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ORIGINAL RESEARCH

Aortic Dimensions Are Larger in Patients With Fibromuscular Dysplasia

Arielle M. Schwartz, MD; Esther Kim, MD, MPH; Patrick Gleason, MD; Xiaona Li, MPH; Yi-An Ko, PhD; Bryan J Wells, MD

BACKGROUND: Fibromuscular dysplasia (FMD) is a disease of unknown etiology that causes stenosis, aneurysmal dilatation, and dissection of vascular beds. Known to affect medium-sized arteries, FMD is not typically considered to affect the aorta. We tested the hypothesis that aortic size in FMD is abnormal compared with age- and sex-matched controls.

METHODS AND RESULTS: Medical records and computed tomography angiography images were reviewed in female patients with a diagnosis of FMD who were seen in the vascular medicine clinic at Emory Healthcare. Aortic dimensions were measured at 6 different landmarks. Using 2 sample *t* tests, the aortic measurements and height-indexed measurements were compared with published normal values in healthy women of a similar age. A total of 94 female patients were included in the study. The median age was 57 (interquartile range, 50–65). FMD involvement was present most commonly in the extracranial carotid (77.7%) and renal (43.6%) arteries. All 6 aortic segments were found to be larger in both absolute measures and height-indexed measures in the FMD population ($P<0.001$). The largest differences were observed within the absolute measures of the sinotubular junction with mean±SD (mm) (29.9±4.1) versus (27±2.5), ascending aorta (32.7±4.4) versus (30.0±3.5), and descending aorta (24.7±3.0) versus (22.0±2.0) ($P<0.001$).

CONCLUSIONS: Aortic diameters in female patients with FMD are larger when compared with published age- and sex-matched normal values. These findings suggest that FMD may also affect the large-sized arteries.

Key Words: aneurysm ■ aorta ■ fibromuscular dysplasia ■ vascular ■ women's health

Fibromuscular dysplasia (FMD) is a disease of unknown etiology that affects the arterial system and can result in stenosis, aneurysmal dilatation, and dissection of involved vessels.[1–5] FMD is typically described in medium-sized arterial beds, which are branches of the aorta and most commonly affects the carotid and renal arteries.[1–3]

Historically, FMD was diagnosed and characterized histologically; however, because of the practical identification of characteristic features on imaging, FMD is now diagnosed on the basis of angiographic criteria.[6] Classic imaging features include a multifocal "string of beads" appearance and/or a focal tubular stenosis in the affected artery.

There is a low reported prevalence of FMD in large-sized vessels. For example, of the first 447 patients enrolled in the US registry, no patients were reported to have aortic involvement.[2] As patients with FMD have received more extensive cross-sectional imaging, aortic aneurysms and dissections are increasingly recognized.[2,7] Case reports describe findings such as aortic aneurysm and/or rupture.[8] Recent data also suggest that patients with FMD have larger common carotid arteries.[9] Thus, the phenotype of FMD is expanding to include vessel tortuosity, aneurysm, and dissection of large vessels as well.[10]

We hypothesize that FMD affects the aorta, resulting in larger aortic diameters compared with a non-FMD comparison group. We sought to systematically

Correspondence to: Arielle M. Schwartz, MD, 49 Jesse Hill Jr Dr SE, Atlanta, GA 30303. Email: amschw2@emory.edu

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CLINICAL PERSPECTIVE

What Is New?

- This is the first study to demonstrate aortic involvement of fibromuscular dysplasia, a condition classically described in medium-sized arterial vessels such as the renal artery.

What Are the Clinical Implications?

- The clinical implications of the above-mentioned observation are not yet known but may suggest that this patient population is at higher risk for aortic aneurysm and dissection.

Nonstandard Abbreviations and Acronyms

CTA	computed tomography angiography
FMD	fibromuscular dysplasia

investigate the aortic dimension of patients with multifocal FMD compared with a normal comparison group to determine if FMD may be a systemic arteriopathy that involves not only the medium-sized vessels but also the aorta.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request. The study was approved by the Emory Institutional Review Board. This study was approved for a waiver of informed consent. The data were based on a retrospective review that had been collected for standard of care. The procedures followed were in accordance with institutional guidelines.

Study Cohort

This is a single center, retrospective study of patients with FMD who were seen at Emory University Hospital in the vascular medicine clinic between January 1, 2015, and January 1, 2020. Patients were included if they were women aged ≥18 years with a confirmed diagnosis of multifocal FMD and had cross-sectional imaging with computed tomography angiography (CTA) of the chest and/or abdomen available to review.

Normal controls were healthy women of a similar age range to our cohort included in the Copenhagen General Population Study.

Data Collection

Patient demographics, medical history, family history, medications, and FMD characteristics including age at diagnosis, vascular bed involvement, and the presence of a dissection or aneurysm were collected from the electronic medical record. Hypertension was defined as any diagnosis listed in the patient's chart and/or treatment with any antihypertensive medications. Tobacco use was defined by any former or current tobacco use documented in the patient's medical record.

The TeraRecon imaging system (TeraRecon Inc, Durham, NC) was used to obtain measurements from specific landmarks.

Imaging and Measurement Protocol

All CTAs were non-ECG gated exams of the chest and abdomen obtained on a multidetector scanner using omnipaque 350 with an injection rate of 4 cc/s. The scans were triggered with a region of interest marker in the descending thoracic aorta at a threshold of 150 Hounsfield Units and a 6-second delay from the time of trigger to scan. Images were reconstructed in 1.0-mm slice thickness with image evaluation and interpretation performed using TeraRecon (Foster City, CA) software. Outside images were imported into the Emory picture archiving and communication system and reviewed in TeraRecon, similar to studies performed within the hospital system.

The following aortic anatomic sites were measured: sinus of Valsalva, sinotubular junction, ascending aorta, descending aorta, the aorta at the level of the diaphragm, and the aorta at the level of the kidneys. Measurements were corrected to the center of the aorta perpendicular to blood flow in an axial plane (Figure 1), a technique recommended in the American College of Cardiology guidelines to improve accuracy and reproducibility.[11] Although outer-to-outer wall dimensions are recommended in the American College of Cardiology guidelines, inner-to-inner wall measurements were measured in the comparison group protocol.[11–13] Thus, aortic dimensions were measured using the inner-to-inner wall method in the current study (Figure 2).

The sinus of Valsalva was measured from the cusp to the corresponding furthest commissure for all leaflets and the sinotubular junction was measured at the narrowest level between the aortic root and the ascending aorta, which were consistent with the comparison study protocol.[12] The ascending aorta and descending aorta were noted in the control study to be measured at a "shared anatomical landmark at the pulmonary artery trunk level." Given this description and the varied diameter throughout the pulmonary trunk level, we measured the ascending and descending aorta with the largest diameter, as is the recommended standardized method.[11] Landmarks

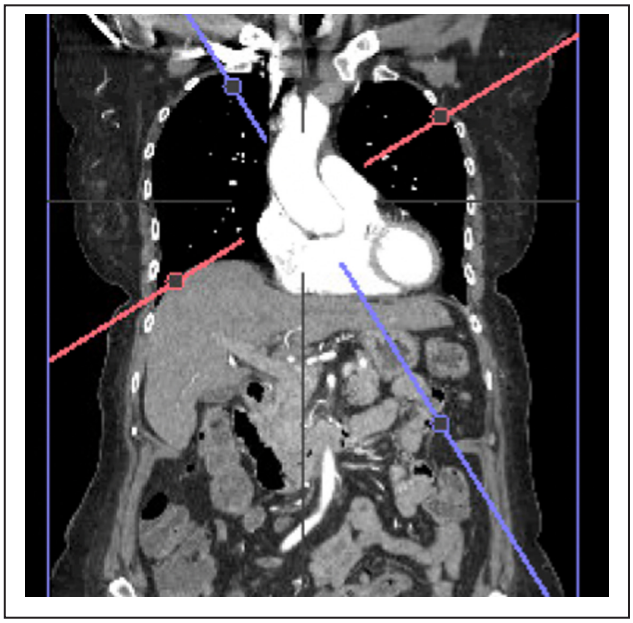

Figure 1. Measurement of ascending aorta using TeraRecon Imaging System.
The vectors were corrected to the center of the aorta perpendicular to blood flow.

within the abdominal aorta included the level of the diaphragm and the infrarenal aorta, which were measured in a fashion consistent with the comparison study protocol.[12]

Two trained imaging readers conducted all of the measurements. Reader 1 is a member of the house staff at our institution with training in advanced imaging modalities. Reader 2 is a member of the cardiology faculty specialized in advanced imaging techniques and is director of cardiac computed tomography at our institution. Reader 1's initial measurements were measured 2 weeks before reader 1's second round of measurements.

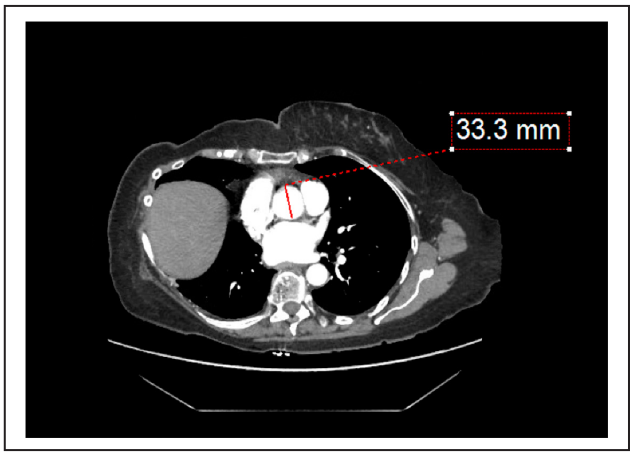

Figure 2. Measurement of inner-to-inner wall of the sinotubular junction.

Reader Variability

To evaluate the degree of intrareader variability, measurements were taken twice by the same reader for 15 different patients. In addition, measurements of 10 patients were taken by an expert reader independent of the original reader. These measurements were compared with the other reader's to assess interreader variability.

Statistical Analysis

Indexing of aortic dimension for body height to the power of 2.7 was performed as it was in the comparison study.[12] Continuous variables were summarized as mean±SD, and categorical variables were summarized as n (%). The aortic measurements and height-indexed measurements were compared with the control study[12] using 2 sample *t* tests. To evaluate intra- and interobserver agreement, the differences in each aortic measurement were calculated between 2 independent observers and 2 separate measurements within the same observer. The results were summarized as mean±SD and percent coefficient of variation: coefficient of variation=SD×100/mean average.

Linear regression modeling was used to examine the association between patient demographics, smoking, and FMD characteristics with aortic diameter at each of the 6 aortic landmarks. The covariates included age (years), body surface area, tobacco use, hypertension, family history of aneurysm, history of dissection or aneurysm, and multisite FMD (defined as disease involving >1 vascular bed). Model diagnostics were examined. *P* values of <0.05 were considered statistically significant. All statistical analysis was performed using R version 3.6.3 software (R Foundation for Statistical Computing, Vienna, Austria).

Using the Bonferroni correction (assuming independence among all the aortic dimension measurements) is inherently conservative. We adopted the procedure using the effective number of independent tests to handle multiple testing for correlated tests. That is, we replaced the actual number of tests being tested by the effective number of independent markers. This results in a modified significance threshold for each test: $\alpha^* = \alpha$ / effective number of independent markers, which controls the family-wise error rate at the level of α. To estimate effective number of independent markers, we applied the method proposed by Galwey (2009) and obtained effective number of independent markers=9. Thus, the test-wise significance level was 0.05/9=0.00556.[14]

RESULTS

Ninety-four patients met all study inclusion criteria and were included in the study. The median age was 57 years.

In the healthy comparison group, 506 women were included with a median age of 52 years. Table 1 summarizes the baseline clinical characteristics of both the FMD and the healthy control groups. A history of hypertension and smoking was present in 61.7% and 8.5% of the FMD study group, respectively. The majority of patients with FMD had extracranial carotid involvement (n=73; 77.7%) with renal involvement being the next most commonly involved vascular bed (n=41; 43.6%) (Figure 3).

The absolute and height-indexed measurements at all 6 aortic landmarks were significantly larger in the FMD group than in the comparison group (Table 2). In the multivariable analyses, age was associated with increased aortic diameter at the descending aorta (Table S1) 1.023 mm per 10-year increase in age (0.327–1.719; P=0.05) as well as at the level of the diaphragm (Table S2) 0.655 mm per 10-year increase in age (0.145–1.165; P=0.012) and kidneys (Table S3) 0.698 mm per 10-year increase in age (0.018–1.378; P=0.044), but not with the dimensions at the other aortic landmarks (Tables S4 through S6). This association persisted despite adjusting for variables including tobacco and hypertension. Body surface area was associated with larger aortic diameter only at the level of the diaphragm (Table S2) when adjusted for the other variables 3.093 m^2 (0.327–5.858; P=0.029). Height, hypertension, tobacco use, and family history of aneurysm were not significantly associated with aortic size at any of the aortic landmarks (aside from the aforementioned associations).

Inter- and intraobserver variability for each aortic segment was assessed (Table 3). The range of mean difference in interobserver measurements in our study ranges from −0.69 to 0.91 (range of 1.6 mm) which is similar to the comparison study interobserver range from −0.8 to 0.5 (range of 1.3 mm). The intraobserver range in our study ranges from −1.31 to 1.07 (range of 2.38 mm), which is larger than intraobserver range in the comparison group ranges from −0.06 to 0.6 (0.66 mm).

Table 1. Descriptive Baseline Characteristics of 94 Patients With FMD Seen in the Vascular Medicine Clinic

	Patients with FMD (n=94)
Age, y, median (IQR)	57 (15)
Age at first FMD-related symptoms, y, median (IQR)	46 (13)
Age at diagnosis of FMD, y, median (IQR)	52 (17)
Body surface area (m^2), mean±SD	1.8±0.2
Race, White, n (%)	63 (67.0)
Hypertension, n (%)	58 (61.7)
Hyperlipidemia, n (%)	28 (29.8)
Diabetes, n (%)	5 (5.3)
Tobacco, n (%)	8 (8.5)
Depression, n (%)	30 (31.9)
Headache/migraines, n (%)	51 (54.3)
Tinnitus, n (%)	44 (46.8)
History of MI, n (%)	8 (8.5)
History of CVA, n (%)	15 (16.0)
History of TIA, n (%)	10 (10.6)
CKD, n (%)	2 (2.1)
Family history of known aneurysm, n (%)	12 (12.8)
Family history of CVA, n (%)	27 (28.7)
Family history of MI, n (%)	38 (40.4)
Aspirin, n (%)	74 (78.7)
Beta blocker, n (%)	28 (29.8)
ACE inhibitor or ARB, n (%)	31 (33.0)
Calcium channel blocker, n (%)	28 (29.8)
Antidepressant, n (%)	32 (34)
Plavix, n (%)	14 (14.9)
Statin, n (%)	27 (28.7)
Oral contraceptives, n (%)	4 (4.3)
Hormones, n (%)	12 (12.8)
Anticonvulsants, n (%)	15 (16.0)
Other hypertension medications, n (%)	20 (21.3)
Multisite FMD, n (%)	51 (54.3)

ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; CVA, cerebrovascular accident; FMD, fibromuscular dysplasia; IQR, interquartile range; MI, myocardial infarction; and TIA, transient ischemic attack.

DISCUSSION

To our knowledge, this is the first study to identify larger aortic dimensions in patients with FMD compared with a cohort of healthy individuals of a similar age range. Female patients with FMD have larger aortic dimensions by both the absolute and height-adjusted dimensions at the sinus of Valsalva, sinotubular junction, ascending aorta, descending aorta, the aorta at the level of the diaphragm, and the aorta at the level of the kidneys compared with healthy female controls of a similar age.

Tobacco use, hypertension, family history of aneurysm or dissection, and the presence of multisite FMD were not associated with aortic size even when adjusted for the other factors. The only variables that were associated with aortic size were age (significant only in the descending aorta, level of the diaphragm, and infrarenal aorta) and body surface area (significant only at the diaphragm level when adjusted for the other factors). This suggests that FMD is an independent predictor of aortic size, which is not explained by baseline characteristics.

While patients with FMD have been reported to have aortic aneurysms and dissections,[7,8] larger aortic dimensions in the absence of these manifestations have never been identified. The clinical significance

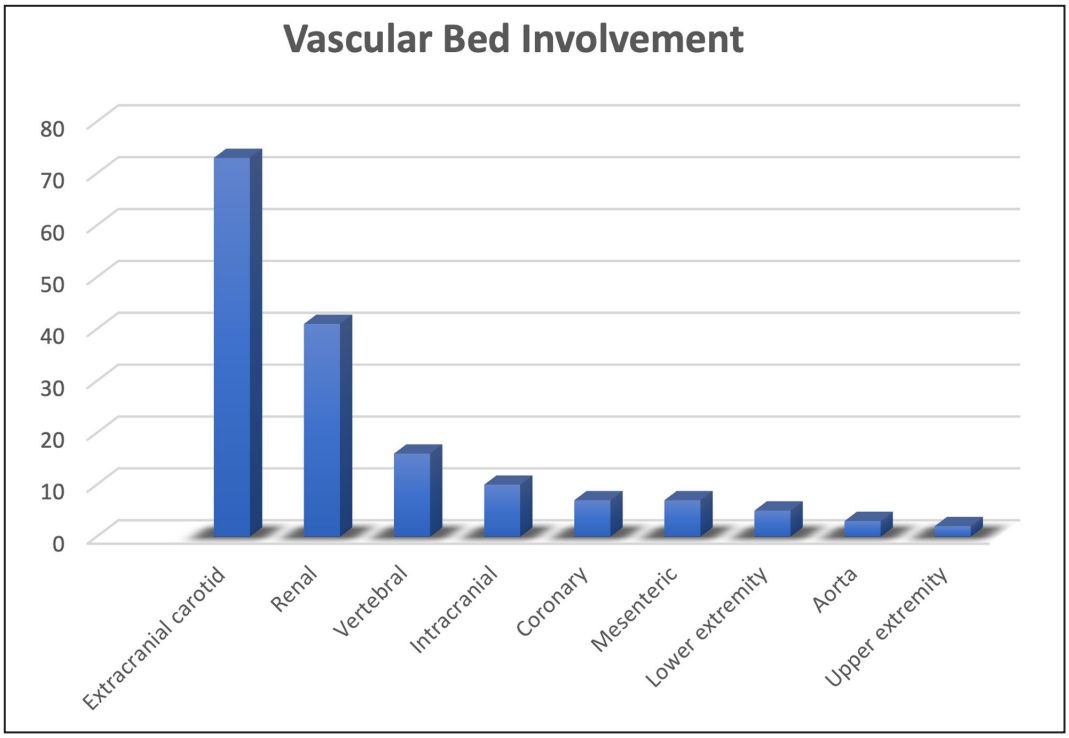

Figure 3. Vascular bed involvement of patients with fibromuscular dysplasia as reported in clinical notes.
The extracranial carotid artery was the most implicated vessel followed by the renal artery.

of this study's findings is not yet known but should be investigated in future studies. More specifically, if larger aortic diameters in this population were found to be a predictor of aneurysm and dissection, surveillance and cardioprotective strategies would be indicated.

While FMD has classically been described in medium-sized vessels such as the renal and internal carotid arteries, our data reveal large-sized vessel involvement. Recent data also support this idea: Lippmann et al[9] found that the common carotid diameter in a cohort of 74 patients with FMD were significantly larger than age- and sex-matched controls; however, this group found no significant difference in aortic diameters between the 2 cohorts. Some reasons for the discrepancy in the results may be differences in study

Table 2. Absolute and Height-Indexed Aortic Diameters in FMD Versus Comparison Group

	FMD (n=94)	Healthy control (n=506)	*P* value
Absolute aortic diameters			
Sinus of Valsalva	30.4±3.3	29.0±2.5	<0.001
Aorta at level of sinotubular junction	29.9±4.1	27.0±2.5	<0.001
Ascending aorta	32.7±4.4	30.0±3.5	<0.001
Descending aorta	24.7±3.0	22.0±2.0	<0.001
Aorta at diaphragm level	22.5±2.5	21.0±2.0	<0.001
Aorta at infrarenal level	19.3±3.1	17.0±1.5	<0.001
Height-indexed aortic diameters			
Sinus of Valsalva	7.8±1.1	7.2±0.8	<0.001
Aorta at level of sinotubular junction	7.6±1.3	6.9±0.8	<0.001
Ascending aorta	8.3±1.4	7.5±1.1	<0.001
Descending aorta	6.4±1.0	5.5±0.7	<0.001
Aorta at diaphragm level	5.8±0.8	5.2±0.7	<0.001
Aorta at infrarenal level	5.0±0.9	4.4±0.5	<0.001

All measurements reported as mean±SD (mm). All 6 aortic segments were found to be larger in both absolute measures and height-indexed measures in the FMD. FMD indicates fibromuscular dysplasia.

Table 3. Inter- and Intraobserver Variability

Aortic region, mm	Interobserver		Intraobserver	
	Mean difference±SD (mm)	CV, %	Mean difference±SD (mm)	CV, %
Sinus of Valsalva (R) coronary leaflet to commissure	0.91±2.75	10.48	−1.31±2.00	7.00
Sinus of Valsalva (L) coronary leaflet to commissure	0.62±2.01	7.22	−1.01±2.97	10.10
Sinus of Valsalva noncoronary leaflet to commissure	0.75±2.45	8.63	−1.19±1.31	4.43
Sinotubular junction	−0.69±2.21	8.14	0.67±1.32	4.51
Ascending aorta largest diameter	−0.36±2.64	8.22	0.94±1.89	5.61
Isthmus end of left subclavian	−0.29±1.72	7.04	1.07±1.48	5.71
Descending aorta largest	−0.30±2.35	9.63	0.11±2.86	11.47
Level of diaphragm	−0.42±0.90	4.11	−0.26±1.13	5.06
Level of kidney	0.06±0.70	3.74	−0.18±1.78	9.31

CV indicates coefficient of variation.

populations and measurement methodology. Our study was larger, and the control group in our study was a healthy group of women without any medical comorbidities or medication use, whereas the control group in the Lippmann study included patients with Hodgkin disease with varying medical comorbidities. Aortic dimensions in this study were obtained by measuring intraluminal diameters, whereas the Lippmann study used extraluminal diameters.

The etiology of FMD is not known, as studies thus far investigating the causes are inconclusive, highlighting the need for more research in this disease process. There are thought to be both genetic and nongenetic contributors. Leading hypotheses of the pathophysiology include mechanical stretch of the vessels leading to phenotypic changes from smooth muscles to a fibroproliferative state and hormonal impact on vasculature given the disproportionate effect on women.[15] Additionally, a number of inflammatory markers have been associated with severe FMD, which could point toward an inflammatory etiology.[16]

Limitations

This study has several limitations. This is a retrospective, observational, single-center study, thereby introducing potential for confounding error and bias. Additionally, differences in baseline characteristics of the FMD group and comparison group may have contributed to observed differences in aortic dimensions: Race data were not described in the comparison study. Additionally, those with a history of hypertension were excluded from the comparison study. The mean±SD systolic and diastolic blood pressures of the healthy group were 126±16 and 78±9. It should be noted, however, that hypertension in this study was not significantly associated with aortic size in either linear or multivariable regression analysis (and neither were tobacco use, family history of aneurysm or dissection, and/or the presence of multisite FMD). A smoking history was present in 8.5% of the FMD study population and in 13% of the comparison group. Additionally, propensity score matching was not possible given the limitations of the available comparison data. Instead, we compared the summary statistics from the Pham et al paper[12] to our data. This limitation likely contributed to selection bias.

The imaging protocols and measurements of the study group and the control group were performed at different institutions. Every effort was made to duplicate the reading methodology used in the healthy control study.[12] However, the difference between the gated protocol used for the comparison study and the nongated protocol used to acquire the FMD CTAs should be addressed. In the comparison group, cardiac CTA was acquired using a gated protocol, and the abdomen was nongated. In our study, the whole CTA was nongated. The difference in protocols certainly could contribute to differences in the proximal aortic measurements between the 2 study groups, but does not explain the differences in size throughout the entire aorta. In other words, if the gating versus nongating protocols accounted for the significant difference in aortic size of the FMD population, one would expect these differences to be significant only in the proximal aortic measurements. Instead, all aortic measurements were found to be significantly larger in the FMD group.

The strength of this study would be improved if the imaging performed on the study group and control group were performed at the same institution. The retrospective nature of the study limited the ability to do so, as finding a sizeable number of CTAs from healthy middle-aged women without aortic pathology was challenging.

Reported aortic measurements can be flawed because of inherent variability, differences in measurement technique, and cross-sectional diameter variability based on the hemodynamic changes throughout the cardiac cycle.[11] An expert aortic specialist may measure identical images of the aorta with up to 3 mm of difference.[11,17–19] While the interobserver variability in this study was similar to the comparison study (1.6 mm compared with 1.3 mm), the intraobserver variability range was larger in this study compared with the comparison study (2.38 mm versus 0.66 mm). The larger intraobserver variability may have been a result of this reader with relatively less reading experience given she is a member of the house staff who has been trained on the imaging technique.

Finally, there may have been unidentified variables that may have contributed to the larger aortic size observed in our FMD cohort compared with the control group.

CONCLUSIONS

This study demonstrates larger aortic dimensions in women with FMD compared with healthy female controls of a similar age. This suggests that FMD is a systemic process that likely also affects large-sized arteries.

ARTICLE INFORMATION

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Affiliations

Willis Hurst Internal Medicine Residency Program, Emory University, Atlanta, GA (A.M.S.); Division of Cardiovascular Medicine, Department of Medicine, Vanderbilt University Medical Center, Nashville, NC (E.K.); Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, GA (P.G., B.J.W.); and Department of Biostatistics and Bioinformatics, Rollins School of Public Health, Emory University, Atlanta, GA (X.L., Y.K.).

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Disclosures

None.

Supplemental Material

Tables S1–S6

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SUPPLEMENTAL MATERIAL

Table S1. Associations between factors (demographics, smoking, and disease history) and the diameter of the descending aorta (mm)

	Univariable		Multivariable	
Predictor variable	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value
Age (per 10 years)	1.099 (0.469, 1.729)	0.001	1.023 (0.327, 1.719)	0.005
BSA (m^2)	0.977 (-3.069, 5.050)	0.634	0.246 (-3.839, 4.332)	0.905
Tobacco	-1.069 (-3.603, 1.467)	0.404	-1.339 (-3.895, 1.216)	0.299
Hypertension	1.202 (-0.185, 2.588)	0.088	1.048 (-0.411, 2.507)	0.156
Family history of aneurysm	-0.759 (-2.894, 1.377)	0.481	-0.268 (-2.406, 1.869)	0.803
History of dissection	-0.768 (-2.894, 1.377)	0.309	-0.611 (-2.123, 0.901)	0.423
History of aneurysm	0.029 (-1.800, 1.857)	0.975	-0.681 (-2.503, 1.142)	0.458
Multisite FMD	0.210 (-1.195, 1.615)	0.767	0.145 (-1.328, 1.617)	0.845

Table S2. Associations between factors (demographics, smoking, and disease history) and the diameter of the aorta at level of diaphragm (mm)

	Univariable		Multivariable	
Predictor variable	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value
Age (per 10 years)	0.753 (0.275, 1.231)	0.002	0.655 (0.145, 1.165)	0.012
BSA (m^2)	2.664 (-0.056, 5.384)	0.055	3.093 (0.327, 5.858)	0.029
Tobacco	0.001 (-1.829, 1.831)	0.999	-0.284 (-2.099, 1.532)	0.757
Hypertension	0.941 (-0.094, 1.976)	0.074	0.557 (-0.545, 1.659)	0.318
Family history of aneurysm	-0.910 (-2.441, 0.621)	0.241	-0.915 (-2.431, 0.602)	0.234
History of dissection	0.114 (-1.029, 1.257)	0.844	0.330 (-0.835, 1.494)	0.575
History of aneurysm	0.118 (-1.109, 1.345)	0.849	-0.128 (-1.353, 1.097)	0.836
Multisite FMD	0.301 (-0.726, 1.328)	0.562	0.784 (-0.929, 1.228)	0.784

Table S3. Associations between factors (demographics, smoking, and disease history) and the level of kidney (mm)

	Univariable		Multivariable	
Predictor variable	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value
Age (per 10 years)	0.725 (0.093, 1.356)	0.025	0.698 (0.018, 1.378)	0.044
BSA (m^2)	1.591 (-1.924, 5.105)	0.371	1.847 (-1.792, 5.485)	0.315
Tobacco	-0.378 (-2.662, 1.907)	0.743	-0.323 (-2.676, 2.030)	0.785
Hypertension	1.085 (-0.234, 2.403)	0.106	0.728 (-0.727, 2.184)	0.322
Family history of aneurysm	-1.696 (-3.612, 0.220)	0.082	-1.452 (-3.424, 0.519)	0.146
History of dissection	-0.415 (-1.850, 1.020)	0.567	-0.080 (-1.604, 1.444)	0.917
History of aneurysm	-0.089 (-1.628, 1.451)	0.909	-0.331 (-1.934, 1.272)	0.682
Multisite FMD	-0.706 (-2.009, 0.597)	0.285	-0.775 (-2.190, 0.641)	0.279

Table S4. Associations between factors (demographics, smoking, and disease history) and the Sinus of Valsalva (SOV) (mm)

	Univariable		Multivariable	
Predictor variable	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value
Age (per 10 years)	-0.048 (-0.993, 0.897)	0.919	0.114 (-0.848, 1.075)	0.813
BSA (m^2)	-3.405 (-9.318, 2.507)	0.253	-1.167 (-7.180, 4.846)	0.698
Tobacco	0.689 (-2.801, 4.179)	0.694	1.683 (-1.662, 5.028)	0.317
Hypertension	0.302 (-1.688, 2.292)	0.762	-0.419 (-2.476, 1.638)	0.684
Family history of aneurysm	-1.720 (-4.756, 1.315)	0.261	-1.423 (-4.332, 1.486)	0.330
History of dissection	1.525 (-0.591, 3.641)	0.154	0.560 (-1.639, 2.758)	0.611
History of aneurysm	-0.058 (-2.560, 2.444)	0.963	0.311 (-2.103, 2.725)	0.797
Multisite FMD	-0.061 (-2.052, 1.931)	0.952	0.274 (-1.855, 2.402)	0.797

Table S5. Associations between factors (demographics, smoking, and disease history) and the Sinotubular (ST) Junction (mm)

	Univariable		Multivariable	
Predictor variable	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value
Age (per 10 years)	0.362 (-0.606, 1.330)	0.458	0.216 (-0.837, 1.269)	0.683
BSA (m^2)	-1.140 (-7.149, 4.869)	0.706	0.402 (-6.000, 6.804)	0.901
Tobacco	-0.186 (-4.036, 3.664)	0.923	-0.079 (-4.034, 3.876)	0.968
Hypertension	-0.397 (-2.408, 1.615)	0.695	-0.571 (-2.771, 1.629)	0.606
Family history of aneurysm	-1.268 (-4.371, 1.835)	0.417	-1.219 (-4.467, 2.029)	0.456
History of dissection	2.257 (0.159, 4.356)	0.035	2.258 (-0.020, 4.536)	0.052
History of aneurysm	0.134 (-2.499, 2.768)	0.919	0.189 (-2.552, 2.930)	0.891
Multisite FMD	0.571 (-1.438, 2.579)	0.573	0.422 (-1.769, 2.614)	0.701

Table S6. Associations between factors (demographics, smoking, and disease history) and the Ascending Aorta (mm)

	Univariable		Multivariable	
Predictor variable	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value
Age (per 10 years)	0.462 (-0.576, 1.500)	0.377	0.311 (-0.853, 1.475)	0.595
BSA (m^2)	1.258 (-5.150, 7.666)	0.696	1.208 (-5.809, 8.226)	0.731
Tobacco	-1.434 (-5.523, 2.655)	0.486	-1.827 (-6.178, 2.524)	0.404
Hypertension	1.038 (-1.110, 3.185)	0.338	0.909 (-1.512, 3.329)	0.455
Family history of aneurysm	-1.425 (-4.788, 1.938)	0.400	-0.949 (-4.511, 2.614)	0.596
History of dissection	1.324 (-0.978, 3.626)	0.255	1.506 (-0.999, 4.011)	0.233
History of aneurysm	1.225 (-1.671, 4.120)	0.401	1.063 (-2.047, 4.173)	0.496
Multisite FMD	0.428 (-1.746, 2.603)	0.695	0.247 (-2.221, 2.715)	0.842