High Prevalence of Multiple Arterial Bed Lesions in Patients With Fibromuscular Dysplasia

The ARCADIA Registry (Assessment of Renal and Cervical Artery Dysplasia)

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See Editorial Commentary, pp 488–489

Abstract—Fibromuscular dysplasia (FMD) commonly affects the renal and cervical arteries but has been described to affect other vascular beds as well. The prevalence of and clinical characteristics associated with multisite FMD (string-of-beds or focal stenoses affecting at least 2 vascular beds) are not known. In the prospective ARCADIA registry (Assessment of Renal and Cervical Artery Dysplasia), symptomatic patients with renal artery (RA) FMD underwent tomographic- or magnetic resonance-angiography from the aortic arch to the intracranial arteries and those with cervical FMD from the diaphragm to the pelvis. Of 469 patients (84.0% women), 225 (48.0%) had multisite FMD. In addition, 86 of 244 patients with single-site disease had dissections or aneurisms affecting other vascular beds, totaling 311 patients (66.3%) with lesions in >1 vascular bed. Among patients with a cerebrovascular presentation, the prevalence of RA lesions was higher in patients with than in those without hypertension (odds ratio, 3.4; 95% confidence interval, 1.99–6.15). Among patients with a renal presentation, the prevalence of cervical lesions was higher in patients with bilateral than in those with unilateral RA lesions (odds ratio, 1.9; 95% confidence interval, 0.99–3.57). In conclusion, FMD is a systemic arterial disease. At least 2 vascular beds were affected by dysplastic stenoses in 48.0% of cases and by dysplastic stenoses, aneurysms, and dissections in 66.1% of cases. RA imaging should be proposed to hypertensive patients with a cerebrovascular presentation. Cervical artery imaging should be considered in patients with a renal presentation and bilateral RA lesions.

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Fibromuscular dysplasia (FMD) is a group of idiopathic, nonatherosclerotic, and noninflammatory diseases of the arterial walls that mostly affects women, leading to stenosis of small and medium-sized arteries.[1,2] It is currently classified by angiography into 2 subtypes, multifocal and focal.[1–5] Multifocal FMD, with a typical string-of-beads pattern, is the angiographic presentation of medial FMD and is at least 4× more frequent than focal FMD.[1–6] FMD most commonly affects the renal (RA) and extracranial carotid and vertebral arteries (eCVA) but has been described in almost every vascular bed.[1–8] FMD may be clinically silent and discovered incidentally,[1,2,7,9] but many patients with the condition present with hypertension, migraine, or complications because of RA or eCVA involvement, including renal infarction, stroke, transient

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ischemic attack, subarachnoid hemorrhage (SAH), and cervical artery dissection (CeAD).[1–7]

The prevalence of multifocal or focal FMD lesions affecting 2 or more vascular beds, here called multisite FMD, is unknown. Several studies report prevalence estimates from 7 to 47%[4,6,10–14] (Table S1 in the online-only Data Supplement), but no study has systematically assessed multisite involvement. No data concerning patient characteristics associated with multisite involvement have been reported, although screening for multisite FMD lesions may have clinical relevance.[2]

We designed the ARCADIA (Assessment of Renal and Cervical Artery Dysplasia) international registry to (1) assess the prevalence of multisite FMD in adults at first presentation of RA or eCVA FMD, (2) compare the clinical and radiological phenotypes between FMD patients with a renal or cerebrovascular presentation, and (3) compare the clinical and radiological phenotypes between patients with single-site or multisite FMD.

Methods

Patients

Women and men aged ≥18 years, diagnosed with RA or eCVA FMD, were prospectively recruited at 16 university hospitals in France and Belgium. Most participating centers were approved by the European Society of Hypertension as Hypertension Excellence Centers[15] or by the French Ministry of Health as FMD Competence Centers. Specialists in hypertension, vascular medicine, vascular neurology, and vascular radiology were available in all centers. The protocol was approved by the Comité de Protection des Personnes Ile-de France II. All participants provided written informed consent. The procedures followed were in accordance with the institutional guidelines.

The diagnosis of FMD had to be confirmed in the vascular bed where the condition was presumed to be symptomatic by recent (<2 years) good quality (confirmed by 2 radiologists) angiography using either computed tomographic angiography (CTA), magnetic resonance angiography (MRA), or digital subtraction angiography. FMD was diagnosed as nonatherosclerotic arterial encroachment or stenoses affecting the trunk or branches of medium size arteries, in the absence of aortic wall thickening, biochemical evidence of inflammation, and known syndromic arterial disease.[1,3] Patients with aneurysms or artery dissections alone, without artery stenosis, were not considered to have FMD.[2] The diagnosis of multifocal FMD could be asserted by local investigators/radiologists, whereas focal FMD had to be confirmed centrally by 2 independent investigators (Pierre-François Plouin and Emmanuel Touzé) before inclusion.

Clinical Data

Circumstances leading to the diagnosis of FMD were (1) renal presentations, including hypertension, acute kidney infarction, and miscellaneous conditions leading to RA imaging, or (2) cerebrovascular presentations, including acute neurological events (stroke, transient ischemic attack, SAH, and CeAD); migraine, and other neurological signs or symptoms (cervical bruit, cervical pain, nonmigraine headache, tinnitus, and other); and unruptured intracranial aneurysm.

We recorded the following patient characteristics: sex, age at FMD diagnosis, ethnicity, family history of FMD, stroke or SAH, presentation, history of hypertension, diabetes mellitus or migraine, tobacco use, blood pressure, body mass index, estimated glomerular filtration rate, and FMD subtype (multifocal or focal). A family history of FMD, stroke, or SAH was considered to be present if at least one first degree relative had documented FMD by angiography or histology or had experienced a stroke or a SAH. Hypertension was defined as known hypertension or current antihypertensive medication, and diabetes mellitus as known diabetes mellitus or current antidiabetic medication. We used a prespecified questionnaire to diagnose migraine, with or without aura, in accordance with the international classification of headaches.[16] Tobacco use was classified into ever and current smokers as previously reported.[17] Body mass index was calculated as body weight (kg) divided by the square of body size (cm). Glomerular filtration rate was estimated using the Cockcroft–Gault formula, considering that many creatinine measurements were not performed using current standards.[18]

Imaging

After inclusion, patients with RA FMD underwent CTA or MRA from the aortic arch to the intracranial arteries, and those with eCVA FMD underwent CTA or MRA from the diaphragm to the pelvis. The thoracic aorta and the coronary, brachial, and femoral arteries were not examined. CTA was the preferred procedure. Arterial phase contrast-enhanced images of CTAs were obtained using computed tomography scanners with at least a 40-detector row, 0.5 to 0.8 slice thickness, <250 mm field of view, covering extracranial/intracranial arteries from the brain to the aortic arch and abdominal arteries from the diaphragm to the femoral bifurcation. All arteries were analyzed on dedicated work stations with images reformatted longitudinally and orthogonally to each artery centerline. Contrast-enhanced MRA using gadoterate meglumine was accepted, particularly in patients with a cerebrovascular presentation and was recommended for patients with diabetes mellitus, renal insufficiency, or iodine-contrast intolerance. We used images recorded before angioplasty for patients who had digital subtraction angiography as the diagnostic procedure. For all patients, additional CTA or MRA was required if arterial imaging had been selective or unilateral.

Images were read in each participating center by at least 2 readers familiar with FMD. The following items were recorded for each arterial segment (Table S2): presence of FMD lesions; FMD subtype (focal or multifocal); and presence of dissection or aneurysm. Focal FMD corresponded to a single stenosis on a given vessel, regardless of its length, and multifocal FMD to ≥2 stenoses on a given vessel segment, as previously reported (Figure 1).[4]

Patients with FMD lesions (focal stenoses or the string-of-beads pattern) affecting at least 2 of the 4 predefined vascular beds (RA, eCVA/intracranial arteries, mesenteric/splenic arteries, and iliac arteries) were classified as having multisite FMD, and the others (irrespective of the presence of unilateral or bilateral FMD lesions of the RA or eCVA) were classified as single-site FMD. We also recorded patients with single-site FMD stenosing lesions and aneurysms or dissections affecting at least one other vascular bed because aneurysms and dissections are frequently associated with or are complications of FMD.[1–3]

All angiographies from patients diagnosed locally with multisite FMD were reviewed centrally by a core imaging committee (Arshid Azarine, Elie Mousseaux [chair], Catherine Oppeheim, Pierre-François Plouin, Emmanuel Touzé, and Frédéric Thony) to confirm multisite status.

Statistical Analysis

The ARCADIA study was powered to insure a precision of 3.5% around a 20% expected prevalence of multisite FMD. Categorical variables were compared with Pearson $\chi 2$ test and continuous variables with 2-tailed t tests. Associations between multisite FMD and potential determinants were assessed by calculations of crude and adjusted odds ratios (ORs; 95% confidence interval [CI]). Variables that were associated with multisite FMD at a level of $P \leq 0.10$ were entered into a logistic regression model. Calculations were performed using statistical analysis system (SAS) software, version 9.3 (SAS Institute, Cary, NC).

Results

From November 2009 to October 2014, 499 patients were recruited. Thirty patients were excluded, leaving 469 patients with confirmed FMD available for analysis (study flowchart in Figure 2). Overall, 394 (84.0%) patients in the analyzed population were women, 415 (88.5%) were white, and 429 (91.5%) had multifocal-type FMD. The mean age±SD at diagnosis of FMD was 53±13.4 years. RA FMD was documented by CTA

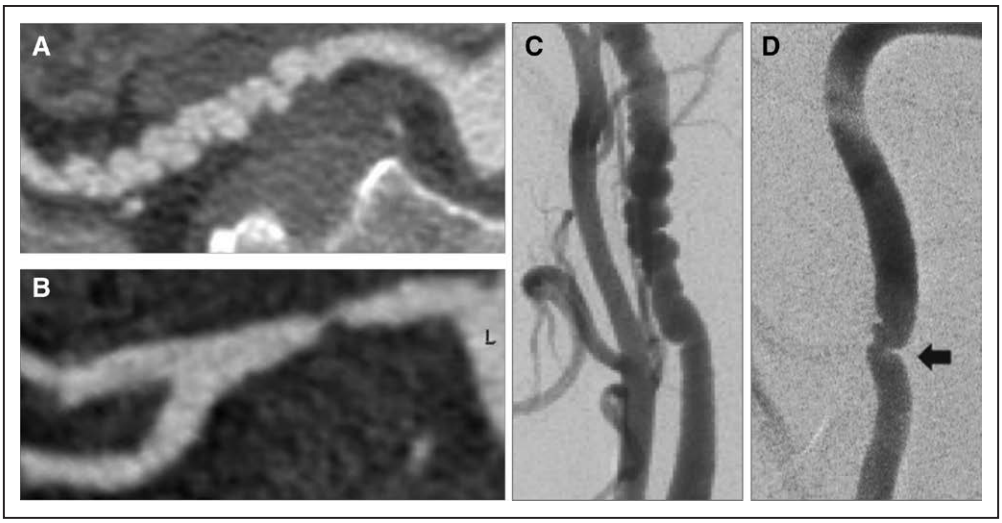

Figure 1. Angiographic subtypes of fibromuscular dysplasia (FMD). FMD affecting renal arteries: multifocal (**A**) and focal (**B**) lesions. FMD affecting carotid arteries: multifocal (**C**) and focal (**D**) lesions.

in 439 patients and MRA in 30. eCVA FMD was documented by CTA in 350 patients and MRA in 118.

Patient Characteristics by Presentation

The clinical presentation of FMD was renal in 304 (64.8%) patients, including 268 with hypertension and 11 with acute renal infarction. It was cerebrovascular in 165 (35.2%) patients, including 100 with acute cerebrovascular events (isolated CeAD, 25; stroke, 21; SAH, 21; transient ischemic attack, 13; CeAD with stroke, 10; CeAD with transient ischemic attack, 9; and CeAD+SAH, 1). As expected, patients with renal presentation more often had a history of hypertension or received antihypertensive medication and had higher blood pressure levels than those with cerebrovascular presentation (Table 1).

Multisite Versus Single-Site FMD

We found multisite FMD lesions in 225 of 469 (48.0%; 95% CI, 43.5–52.5) patients, of whom 217 of 429 (50.6%; 95% CI, 45.9–55.3) had multifocal FMD. Patients with multisite FMD were older and had lower estimated glomerular filtration rate levels, less frequently a history of hypertension, and more frequently multifocal-type FMD than patients with single-site FMD (Table 2). They also tended to have a lower body mass index, a white origin, and a cerebrovascular presentation. Sixty-one of the 100 patients with acute cerebrovascular events had multisite FMD. The age at diagnosis of FMD (OR, 10.3 per decade; 95% CI, 10.1–10.5; P=0.004) and cerebrovascular presentation (OR, 1.68; 95% CI, 1.08–2.60; P=0.02) were independently associated with multisite FMD in a multivariate logistic model, taking into account age, clinical presentation, white origin, body mass index, estimated glomerular filtration rate levels, and FMD subtype.

Lesions affecting the RA, eCVA/intracranial arteries, mesenteric/splenic arteries, or iliac arteries were present in 393, 236, 82, and 69 patients, respectively. Ten patients (2.1%) had intracranial FMD lesions, of whom 5 also had eCVA FMD. The distribution of FMD lesions between patients with multisite and single-site FMD is compared in Figure 3 and Table 3.

The prevalence of bilateral lesions was higher in patients with eCVA FMD (n=178; 75.4%) than in those with RA FMD (n=193; 49.1%) for both single-site and multisite FMD. The prevalence of aneurysms (26.0%) and dissections (15.1%) at any site did not significantly differ between single-site and multisite FMD patients. Twenty-eight patients (6.0%) had intracranial aneurysms, of which 24 had eCVA FMD lesions. Among the 244 patients with single-site FMD, 86 also had at least one aneurysm or one dissection affecting another vascular bed. Therefore, a total of 225+86=311 (66.3%) patients had FMD lesions, aneurysms, or dissections affecting at least 2 vascular beds.

Among the 165 patients with a cerebrovascular presentation, the prevalence of RA FMD was 63 of 95 (66.3%) if they had a history of hypertension and 29 of 70 (41.4%) in the absence of such history (OR, 3.4; 95% CI, 1.99–6.15). Among the 301 patients with a renal presentation (data missing for 3 patients), the prevalence of eCVA FMD was 60 of

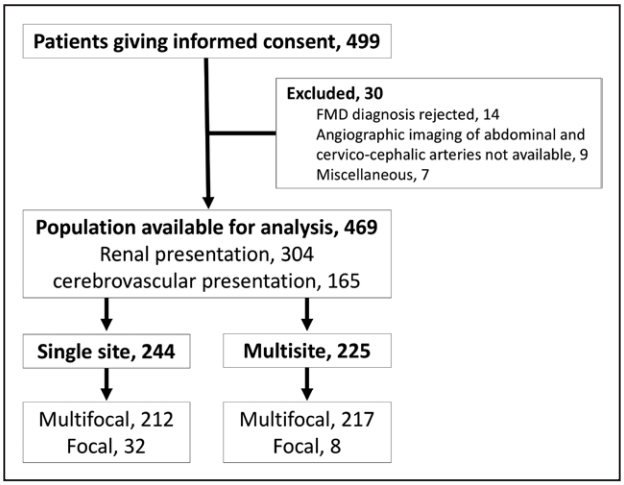

Figure 2. Flow chart showing the selection of patients with fibromuscular dysplasia (FMD). Miscellaneous causes for exclusion were invalid informed consent form (**3**); FMD subtype not reported (**2**); FMD diagnosed >2 y before inclusion (**1**); patient with genetically-documented vascular Ehlers–Danlos syndrome (**1**).

Table 1. Clinical Phenotype and FMD Subtype in Patients With Renal or Cerebrovascular Presentation

Variables	Renal Presentation, 304		Cerebrovascular Presentation, 165		OR	95% CI	*P* Value
	n*	Values	n*	Values			
Women	304	257 (84.5)	165	137 (83.0)	1.12	0.67–1.86	0.67
Age at diagnosis of FMD, y	304	52.7±14.0	165	53.9±12.2	1.01	0.99–1.02	0.36
White	304	269 (88.5)	165	146 (88.5)	1.00	0.55–1.81	1.00
Family history of FMD	296	8 (2.7)	160	3 (1.9)	0.69	0.18–2.62	0.58
Family history of stroke	296	20 (6.8)	160	16 (10.0)	1.53	0.77–3.10	0.22
Family history of SAH	296	14 (4.7)	160	10 (6.3)	1.34	0.58–3.10	0.49
History of hypertension	304	268 (88.2)	165	95 (57.6)	0.18	0.11–0.29	<0.001
History of diabetes mellitus	304	15 (4.9)	165	4 (2.4)	0.48	0.16–1.47	0.20
History of migraine: none	303	226 (74.6)	165	109 (66.1)	…	0.70–2.08	0.07
Yes, without aura		43 (14.2)		25 (15.2)	1.21		…
Yes, with aura		34 (11.2)		31 (18.8)	1.89	1.10–3.24	…
Ever smokers	304	126 (41.5)	165	73 (44.2)	1.12	0.77–1.64	0.56
Current smokers	304	57 (18.8)	165	33 (20.0)	1.08	0.67–1.75	0.74
Systolic blood pressure, mm Hg	301	139±22	163	131±16	0.98	0.97–0.99	<0.001
Diastolic blood pressure, mm Hg	301	83±13	163	80±16	0.98	0.96–1.00	0.02
Patients given antihypertensive drugs	304	236 (77.6)	165	90 (54.5)	0.35	0.23–0.52	<0.001
Body mass index, kg/m^2	304	23.9±4.6	162	23.6±4.1	0.98	0.94–1.02	0.32
Glomerular filtration rate, mL/min	291	91.2±32.5	131	86.3±32.2	1.00	0.99–1.01	0.16
Multifocal FMD	304	275 (90.5)	165	154 (93.3)	1.48	0.72–3.04	0.29

CI indicates confidence interval; FMD, fibromuscular dysplasia; OR, odds ratio; and SAH, subarachnoid hemorrhage.

*The number of patients available for analysis is shown for each variable. Data are expressed as the number of patients (percentage) for categorical variables and the mean±SD for quantitative variables.

147 (40.8%) in patients with bilateral RA FMD and 35 of 154 (22.7%) in those with unilateral RA FMD (OR, 1.88; 95% CI, 0.99–3.57).

Discussion

We found that FMD affected more vascular beds than expected in this prospective study of French and Belgian symptomatic patients with well-defined FMD. Indeed, the systematic angiographic imaging of intra-abdominal and eCVA/intracranial arteries disclosed multisite FMD (focal or multifocal stenoses affecting 2 or more arterial beds) in 48.0% of cases. The prevalence of multisite FMD increased with age and was higher in patients with multifocal FMD. Most patients with multisite FMD had bilateral RA (59.7%) or eCVA (72.5%) FMD lesions. Eighty-six patients with single-site FMD had aneurysms or dissections affecting another vascular bed. Thus, a total of 311 patients (66.1%) had FMD lesions, aneurysms, or dissections affecting at least 2 vascular beds. We identified the presence of hypertension in patients with a cerebrovascular presentation and the presence of bilateral RA lesions in patients with a renal presentation to be clues for the presence of multisite FMD, providing a more rational than systematic approach to vascular screening of patients with FMD.

Seven studies have assessed the extent of lesions in patients presenting with RA or eCVA FMD using conventional angiography, CTA, MRA, or Duplex ultrasound.[4,6,10–14] They reported prevalence estimates for multisite FMD ranging from 7% to 47%. This large range is because of differences in patient presentation, imaging methods, the definition of multisite FMD, and the percentage of patients who had at least 2 vascular beds imaged (Table S1). These reports were subject to referral (most patients had renal presentation) and investigational biases (a systematic assessment of cervical and intra-abdominal arteries by angiography was not obtained for all patients). In the present prospective study, intra-abdominal arteries and eCVA/intracranial arteries were systematically examined in all patients, irrespective of clinical presentation; imaging relied on high-resolution techniques optimized by standardized acquisition protocols between centers; and CTA, MRA, or digital subtraction angiography images from all patients with multisite FMD were reviewed by a core imaging committee.

Our study has potential limitations. First, our findings apply to a symptomatic population. Second, the diagnosis of FMD rested on MRA, CTA, or digital subtraction angiography. Given the different sensitivities and specificities of these techniques, some inclusion bias may have occurred. Lastly, the core imaging committee reviewed images from patients with presumed multisite FMD to avoid false-positive diagnosis of multisite FMD but did not review all images from all patients. The true frequency of multisite FMD may be underestimated because (1) false negatives in the detection of FMD lesions by local radiologists were not sought; (2) we included patients

Table 2. Clinical Phenotype and FMD Subtype in Patients With Single-Site and Multisite FMD

Variables	Single-Site, 244		Multisite, 225		OR	95% CI	*P* Value
	n*	Values	n*	Values			
Women	244	205 (84.0)	225	189 (84.0)	1.00	0.61–1.64	1.00
Age at diagnosis of FMD, y	244	50.6±14.7	225	55.9±11.2	1.03	1.02–1.05	<0.001
Cerebrovascular vs renal presentation	244	76 (31.2)	225	89 (39.6)	1.45	0.99–2.12	0.06
White	244	210 (86.1)	225	205 (91.1)	1.66	0.93–2.98	0.09
Family history of FMD	238	7 (2.9)	218	4 (1.8)	0.62	0.18–2.14	0.45
Family history of stroke	238	19 (8.0)	218	17 (7.8)	0.98	0.50–1.93	0.94
Family history of SAH	238	12 (5.0)	218	12 (5.5)	1.10	0.48–2.50	0.83
History of hypertension	244	198 (81.2)	225	165 (73.3)	0.64	0.41–0.99	0.04
History of diabetes mellitus	244	10 (4.1)	225	9 (4.0)	0.98	0.39–2.45	0.96
History of migraine: none	243	181 (74.5)	225	154 (68.4)	1.05	0.62–1.76	0.12
Yes, without aura		36 (14.8)		32 (14.2)			…
Yes, with aura		26 (10.7)		39 (17.3)	1.76	1.03–3.03	…
Ever smokers	244	110 (45.1)	225	89 (39.6)	0.80	0.55–1.15	0.23
Current smokers	244	50 (20.5)	225	40 (17.8)	0.84	0.53–1.33	0.46
Systolic blood pressure, mm Hg	241	136±20	223	136±20	1.00	0.99–1.01	0.88
Diastolic blood pressure, mm Hg	241	82±12	223	81±13	1.00	0.98–1.00	0.74
Patients given antihypertensive drugs	244	178 (72.9)	225	148 (65.8)	0.71	0.48–1.06	0.09
Body mass index, kg/m^2	242	24.2±4.5	224	23.4±4.5	0.96	0.92–1.00	0.05
Glomerular filtration rate, mL/min	219	95.5±34.6	203	83.3±28.7	0.98	0.98–0.99	<0.001
Multifocal FMD	244	212 (86.9)	225	217 (96.4)	4.09	1.84–9.09	<0.001

CI indicates confidence interval; FMD, fibromuscular dysplasia; OR, odds ratio; and SAH, subarachnoid hemorrhage.

*The number of patients available for analysis is shown for each variable. Data are expressed as the number of patients (percentages) for categorical variables and the mean±SD for quantitative variables.

with renal and cerebrovascular presentations and could have missed patients with signs of mesenteric or limb ischemia; and (3) we did not examine the thoracic aorta, the limb arteries, or the coronary arteries.[1,3,8,20] FMD may be revealed by spontaneous coronary artery dissection—a rare acute complication of FMD that was only described after the start of the ARCADIA registry. None of our patients reported a history of an acute coronary event. We found a high prevalence of dissections and aneurysms in patients with FMD, as previously reported.[20,21] An extensive review of the ARCADIA image database will be necessary to assess their clinical relevance and document aneurysm size, site, and morphology.

Our findings have implications for the guidelines concerning vascular screening of patients with FMD. Patients with FMD should be informed of the possibility of lesions affecting asymptomatic vascular beds, particularly older patients and those with a cerebrovascular presentation because age and cerebrovascular symptoms are independently associated with multisite FMD. Among patients with a cerebrovascular presentation, those with hypertension are 3× more likely to have RA FMD (OR, 3.4; 95% CI, 1.99–6.15) than those without hypertension. Such patients should be screened with RA imaging because hypertension could be amenable to RA angioplasty in selected cases.[1–3,22] Imaging the eCVA could be considered in patients with a renal presentation in whom the first imaging procedure disclosed bilateral RA FMD lesions because they have a higher probability of having eCVA lesions than those with unilateral RA FMD (OR, 1.88; 95% CI, 0.99–3.57).

FMD is likely a systemic rather than local arterial disease, suggested by the high frequency of multisite and bilateral FMD lesions and frequent detection by high-resolution echo tracking of arterial wall alterations that affect the common carotid and radial arteries.[19]

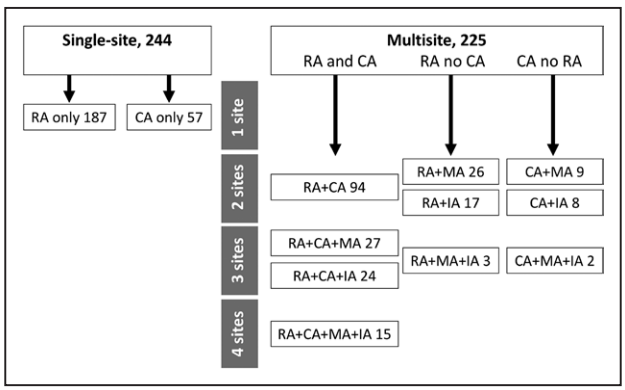

Figure 3. Distribution of fibromuscular dysplasia (FMD) stenoses. CA indicates cervical/intracranial arteries; IA, iliac arteries; MA, mesenteric/splenic arteries; and RA, renal arteries.

Table 3. Distribution of Lesions in Patients With Single-Site and Multisite FMD

Variables	Single-Site, 244		Multisite, 225		OR	95% CI	*P* Value
	n*	Values	n*	Values			
Patients with RA FMD	244	187 (76.6)	225	206 (91.6)	…		
Bilateral RA FMD	187	70 (37.4)	206	123 (59.7)	2.48	1.65–3.72	<0.001
Patients with eCVA/intracranial FMD†	244	57 (23.4)	225	179 (79.6)	…		
Bilateral eCVA/intracranial FMD	57	49 (86.0)	178	129 (72.5)	0.43	0.19–0.93	0.04
Patients with ≥1 aneurysm on any site	244	60 (24.6)	225	62 (27.6)	1.17	0.77–1.76	0.46
Patients with ≥1 dissection at any site	244	32 (13.1)	225	39 (17.3)	1.39	0.84–2.31	0.21

CI indicates confidence interval; eCVA, extracranial carotid and vertebral arteries; FMD, fibromuscular dysplasia; OR, odds ratio; and RA, renal artery.
*The number of patients available for analysis is shown for each variable. Data are expressed as the number of patients (percentages).
†Sixteen patients (14 with multisite FMD) had intracranial FMD lesions, of whom 12 also had eCVA FMD.

Perspectives

Further biological, hemodynamic, and genetic studies are required to better understand the determinants of arterial bed involvement in FMD and the development of stenosing lesions as opposed to aneurysms and dissections.

Stenosing lesions, aneurysms, and dissections are frequently asymptomatic in patients with FMD. Thus, a cost-effective approach to vascular screening that takes into account clinical relevance should be developed.

Prospective studies are required to document the incidence of symptomatic events in patients with FMD, and assess whether the diffusion of FMD lesions increases with age, as suggested by the independent association of multisite status with age. This is an objective of the ongoing study of the PROFILE (progression in fibromuscular lesions) cohort (www.Clinicaltrials.gov; NCT02961868), involving 300 of the patients included in the ARCADIA registry.

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Disclosures

None.

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Novelty and Significance

What Is New?

- Although fibromuscular dysplasia (FMD) lesions are generally symptomatic at a single vascular bed, 2 of 3 patients have stenosing FMD lesions, aneurysms, or dissections that affect additional vascular beds. This suggests that FMD is a systemic rather than a local disease.

What Is Relevant?

- Hypertension is present in most patients with FMD.
- The prevalence of renal artery lesions is much higher in hypertensive patients with a cerebrovascular presentation than in normotensive patients (OR, 3.4; 95% CI, 1.99–6.15). This suggests renovascular hypertension and could be treated by angioplasty in selected cases.

Summary

The ARCADIA registry (Assessment of Renal and Cervical Artery Dysplasia) prospectively included 469 patients with renal artery or extracranial carotid and vertebral artery FMD. Renal artery and extracranial carotid and vertebral artery FMD lesions were bilateral in 49% and 75% of cases, respectively. Stenosing lesions affected at least 2 vascular beds in 48.0% of cases. Stenosing lesions and aneurysms or dissections affected at least 2 vascular beds in 66% of cases.

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ONLINE SUPPLEMENT

High Prevalence of Multiple Arterial Bed Lesions in Patients with Fibromuscular Dysplasia: The ARCADIA Registry

High Prevalence of Multisite FMD

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*A complete list of investigators in the Assessment of Renal and Cervical Artery DysplasIA (ARCADIA) study is provided in the appendix below

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APPENDIX

The following investigators (with the number of patients enrolled given in parentheses) and committee participated in the ARCADIA study:
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Imaging Committee: Arshid Azarine, Elie Mousseaux [chair], Catherine Oppenheim, Pierre-François Plouin, Emmanuel Touzé, Frédéric Thony

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S1 – Frequency of multisite involvement in adult patients with fibromuscular dysplasia (FMD)

First author	Patient presentation	Imaging method	Definition of multisite FMD	No. of patients with ≥2 vascular beds imaged/total No. of patients	Percent with multisite FMD
Stanley, 1975[1]	Renal	Conventional angiography	Coexistent extrarenal and renal arterial fibrodysplastic lesions	Not reported	6.6
Lüscher, 1986[2]	Mostly renal	Conventional angiography	Systemic disease involving two or more different arteries	Not reported	28.3
Pannier, 1997[3]	Renal	Conventional angiography	Presence of cervical artery FMD in patients with renal artery FMD	81/104	11.1
Olin, 2012[4]	Renal or cerebrovascular	CTA, DSA, DU or MRA	FMD in 2 vascular beds in patients with ≥2 vascular beds imaged	357/447	35.3
Savard, 2012[5]	Renal	CTA, DSA or MRA	Presence of cervical artery FMD in patients with renal artery FMD	151/337	47.0
Pasquini, 2015[6]	Cerebrovascular	DSA, CTA or MRA	Presence of renal artery FMD in patients with cervical artery FMD	30/36	43.3
De Groote, 2017[7]	Renal or cerebrovascular	CTA, DSA, DU or MRA	FMD in 2 vascular beds in patients with ≥2 vascular beds imaged	61/123	41.0

Abbreviations: CTA, computed tomographic angiography; DSA, digital subtraction angiography; DU, Duplex Ultrasound; MRA, magnetic resonance angiography

S2 – Classification of arterial sites

Renal artery (left, right) Main Accessory	 ostium, trunk, branch ostium, trunk, branch
Subclavian artery (left, right)	
Extracranial carotid artery (left, right)	Common, internal (origin), internal (subpetrous)
Extracranial vertebral artery (left, right)	V0, V1, V2
Intracranial arteries	Carotid siphon (left, right) Intracranial vertebral artery V4 (left, right) Basilar artery Middle cerebral artery M1, M2 (left, right) Anterior cerebral artery (left, right) Posterior cerebral artery (left, right)