Aortic Arch Width and Cardiovascular Disease in Men and Women in the Community

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Background—We sought to determine whether increased aortic arch width (AAW) adds to standard Framingham risk factors and coronary artery calcium (CAC) for prediction of incident adverse cardiovascular disease (CVD) events in community-dwelling adults.

Methods and Results—A total of 3026 Framingham Heart Study Offspring and Third Generation cohort participants underwent noncontrast multidetector computed tomography from 2002 to 2005 to quantify CAC. We measured AAW as the distance between the centroids of the ascending and descending thoracic aorta, at the level of main pulmonary artery bifurcation or the right pulmonary artery. We determined sex, age group, and body size specific cut points for high (≥90th percentile) AAW from a healthy referent group (N=1471) and dichotomized AAW as high or not high across all study participants. Clinical covariates were obtained at Offspring cycle 7 (1998–2001) or Third Generation cycle 1 (2002–2005) examinations. The primary CVD outcome was a composite of myocardial infarction, coronary insufficiency, cerebrovascular accident, first hospitalization for heart failure, or CVD death. Cox proportional hazards models were used to estimate hazard ratio of high AAW on time-to-incident CVD after adjustment for Framingham risk factors and CAC. Net reclassification improvement was used to assess the effect of adding AAW to the baseline Framingham risk factor+CAC model. A total of 2826 participants (aged 51±11 years, 48% women) had complete covariates and were free of CVD at multidetector computed tomography. Over a median 8.9 years of follow-up, there were 135 incident CVD events. High AAW was independently predictive of CVD events (hazard ratio, 1.55; *P*=0.032) and appropriately reclassified participants at risk: net reclassification improvement, 0.31 (95% confidence interval, 0.15–0.48).

Conclusion—AAW augments traditional CVD risk factors and CAC for prediction of incident adverse CVD events among community-dwelling adults. (*J Am Heart Assoc*. 2018;7:e008057. DOI: 10.1161/JAHA.117.008057.)

Key Words: aorta • computed tomography • epidemiology • population study • risk factor

The thoracic aorta increases in diameter, elongates, and stiffens with advancing age.[1–4] Aortic arch width (AAW)[5,6] also increases with older age. These changes in aortic geometry are cross sectionally associated with excess burden of undesirable hemodynamic and cardiac structural changes.[1,4,6] Furthermore, increasing aortic stiffness may be more a precursor than a result of hypertension.[7] The increased central blood pressures associated with decreased aortic compliance are associated with greater left ventricular mass and concentric remodeling. Greater aortic stiffness, increased left ventricular mass, and concentric left ventricular geometry are all associated with increased risk of future adverse cardiovascular and cerebrovascular events.[8–13] Thus, indexes of altered aortic geometry may be useful for cardiovascular disease (CVD) risk stratification. In particular, AAW may serve as a simple-to-measure summary measure of changes in the thoracic aorta.

The purpose of this study was to determine whether increased AAW adds to standard CVD risk factors as a

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predictor of incident adverse CVD events in a population of community-dwelling adults. We further sought to determine whether AAW adds to standard CVD risk factors and coronary artery calcium (CAC), because AAW can be measured from computed tomography scans performed to determine burden of CAC.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Study Population

Study participants were members of the FHS (Framingham Heart Study) Offspring and Third Generation cohorts who underwent multidetector computed tomography (MDCT) scanning from 2002 to 2005. To be eligible for the MDCT substudy, participants had to be aged $\geq$35 years (men) or $\geq$40 years (women). Female participants were not pregnant, as verified by questionnaire and urine pregnancy test $\leq$24 hours before MDCT study. In addition, each participant had to weigh <160 kg because of MDCT scanner constraints. All participants provided written informed consent. The study was approved by the institutional review boards of the Boston University Medical Center and The Massachusetts General Hospital and is in compliance with the Declaration of Helsinki.

The Offspring and Third Generation cohorts undergo periodic or "cycle" examinations every several years, as

previously described.[14,15] Clinical covariates were obtained at the Offspring cycle 7 (1998–2001) or Third Generation cycle 1 (2002–2005) examinations. Height and weight were measured with participants in light clothing, body mass index was calculated as weight (kilograms) divided by height (meters) squared (kg/m^2), and body surface area was calculated using the Mosteller formula.[16] A morning venous blood draw was obtained after 12-hour overnight fast. Medical history, including smoking status and medications being taken, was obtained via interview and questionnaires.

Brachial blood pressure was measured twice, by a physician using a mercury sphygmomanometer, and the average of the 2 measures was used. Hypertension was defined as having systolic blood pressure $\geq$140 mm Hg, diastolic blood pressure $\geq$90 mm Hg, or use of antihypertensive medication. Hyperlipidemia was serum cholesterol $\geq$240 mg/dL or use of pharmacologic treatment. Diabetes mellitus was defined as a fasting plasma glucose $\geq$126 mg/dL, treatment with insulin, or use of antihyperglycemic medication. Participants were considered current smokers if they smoked $\geq$1 cigarette daily over the past year.

Image Acquisition and Analysis

MDCT scanning was performed on an 8-row system (Lightspeed Ultra; General Electric, Milwaukee, WI) during a single midinspiratory breath hold. Image acquisition was electrocardiographically triggered and prospectively initiated at 50% of the RR cycle. Thoracic scan parameters included 120 kVp with 320-mA tube current (400 mA if body weight was $\geq$100 kg), 500-ms gantry rotation time, and 3:1 table feed. Estimated radiation exposure was 1 mSv (1.25 mSv for 400-mA tube current).

Image analysis was performed off line using commercially available software (Aquarius 3D; TeraRecon Inc, San Mateo, CA). A single trained observer (R.M.M.), blinded to participant identifiers and characteristics, measured AAW directly from the transverse thoracic image at the level of the main pulmonary artery bifurcation or right pulmonary artery as the distance between the centroids of the ascending and descending thoracic aorta (Figure 1). Burden of CAC was quantified from the MDCT scans, using standard methods, as previously described.[17]

CVD and Mortality Follow-Up

FHS participants are monitored by means of cycle examinations supplemented by mailed questionnaires and telephone contact. The follow-up period for this study began after MDCT scanning and continued until the first adverse CVD event, death, unavailability for follow-up, or the most recent follow-up call. Median follow-up was 8.9 years. Adverse CVD events were adjudicated using standardized criteria[18] by 3 physician-
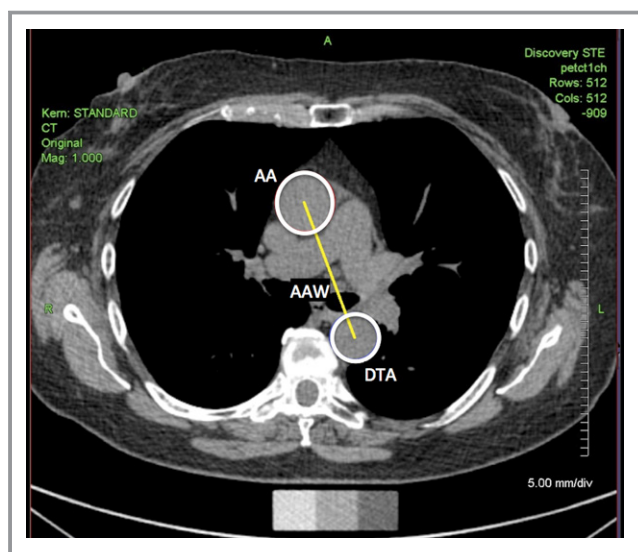
Figure 1. Measurement of aortic arch width (AAW) on noncontrast computed tomography image at the level of the main pulmonary artery bifurcation. AAW is the straight-line distance between the centroids of the ascending aorta (AA) and the descending thoracic aorta (DTA).

investigators after review of all available records, obtained from the participant and directly from treating physicians. The review panel members were unaware of MDCT results. We analyzed the composite CVD outcome of myocardial infarction, coronary insufficiency, ischemic stroke, index admission for heart failure, and CVD death. CVD death was defined as coronary, ischemic stroke, or other atherosclerotic death.

Statistical Analysis

Statistical analyses were performed using SAS, version 9.4 (SAS Institute, Cary, NC). Baseline characteristics were compared between men and women using t test or Wilcoxon rank sum test, as appropriate, for continuous variables. Categorical variables were compared between sexes using the χ^2 test. AAW varies with sex, age, and body surface area. To minimize the effect of sex, age, and body size differences on the relationship between AAW and adverse CVD events, we used age-, sex-, and body surface area–specific upper 90th percentile (P90) cut points (Table S1) derived from a healthy referent subset (N=1471) of the study participants. The healthy referent group was defined by freedom from prevalent CVD, hypertension, hyperlipidemia, diabetes mellitus, and current cigarette smoking. All participants were then stratified into 1 of 2 categories: high AAW, defined by AAW≥P90, or AAW<P90. Participants with history of adverse CVD events before MDCT scanning were identified and excluded from further analyses.

Kaplan-Meier survival curves were constructed for AAW<P90 and AAW≥P90; multivariable-adjusted Cox proportional hazards models were used to estimate hazard ratios

(HRs) for time to event, after adjustment for standard Framingham risk factors (FRFs), including age, sex, systolic blood pressure, total and high-density lipoprotein cholesterol, diabetes mellitus, and smoking. In a second set of models, we adjusted for burden of CAC, as log(CAC+1), in addition to FRFs. We tested the veracity of the proportionality of hazards required for Cox models using a time interaction with each of categorical AAW, continuous AAW, and log(CAC+1). In each case, the interaction term did not attain statistical significance; therefore, the proportional hazards requirement was satisfied.

The incremental effect of adding AAW to FRF-based and FRF+CAC-based models was assessed using the category-free net reclassification improvement (NRI) metric.[19] Category-free NRI assesses the effect of an additional exposure on model performance across all study participants by evaluating the net number of participants whose predicted risk increased or decreased appropriately, on the basis of whether they experienced or did not experience an incident CVD event, after the addition of AAW to the model. We also considered models incorporating FRF, AAW, and aortic diameter, because the diameters of the ascending and descending limbs of the thoracic aorta can be measured from the same image as AAW.

In secondary analyses, we considered only participants with ≥5.0% 10-year American Heart Association/American College of Cardiology cardiovascular risk,[20] on the basis that lower-risk individuals were unlikely to have undergone chest CT for CAC assessment. Finally, in sensitivity analyses, we used continuous AAW in place of dichotomized AAW.

Observer reproducibility was assessed on a subset of 100 participants (proportionally distributed across sex and cohorts to reflect the overall study population) by 2 trained observers, unaware of each other's results, at a time point separate from primary analyses.

Results

Baseline characteristics of the 3026 study participants are shown in Table 1. Women were slightly older than men but had lower blood pressure and more favorable lipid profiles. Both diabetes mellitus and prevalent CVD were more common among men than women. Prevalence of current smoking did not differ between sexes. Men had greater prevalence and quantitative burden of calcium in the coronary arteries and in the descending aorta. Mean AAW was greater in men (79.2±11.8 mm) than women (70.4±10.1 mm; $P<0.0001$). Reproducibility of AAW was high, with intraobserver and interobserver intraclass correlation coefficients of 0.988 and 0.985, respectively.

Among the 3026 study participants, 119 (3.9%) had prevalent adverse CVD events, and 81 were missing ≥1 covariates; these participants were excluded from further analyses, leaving 2826 adults with complete covariates and

Table 1. Baseline Characteristics

Characteristics	Men (n=1560)	Women (n=1466)	P Value
Age, y	49.9±10.7	52.2±9.9	<0.0001
Height, m	1.77±0.07	1.63±0.06	<0.0001
Weight, kg	89.0±15.2	71.8±15.2	<0.0001
Body surface area, m²	2.08±0.19	1.79±0.21	<0.0001
Body mass index, kg/m²	28.4±4.6	27.1±5.92	<0.0001
Systolic blood pressure, mm Hg	124±15	120±18	<0.0001
Diastolic blood pressure, mm Hg	78±9	74±9	<0.0001
Total cholesterol, mg/dL	194±34	198±36	0.013
HDL cholesterol, mg/dL	46±12	61±17	<0.0001
Hypertension	515 (33)	426 (29)	0.018
Diabetes mellitus	103 (7)	70 (5)	0.031
Current smoking	188 (12)	168 (11)	0.23
Prevalent CVD	124 (8)	70 (5)	0.0004
Prevalent coronary artery calcium	823 (53)	489 (33)	<0.0001
Coronary artery calcium, AS	95 (13–417)	51 (9–165)	<0.0001
Aortic arch width, mm	79.2±11.8	70.4±10.1	<0.0001

Data are summarized as mean±SD, number (percentage), or median (interquartile range). AS indicates Agatston score; CVD, cardiovascular disease; HDL, high-density lipoprotein.

free of CVD who were followed up for a median 8.9 years. There were 135 incident CVD events (4.7%), including 6 CVD deaths (4%), 49 myocardial infarctions (36%), 42 cerebrovascular accidents (31%), 34 index admissions for congestive heart failure (25%), and 4 cases of coronary insufficiency (3%). Most adverse CVD events occurred among the older Offspring cohort (N=105 [78%]) versus 30 events (22%) among the younger Third Generation cohort.

Stratification of all study participants by AAW category (<P90 or ≥P90; P90 determined from the healthy reference group) resulted in 19.2% having high AAW (ie, ≥P90). Figure 2 shows Kaplan-Meier curves for survival free from adverse CVD events for participants with and without high AAW. Table 2 shows the multivariate Cox models. Model 1 incorporated standard FRFs alone, and model 2 incorporated both FRF+AAW, where high AAW was associated with 1.69-fold greater hazard of an adverse CVD event (*P*<0.001); the 95% confidence intervals are presented in Table 2. Model 3 is the multivariable-adjusted Cox model for FRF+CAC, exclusive of AAW. Herein, the burden of CAC, as log(CAC+1), was significantly associated with incident adverse events (HR, 1.30; *P*<0.001). Results for FRF+CAC+AAW are shown as

model 4, where log(CAC+1) was minimally attenuated but remained significantly associated with adverse events (HR, 1.29; *P*<0.001). High AAW also remained significantly associated with events (HR, 1.55; *P*=0.032).

We used category-free NRI to assess the effect of incorporating AAW above FRFs only (ie, model 2 versus model 1) and obtained NRI of 0.311 (95% confidence interval, 0.145–0.475; *P*=0.0078). After addition of AAW to the FRF+CAC model (model 4 versus model 3), the category-free NRI was 0.312 (95% confidence interval, 0.148–0.476; *P*=0.00076). Each of these NRIs is significant, indicating overall appropriate movement of individual risks predicted by the AAW-augmented model versus the model without AAW. Finally, in models incorporating FRFs, AAW, and either ascending-aortic or descending-aortic diameter, neither aortic diameter was a significant predictor of incident adverse events, although AAW remained significant (data not shown).

In sensitivity analyses, we considered AAW as a continuous variable (Table 3). In analyses adjusting for FRFs and continuous AAW (model 5), each 10-mm increment of AAW was associated with 1.21-fold greater hazard of an adverse CVD event (*P*=0.036). In a model of FRF+AAW that further adjusted for CAC (model 6), the association of continuous AAW with adverse CVD events was mildly attenuated but became nonsignificant (HR, 1.18 per 10 mm; *P*=0.074), whereas log (CAC+1) remained significant (HR, 1.29; *P*<0.001).

In parallel, secondary, multivariable-adjusted models, we restricted analyses to participants with ≥5.0% 10-year American Heart Association/American College of Cardiology CVD risk (N=922) because these would be the participants more likely to have undergone CAC screening (and perhaps other tomographic chest imaging). In model 4a (identical to model 4, except for being restricted to 922 intermediate and higher-risk participants), both CAC (HR, 1.29; *P*<0.001) and high AAW (HR, 1.60; *P*=0.035) were significant predictors of incident CVD. In model 6a (incorporating continuous AAW and identical to model 6, apart from restriction to 922 intermediate- and higher-risk participants), both CAC (HR, 1.29; *P*<0.001) and continuous AAW (HR, 1.25 per 10 mm; *P*=0.023) were significant predictors of incident CVD.

Discussion

The principal findings of this study are that high AAW is a predictor of incident adverse CVD events over 8.9 years of follow-up in a community-dwelling cohort of adults initially free of clinical CVD. AAW not only added to traditional CVD risk factors in multivariable-adjusted models, but also augmented risk prediction in models incorporating both traditional risk factors and burden of CAC. AAW is a simple measure of aortic geometry that is often available to be measured on standard axial chest CT or magnetic resonance scans.
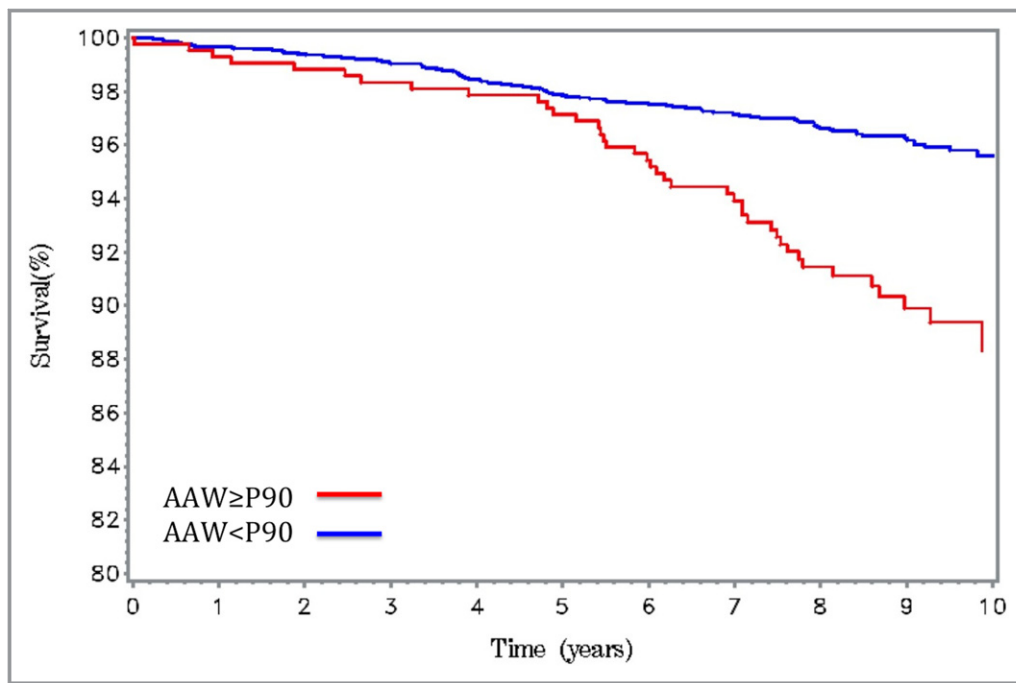
Figure 2. Survival free of adverse cardiovascular disease events over time by high (≥90th percentile [P90]) vs not high (<P90) aortic arch width (AAW).

In the Context of Current Literature

To our knowledge, this is the first study of AAW as a predictor of CVD events in the general population, but some groups have investigated cross-sectional associations between aortic arch geometry and CVD risk factors in smaller patient series. Craiem et al studied 400 men (200 normotensive and 200 hypertensive) with at least 1 CVD risk factor, but no history of overt coronary heart disease, who had undergone noncontrast CT for CAC screening.[5] The size and shape of the aortic arch, including AAW, was characterized using custom software. Mean AAW among the normotensive men was 76.7±9.8 mm, similar to the AAWs of comparably sized and aged normotensive men in our study. In linear regression models, Craiem et al[5] found greater AAW with advancing age (5.6 mm per 10 years) and with prevalent hypertension (2.1 mm).

Redheuil et al used magnetic resonance imaging to determine aortic arch geometry, distensibility, and pulse wave velocity in 100 adults free of cardiac disease, aged 46±16 years. AAW increased with greater age, body weight, and blood pressure.[6] Increased AAW was associated with greater aortic stiffness, as well as increased left ventricular mass and concentricity in models adjusting for age, sex, body size, hypertension, hypercholesterolemia, and smoking.

The studies by Craiem[5] and Redheuil[6] and colleagues quantified aortic arch size and geometry in greater detail than in the present study, but their cross-sectional findings on AAW are in accord with our results. Our study extends the literature in that we were able to demonstrate a significant association between AAW and incident adverse CVD events over 8.9 years of follow-up, in a well-characterized community population with rigorously obtained risk factor and MDCT information, finding that AAW added to models incorporating both FRFs and CAC. We did not characterize the arch in the same detail as in the prior studies for 2 principal reasons. First, we hypothesized that AAW is a simple-to-measure highly reproducible metric of geometric alterations in the thoracic aorta that has predictive value for CVD events. Accordingly, we focused on measuring AAW in a larger cohort rather than on extensively characterizing the entire aortic arch in a smaller study sample. Second, our image data did not encompass the apex of the aortic arch, because our MDCT scanning protocol was optimized for measurement of CAC while minimizing participant exposure to ionizing radiation; scan coverage in the z-direction was limited to that needed to encompass the heart. Thus, our findings in a substantially larger community cohort are both complementary to and consistent with the studies by Craiem[5] and Redheuil[6] and colleagues.

Lee et al measured the straight-line "longest distance between the ascending and descending aortas" in 219 adults who underwent CAC scanning as part of routine health screening.[21] This metric, which they called "unfolding," is essentially AAW plus the radii of the 2 limbs of the aorta in the plane of main pulmonary artery bifurcation. Lee et al[21] found greater unfolding with age, body surface area, hypertension, and burden of CAC. These authors speculated that, because CAC is a

Table 2. Cox Proportional Hazards Models for Incident Adverse CVD Events With 2826 Participants

Variable	Model 1			Model 2			Model 3			Model 4			Model 4a		
	Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value
Female sex	0.87	0.58–1.30	0.49	0.87	0.58–1.31	0.51	1.31	0.85–2.01	0.22	1.30	0.85–1.99	0.23	1.37	0.84–2.24	0.21
Age, per 10 y	2.38	2.01–2.81	<0.001	2.31	1.95–2.73	<0.001	1.71	1.39–2.10	<0.001	1.69	1.38–2.07	<0.001	1.41	1.07–1.86	0.016
Current smoking	2.71	1.66–4.41	<0.001	2.68	1.64–4.37	<0.001	2.43	1.49–3.98	<0.001	2.42	1.48–3.95	<0.001	1.78	0.98–3.24	0.060
Systolic blood pressure, per 10 mm Hg	1.13	1.03–1.24	0.011	1.12	1.02–1.23	0.022	1.10	0.99–1.21	0.054	1.09	0.99–1.20	0.079	1.07	0.97–1.19	0.19
Diabetes mellitus	1.07	0.60–1.93	0.81	1.15	0.64–2.06	0.65	0.91	0.51–1.64	0.76	0.96	0.53–1.72	0.88	0.91	0.50–1.65	0.75
Total cholesterol, per 10 mg/dL	1.00	0.95–1.05	0.98	1.00	0.95–1.06	0.97	1.00	0.95–1.06	0.97	1.00	0.95–1.05	0.99	0.97	0.91–1.03	0.25
HDL cholesterol, per 10 mg/dL	0.72	0.62–0.84	<0.001	0.72	0.62–0.84	<0.001	0.75	0.64–0.87	<0.001	0.75	0.64–0.87	<0.001	0.81	0.69–0.96	0.016
Log(CAC+1)	NA	NA	NA	NA	NA	NA	1.30	1.18–1.42	<0.001	1.29	1.17–1.41	<0.001	1.29	1.16–1.43	<0.001
Aortic arch width ≥P90	NA	NA	NA	1.69	1.13–2.52	0.010	NA	NA	NA	1.55	1.04–2.30	0.032	1.60	1.03–2.48	0.035

Model 1, Framingham risk factors; model 2, Framingham risk factors+aortic arch width; model 3, Framingham risk factors+CAC; model 4, Framingham risk factors+CAC+aortic arch width. Model 4a is identical to model 4 but applied only to the 922 participants with ≥5.0% 10-year American Heart Association/American College of Cardiology risk. Model 2 vs model 1: category-free net reclassification improvement, 0.311 (95% CI, 0.147–0.475; *P*=0.0078). Model 4 vs model 3: category-free net reclassification improvement, 0.312 (95% CI, 0.148–0.476; *P*=0.0076). CAC indicates coronary artery calcium; CI, confidence interval; CVD, cardiovascular disease; HDL, high-density lipoprotein; NA, not in model; P90, upper 90th percentile limit.

Table 3. Sensitivity Analyses: Cox Proportional Hazards Models Incorporating Continuous AAW Among 2826 Participants

Variable	Model 5			Model 6			Model 6a		
	Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value
Female sex	1.05	0.67–1.63	0.84	1.54	0.96–2.46	0.072	1.73	1.01–2.96	0.045
Age, per 10 y	2.12	1.73–2.59	<0.001	1.56	1.24–1.97	<0.001	1.27	0.93–1.73	0.13
Current smoking	2.65	1.63–4.32	<0.001	2.38	1.46–3.90	<0.001	1.77	0.98–3.22	0.059
Systolic blood pressure, per 10 mm Hg	1.12	1.02–1.23	0.023	1.09	0.99–1.20	0.084	1.07	0.96–1.19	0.21
Diabetes mellitus	1.10	0.61–1.98	0.74	0.93	0.52–1.67	0.81	0.90	0.49–1.62	0.72
Total cholesterol, per 10 mg/dL	1.00	0.95–1.06	0.89	1.00	0.95–1.06	0.92	0.97	0.91–1.03	0.32
HDL cholesterol, per 10 mg/dL	0.73	0.62–0.85	<0.001	0.75	0.65–0.87	<0.001	0.82	0.69–0.97	0.019
Log(CAC+1)	NA	NA	NA	1.29	1.17–1.42	<0.001	1.29	1.16–1.44	<0.001
AAW, per 10 mm Hg	1.21	1.01–1.44	0.036	1.18	0.98–1.41	0.074	1.25	1.03–1.51	0.023

Model 5, Framingham risk factors+AAW; model 6, Framingham risk factors+CAC+ascending AAW. Model 6a is identical to model 6 but applied only to the 922 participants with ≥5.0% 10-year American Heart Association/American College of Cardiology risk. AAW indicates aortic arch width; CAC, coronary artery calcium; CI, confidence interval; HDL, high-density lipoprotein; NA, not in model.

recognized predictor of CVD risk, unfolding might also be a CVD risk predictor, but they were unable to test this hypothesis.

Clinical Implications and Future Directions

AAW is a simple, easily determined, highly reproducible parameter often visualized on tomographic imaging of the thorax. In such cases, there is no additional imaging overhead to determine AAW, and analysis burden is trivial, consisting of a single linear measurement after identification of the correct imaging plane. AAW augments CAC in prediction of CVD risk, and it bears emphasizing that AAW can be determined from scans performed to assess CAC. In recognition of this, we performed secondary analyses restricted to Offspring and Third Generation participants with ≥5.0% 10-year American Heart Association/American College of Cardiology risk for CVD, because such participants would be more likely to undergo scanning for CAC assessment. We found that AAW augmented prediction of incident CVD events above FRFs and CAC in this population as well. These practical attributes suggest that AAW offers essentially "free" prognostic information in many thoracic scans performed for various clinical indications and can additionally improve the predictive value of CAC scans performed for CVD risk stratification. Moreover, the observation that AAW predicts increased risk independent of CAC supports the notion that AAW predicts another dimension of CVD risk, in that vascular calcification and width of the aortic arch appear to provide complementary CVD risk prediction. We do not propose that thoracic imaging be performed solely to measure AAW, but note that when

appropriate images have been obtained for other purposes, measurement of AAW offers additional information without any excess burden to the patient.

Our novel finding that AAW has prognostic value above FRFs and CAC for incident adverse CVD events remains to be extended to other cohorts; ideally, these additional studies would be among ethnically diverse populations. Our primary analyses used dichotomized (high or not high) AAW because that is amenable to a perhaps more clinically applicable "table look-up" method. Cut points for high AAW may need to be recalibrated in other ethnic groups, because the FHS Offspring and Third Generation cohorts are largely of European descent. Whether AAW has differential predictive value for subtypes of adverse CVD event (eg, stroke versus myocardial infarction) remains to be determined. Adequately powered studies to assess subtypes of CVD would require additional numbers of events, either through extended duration of follow up or by pooling data across cohorts.

Study Strengths and Limitations

Study participants underwent CT scanning per research protocol as part of their participation in the FHS Offspring and Third Generation cohorts, as opposed to being self- or physician-referred to CT for CAC-based CVD risk stratification. The present study population may be more representative of CVD risk among community-dwelling adults than a population functionally selected for excess CVD. The FHS participants have been meticulously characterized; history and contemporaneous FRFs were measured by investigators rather than

based on self-report. Furthermore, adverse CVD events were adjudicated after extensive review of all available records by a panel of physician-investigators using standardized criteria, as opposed to being based solely on participant self-report or summary diagnostic codes.

The FHS Offspring and Third Generation cohorts are predominantly of European descent; generalization of our results to other ethnicities may be limited. In particular, cut points for high AAW may need recalibration in other populations. Other aspects of aortic arch geometry may have superior predictive value for incident adverse CVD events, but our scans, initially acquired for assessment of CAC, did not encompass the entire aortic arch, so we were not able to fully characterize the arch.

Conclusion

We determined AAW from CT scans performed to measure CAC in a community-dwelling cohort. Over a median 8.9 years of follow-up among the 2826 adults with complete covariates who were free of prevalent CVD events at time of scanning, AAW added predictive value to models incorporating both standard FRFs and CAC. AAW is commonly visualized incidentally on many magnetic resonance or CT scans of the chest, and is trivially simple to measure. These attributes suggest that AAW has utility for CVD risk stratification and may be suitable for the clinical setting. The findings of the present study remain to be extended to other ethnically diverse research cohorts and patient populations.

Sources of Funding

Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. **Upper ninetieth percentile (P90) values for aortic arch width (in mm) among referent participants by age, sex and body surface area.**

AAW, mm	N	P90		N	P90
Men age <45 yr	386		Women age <45 yr	278	
BSA < 1.9	76	74.1	BSA < 1.7	116	67.3
BSA 1.9 – 2.09	165	76.6	BSA 1.7 – 1.89	106	69.2
BSA ≥ 2.10	145	83.8	BSA ≥ 1.90	56	72.9
Men age 45-54 yr	229		Women age 45-54 yr	273	
BSA < 1.9	34	80.1	BSA < 1.7	104	70.1
BSA 1.9 – 2.09	93	86.7	BSA 1.7 – 1.89	104	75.5
BSA ≥ 2.10	101	89.1	BSA ≥ 1.90	65	79.7
Men age 55-64 yr	79		Women age 55-64 yr	114	
BSA < 1.9	15	88.5	BSA < 1.7	43	74.8
BSA 1.9 – 2.09	34	89.3	BSA 1.7 – 1.89	44	78.9
BSA ≥ 2.10	28	97.1	BSA ≥ 1.90	27	86.3
Men age ≥65 yr	44		Women age ≥65 yr	68	
BSA < 1.9	9	98.5	BSA < 1.7	26	87.8
BSA 1.9 – 2.09	21	99.5	BSA 1.7 – 1.89	34	89.6
BSA ≥ 2.10	14	104.3	BSA ≥ 1.90	8	96.6

P90 = upper 90th percentile limit, AAW = aortic arch width, BSA = body surface area (m^2), yr =

years.