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Thoracic versus coronary calcification for atherosclerotic cardiovascular disease events prediction

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Abstract

Objective: This study compared the prognostic value of quantified thoracic artery calcium (TAC) including aortic arch on chest computed tomography (CT) and coronary artery calcium (CAC) score on electrocardiography (ECG)-gated cardiac CT.

Methods: A total of 2412 participants who underwent both chest CT and ECG -gated cardiac CT at the same period were included from the Multi-Ethnic Study of Atherosclerosis (MESA) Exam 5. All participants were monitored for incident atherosclerotic cardiovascular disease (ASCVD) events. TAC is defined as calcification in the ascending aorta, aortic arch, and descending aorta on chest CT. The quantification of TAC was measured using the Agatston method. Time-dependent receiver-operating characteristic (ROC) curves were used to compare the prognostic value of TAC and CAC score.

Results: Participants were 69 ± 9 years of age and 47% male. The Pearman correlation between TAC and CAC score was 0.46 ($p<0.001$). During the median follow-up period of 8.8 years, 234 participants (9.7%) experienced ASCVD events. In multivariable Cox regression analysis, TAC score was independently associated with increased risk of ASCVD events (hazard ratio 1.31, 95% confidence interval 1.09–1.58) as well as CAC score (hazard ratio 1.82, 95% confidence interval 1.53–2.17). However, the area under the time-dependent ROC curve for CAC score was greater

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Author's Contribution

Keishi Ichikawa: Conceptualization, Methodology, Writing – Original Draft, **Rui Wang:** Data curation, Formal analysis, **Robyn L McClelland:** Data curation, Formal analysis, **Venkat S. Manubolu:** Writing – Review & Editing, **Shriraj Susarla:** Data collection, Writing – Review & Editing, **Duo Lee:** Data collection, Writing – Review & Editing, **Leili Pourafkari:** Writing – Review & Editing, **Hooman Fazlalizadeh:** Writing – Review & Editing, **Jairo Aldana-Bitar:** Writing – Review & Editing, **Rick Robin:** Data collection, Writing – Review & Editing, **April Kinninger:** Data curation, Writing – Review & Editing, **Sion Roy:** Writing – Review & Editing, **Wendy S. Post:** Writing – Review & Editing, **Matthew Budoff:** Writing – Conceptualization, Methodology, Writing – Review & Editing, Supervision.

Conflict of interest

All authors declare no conflicts of interest associated with this manuscript.

than that for TAC score in all participants (0.698 and 0.641, p = 0.031). This was particularly pronounced in participants with borderline/intermediate and high 10-year ASCVD risk scores.

Conclusions: Our study demonstrated a significant association between TAC and CAC score but a superior prognostic value of CAC score for ASCVD events. These findings suggest TAC on chest CT provides supplementary data to estimate ASCVD risk, but does not replace CAC on ECG-gated cardiac CT.

Keywords

Thoracic artery calcium; Coronary artery calcium; Atherosclerotic cardiovascular disease; Computed tomography; risk assessment

Introduction

Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of mortality in the United States, which highlights the need for ASCVD risk assessment and early intervention[1]. Coronary artery calcium (CAC) score, determined by electrocardiography (ECG) -gated cardiac computed tomography (CT), is a well-known marker indicating the total burden of coronary atherosclerosis, and is established as a powerful predictor of ASCVD events[2] [3]. Based on this abundant evidence, CAC score is used not only as a tool for risk stratification but also as a decision-making guideline for preventive therapies. However, the use of CAC score is relatively limited in clinical practice, as the current guidelines do not recommend routine CAC screening for primary prevention, and most insurance companies do not cover CAC screening costs[4] [5].

Standard non-contrast chest CT is more widely used, as seen in lung cancer screenings. According to previous reports, approximately 10.6 million non-contrast chest CT scans are done in the United States annually, compared to only 0.5 million CAC scans[6]. Thoracic artery calcium (TAC) is the most common form of extra-coronary calcification and is a frequent incidental finding on chest CT scans. Furthermore, TAC can be accurately assessed on chest CT scans without ECG gating. Previous population-based studies have shown that the presence and extent of TAC is associated with CAC score and ASCVD events[7] [8] [9]. However, the majority of existing TAC data were assessed by visual qualitative method or assessed only in the partial ascending aorta and descending aorta detected by cardiac CT for CAC [10] [11]. A few studies have assessed the comparison of quantified TAC score including the aortic arch and CAC score; however, the CAC scores used were determined by chest CT, which is not the gold standard method for CAC quantification [12, 13]. Although TAC score could be a more reproducible and reliable quantitative method, the primary prevention potential of TAC has not been fully utilized clinically. If quantified TAC scores on non-contrast chest CT can be a substitute for CAC scores, non-contrast chest CT can provide critical information for ASCVD prevention in addition to its primary clinical purpose.

The Multi-Ethnic Study of Atherosclerosis (MESA) is a large, ethnically diverse cohort study with participants that had both chest CT and ECG-gated cardiac CT during the same period, with follow up data. Therefore, MESA is an excellent cohort to conduct direct and

reliable comparisons between TAC including the aortic arch and CAC. In this study, we aim to clarify the relationship between quantified TAC score including aortic arch and CAC score, and to compare their predictive values for ASCVD events.

Materials and Methods

Study population

The MESA study is a prospective cohort study designed to investigate the prevalence and progression of subclinical ASCVD, and to identify risk factors for incident ASCVD in a racially and ethnically diverse community-based sample. From July 2000 through August 2002, 6814 men and women aged 45 to 84 years and free of clinical cardiovascular disease were recruited from 6 different sites in the United States (Baltimore, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles, California; New York, New York and St. Paul, Minnesota). The study design of MESA has been previously published [14].

This study included all the participants who underwent both non-contrast chest CT scans and ECG-gated cardiac CT in MESA Exam 5 (April 2010 to December 2011). A total of 2607 participants had both chest and ECG-gated cardiac CT. Of these, we excluded 154 participants who had experienced ASCVD events prior to MESA Exam 5. Additionally, 41 participants were excluded due to missing data. After these exclusions, 2412 participants were included in this study. All study participants provided written informed consent, and the aggregated data was de-identified. The study was approved by the Institutional Review Board at each field center and the data coordinating center. Each Institutional Review Board is certified by the U.S. Office of Human Research Protections: Wake Forest University (IRB number IRB00008492 under Federal-wide Assurance- FWA00001435), Columbia University (IRB number IRB00002973 under Federal-wide Assurance- FWA00002636), Johns Hopkins University (IRB number 00001656 under Federal-wide Assurance- FWA00005752), University of Minnesota (IRB number IRB00000438 under Federal-wide Assurance- FWA00000312), Northwestern University (IRB number IRB00005003 under Federal-wide Assurance- FWA00001549), University of California Los Angeles (IRB number 00000172 under Federal-wide Assurance- FWA00004642), University of Washington (IRB number STUDY00009029 under Federal-wide Assurance- FWA00006878).

Assessment of CAC score and TAC score

Participants in this study underwent both chest CT and ECG-gated cardiac CT scans at MESA scanning centers, and more than 95% of participants had these CT scans performed on the same day. Non-contrast chest CT scans were acquired at full inspiration following a standardized protocol with reconstruction in 0.625–0.75mm slice thickness[15]. A detailed description of the TAC score measurement protocol has been published [16]. In brief, TAC was defined as calcification on chest CT in the ascending aorta, aortic arch and descending aorta inferior to the cardiac apex. All images were analyzed in blinded fashion by trained technologists at the CT Reading Center (Lundquist Research Institute, Torrance, California), the same group that has analyzed all CT findings since the MESA's inception. The TAC score was quantified by the Agatston method, using the Philips Heart Beat CS software

program (Philips Company, Cleveland, Ohio). Intra-reader and inter-reader reproducibility for the TAC score were very good at 99% and 97%, respectively. CAC scores by cardiac CT were also calculated using the Agatston method [17]. All cardiac CT images were also interpreted at the MESA CT reading center (Lundquist Research Institute, Torrance, California). We transformed the TAC and CAC scores by taking the log (TAC score+1) and log (CAC score+1) in order to reduce the skewness of TAC and CAC measures. The CAC scores were also categorized by range as 0, 1–100, 101-300, and > 300[18].

Assessment of covariates

Relevant covariates were obtained from the MESA Exam 5 questionnaire and Exam 5 physiologic assessments. Covariates in this analysis included age, sex, race and ethnicity, education, smoking status, body mass index (BMI), systolic blood pressure, antihypertensive medication use, lipid lowering medication use, total cholesterol, high-density lipoprotein (HDL) cholesterol, and prevalent diabetes.

Interview-administered questionnaires were used to assess education and smoking status. Education was categorized as: less than high school, high school graduate, some college, or college graduate and above. Participants were asked if they currently smoke cigarettes and were categorized as: current, former, or never. Moreover, trained staff collected height, weight, blood pressure, and fasting blood measures. BMI was calculated as weight (kilograms) divided by height (meters) squared. Blood pressure was measured 3 times in the seated position using a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon, Tampa, Florida), and the final 2 measurements were averaged. Total cholesterol and HDL cholesterol levels from blood samples obtained after a 12-hour fast were measured at the Collaborative Studies Clinical Laboratory (Fairview University Medical Center, Minneapolis, Minnesota). Diabetes was defined as fasting blood glucose concentration ≥126mg/dL, self-reported physician diagnosis, or use of hypoglycemic drugs. The 10-year ASCVD risk score was calculated from the pooled cohort equation [19]. In this study, we classified the study population into three groups based on their risk level: low (<5%), borderline/ intermediate (5–20%), and high-risk (>20%) [20].

Outcome data

Participants were regularly contacted via follow-up calls through 2019 to inquire about interim hospital admissions, cardiovascular outpatient diagnoses, and deaths. To verify self-reported diagnoses, information was collected from death certificates and medical records for all hospitalizations and outpatient cardiovascular diagnoses. Detailed description of follow-up of MESA participants is available online (www.mesa-nhlbi.org). ASCVD events were defined as: definite or probable myocardial infarction, definite angina, probable angina followed by coronary revascularization, resuscitated cardiac arrest, fatal or non-fatal stroke (not transient ischemic attack), coronary heart disease death, and other atherosclerotic death. In the subsequent analysis, we divided ASCVD events into cardiac events (ASCVD events excluding stroke) and stroke. A detailed description of the adjudication process has been published [14].

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation or median with interquartile range. Dichotomous variables are expressed as numbers (percentages). Participants were classified into four groups according to quartiles of TAC score. For approximately normally distributed continuous variables, a one-way analysis of variance was used to evaluate intergroup differences. For continuous variables with a non-normal distribution, the Kruskal-Wallis rank sum test was used. Categorical variables are presented as percentages and frequencies, and comparisons were made using the $\chi 2$ test. In subsequent analyses, TAC score and CAC score were log-transformed after adding 1 to all scores to manage values of 0 [log(TAC score +1), log(CAC score +1)] owing to their highly skewed distribution. A bar plot for the proportion of participants in each CAC category was shown by levels of TAC score. Pearson's correlation coefficient was employed to evaluate the association between log(TAC score +1) and log(CAC score +1), and a scatter plot of was presented to show their positive correlation. Cumulative survival estimates were calculated using the Kaplan-Meier method and compared with the log-rank test. For this study time ‘at-risk’ began at the time of the Exam 5 CT scan, and participants who had experienced ASCVD events before that time were excluded. Univariate Cox proportional hazards models were fit to assess the association between each of the predictors (including standard risk factors, log(TAC score +1) and log(CAC score +1)), and incident ASCVD events). Two additional multivariable Cox proportional hazards models were fit: standard risk factors + log(TAC score +1) and risk factors + log(CAC score+1), which were included in each model respectively. The satisfaction of the proportional hazards assumption of Cox proportional hazards models was evaluated by examining and testing Schoenfeld residuals. Global tests were non-significant, but mild violations were indicated for log(TAC score +1) and log(CAC score +1). Inspection of smoothed residual plots indicated that the average (non-time-varying) estimates presented are a good approximation despite the statistically significant tests. Time-dependent receiver operator characteristics (ROC) curves (at 5 years of follow-up) were constructed to evaluate the predictive value of TAC and CAC in all participants and subgroups. We also assessed the discrimination for incident ASCVD when TAC score was added to CAC score by comparing the area under the time-dependent ROC curves. All results were considered significant with values of $p<0.05$. Statistical analyses were performed using the R statistical packages (version 4.2.1; R Foundation for Statistical Computing, Vienna, Austria).

Results

Participant characteristics

At the time of this study, the mean age of the participants was 69 years old; 47% were men, 38% identified as White, 26% identified as Black, 22% identified as Hispanic, and 13% identified as Chinese American. The overall median TAC score was 274, and 144 participants (6.0%) had no TAC. Participants were divided into quartiles based on TAC score. The median (range) of the TAC score quartiles were 6 (0 – 44), 133 (44 – 274), 556 (274 – 1067), and 2730 (1068 – 30900), in Q1, Q2, Q3, and Q4, respectively. Table 1 shows the main clinical and laboratory baseline characteristics of the study participants in the different quartiles. Participants in Q4 were older ($p<0.001$), had lower educational

attainment (p<0.001), and had higher prevalence of ever smoking (p=0.001), white race (p<0.001) and diabetes (p=0.010). In addition, lipid lowering and hypertensive medications were most frequently used in the Q4 group (p<0.001).

Association between TAC and CAC score

The overall median CAC score in the study participants was 30, and 801 participants (33.2%) had no CAC. The median CAC score increased across TAC groups (Q1=0, Q2=12, Q3=50, Q4=219, p<0.001). The distribution of CAC score categories in each group are shown in Figure 1A. Participants in Q4 had the highest prevalence of CAC score >300 (45.5%) and lowest prevalence of CAC score 0 (9.2%). On the other hand, participants in Q1 had the highest prevalence of CAC score 0 (57.9%) and lowest prevalence of CAC score >300 (7.0%). In the Pearson correlation analysis, log (TAC+1) was significantly correlated with log (CAC+1) (correlation coefficient 0.46; p<0.001) (Figure 1B).

Association of TAC score and ASCVD events in all participants

During the follow-up period (median 8.8 years), 234 ASCVD events (coronary heart disease death [n=23], myocardial infarction [n=52], resuscitated cardiac arrest [n=3], definite angina [n=37], probable angina followed by coronary revascularization [n=6], stroke [n=74], other cardiovascular death [n=39) were recorded. Figure 2. shows the Kaplan-Meier curves according to TAC score quartiles. Participants with higher levels of TAC exhibited a notably increased risk of incident ASCVD events during follow-up (log-rank, p <0.001). As shown in Table 2, univariate Cox regression analysis identified that log (TAC score +1) was significantly associated with ASCVD events (HR, 95% CI 1.79, 1.53–2.09, p<0.001). Furthermore, multivariable Cox regression analysis identified that log (TAC score +1) was independently associated with ASCVD events after adjustment for clinical risk factors (HR, 95% CI 1.31, 1.09–1.58, p=0.005). Similarly, log (CAC score +1) was an independent factor for ASCVD events after adjustment for clinical risk factors (HR, 95% CI 1.82, 1.53–2.17, p< 0.001).

Comparison of prognostic value of TAC and CAC score

Table 3 shows the comparison of prognostic value of TAC score and CAC score for prediction of ASCVD events. Among all participants, the area under the time-dependent ROC curve for CAC demonstrated a meaningful superiority over TAC (0.698 and 0.641, p=0.031). This difference is particularly meaningful in a clinical context as it suggests the CAC may be a more effective tool for ASCVD risk stratification. We conducted a further analysis by categorizing ASCVD events into cardiac events and stroke. For the prediction of cardiac events, the area under the time-dependent ROC curve for CAC exceeded that for TAC, although the difference did not reach statistical significance (0.771 vs. 0.737, p=0.086). Despite the lack of statistical significance, the observed numerical superiority in favor of CAC suggests a potential trend towards improved predictive value for cardiac events. Conversely, in the prediction of stroke, no substantial differences were observed between CAC and TAC (0.675 and 0.684, p=0.512). Furthermore, subgroup analyses were performed to compare the prognostic value of TAC and CAC in each group stratified by 10-year ASCVD risk score and gender. The number of ASCVD events in each risk group and gender was 15 (low/borderline-risk group), 84 (intermediate-risk group), 135 (high-risk

group), 137 (male), and 97 (female), respectively. The area under the time-dependent ROC curve for CAC was more pronounced compared to TAC among individuals with borderline/intermediate 10-year ASCVD risk score (0.698 and 0.561, p=0.004) and high 10-year ASCVD risk score (0.642 and 0.559, p=0.033). These differences suggest a more effective performance of CAC in assessing ASCVD risk within these specific risk categories. Additionally, we observed a trend where CAC tended to provide better predictive value than TAC in male participants (0.693 and 0.647, p=0.160). Finally, we analyzed the incremental prognostic value of TAC score when it is added to CAC score. The change of the area under the time-dependent ROC curve adding log (TAC score+1) to log (CAC score +1) alone was not significant in all participants (0.698 to 0.706, p=0.226), in participants with high ASCVD risk score (0.642 to 0.641, p=0.895), nor in borderline/intermediate ASCVD risk score (0.698 to 0.699, p=0.880). Among participants with low ASCVD risk scores, we observed a substantial improvement in predictive value for ASCVD events with the increase of the area under the time-dependent ROC curve from 0.629 to 0.758 (p=0.007).

Discussion

Our study conducted the first direct comparison of TAC including aortic arch on non-contrast chest CT, and CAC on ECG-gated cardiac CT in a large community-based cohort. TAC was positively associated with CAC, and TAC and CAC were both independently associated with ASCVD events. However, the prognostic value of TAC was lower than that of CAC, primarily attributed to the difference in the prediction of cardiac events. Moreover, the distinction in prognostic value for ASCVD events was conspicuous, particularly in participants with borderline/intermediate and high 10-year ASCVD risk scores.

To date, there have been many studies which evaluated the association between TAC and CAC. The majority of these studies reported that the association with ASCVD events is stronger for CAC than for TAC, which are consistent with our findings [11] [21] [22] [10] [23]. However, results from previous studies should be approached with caution for several reasons. First, several studies assessed TAC by visual qualitative method and used a binary assessment, which is less robust from a methodological perspective [10]. Second, most previous studies assessed TAC by cardiac CT scans, which do not include the aortic arch segments [11] [21] [22] [23]. The aortic arch has been reported as one of the most common sites of calcification[24], and thus assessment of TAC without this segment leads to an underestimation. One previous study that assessed TAC on cardiac CT reported that the prevalence of TAC =0 was 70.5%, which was much higher than in our study (6.0 %) [25]. Aortic arch atherosclerosis has also been reported to be the strongest indicator for both cardiovascular and non-cardiovascular mortality[26]. These reports suggest the importance of including the aortic arch when comparing the prognostic value of TAC and CAC. Third, the few existing studies with TAC including the aortic arch have utilized CAC score determined by non-gated chest CT scans[27, 28], which has not been fully endorsed due to intra-observer variability caused by motion artifact. Therefore, the strength of our study is in the comparison of TAC and CAC by the most reliable methods, which enables us to reinforce the valid findings of previous studies. Furthermore, our study demonstrated that the superior prognostic value of CAC over TAC was primarily due to

its more accurate prediction of cardiac events. This result is reasonable considering that CAC directly measures the amount of calcification in the coronary arteries.

In clinical settings, CAC scans are most frequently used for individuals with borderline/intermediate (5–20%) 10-year ASCVD risk scores. Among these individuals, CAC score is used not only for risk estimation but also for treatment decision-making[20]. In our study, the difference in the prognostic value of TAC and CAC was the most prominent in this group. Furthermore, an incremental prognostic value of TAC over CAC was not demonstrated. Thus, this result does not support the expansion of the field of view to include TAC, as individuals with borderline/intermediate (5–20%) 10-year ASCVD risk score have CAC screening for primary prevention. On the other hand, TAC had incremental prognostic value over CAC in participants with low (<5%) ASCVD risk score, suggesting a potential role for TAC. However, we cannot deny that the number of ASCVD events in this group may have affected our findings. Therefore, we need to confirm our findings in larger populations. Nevertheless, considering that the current guidelines do not endorse routine CAC measurements in this cohort, coupled with the low incidence of events, it might pose a challenge to conduct a substantial study to validate our findings. Future research may reveal the efficacy of combined TAC and CAC assessment if chest CT-CAC measurements using deep learning become more prevalent[29], thereby demonstrating their utility in a larger population with chest CT evaluations.

Our study did not demonstrate the superiority of TAC over CAC in terms of predictive ability for future ASCVD events. However, knowing the extent of TAC has other potential benefits in primary prevention settings. Identifying the extent of TAC may lead clinicians to reconsider a patient's future ASCVD risk, or to increase opportunities for ECG-gated cardiac CT scans to evaluate CAC score. Furthermore, TAC has potential benefits for modifying patient behavior. Patients with visualized TAC may experience improvements in lifestyle, risk factor control, and medication adherence. Although identification of CAC on chest CT has also been shown to have similar effects[30], TAC can detect more patients with subclinical atherosclerosis. Future research is needed to evaluate the impact of identifying TAC on clinicians' practice and patients' behavior.

Our study revealed a robust correlation between TAC and CAC, yet it was observed that a subset of participants exhibited substantial levels of TAC with minimal or no CAC, and vice versa. Calcification within the arterial wall occurs in two distinct locations, the intima and the media. Intimal calcification is the most common distribution in atherosclerosis. In contrast, calcification occurring in the medial smooth muscle is frequently linked with chronic kidney disease, diabetes mellitus, systemic inflammatory diseases, and radiation-associated cardiac disease [31]. Currently, the absence of non-invasive imaging techniques capable of differentiating between intimal and medial calcification hinders the accurate determination of the prevalence of medial calcification within TAC and CAC. The discrepancies observed between TAC and CAC in certain participants may suggest variability in the calcification location. Consequently, further research is imperative to elucidate the factors contributing to these discrepancies and to assess their prognostic implications.

Our study has some limitations. First, the MESA 5 Exam was conducted approximately 10 years after MESA initiation, and hence our study population had an average age of almost 70. Therefore, our results may not be generalizable to younger populations. Thus, our findings should be confirmed and validated through another cohort study. Second, the data regarding CAC on chest CT is not yet available in this cohort. CAC on non-gated chest CT is recommended to make qualitative assessments of CAC as present or not present, or as mild, moderate or severe[13]. A combination of CAC data and TAC score may improve the predictive ability of chest CT. Third, TAC scores were used as continuous variables, as there are no accepted thresholds for TAC score at present. Future studies are needed to determine thresholds for TAC score and to further compare their prognostic value with CAC score.

Conclusions

In this study, a positive association between TAC including aortic arch on chest CT and CAC on ECG-gated cardiac CT was found. TAC and CAC were both associated with increasing risk of ASCVD events. However, the prognostic value of TAC was lower than that of CAC, especially in participants with borderline/intermediate and high 10-year ASCVD risk scores. TAC on chest CT provides supplementary data to estimate ASCVD risk, but does not replace CAC on ECG-gated cardiac CT.

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Key messages

What is already known on this topic

Thoracic artery calcium (TAC) on standard non-contrast chest CT has been expected to be a substitute for coronary artery calcium (CAC) scores in primary prevention. However, no study has conducted direct and reliable comparisons between TAC including the aortic arch and CAC in regard to predictive ability for future ASCVD events.

What this study adds

This study showed a positive association between TAC including aortic arch on chest CT and CAC on electrocardiography (ECG) -gated cardiac CT. In addition, TAC and CAC were both associated with increased risk for atherosclerotic cardiovascular disease (ASCVD) events. However, the prognostic value of TAC was lower than that of CAC. TAC on chest CT provides supplementary data to estimate ASCVD risk, but does not replace CAC on ECG-gated cardiac CT

How this study might affect research, practice or policy

Assessing TAC should raise awareness for subclinical atherosclerosis and can be an early opportunity to intensify cardiovascular disease prevention efforts. Future studies are needed to evaluate the impact of identifying TAC on clinicians' practice and patients' behavior.

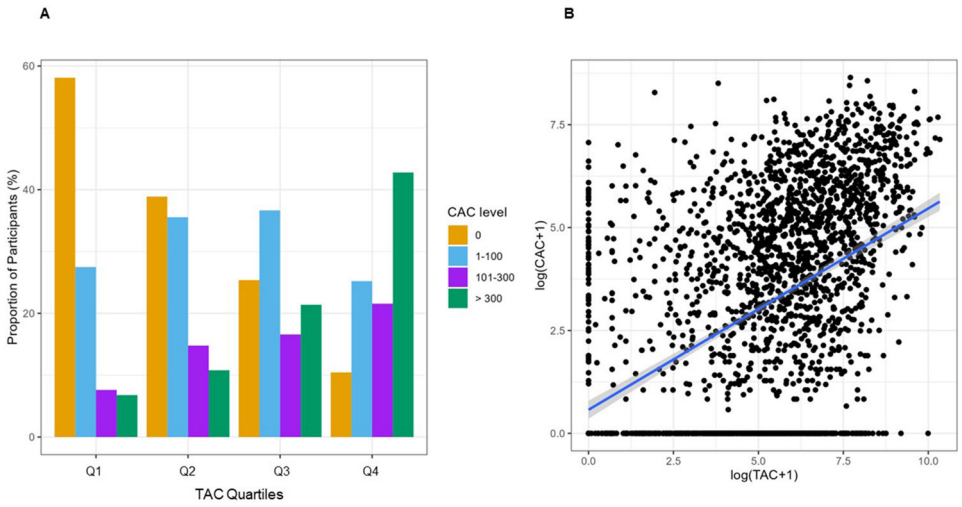

Figure 1. The association between TAC score and CAC score.

(A) Distribution of CAC score categories in participants stratified by TAC score quartiles.

(B) Correlation between TAC score and CAC score.

CAC, coronary artery calcium; TAC, thoracic artery calcium.

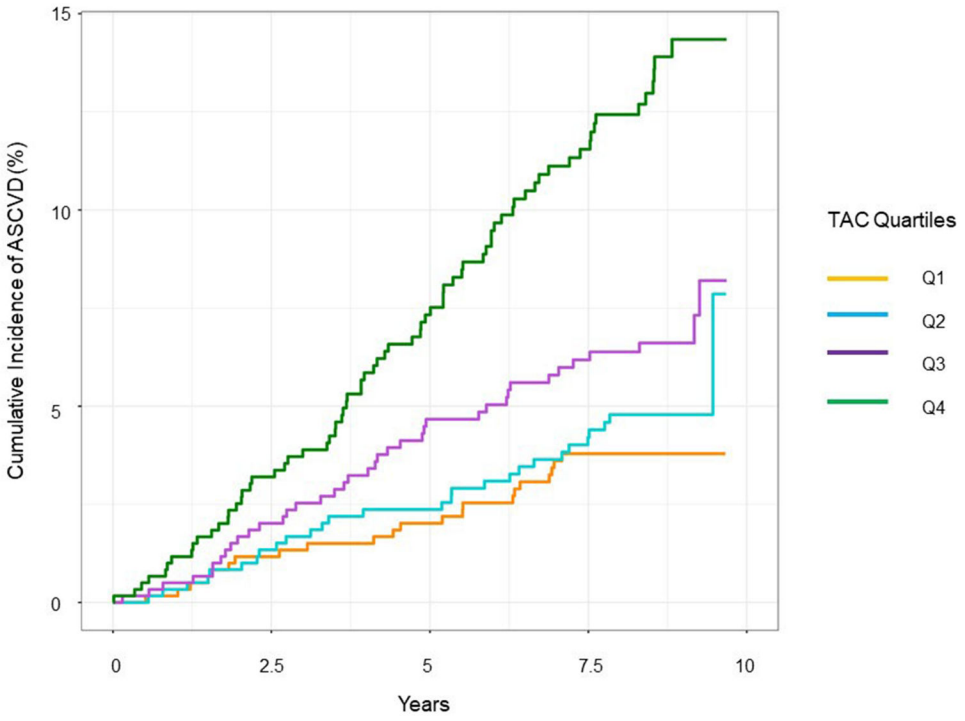

Figure 2. Kaplan-Meier analyses of incident ASCVD stratified by TAC score quartiles.
ASCVD, atherosclerotic cardiovascular disease; TAC, thoracic artery calcium.

Table 1

Baseline clinical and laboratory characteristics of the study population according to TAC score quartiles

	All	Q1 (0-44)	Q2 (44-274)	Q3(274-1067)	Q4(1068-30900)	p-value
n	2412	604	602	603	603	
Age, years	69.1±9.2	62.6 ±6.6	66.6± 7.7	70.3± 8.2	76.5± 8.0	<0.001
Male sex, n (%)	1127 (47)	300 (50)	278 (46)	281 (47)	268 (44)	0.329
Race/ethnicity						<0.001
White, n (%)	913 (38)	234 (39)	209 (35)	211 (35)	259 (43)	
Chinese American, n (%)	320 (13)	61 (10)	64 (11)	97 (16)	98 (16)	
Black, n (%)	638 (26)	175 (29)	182 (30)	158 (26)	123 (20)	
Hispanic, n (%)	541 (22)	134 (22)	147 (24)	137 (23)	123 (20)	
Body mass index, kg/m^2	28.4±5.5	28.8 ±5.5	28.9±5.7	28.3±5.4	27.7±5.3	<0.001
smoking status						0.003
Never, n (%)	1120 (46)	319 (53)	282 (47)	271 (45)	248 (41)	
Former, n (%)	1106 (46)	236 (39)	276 (46)	286 (47)	308 (51)	
Current, n (%)	186 (8)	49 (8)	44 (7)	46 (8)	47 (8)	
Education						<0.001
Less than high school, n (%)	333 (14)	49 (8)	77 (13)	102 (17)	105 (17)	
High school, n (%)	1129 (47)	268 (44)	282 (47)	266 (44)	313 (52)	
Some college, n (%)	442 (18)	128 (21)	117 (19)	105 (17)	92 (15)	
College and above, n (%)	508 (21)	159 (26)	126 (21)	130 (22)	93 (15)	
Total cholesterol, mg/dl	184.4±36.3	188.8±35.6	187.7±35.7	180.8±36.3	180.2±36.9	<0.001
HDL cholesterol, mg/dl	55.9±16.7	55.7±17.4	56.0±17.0	55.9±16.6	56.2 ±16.0	0.962
Diabetes, n (%)	450(19)	101 (17)	93 (15)	123 (20)	133 (22)	0.010
Systolic blood pressure, mmHg	123.7±20.1	117.7±17.7	122.0±19.9	123.9±19.0	131.0±21.4	<0.001
Lipid lowering medications, n (%)	891 (37)	156 (26)	196 (33)	241 (40)	298 (49)	<0.001
Hypertensive medications, n (%)	1291 (54)	236 (39)	294 (49)	332 (55)	429 (71)	<0.001
CAC score	30[0, 212]	0[0, 30]	12[0, 102]	50[0, 229]	219[37, 682]	<0.001

Data are presented as mean ± standard deviation, number (%), or median [25th, 75th percentile].

CAC, coronary artery calcium; HDL, high-density lipoprotein; TAC, thoracic artery calcium.

Table 2

The factors associated with atherosclerotic cardiovascular disease events. Multivariable analysis including TAC score (Multivariable-1) and CAC score (Multivariable-2).

	Univariate		Multivariable-1		Multivariable-2	
	HR (95%CI)	**P-value**	**HR (95%CI)**	**P-value**	**HR (95%CI)**	**P-value**
Age, years	1.74 [1.53,1.98]	<0.001	1.43 [1.21,1.69]	<0.001	1.33 [1.14,1.55]	<0.001
Male sex	1.66 [1.28,2.15]	<0.001	1.55 [1.15,2.09]	0.004	1.20 [0.89,1.63]	0.230
Chinese American	0.85 [0.56,1.30]	0.462	0.76 [0.49,1.20]	0.246	0.85 [0.54,1.34]	0.497
Black	0.86 [0.62,1.19]	0.368	0.86 [0.61,1.22]	0.393	0.97 [0.68,1.37]	0.850
Hispanic	0.97 [0.69,1.35]	0.837	0.92 [0.63,1.35]	0.666	1.00 [0.68,1.46]	0.993
Body mass index, kg/m^2	0.91 [0.80,1.04]	0.185	0.90 [0.76,1.06]	0.200	0.86 [0.73,1.01]	0.070
Former smoker	1.36 [1.04,1.77]	0.026	1.14 [0.86,1.51]	0.365	1.11 [0.84,1.47]	0.461
Current smoker	1.10 [0.66,1.84]	0.722	1.22 [0.71,2.07]	0.475	1.14 [0.67,1.95]	0.628
High school	0.89 [0.61,1.29]	0.527	1.01 [0.68,1.51]	0.946	0.95 [0.64,1.42]	0.807
Some college	0.64 [0.40,1.03]	0.069	0.75 [0.45,1.26]	0.286	0.69 [0.41,1.15]	0.153
College and above	0.90 [0.59,1.37]	0.616	1.12 [0.69,1.82]	0.644	0.98 [0.61,1.59]	0.937
Total cholesterol, mg/dl	0.85 [0.75,0.97]	0.018	1.05 [0.91,1.22]	0.498	1.04 [0.90,1.21]	0.615
HDL cholesterol, mg/dl	0.80 [0.69,0.93]	0.003	0.80 [0.67,0.95]	0.010	0.80 [0.68,0.95]	0.011
Diabetes	1.27 [0.93,1.72]	0.132	1.08 [0.78,1.50]	0.643	1.00 [0.71,1.39]	0.982
Systolic blood pressure, mmHg	1.31 [1.16,1.47]	<0.001	1.15 [1.01,1.30]	0.042	1.13 [0.99,1.29]	0.063
Lipid lowering medications	1.22 [0.94,1.58]	0.137	0.93 [0.69,1.24]	0.604	0.81 [0.61,1.09]	0.167
Hypertensive medications	1.93 [1.47,2.54]	<0.001	1.51 [1.12,2.04]	0.006	1.47 [1.09,1.98]	0.011
Log(TAC score+1) per SD	1.79 [1.53,2.09]	<0.001	1.31 [1.09,1.58]	0.005		
Log(CAC score+1) per SD	2.20 [1.89,2.55]	<0.001			1.82 [1.53,2.17]	<0.001

CAC, coronary artery calcium; CI, confidential interval; HDL, high-density lipoprotein; HR, hazard ratio; TAC, thoracic artery calcium.

Table 3

The comparison of prognostic value of TAC score and CAC score in all participants and risk subgroups

	The area under the time-dependent ROC curve		
	Log (TAC score+1)	**Log (CAC score+1)**	**p value**
All participants	0.641	0.698	0.031
10-year ASCVD risk			
Low	0.750	0.629	0.141
Borderline/Intermediate	0.566	0.698	0.004
High	0.559	0.645	0.033
Gender			
Male	0.647	0.693	0.160
Female	0.643	0.658	0.722

ASCVD, atherosclerotic cardiovascular disease; CAC, coronary artery calcium; TAC, thoracic artery calcium; ROC, receiver-operating characteristic.