

# Dissection and Aneurysm in Patients With Fibromuscular Dysplasia



## Findings From the U.S. Registry for FMD

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### ABSTRACT

**BACKGROUND** Fibromuscular dysplasia (FMD) is a noninflammatory arterial disease that predominantly affects women. The arterial manifestations may include beading, stenosis, aneurysm, dissection, or tortuosity.

**OBJECTIVES** This study compared the frequency, location, and outcomes of FMD patients with aneurysm and/or dissection to those of patients without.

**METHODS** The U.S. Registry for FMD involves 12 clinical centers. This analysis included clinical history, diagnostic, and therapeutic procedure results for 921 FMD patients enrolled in the registry as of October 17, 2014.

**RESULTS** Aneurysm occurred in 200 patients (21.7%) and dissection in 237 patients (25.7%); in total, 384 patients (41.7%) had an aneurysm and/or a dissection by the time of FMD diagnosis. The extracranial carotid, renal, and intracranial arteries were the most common sites of aneurysm; dissection most often occurred in the extracranial carotid, vertebral, renal, and coronary arteries. FMD patients with dissection were younger at presentation (48.4 vs. 53.5 years of age, respectively;  $p < 0.0001$ ) and experienced more neurological symptoms and other end-organ ischemic events than those without dissection. One-third of aneurysm patients (63 of 200) underwent therapeutic intervention for aneurysm repair.

**CONCLUSIONS** Patients with FMD have a high prevalence of aneurysm and/or dissection prior to or at the time of FMD diagnosis. Patients with dissection were more likely to experience ischemic events, and a significant number of patients with dissection or aneurysm underwent therapeutic procedures for these vascular events. Because of the high prevalence and associated morbidity in patients with FMD who have an aneurysm and/or dissection, it is recommended that every patient with FMD undergo one-time cross-sectional imaging from head to pelvis with computed tomographic angiography or magnetic resonance angiography. (J Am Coll Cardiol 2016;68:176–85) © 2016 by the American College of Cardiology Foundation.



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**F**ibromuscular dysplasia (FMD) is a noninflammatory arterial disease that affects predominantly women. Arterial manifestations include beading, stenosis, aneurysm, dissection, and arterial tortuosity (**Central Illustration**) (1,2). The most common histological type of FMD is medial fibroplasia, which results in an artery with a “string of beads” appearance, representing alternating areas of stenosis due to fibrous webs and post-stenotic dilation. Due to the increasing use of endovascular therapy, tissue samples are rarely obtained in the current era; thus, it has been recommended that an angiographic classification scheme replace the previously used histopathological classification (3,4). The

string-of-beads type is now called “multifocal” FMD (3,4) (**Figure 1A**), whereas “focal” FMD denotes a single area of concentric or tubular stenosis, most commonly due to intimal fibroplasia, pathologically (**Figure 1B**) (3,5,6).

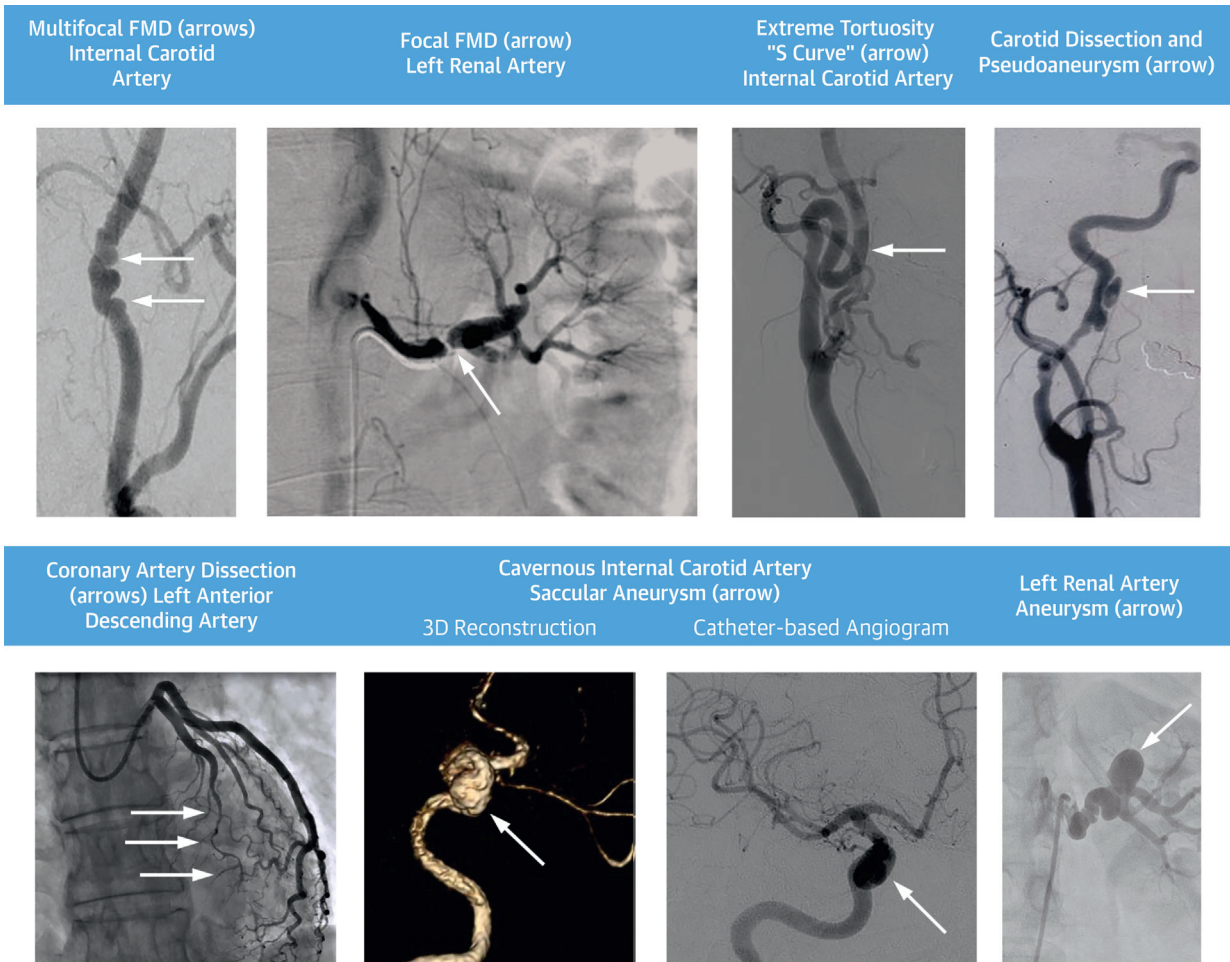
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The prevalence of FMD remains unknown; however, data from asymptomatic kidney donors suggest that up to 4% of the general population may have FMD (1,7). Prevalence may be even higher in patients with resistant hypertension (8). FMD affects predominantly women 20 to

**ABBREVIATIONS  
 AND ACRONYMS**

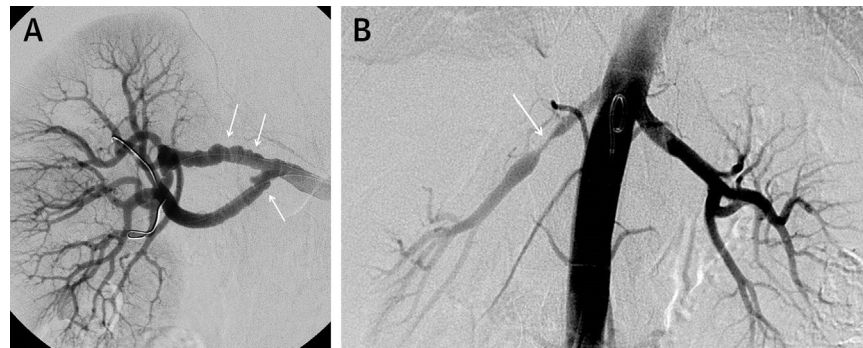
- CTA** = computed tomographic angiography
- FMD** = fibromuscular dysplasia
- MRA** = magnetic resonance angiography
- SAH** = subarachnoid hemorrhage
- SCAD** = spontaneous coronary artery dissection
- TIA** = transient ischemic attack

**CENTRAL ILLUSTRATION The Many Faces of Fibromuscular Dysplasia**



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Imaging characteristics of FMD include a “string of beads” appearance to the artery, a focal area of stenosis, extreme tortuosity, dissection of a coronary or peripheral artery, and/or aneurysm of a peripheral artery, an intracranial artery, or the aorta. 3D = 3-dimensional; FMD = fibromuscular dysplasia.

**FIGURE 1** Multifocal and Focal FMD

Catheter-based angiography shows (A) multifocal FMD involving the right renal artery branches (arrow) and (B) focal FMD (arrow) involving the right renal artery. FMD = fibromuscular dysplasia.

60 years of age, although men and patients of all ages can be affected (4,9). In the U.S. Registry for FMD, 93.5% of patients are women (9). Disease manifestations depend on the arterial bed involved: most often the extracranial carotid or vertebral arteries are associated with headache (generally migraine-type), pulsatile tinnitus, transient ischemic attack (TIA), or stroke, whereas the renal arteries are often associated with hypertension (1,4,7,9,10). Asymptomatic FMD may occur in some patients, although again, the frequency is unknown. Savard *et al.* (6) showed there was an average delay of 4 years from the onset of hypertension until diagnosis in patients with focal FMD and 9 years in patients with multifocal FMD. A similar delay of 4.1 years to diagnosis was reported in the registry (9).

Dissection may result in devastating outcomes for the typically young and otherwise healthy FMD patient. Spontaneous carotid or vertebral artery dissection accounts for approximately 20% of strokes in patients  $\leq 45$  years of age (11), and spontaneous coronary artery dissection (SCAD) has been reported to account for 24% of myocardial infarctions (MI) in women  $\leq 50$  years of age (12-14). Multiple studies have demonstrated an increased prevalence of FMD in patients who experience carotid or vertebral artery dissection (15% to 20%), coronary artery dissection (45% to 86%) (11,14-19), or renal artery dissection (20). It is not uncommon for FMD patients to have dissections in more than 1 artery (19,21-23).

While small aneurysms are likely to be asymptomatic, a ruptured aneurysm, especially if intracranial, may result in a disabling stroke or death.

Intracranial FMD most often manifests as aneurysm, with an estimated prevalence of approximately 7%, which is higher than the 2% to 5% rate reported in the general population (24,25). In FMD patients who have developed subarachnoid hemorrhage (SAH) (7,9), estimates of cerebral aneurysm prevalence may be as high as 50% (26,27). Despite a clear association, there is a poor understanding of the prevalence and clinical presentation of aneurysm in patients with FMD, as well as long-term prognosis for these events. In addition to intracranial aneurysms, FMD is a predisposing factor in the development of renal artery aneurysms (28,29) and aneurysms in other vascular beds.

The goal of the U.S. Registry for FMD is to increase understanding of the epidemiology, clinical characteristics, management, and outcomes of patients with FMD. The objective of this report was to define the prevalence of aneurysm and dissection in this cohort of FMD patients and better understand the associated clinical phenotypes and outcomes of these patients.

## METHODS

The U.S. Registry for FMD was started in 2008, and details of its management have been described previously (9). Since publication of the first report involving 447 patients, an additional 561 patients were enrolled as of October 17, 2014. Complete information regarding aneurysm and dissection was available for 921 patients (91.4%). Aneurysm and dissection location was recorded in the subjects' past medical history and presenting signs/symptoms,

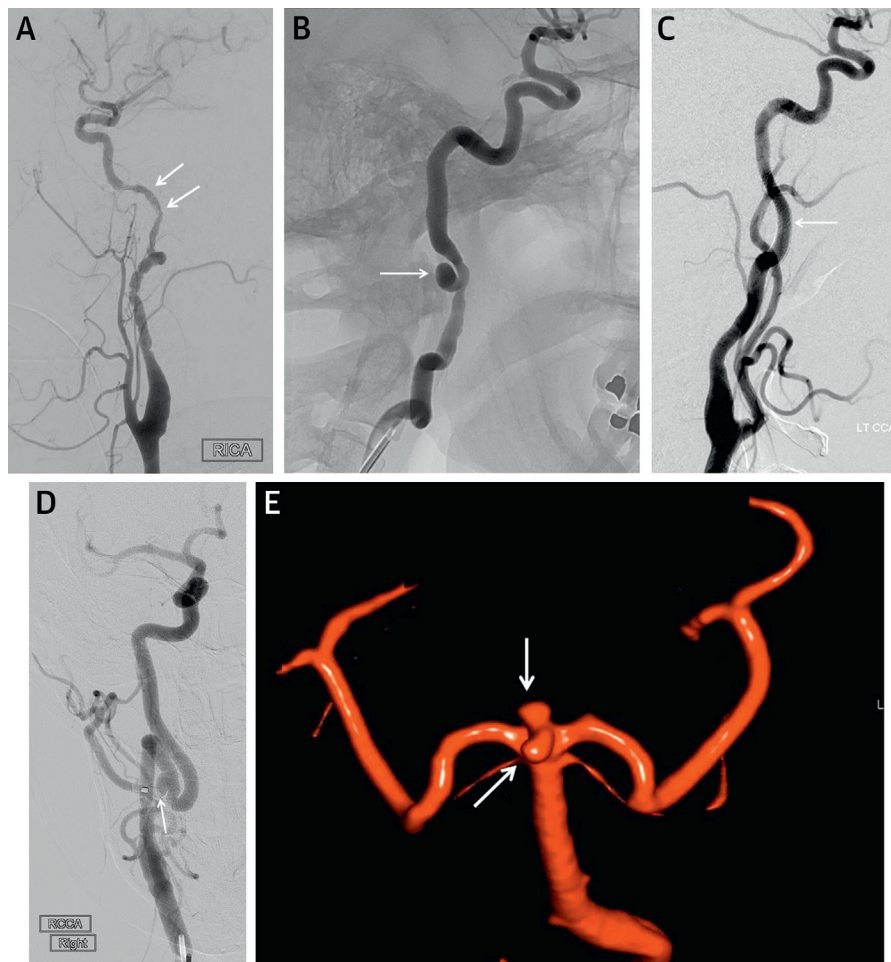
although not all vascular beds were imaged in all patients. Follow-up information after registry enrollment was not included in this report. In order to attribute an aneurysm or dissection to FMD, there must have been evidence of focal or multifocal FMD in another vascular bed (**Figure 2**).

**STATISTICAL ANALYSIS.** Analysis was performed using SAS version 9.3 software (SAS Institute Inc., Cary, North Carolina). Continuous variables are presented as mean  $\pm$  1 SD, median, range, and interquartile range (IQR). Student *t* tests and Wilcoxon rank sum tests were used to examine differences in means. Categorical variable data are expressed as counts and percentages. Chi-square and Fisher exact tests were performed for comparisons.

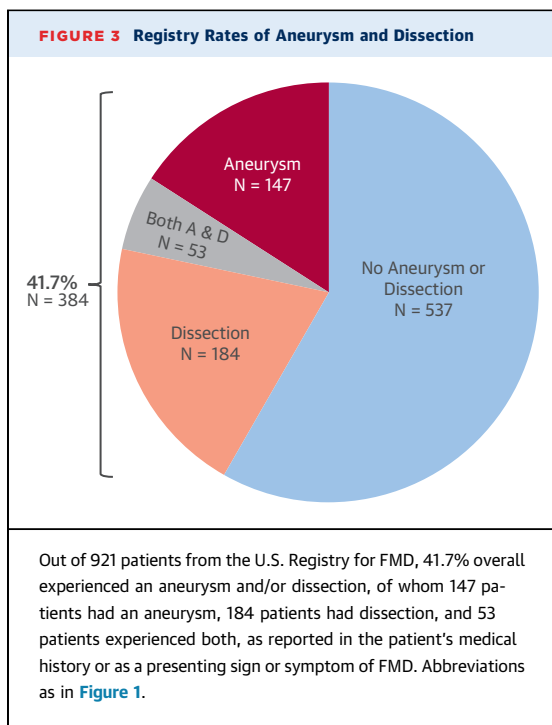
## RESULTS

Among 921 patients with complete data, 861 patients (93.5%) were female. The majority of patients were white (91%), with no significant differences in race between patients with or without aneurysm or dissection. The mean age was  $48.1 \pm 14.0$  years at the onset of symptoms/signs and  $52.2 \pm 13.4$  years at FMD diagnosis. An aneurysm or dissection occurred in 384 patients (41.7%) (**Figure 3**). Aneurysm was present in 200 patients (21.7%) and dissection in 237 patients (25.7%) (**Table 1**); 53 patients (5.8%) had both an aneurysm and a dissection. Men accounted for a minority of the FMD population overall (**Table 2**); however, they were more likely to experience aneurysm

**FIGURE 2** Catheter-Based Angiography in Patients With Dissection and Aneurysm



Angiography displays (A) dissection (arrows) in the mid and distal right internal carotid artery, above an area of multifocal FMD; (B) dissection of the mid internal carotid artery with a pseudoaneurysm present (arrow); (C) post-successful stent graft placement (arrow) to exclude the pseudoaneurysm; (D) extreme tortuosity (S curve) of the right internal carotid artery with the presence of a saccular aneurysm (arrow); and (E) bilobed basilar artery aneurysm (arrows). Abbreviations as in **Figure 1**.



(32 of 60 [53.3%] patients) and/or dissection (25 of 60 [41.7%] patients). Of the 861 women included in this analysis, 175 patients (20.3%) had an aneurysm, and 205 patients (23.8%) had a dissection.

**ANEURYSMS.** The location and prevalence of aneurysms and dissection are shown in [Table 1](#). The majority of patients with aortic aneurysm were female (14 of 20), and had hypertension (18 of 20) and a history of tobacco use (12 of 19). The most common location of aortic aneurysm was in the thoracic aorta: 9 of 20 aneurysms occurred in the ascending segment, and all of these patients had a tricuspid aortic valve. Aneurysm patients more often experienced previous SAH ([Table 2](#)) than patients without an aneurysm (8.4% vs. 1.3%, respectively;  $p < 0.0001$ ). Tobacco exposure was more commonly reported in patients with aneurysm than in those without (41.7% vs. 32.9%, respectively;  $p = 0.025$ ). There were no differences in the prevalence of hypertension.

**DISSECTION.** Dissection most often occurred in the extracranial carotid and vertebral arteries ([Table 1](#)). Of 177 patients (37.3%) with extracranial carotid or vertebral artery dissection, 66 experienced dissection of more than 1 cervical artery (carotid and/or vertebral). All dissections of the aorta were localized to the descending thoracic and abdominal segments. Of the 8 patients with aortic dissection, 7 had a history of

hypertension and renal artery involvement of FMD, 6 were women, and 5 had a confirmed history of tobacco use. All 25 patients with spontaneous coronary artery dissection were women. The most common artery affected was the left anterior descending ( $n = 15$ ), followed by the circumflex and right coronary arteries. Six patients had multiple coronary artery involvement, 3 had dissections elsewhere (extracranial carotid, vertebral, mesenteric), and 3 also experienced an aneurysm in another vascular bed (2 in the ascending aorta, 1 in the extracranial carotid artery). No patient had a coronary aneurysm.

Dissection patients were younger at presentation and at FMD diagnosis than those without dissection ([Table 2](#)). Patients with dissection had a lower prevalence of hypertension. Headache, neck pain, and neurologic symptoms were more common with dissection, as was end-organ ischemia (stroke, renal infarct, or MI). Physical examination at diagnosis mirrored these findings, with higher rates of pupil asymmetry and cranial nerve and focal neurological deficits in patients with dissection.

Family members of patients with dissection more often experienced sudden death (21.4% vs. 13.3%, respectively;  $p = 0.009$ ). There were no significant differences in family history of aneurysm, dissection, or stroke between patients with or without aneurysm or dissection. Overall, the rate of stroke in first- and second-degree family members of patients with FMD was 29.2%, and the mean age at stroke occurrence was  $63.4 \pm 14.9$  years.

Overall, 348 of 921 patients (37.8%) in the registry underwent endovascular or surgical procedure, most often for hypertension (60.1%). Other indications for a procedure were management of dissection (11.8%) and aneurysm (18.1%) ([Table 3](#)). Reported indications were not mutually exclusive. Of 200 patients with an aneurysm, 63 (31.5%) underwent procedures for the treatment of an aneurysm, most often in the carotid, renal, and cerebral artery distributions ([Figure 4](#)). For 36 of these patients (57.1%), endovascular therapy (most commonly coil embolization) of the aneurysm was performed, and surgery was performed in 26 patients (41.3%). Sixteen of 44 patients (36.4%) with an intracranial aneurysm had a procedure to prevent aneurysm rupture. Of 237 patients with dissection, 41 (17.3%) underwent procedures for the treatment of dissection most often in the carotid and renal arteries. Eight patients (32%) with coronary dissection underwent procedures for management of this dissection. For dissections, percutaneous transluminal angioplasty alone (30.6%) and percutaneous transluminal angioplasty plus stent implantation (45.9%) were the procedures most frequently performed.

## DISCUSSION

The prevalence of aneurysm and dissection among FMD patients has increased since the first registry report (9), likely due to the increased sample size of the U.S. registry for FMD and standardization of clinical practice, resulting in more comprehensive imaging of FMD patients for occult aneurysm. Of the 921 patients in this cohort, 41.7% had a diagnosis of an aneurysm and/or dissection: approximately 1 of 5 patients had an aneurysm, and 1 of 4 patients had a dissection. Of note, these numbers likely remain an underestimate of prevalence, as not all patients were systematically screened with imaging of all vascular beds. Due to the high prevalence of aneurysms and/or dissections in patients with FMD, these data support the recommendation to perform cross-sectional imaging with computed tomographic angiography (CTA) our preferred modality because of better resolution than magnetic resonance angiography (MRA) or MRA from head to pelvis, once, in all patients with FMD, regardless of the initial site of disease.

The most common sites of dissection-extracranial carotid and vertebral arteries, coronary arteries, and renal arteries—may result in potentially debilitating or fatal clinical events such as stroke, MI, and renal infarction. These events may cause impaired quality of life, chronic pain, mood disorders, and post-traumatic stress disorder in a cohort of young and otherwise healthy women (30,31). The age of diagnosis of FMD was younger in patients with dissection than in those without ( $48.4 \pm 9.6$  years of age vs.  $53.5 \pm 14.3$  years of age, respectively;  $p < 0.0001$ ). This suggests that FMD is diagnosed earlier in the acute period following a dissection, and therefore, these patients may not be subject to the prolonged delay to diagnosis that patients with subtle manifestations of FMD experience.

Multiple cervical artery dissections were common in this cohort (37.3%), which is consistent with previous reports noting a higher rate of multiple artery dissections in patients with underlying FMD (19,21,23,32). Compared to CADISP (Cervical Artery Dissection and Ischemic Stroke Patients) registry patients, a cohort of cervical artery dissection patients not limited to FMD, our cohort of patients with cervical artery dissections was associated with a much lower rate of ischemic stroke at presentation (19% vs. >50%, respectively) (32). Because the U.S. registry for FMD is still in its early years of follow-up, we do not have reliable information regarding the recurrence rate of cervical artery dissection or outcomes in the long term. It should be noted that asymptomatic

**TABLE 1 Location of Aneurysm and Dissection**

	Aneurysm	Dissection
Number of patients with aneurysm and dissection*	200 (21.7)	237 (25.7)
Total number of aneurysms or dissections	291	360
Aneurysms/dissections per patient	$1.5 \pm 0.8$	$1.5 \pm 0.9$
Median	1	1
Range	1-5	1-7
IQR (Q1-Q3)	1-2	1-2
Patients with 1 aneurysm/dissection	138 (69)	150 (63.3)
Patients with >1 aneurysm/dissection	62 (31)	87 (36.7)
Different aneurysm/dissection locations per patient	$1.2 \pm 0.5$	$1.2 \pm 0.5$
Median	1	1
Range	1-4	1-5
IQR (Q1-Q3)	1-1	1-1
Patients with 1 unique location	170 (85)	201 (84.8)
Patients with >1 unique location	30 (15)	36 (15.2)
Vascular territories involved		
Carotid†	62 (31)	151 (63.7)
Renal	68 (34)	26 (11)
Vertebral‡	8 (4)	49 (20.7)
Mesenteric/cealic	26 (13)	14 (5.9)
Intracranial‡	43 (21.5)	0 (0)
Aorta	20 (10)	8 (3.4)
Ascending	9 (4.5)	0 (0)
Thoracic descending	4 (2)	5 (2.1)
Abdominal	7 (3.5)	6 (2.5)
Coronary	0 (0)	25 (10.5)
Iliac	6 (3)	5 (2.1)
Popliteal	2 (1)	0 (0)
Subclavian	1 (0.5)	0 (0)

Values are n (%) or mean  $\pm$  SD. \*Some patients had an aneurysm and/or dissection in more than 1 location. †Extracranial portions only. ‡Intracranial aneurysm included cerebral aneurysms in the posterior, anterior, and mid circulations, basilar, anterior, and posterior communicating arteries. IQR = interquartile range.

dissection is not uncommon when images are obtained for another indication (e.g., aneurysm screening or evaluation for possible FMD).

In contrast to FMD patients with dissection, the age at diagnosis for FMD patients with aneurysm was the same as the overall cohort (52 years of age), and these patients were subject to previously reported delays to FMD diagnosis (6,9). There were no symptoms or features identified among patients with aneurysm compared to those without, suggesting that most aneurysms are identified only when imaging is performed. The most commonly identified aneurysm locations mirrored the arterial beds most frequently affected and imaged for FMD: the extracranial carotid and renal arteries. The intracranial circulation was the third most common location for aneurysms, occurring in 21.5% of all patients with aneurysms and 4.7% of the 921 patients in the general cohort. Of

**TABLE 2 History and Clinical Presentation of Patients with FMD**

	Aneurysm	No Aneurysm	p Value	Dissection	No Dissection	p Value	Neither Aneurysm or Dissection
n (%)	200 (21.7)	721 (78.2)	<0.0001	237 (25.7)	684 (74.3)	<0.0001	537 (58.3)
Males	25 (12.5)	35 (4.8)	0.00029	32 (13.5)	28 (4.1)	<0.0001	14 (2.6)
Females	175 (87.5)	686 (95)	0.00029	205 (86.5)	656 (95.9)	<0.0001	523 (97.4)
Age at diagnosis, yrs	52.3 ± 14.2	52.2 ± 13.2	0.78	48.4 ± 9.6	53.5 ± 14.3	<0.0001	53.9 ± 14.0
Age at first symptom of FMD, yrs	47.5 ± 15.3	48.3 ± 13.7	0.79	45.6 ± 9.7	49.1 ± 15.2	<0.0001	49.6 ± 14.8
History of tobacco use	78/187 (41.7)	231/703 (32.9)	0.025	89/230 (38.7)	220/660 (33.3)	0.15	168/525 (32.0)
History of contraceptive hormone use*	82/130 (63.1)	344/489 (70.3)	0.14	99/132 (75)	327/487 (67.1)	0.091	265/386 (68.7)
Hypertension	147/197 (74.6)	480/711 (67.5)	0.067	123/229 (53.7)	504/679 (74.2)	<0.0001	393/533 (73.7)
Age at onset, yrs	40.8 ± 15.1	44.5 ± 14.1	0.027	42 ± 10.9	44 ± 15.1	0.11	45.1 ± 14.6
Headache	119/185 (64.3)	432/649 (66.6)	0.6	168/220 (76.4)	383/614 (62.4)	0.00018	298/478 (62.3)
Migraine	63/119 (52.9)	218/432 (50.5)	0.68	91/168 (54.2)	190/383 (49.6)	0.36	146/298 (49.0)
TIA	20/183 (10.9)	77/697 (11)	1.0	33/224 (14.7)	64/656 (9.8)	0.048	51/522 (9.8)
Stroke	21/194 (10.8)	64/706 (9.1)	0.49	46/229 (20.1)	39/671 (5.8)	<0.0001	25/529 (4.7)
Amaurosis fugax	8/188 (4.3)	40/693 (5.8)	0.47	22/224 (9.8)	26/657 (4)	0.0018	21/521 (4.0)
Subarachnoid hemorrhage	16/190 (8.4)	9/700 (1.3)	<0.0001	8/229 (3.5)	17/661 (2.6)	0.49	6/521 (1.2)
Myocardial infarction	3/123 (2.4)	27/419 (6.4)	0.12	24/154 (15.6)	6/388 (1.5)	<0.0001	5/301 (1.7)
Coronary revascularization	3/123 (2.4)	24/418 (5.7)	0.16	18/154 (11.7)	9/387 (2.3)	<0.0001	8/300 (2.7)
Renal infarction	4/119 (3.4)	12/410 (2.9)	0.77	10/152 (6.6)	6/377 (1.6)	0.0045	5/294 (1.7)

Values are n (%), mean ± SD, or n/N (%). \*Women only.  
FMD = fibromuscular dysplasia; TIA = transient ischemic attack.

note, only 593 patients in this cohort had confirmed brain imaging, suggesting that 4.7% likely underestimates the prevalence of intracranial aneurysms. In fact, an additional 9 patients without a known aneurysm had a history of SAH. As most SAH is due to a ruptured aneurysm, the prevalence of brain aneurysms might account for 24.8% of all aneurysms and 5.6% of the total population. More than one-third of patients with intracranial aneurysms underwent a procedure to treat the aneurysm and prevent rupture. These findings strongly support the recommendation for obtaining at least 1 intracranial CTA or MRA in all patients with FMD (4,33), but do not allow specific recommendations to be made regarding what size of intracranial aneurysm should be treated. Therefore, existing aneurysm treatment guidelines apply. Patients with smaller aneurysms can be placed in a

surveillance program, reserving intervention for larger or expanding aneurysms (25,34-38).

FMD is a common finding when populations of patients with spontaneous cervical artery dissection or intracranial aneurysm are investigated. Rates of identification of cervical artery FMD approached 23% to 30% of patients with ruptured intracranial aneurysms, if the neck was imaged (39-41). In a series of patients with cervical artery dissection, rates of carotid and/or vertebral artery FMD varied from 5.6% to 21%, depending on the number of patients screened (range: 4% to 90% of the population) and the imaging modality used (19,21,42). It is unknown with what frequency FMD occurred in the renal arteries or other vascular territories in these reports; however, it is likely that the association with FMD has been underappreciated due to lack of screening.

Recently, a high prevalence of FMD among patients with SCAD has been identified through evaluation of extracoronary vessels with cross-sectional imaging of the head, neck, chest, abdomen, and pelvis. In the Mayo SCAD series, 45% of patients had extracoronary FMD (43) compared to 72% of patients in the Canadian SCAD series (44); 14% of patients in the Canadian series also had a concomitant intracranial aneurysm (44). A similar screening approach for patients with intracranial and extracranial cervical artery aneurysm or dissection may be useful to identify FMD, especially given the high rate of these events in the current report.

**TABLE 3 Therapeutic Procedures and Complications**

Complication	Aneurysm (n = 200)	Dissection (n = 237)
Patients who had a procedure	114/200 (57)	85/237 (35.9)
Patients who had aneurysm or dissection as an indication for procedure*	63/114 (55.3)	41/85 (48.2)
Other indications for procedures		
Pseudoaneurysm	3/114 (2.6)	10/85 (11.8)
Hypertension	48/114 (42.1)	22/85 (25.9)
Myocardial infarction	1/114 (0.9)	14/85 (16.5)

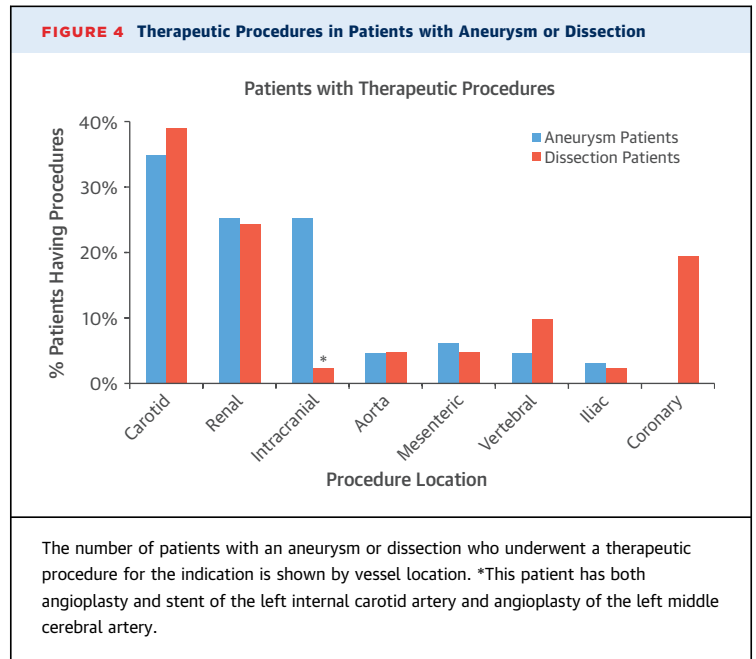
Values are n/N (%). \*Reported indications were not mutually exclusive.

There were no deaths related to aneurysm or dissection in this cohort, consistent with an earlier report from the U.S. registry (45), although long-term follow-up data are lacking. Future studies and follow-up data from this registry will be of interest with regard to these outcomes.

Finally, it is entirely possible that the outcomes and vascular events in FMD may be related to intrinsic and extrinsic factors, such as patient sex, tobacco use, and genetics or epigenetics. Consistent with an earlier report from the registry (46), we observed a higher rate of aneurysm and dissection in men with FMD, although men accounted for a minority of FMD patients overall. When present, tobacco use appeared to result in a more virulent course: tobacco exposure and early onset hypertension were more often reported in patients with aneurysm, consistent with previous publications, demonstrating increased renal artery involvement and aneurysm formation with tobacco use in FMD (47,48). As for dissection, an overall association with tobacco use was not observed. For the patients with aortic dissection, the majority had hypertension and renal artery FMD.

A genetic contribution to FMD undoubtedly exists. Previous studies reported prevalence of FMD in first- or second-degree relatives of 7% to 11% of patients (9,49). Additionally, a high rate of stroke and sudden death in family members was reported in this FMD patient cohort, suggesting the possibility that these family members may have experienced silent, undiagnosed events related to FMD, such as aneurysm rupture and/or dissection. Previous investigations did not yield significant overlap with identifiable heritable connective tissue diseases (50), similar to reports in spontaneous cervical artery dissection from the CADISP study (51). Recently, a novel gene association was identified in the CADISP cohort, with modest effects on the risk of cervical artery dissection (52); and the same gene association was recently reported for FMD (53). There are a number of ongoing studies that will hopefully shed more light on the genetics and cause of FMD (NCT01967511; NCT01935752; institutional review board number HUM00044507, French Arcadia Registry).

**STUDY LIMITATIONS.** First, registry data are subject to referral and retrieval bias and may not be a true representation of the general population. Second, because this is a registry and not a randomized trial, patients were imaged and treated at clinician discretion at each registry center. Not all physicians manage patients with FMD in an identical fashion;



therefore, there may be missing data points. Not all vascular beds were systematically imaged, resulting in differing denominators in the various circulations studied. This may limit broad application of these findings. Also, a disease-based registry is subject to participants recall bias, as patients with known arteriopathy (FMD) are more likely to volunteer symptoms and family history, as are their family members. Finally, the U.S. registry for FMD is relatively new, and therefore prospective long-term follow-up data are limited. Future reports regarding long-term outcomes and recurrence of events will be reported as the registry matures. Despite these limitations, registry data are extremely important to study less common diseases, in which randomized trials are not possible and single-center experience may be limited or biased. Previous studies related to FMD involved extremely small sample sizes, and there continue to be case reports and small case series published every year. A registry such as the U.S. Registry for FMD allows the characterization of a much larger cohort of patients with FMD with much wider geographic distribution.

**CONCLUSIONS**

There is a high prevalence of aneurysm and dissection among patients with FMD. Dissection most often occurred in the extracranial cervical arteries, renal, and coronary arteries and was associated with



increased rates of end-organ ischemia and pain syndromes. Aneurysm was most often identified in the carotid, renal, and intracranial arteries and was associated with higher rates of therapeutic intervention to repair the aneurysm. These findings support the recommendation that all patients with FMD obtain cross-sectional imaging once (CTA or MRA) from head to pelvis. Long-term outcome data are lacking, but no patient in this cohort died due to FMD or associated vascular events. Future efforts should focus on uncovering the genetic and predisposing factors for these vascular events in FMD, as well as treatment and long-term management strategies for patients with FMD.

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## PERSPECTIVES

**COMPETENCY IN MEDICAL KNOWLEDGE:** Patients with FMD have a high prevalence of arterial aneurysms and spontaneous dissections in diverse vascular territories.

**COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS:** Patients with FMD should undergo cross-sectional imaging of arteries of the head, neck, chest, abdomen, and pelvis with CTA or MRA to assess the extent of disease and identify aneurysms and/or dissections that require intervention or surveillance.

**TRANSLATIONAL OUTLOOK:** More studies are needed to explore genetic and environmental factors that contribute to arterial aneurysms and dissections in patients with FMD and to develop effective strategies for prevention and management of these complications.

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**KEY WORDS** angiography, beading, stenosis, tortuosity