Incidental Thoracic Aortic Dilation on Chest Computed Tomography in Patients With Atrial Fibrillation

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Patients with atrial fibrillation (AF) have risk factors that predispose to thoracic aneurysmal disease (TAD) and atherosclerosis. In this study in patients with AF, we assessed the occurrence of incidental TAD and assessed if a validated predictive score used to predict AF, the CHARGE-AF score, was associated with greater aortic dimensions. We also assessed the prevalence of coronary calcification. We conducted a cross-sectional study of 1,000 consecutive patients with AF undergoing chest multidetector CT during evaluation for pulmonary vein isolation. A dilated aortic root or ascending aorta (AA, dimension/body surface area >2.05 cm/m^2) were found in 195 (20%). A total of 12 (1%) had significant aortic aneurysmal enlargement of > 5.0 cm. Advancing age, a bicuspid aortic valve, hypertension, and male gender were associated with increased aortic dimensions. Aortic root dimensions increased linearly ($p < 0.001$) and ascending aortic dimensions increased nonlinearly across CHARGE-AF deciles ($p < 0.001$). Nearly two-thirds (63%) had coronary calcification, 38% of whom were not on lipid-lowering therapy. In conclusion, in patients with AF undergoing gated chest CT, 1 in 5 had previously undetected TAD, with a small proportion having significantly aneurysmal dimensions approaching surgical thresholds. Risk factors previously established to increase the propensity to develop AF are also associated with increased TAD. These findings raise the need to consider a surveillance strategy for TAD in patients with AF, particularly in those with other risk factors for aortic disease. A high prevalence of coronary calcium was also detected, representing an opportunity to optimize statin therapy in patients with AF. **(Am J Cardiol 2021;140:78−82)**

Thoracic aneurysmal disease (TAD) leads to devastating complications and is a leading cause of death in the United States.[1] Reduction in mortality in recent years is related to improved surveillance strategies that permit earlier detection and treatment.[2] TAD is associated with several risk factors such as advancing age and hypertension.[3] Although patients with atrial fibrillation (AF) also have risk factors that would predispose to TAD and atherosclerosis,[4,5] the prevalence of occult TAD in patients with AF has not been defined. The aim of this study in AF was to assess the presence of TAD detected incidentally on chest multidetector computed tomography (CT) as part of evaluation for pulmonary vein isolation. We assessed if a validated predictive score used to predict AF, the CHARGE-AF score,[6,7] was associated with greater aortic dimensions. As a secondary aim, we also sought to assess the prevalence of coronary artery calcification.

Methods

We conducted a cross-sectional, single-center study of patients with AF after institutional review board approval. As this was a pilot, observational study, the sample size was predefined arbitrarily as 1,000 consecutive patients. This sample size has a power of 89% to detect a correlation coefficient r of 0.1 or more. We included consecutive patients undergoing a standardized pulmonary venous CT as part of work-up for pulmonary venous isolation between December 2018 and October 2019. Baseline demographic and clinical data were obtained. No patient had a documented history of connective tissue disorder or TAD.

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

The CT protocol comprised sequential axial imaging with prospective triggering in the systolic phase with 1.5 mm slice reconstruction following intravenous contrast administration (Siemens scanner, Siemens, Erlangen, Germany). Aortic dimensions were measured by the investigators retrospectively for the purpose of the present study. Using multiplanar reconstruction, aortic root (AR) and

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proximal ascending aorta (AA) dimensions were measured perpendicular to the centre line.[8] Diameters were measured from the outside to outside wall using electronic calipers with a zoom function.[8,9] The AR was measured using the sinus-to-sinus technique. With standard centerline techniques, the "diameter" of the aorta at the sinuses of Valsalva is determined by running a line from the deepest point of one sinus perpendicularly through the "center" to the adjacent sinus.[8,9] This technique is recommended by contemporary guidelines owing to similarity to monoplane CT measurements, close correlation with echocardiographic measurements, and easier application to bicuspid aortic valves.[8,9] Furthermore, from a biomechanical perspective, this diameter is believed to be most representative of the highest wall tension in the aorta and thus more naturally predictive of aortic events.[10]

For both AR and AA, aortic size index (dimension/body surface area, dilated >2.05 cm/m^2), aortic height index (dimension/height, dilated >2.43 cm/m), aorta area/height ratio and AR Z-score were calculated as previously described.[1,11] Presence of coronary calcification was recorded (present / absent).

The CHARGE-AF risk score was developed in 2013 to predict risk of AF in the general population.[6] It was derived from the Framingham Heart Study, the Cardiovascular Health Study, and the Atherosclerosis Risk In Communities study and validated in the Age, Gene/Environment Susceptibility Study, and the Rotterdam Study, with more than 26,000 patients of European, European-American, and African-American ancestry in total.[6] The CHARGE-AF risk score was calculated as follows: 0.508 × age (5 years) + 0.248 × height (10 cm) + 0.115 × weight (15 kg) + 0.197 × systolic blood pressure (20 mm Hg) - 0.101 × diastolic blood pressure (10 mm Hg) + 0.359 × current smoker + 0.349 × antihypertensive medication + 0.237 × diabetes + 0.701 × congestive heart failure + 0.496 × myocardial infarction. The coefficients for each risk factor are from the derivation study for the CHARGE-AF risk score.[6,7] We did not include race because it was not disclosed by many of the study participants though where collected, the majority of the participants were of European-American ancestry where the CHARGE-AF score has previously been independently validated.[7]

Baseline demographic data, risk factors, and clinical variables were descriptively summarized with continuous variables expressed as mean ± SD and categorical data presented as percentage frequency. The primary outcome of interest was the incidence of a dilated AR or AA. Continuous data are reported as mean ± SD or median with interquartile range and categorical data as percentage. We assessed potential predictors of aortic size using General Linear Model analysis of variance (ANOVA). To circumvent the correlation between gender and body size, ($p < 0.0001$ by Spearman's rho for body height in our sample), we normalized AR and AA diameters by height. Given that cross correlation matrix revealed a very significant correlation between hypertension and age ($p < 0.0001$ by Spearman's rho), separate multivariable models were built for these 2 variables. To assess the relation between the CHARGE-AF score and diameters of AR and AA, patients were first divided into 10 equal groups based on the deciles of the CHARGE-AF score.[12] We then applied ANOVA with polynomial contrast analysis. A 2-tailed $p < 0.05$ was interpreted as significant. Statistical analysis was performed using STATA version 15.1 (Statacorp., College Station, Texas) and SPSS version 23.0 (IBM, Armonk, New York)

Results

Baseline characteristics are shown in Table 1. Mean age was 66 years and the cohort was mostly male. Cardiovascular risk factors were prevalent such as diabetes, hypertension, and hyperlipidemia. A total of 40 patients had a bicuspid aortic valve (4%).

A dilated AR or AA (dilated aortic size index >2.05 cm/m^2) was found in 195 (20%). A total of 96 (10%) had AR or AA > 4.5 cm and 12 (1%) had significant AR or AA aneurysmal enlargement of > 5.0 cm. A total of 26 patients (2.6%) had an AR or AA area/ height ratio of > 10 cm^2/m, an index shown to be predictive of death[13] and is included

Table 1
Baseline characteristics

Variable	N = 1,000
Age (years)	66 ± 11
Men	681 (68%)
Height (cm)	176 [168−183]
Weight (kg)	92 [78−106]
Body surface area (m^2)	2.1 [1.9−2.3]
Body mass index (kg/ m^2)	29 [26−34]
Hypertension	645 (65%)
Smoking history	415 (42%)
Diabetes mellitus	194 (19%)
Hyperlipidemia	510 (51%)
Bicuspid aortic valve	40 (4%)
Beta-blockers	706 (71%)
Lipid lowering therapy	516 (52%)
ACE-I / ARB	414 (41%)
Aortic root diameter (cm)	3.7 [3.4−4.1]
Aortic root size index (cm/ m^2)	1.8 [1.6−1.9]
Aortic root height index (cm/ m)	2.1 [2.0−2.3]
Aortic root diameter ≥ 4.5cm	78 (8%)
Aortic root diameter ≥ 5.0 cm	10 (1%)
Aortic root Z score > 2	146 (15%)
Aortic root height index ≥ 2.43 cm/m	118 (12%)
Aortic root cross-sectional area/height ratio ≥10 cm^2/ m^2	23 (2%)
Ascending aorta diameter (cm)	3.5 [3.2−3.8]
Ascending aorta size index (cm/ m^2)	1.7 [1.5−1.8]
Ascending aorta height index (cm/ m)	2.0 [1.9−2.2]
Ascending aorta diameter > 4.5cm	32 (3%)
Ascending aorta diameter > 5.0cm	3 (0.3%)
Ascending aorta Height index ≥ 2.43 cm/m	52 (5%)
Ascending aortic cross-sectional area/height ratio ≥10 cm^2/ m^2	6 (0.6%)

ACE-I = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker.

Data are presented as median [25th−75th percentile] or mean (standard deviation) as noted for continuous variables and frequencies for categorical variables.

Hyperlipidemia was defined according to the fulfillment of one of the following criteria: clinical history of hyperlipidemia, total cholesterol levels >200 mg/dL, LDL cholesterol ≥130 mg/dL, HDL cholesterol <40 mg/dL or lipid lowering therapy

Table 2
Predictors of aortic size using General Linear Model Analysis of variance

N = 1,000	Variables	B (95% Confidence Interval)	p Value
Model 1: *Ascending aorta* indexed to height	Age	0.005 (0.004−0.006)	<0.001
	Bicuspid valve	0.178 (0.102−0.254)	<0.001
	Male	−0.19 (−0.51−0.013)	0.248
Model 2: *Ascending aorta* indexed to height	Hypertension	0.083 (0.052−0.115)	<0.001
	Bicuspid valve	0.183 (0.106−0.259)	<0.001
	Male	−0.033 (−0.066− −0.001)	0.042
Model 3: *Aortic root* indexed to height	Age	0.002 (0.001−0.004)	0.004
	Bicuspid valve	0.097 (0.021−0.173)	0.013
	Male	0.110 (0.078−0.142)	<0.001
Model 4: *Aortic root* indexed to height	Hypertension	0.013 (-0.019−0.044)	0.427
	Bicuspid valve	0.097 (0.021−0.174)	0.013
	Male	0.104 (0.072−0.136)	<0.001

in the most recent guidelines as an indication for elective aortic repair in high-risk patientspatients.[1] In the patients with thoracic aorta dilation (n = 195), a subsequent chest x-ray or echocardiogram was available in 144 patients and identified thoracic aortic dilation in only 44 (31%)

General Linear Model (ANOVA) was used to assess potential predictors of aortic size adjusted to height (Table 2). Patients with bicuspid aortic valve had a 1.78 mm/m larger AA compared with those with trileaflet aortic valves (Table 2, model 1, $p < 0.001$). Ascending aortic size adjusted to height increased by 0.5mm/m for increase in age by a decade (Table 2, model 1, $p < 0.001$). Gender did not consistently influence height adjusted-ascending aortic dimension. The presence of hypertension increased the size of the height-adjusted aorta by 0.83 mm/m (Table 2, model 2, $p < 0.001$). With regard to measurements at the level of the AR, height adjusted AR was larger in men by 1.1 mm/m (Table 2, model 3, $p < 0.001$). Similarly, AR normalized for height increased by 0.2 mm/m for increase in age by a decade (Table 2, model 3, $p = 0.001$). There was no effect of hypertension on AR measures (Table 2, model 3, p = NS).

The relation between AR and ascending aortic dimensions across deciles of CHARGE-AF score are shown in Figures 1 and 2 respectively. AR dimensions increased linearly across CHARGE-AF deciles ($p < 0.001$). Mid ascending aortic dimensions increased nonlinearly with CHARGE-AF deciles ($p < 0.001$), with significant first and second order components ($p < 0.001$ and $p = 0.003$).

A total of 631 (63%) participants had coronary calcification, and 242 (38%) of these patients were not on lipid-lowering therapy.

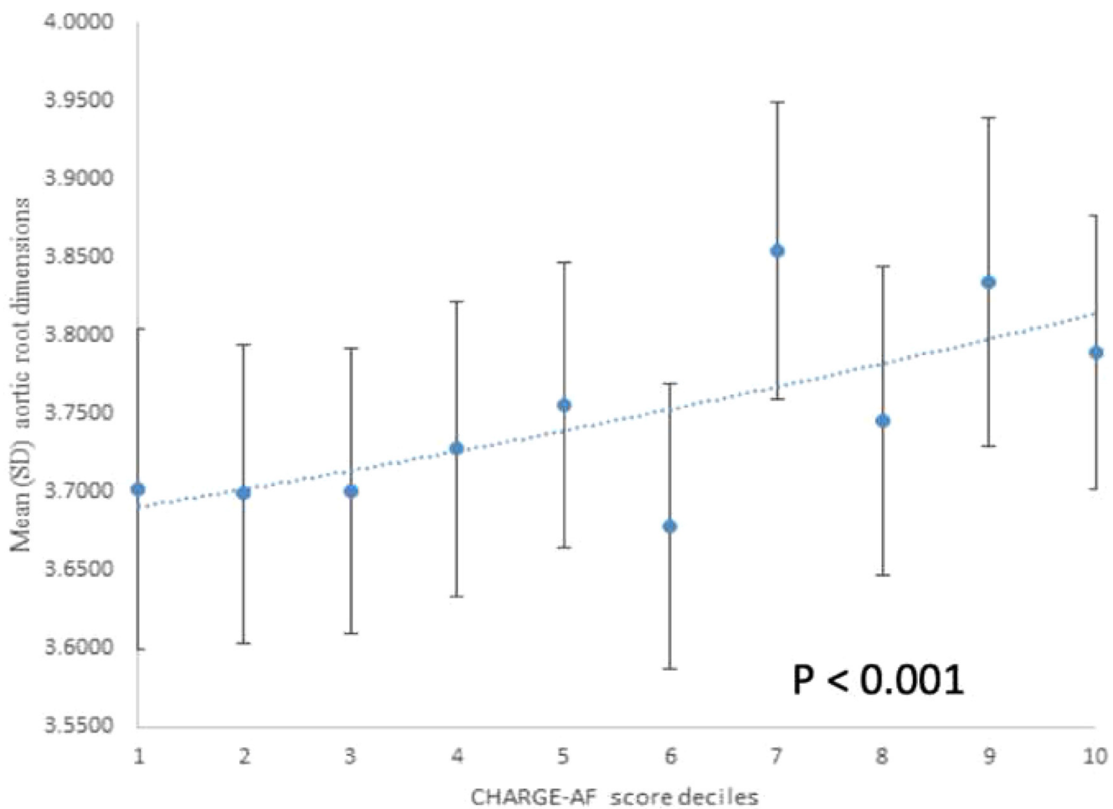

Figure 1. Aortic root dimensions according to CHARGE-AF score. The relation between aortic root dimensions across deciles of CHARGE-AF score. Aortic root dimensions increased linearly across CHARGE-AF deciles ($p < 0.001$). The y-axis represents mean and standard deviation of aortic dimensions across CHARGE = AF deciles (x-axis). SD = standard deviation.

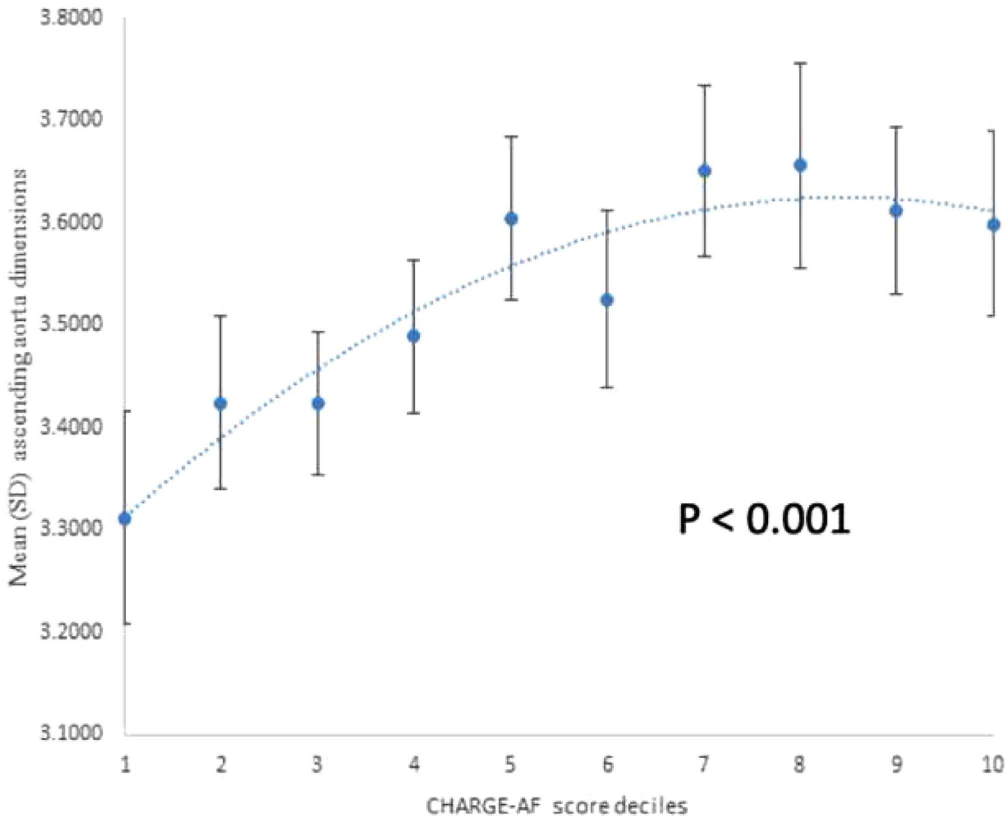

Figure 2. Ascending aortic dimensions according to CHARGE-AF score. Mid ascending aortic dimensions increased nonlinearly with CHARGE-AF deciles ($p < 0.001$), with significant first and second order components ($p < 0.001$ and $p = 0.003$). The y-axis represents mean and standard deviation of aortic dimensions across CHARGE=AF deciles (x-axis). SD = standard deviation.

Discussion

The key finding in this study is that in patients with AF who underwent gated chest CT as part of evaluation for pulmonary vein isolation, 1 in 5 had a dilated proximal thoracic aorta, and 1% of the cohort had aneurysmal dimensions approaching surgical repair thresholds. The prevalence of significantly aneurysmal dimensions (>5.0cm) in this cohort with AF is numerically higher compared with a separate primary prevention 'control' population without AF that we previously reported (1% vs 0.1%).[11]

The underlying mechanisms underpinning high aortic dimensions in AF remains to be understood. AR dimensions and mid ascending aortic dimensions increased across CHARGE-AF deciles suggesting that factors previously established to increase the propensity to develop AF are also associated with increases in aortic dimensions.[6]

These findings raise the need to consider a surveillance strategy for thoracic aortic enlargement in patients with AF particularly in those with concurrent risk factors for aortic disease. Our results are expected to stimulate further research in this patient population and the findings need confirmation in large, independent cohorts if routine screening for TAD is to be recommended in this patient group. To balance the risk of ionizing radiation and costs, the optimal surveillance strategy should be targeted at patients with the highest risk for TAD for example in those who also have other risk factors identified on the present study such as advancing age, a bicuspid aortic valve, hypertension, and male gender.

Remarkably, nearly two-thirds of the population had coronary calcification, a known powerful predictor of atherosclerotic cardiovascular disease events.[14] A large subset (38%) of these patients were not on lipid lowering therapy. Our findings thus emphasize the added utility of pulmonary venous CT to optimize atherosclerotic cardiovascular disease primary prevention strategies. This is of particular relevance considering the most recent cholesterol clinical practice guidelines recommend initiation of statin therapy in those with intermediate risk of atherosclerotic cardiovascular disease in the presence of coronary artery calcification.[15] Randomized controlled trials are needed to determine if more intensive lifestyle and/or pharmacological interventions improve outcomes in this cohort of patients with AF. Until then, it would seem reasonable to use this information to complement guideline driven clinical strategies in cardiovascular risk screening and help improve the timely initiation of cardiovascular risk management in eligible patients.

The strengths of this study include the large patient population, precise measurement of the aorta using gated CT with contrast and multiplanar reconstruction to measure aortic size perpendicular to the centre line. The study has a number of limitations. Our results are applicable only to the subset of patients underwent CT as part of evaluation for pulmonary vein isolation for AF. Results may therefore not be applicable to the patients who are not candidates for pulmonary vein isolation AF. Secondly, the entire aorta was not completely assessed due to the range included as part of the pulmonary vein CT protocol and as such dilation in regions not covered such as the aortic arch or distal descending thoracic aorta may have been missed. Lastly, coronary artery calcium was assessed qualitatively using a contrast-enhanced CT scan. This method avoids the additional costs/ radiation exposure with a dedicated coronary artery calcium score scan.

To conclude, to our knowledge this study of patients with AF underwent gated chest CT demonstrates that 1 in 5 patients has a dilated proximal thoracic aorta, with 1% of the cohort having incidental but significant aneurysmal dimensions approaching surgical thresholds. None of those with dilated aortas had dissection or rupture negating the need for acute operative intervention on these patients.

Authors contribution

Jay Ramchand: Conceptualization, Methodology, data curation, formal analysis, writing − original draft **Agam Bansal:** investigation − data collection **Mnahi Bin Saeedan:** investigation − data collection **Tom Kai Ming Wang**: investigation − data collection **Ritu Agarwal:** investigation − data collection **Mohamed Kanj:** data interpretation and the critical revision of the manuscript. **Oussama Wazni:** data interpretation and the critical revision of the manuscript. **Lars G. Svensson**: data interpretation and the critical revision of the manuscript **Milind Y. Desai**: data interpretation and the critical revision of the manuscript. **Serge C. Harb:** resources, data interpretation and the critical revision of the manuscript. **Paul Schoenhagen:** data interpretation and the critical revision of the manuscript. **Louise M. Burrell:** data interpretation and the critical revision of the manuscript **Brian P Griffin:** resources, data interpretation and the critical revision of the manuscript **Zoran B. Popović:** supervision, formal analysis and the critical revision of the manuscript **Vidyasagar Kalahasti**: supervision, project administration, data interpretation and the critical revision of the manuscript

Disclosures

The authors have reported that they have no relations relevant to the contents of this study to disclose.

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