REVIEW ARTICLES

Richard P. Cambria, MD, Section Editor

Diagnosis, management, and future developments of fibromuscular dysplasia

Jeffrey W. Olin, DO, and **Brett A. Sealove, MD,** *New York, NY*

Fibromuscular dysplasia (FMD) is a nonatherosclerotic noninflammatory vascular disease that primarily affects women from age 20 to 60, but may also occur in infants and children, men, and the elderly. It most commonly affects the renal and carotid arteries but has been observed in almost every artery in the body. FMD has been considered rare and thus is often underdiagnosed and poorly understood by many health care providers. There are, however, data to suggest that FMD is much more common than previously thought, perhaps affecting as many as 4% of adult women. When it affects the renal arteries, the most common presentation is hypertension. When it affects the carotid or vertebral arteries, the patient may present with transient ischemic attack or stroke, or dissection. An increasing number of patients are asymptomatic and are only discovered incidentally when imaging is performed for some other reason or by the detection of an asymptomatic bruit. FMD should be considered in the differential diagnosis of a young person with a cervical bruit; a "swishing" sound in the ear(s); transient ischemic attack, stroke, or dissection of an artery; or in individuals aged ≤35 years with onset hypertension. Treatment consists of antiplatelet therapy for asymptomatic individuals and percutaneous balloon angioplasty for patients with indications for intervention. Patients with aneurysms should be treated with a covered stent or open surgical repair. Little new information has been published about FMD in the last 40 years. The recently instituted International Registry for Fibromuscular Dysplasia will remedy that situation and provide observational data on a large numbers of patients with FMD. (J Vasc Surg 2011;53:826-36.)

Fibromuscular dysplasia (FMD) was first described in 1938 by Leadbetter and Burkland,[1] and in the same year, McCormack et al[2] introduced the term when they reported on three patients with renal artery stenosis and hypertension. FMD is a noninflammatory, nonatherosclerotic arterial disease that most commonly affects the renal and carotid arteries but has been observed in almost every artery in the body.[3] Stenosis, aneurysm, dissection, and occlusion may occur, or the patient may be entirely asymptomatic.[3,4] FMD occurs most frequently in women aged between 20 and 60, but may also be seen in men or older individuals.[5] FMD may also be encountered in the pediatric population; however, the presentation and natural history of FMD in infants and children is quite different from adults and, thus, will not be discussed further in this review.[6]

Although most clinicians believe FMD is a rare disease, the prevalence in the general population is not known. There are three pieces of evidence that suggest that FMD is more common than previously thought:

1. **Potential renal donors.** Cragg et al[7] reviewed the results of 1862 renal arteriograms in potential renal donors and found FMD in 3.8%. A similar prevalence was found in a more recent review.[8] In a study by Neymark et al,[9] 47 of 716 potential renal donors (6.6%) demonstrated evidence of FMD on arteriography. It is estimated that there are 151.5 million women aged ≥18 in the United States (http://www.census.gov/population/www/socdemo/age/agebyage). If the data regarding the prevalence of FMD in "normal" renal donors are correct, then approximately 5.8 to 8.6 million women in the United States may have this disorder. Thus, this condition is underdiagnosed and has been for >40 years.[4,10]
2. **Incidentally discovered on imaging.** Since the advent of better imaging techniques, FMD is frequently found incidentally when computed tomography angiography (CTA), magnetic resonance angiography (MRA), duplex ultrasound

From the Zena and Michael A. Wiener Cardiovascular Institute and The Marie-Josée and Henry R. Kravis Center for Cardiovascular Health, Mount Sinai School of Medicine.

Competition of interest: Jeffrey W. Olin is (1) Chair, Medical Advisory Board, Fibromuscular Dysplasia Society of America (FMDSA). He receives no funds or gifts for this activity; it is voluntary. (2) Chair of the Steering Committee and Principal Investigator of the International Registry for Fibromuscular Dysplasia. The funding for this is from the FMDSA and goes entirely to the data coordinating center at the University of Michigan. Drs James Froehlich and Kim Eagle oversee this activity. Neither Dr Olin nor his institution receives any funding for his activities related to the registry. His activities are voluntary. (3) Chair of a Scientific Statement Committee on FMD for the American Heart Association. This activity is voluntary.

Additional material for this article may be found online at www.jvascsurg.org.

Reprint requests: Jeffrey W. Olin, DO, Professor of Medicine, Director, Vascular Medicine, The Zena and Michael A. Wiener Cardiovascular Institute and The Marie-Josée and Henry R. Kravis Center for Cardiovascular Health, One Gustave L. Levy Pl, Box 1033, New York, NY 10029 (e-mail: jeffrey.olin@mountsinai.org).

The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a competition of interest.

0741-5214/$36.00

doi:10.1016/j.jvs.2010.10.066

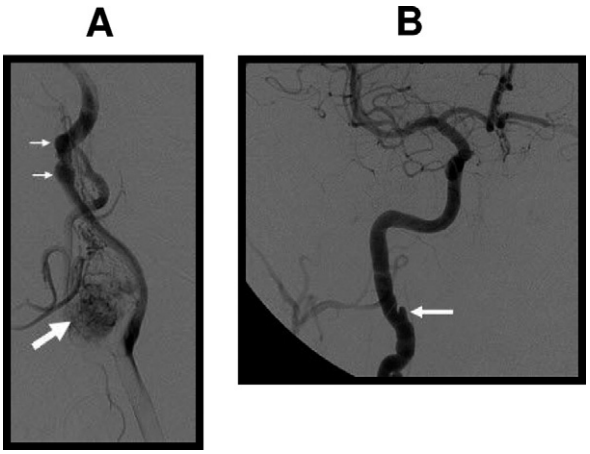

Fig 1. A 54-year-old woman underwent angiography of the carotid arteries before surgery for a carotid body tumor. **A**, Left carotid artery injection demonstrates a carotid body tumor (*arrow*), and medial fibroplasia (*small arrows*) that were incidentally discovered. **B**, Outpouching (*arrow*) commonly seen in patients with medial fibroplasia may represent a small pseudoaneurysm. (Han DK, Fishman EW, Walkup MH, Olin JW, Marin ML, Faries PL. A rare case of familial carotid body tumor in a patient with bilateral fibromuscular dysplasia. J Vasc Surg 2010;52:746-50.)

(DUS) imaging, or catheter-based angiograms are performed for reasons unrelated to the FMD (Fig 1).

3. **Incidentally discovered in the clinic.** In patients presenting to a vascular clinic for other reasons (ie, leg swelling, leg ulcers, venous thrombosis), FMD may be diagnosed after a carotid or abdominal bruit is heard. Nine such patients have been encountered in the last 18 months (unpublished data).

EPIDEMIOLOGY AND ETIOLOGY

Renal artery FMD occurs in approximately 75% of patients with FMD and is bilateral in >35% of patients.[3,11,12] There is frequently a delay in diagnosis that leads to a delay in the most appropriate treatment.

Renal artery FMD may be associated with dissection and aneurysms (Fig 2). Few contemporary data are available on the prevalence of renal artery aneurysms in patients with FMD.[13] In a study from 1968, Kincaid et al[14] reported a 9.6% prevalence of renal artery aneurysms. A more recent study of 41 patients with renal artery FMD documented 4 patients with renal artery aneurysms (prevalence of 9.8%).[9]

Extracranial cerebrovascular FMD most commonly occurs in the internal carotid artery near the level of C1-C2. In the past it was often stated that carotid artery FMD affected 25% to 30% of patients with FMD.[15,16] However, in the first 200 patients entered into the International Registry for Fibromuscular Dysplasia, approximately 70% had extracranial cerebrovascular FMD (unpublished data, 2010). Vertebral artery involvement is less common (7% to 19%); however, the prevalence of both in the general population is not known.[17,18]

There is an increased prevalence of intracranial aneurysms in patients with extracranial cerebrovascular FMD compared with the general population. In a meta-analysis of 18 studies involving 615 patients with carotid or vertebral artery FMD, the overall prevalence of intracranial aneurysms was 22%. However, when patients presenting with subarachnoid hemorrhage were excluded, the prevalence of intracranial aneurysms was only 7.3% ± 2.0%.[19] Other investigators have reported a prevalence of 22% to 51%.[10,11,18,19]

Although many theories have been proposed, including environmental factors, such as tobacco and estrogen, as well as genetic factors, the cause of FMD is unknown. FMD overwhelmingly affects the female sex by a 9/1 ratio.[4,20] Some investigators have promulgated a theory that links estrogen with a predisposition to the development of FMD.[21] However, neither oral contraceptives nor pregnancy appears to increase the risk for developing FMD.[22]

FMD is likely, at least in part, a genetic disorder. Mettinger and Ericson[10] examined the pedigree of 37 patients and concluded that there was a dominant trait with reduced penetrance. Rushton et al[23] examined 20 families and found that 60% of FMD cases were due to an autosomal-dominant trait with variable penetrance and speculated that the remaining 40% were due to acquired mutations. Subsequently, Perdu et al[24] reported an 11% incidence of FMD among first-degree relatives of individuals with FMD. Until first-degree relatives of patients with FMD are formally studied in larger numbers, we will not know the patterns of inheritance or the percentage of patients who pass this on to their offspring.

PATHOLOGIC CLASSIFICATION OF FMD

FMD is classified into three categories related to the pathologic layer of the arterial wall that is affected—intima, media, and adventitia (periarterial).[12,25] Medial FMD is by far the most common type and is further subdivided into medial fibroplasia, perimedial fibroplasia, and medial hyperplasia.[15,25,26] Although this classification was initially proposed for the renal arteries, it is also applicable to other arterial beds and has been angiographically correlated with the disease elsewhere.[3]

Medial fibroplasia accounts for 80% to 90% of all types of FMD.[11,20] This subtype is defined histologically by alternating areas of thinned media and thickened collagen-containing medial ridges. Multiple stenotic "webs" cause arterial stenosis and poststenotic dilation, often displaying the typical "string of bead" appearance on angiography (Fig 2). The "bead" component is often larger than the normal arterial lumen, and in a subset of patients with FMD, aneurysms are present that may require treatment (Fig 2).[9,27]

Intimal fibroplasia accounts for approximately 10% of all FMD. Intimal fibroplasia is due to a collagen deposition within the intima complicated by an often fragmented or duplicated internal elastic lamina.[11,25] Angiography shows it is distinct from medial disease because the intima often causes a focal fibrotic band-like constriction that results in a concentric stenosis (Fig 3) or long tubular lesion.[15,26,28]

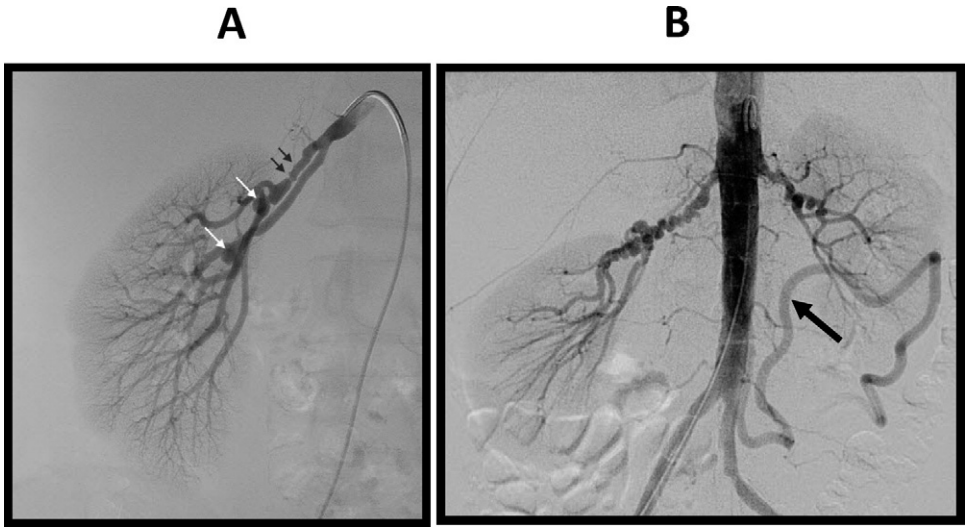

Fig 2. A, A catheter-based angiogram in a 35-year-old woman with new-onset of severe high blood pressure demonstrated fibromuscular dysplasia of the right renal artery (*black arrows*) and two small aneurysms (6 mm) more distally (*white arrows*). **B,** Aortogram in a patient with medial fibroplasia of the middle and distal renal arteries and the branches shows a large marginal artery (*arrow*) indicating severe disease or occlusion of the superior mesenteric artery. There is also fibromuscular dysplasia of the celiac and superior mesenteric artery (not shown).

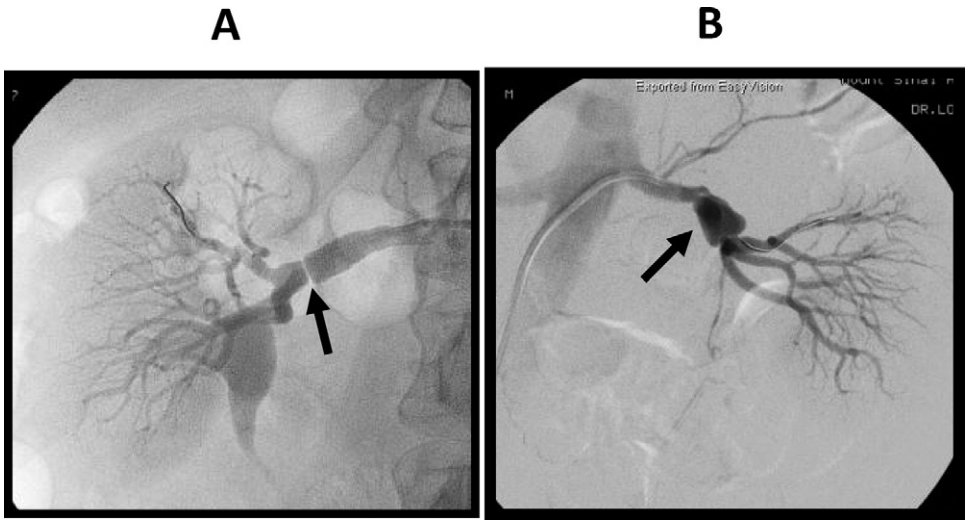

Fig 3. A 48-year-old man presented with bilateral flank pain and increased serum creatinine. **A**, There is a concentric severe stenosis (*arrow*) of the right renal artery characteristic of intimal disease. **B**, There is a dissection (*arrow*) in the left renal artery with dilatation of the distal main renal artery and infarction of the upper pole of the left kidney (not shown). (Reproduced with permission from Olin JW, Pierce M. Contemporary management of fibromuscular dysplasia. Curr Opin Cardiol 2008;23(6):527-36.)

Perimedial fibroplasia (less numerous and smaller beads than medial fibroplasia) is quite uncommon and usually occurs in young girls aged between 5 and 15 who present with hypertension and renal impairment.[3]

Medial hyperplasia is extremely rare and requires a pathologic specimen for diagnosis.

Adventitial fibroplasia has an unknown frequency. Weiner et al[29] recently reported adventitial FMD was diagnosed by intravascular ultrasound (IVUS) imaging.[29] The angiographic appearance looks similar to intimal disease.

CLINICAL PRESENTATION AND NATURAL HISTORY

Renal artery FMD. The most common clinical presentation of FMD of the renal arteries is hypertension in a young

woman. However, FMD can occur in both sexes and present at any age.[30] The development of noninvasive imaging such as CTA and MRA has led to the identification of FMD in patients being imaged for other indications.[31] In these situations, the FMD is asymptomatic and often an incidental finding (Fig 1). FMD is now commonly identified in older patients and it is also not uncommon to see both atherosclerosis and FMD in the same patient.[5] Other clinical manifestations of renal artery FMD include aneurysm, dissection, or occlusion of the renal artery. Dissection is the most common cause of renal infarction in patients with FMD (Fig 3).

Before 1990, the average age for the diagnosis of renal artery FMD was reported to be 39 in women and 31 in men. More recent data, however, suggest that the typical patient presenting with renal artery involvement is older, has had a longer duration of hypertension, and possesses more involvement of the renal branches.[32] This in all likelihood is due to failure to diagnose FMD when patients aged <35 years present with hypertension.

Two angiographic studies have reported the progression rate of renal artery disease secondary to FMD. Goncharenko et al[33] evaluated 42 patients and found that all demonstrated progression of disease. Schreiber et al[34] evaluated 66 patients with medial fibroplasia and reported progression in 33%, with only 2 patients demonstrating worsening renal function and no lesion progressing to occlusion. Both of these studies have significant methodologic problems that cast doubt on these conclusions. The only way to determine whether progression has occurred is to observe new lesions where lesions did not exist in the past. It is impossible to assess whether a given lesion has more stenosis because the degree of stenosis cannot be accurately gauged on arteriography or any other imaging modality.

Medial fibroplasia may be present with normal blood pressure or may present with difficult to control hypertension. There is rarely renal dysfunction with medial fibroplasia unless a dissection occurs. Intimal and perimedial fibroplasia may be associated with renal dysfunction, dissection, and progression to occlusion.[4]

Extracranial cerebrovascular FMD. Carotid FMD is most frequently located in the middle and distal part of the internal carotid arteries and is usually bilateral (Fig 4).[3,10,18] The vertebral arteries may also be involved. Carotid or vertebral artery FMD may be asymptomatic and only discovered when a cervical bruit is heard or when imaging is performed for another reason (Fig 1).[4] In the Mayo Clinic experience, none of the 27 asymptomatic individuals incidentally diagnosed with carotid artery FMD had neurologic symptoms during a 6.5-year follow-up.[35]

There are a myriad of nonspecific symptoms or signs that frequently occur in patients with carotid or vertebral artery FMD, such as dizziness, headache, altered mentation, pulsatile tinnitus, neck pain, headache, wooziness, and a swishing (swooshing, whooshing) sound in the ears. More focal and specific neurologic signs and symptoms that may occur include transient ischemic attack (TIA), cerebral infarction, subarachnoid hemorrhage, syncope, Horner syndrome, and cranial nerve palsies.[10,18,36] Symptoms may be related to one or more of the following mechanisms: (1) severe stenosis producing hypoperfusion, (2) embolization, (3) thrombosis, (4) dissection,[37] or (5) aneurysm rupture.[15]

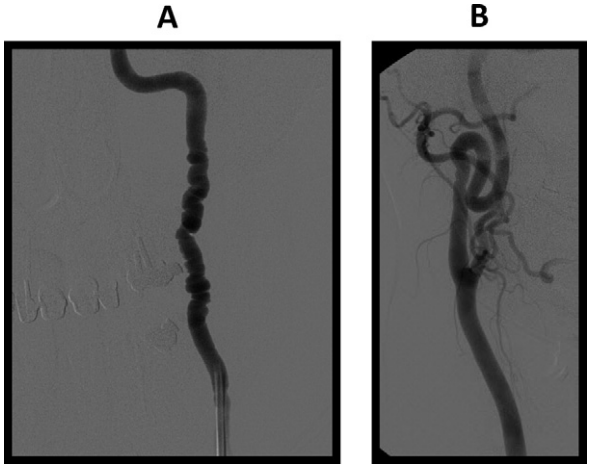

Fig 4. A, Typical medial fibroplasia of the right internal carotid artery. Note the "beading" is located in the middle and distal portion of the internal carotid artery, whereas atherosclerosis occurs at the origin of the internal carotid artery. **B**, This 51-year-old patient demonstrates severe tortuosity of the left internal carotid artery. She has medial fibroplasia of the renal arteries and an occluded right internal carotid artery from dissection.

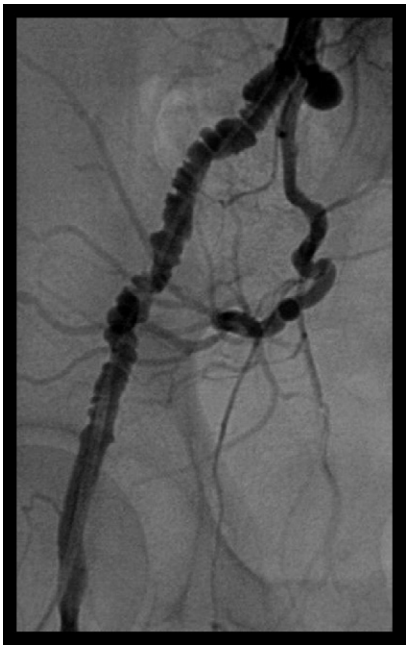

Fig 5. Medial fibroplasia of the external iliac arteries in a patient who presented with claudication. (Photograph courtesy of J. Michael Bacharach, MD.)

Other arterial beds. FMD has been reported to affect the celiac, superior and inferior mesenteric (Fig 2, *B*),

Table I. Common misconceptions regarding fibromuscular dysplasia

Misconception	*Fact*
All coronary, carotid, and renal artery disease is due to atherosclerosis	• FMD can cause renal, visceral, cerebrovascular, extremity, and coronary disease • Most patients are young or middle-age females, with few or no atherosclerotic risk factors • Whereas atherosclerosis occurs at the origin or proximal portion of the vessel, FMD occurs in the mid and distal part of the artery
The severity of medial fibroplasia (beading) can accurately be ascertained by visual inspection of the angiogram	• There is no accurate way to determine the degree of stenosis by visual inspection of an arteriogram or other imaging studies • IVUS or measurement of pressure gradient should be obtained in the renal arteries before and after angioplasty in patients with FMD • As many as one-third of patients have no demonstrated angiographic stenosis after angioplasty yet have residual stenosis by pressure gradient or IVUS imaging
Duplex ultrasound velocities predict degree of carotid or renal FMD severity, or both	• The degree of "stenosis" cannot be determined by Doppler velocity shift • Contrary to the Doppler assessment in atherosclerotic carotid or renal artery disease, no diagnostic velocity criteria exist for cerebrovascular or renal FMD • Rather than one area of stenosis in atherosclerosis, there are multiple areas of stenosis and dilatation in FMD, making the flow characteristics completely different from patients with atherosclerosis • On ultrasound reports, we recommend a statement such as: "there is an increased velocity (PSV 450 cm/s), turbulence and tortuosity in the mid and distal renal (or carotid) artery consistent with fibromuscular dysplasia,"[a] which is a much more accurate statement than assigning a degree of stenosis (ie, 50%-70%) to an artery
Patients with renal or carotid artery fibromuscular dysplasia undergoing intervention should receive a stent	• There is no indication for stent placement in fibromuscular dysplasia under most circumstances • Angioplasty alone is all that is needed to resolve the pressure gradient and normalize the appearance on IVUS • FMD occurs in the mid-to-distal portion of the blood vessel; therefore, a stent in the renal artery in which restenosis occurs will make surgical repair more complex • The only indications for stent implantation are failure to achieve a desirable result with PTA alone (rare) or dissection during the procedure
The most common presentation for carotid FMD is transient ischemic attack or stroke	• Although TIA and stroke can occur with carotid FMD, the most common presentations are asymptomatic and detected incidentally via imaging for another reason and cervical bruit • Nonspecific symptoms, such as headaches, dizziness, light-headed, audible swishing (or whooshing) sound in the ear

FMD, Fibromuscular dysplasia; *IVUS,* intravascular ultrasound imaging; *PSV,* peak systolic velocity; *PTA,* percutaneous transluminal angioplasty; *TIA,* transient ischemic attack.

[a]If the presence of "beading" is demonstrated on ultrasound imaging (B-mode, color Doppler, or power angiography), it should be noted in the conclusions.

hepatic, splenic, extremity (Fig 5), and coronary arteries. In the viscera, FMD usually involves more than one vessel. Although typically asymptomatic, mesenteric ischemia can occur but rarely results in infarction due to extensive collateralization.

Epicardial coronary artery involvement has been infrequently reported. Coronary FMD typically appears as a well-demarcated, long, smooth lesion in the distal portion of the artery. There is an abrupt transition from an angiographically normal coronary artery to the abnormal area.[38] Rarely, the "string of beads" appearance will occur in the coronary arteries.

DIAGNOSTIC EVALUATION

Renal artery. Catheter-based angiography remains the most accurate imaging technique to diagnose and evaluate FMD. It can visualize the main renal arteries as well as the smaller branch vessels. In fact, catheter-based angiography is the only imaging modality that can accurately identify the changes of FMD, aneurysm formation, and dissection in the branch vessels.[39] In addition, catheter-based angiography has an advantage in that a pressure wire and IVUS imaging can be used to help determine the hemodynamic significance of a lesion.[40-42] Gowda et al[42] evaluated 20 consecutive patients with suspected renal artery stenosis with DUS imaging, renal angiography, and IVUS imaging. On IVUS imaging, eccentric ridges, fluttering membranes, or spiraling folds were present in areas where DUS and angiography demonstrated abnormalities (8 patients). However, similar defects were detected by IVUS imaging when angiography was borderline (7 patients) or normal (5 patients).[42] Although catheter-based angiography has been considered the gold standard for the diagnosis of FMD, it is important to not just rely on visual inspection of the angiogram, because the stenosis can be subtle and only detected with the measurement of pressure gradient or use of IVUS imaging (Table I).

CTA and MRA have been successfully used in the diagnosis of renal artery FMD. Neither imaging modality has good enough resolution to identify branch vessel disease.[39] Both techniques can accurately identify aneurysms.[31,43,44]

DUS is accurate in the diagnosis of atherosclerotic renal artery stenosis and is valuable as a surveillance modality after endovascular intervention.[45] Although no large-scale studies have compared DUS imaging with angiography for patients with FMD, smaller reports have shown accuracy in patients with FMD.[46,47] The typical string of beads may occasionally be seen on DUS imaging, but a more common finding is turbulence, tortuosity, and a velocity shift in the middle and distal arteries. It is important to visualize the middle and distal renal arteries using an oblique, subcostal, or flank approach in addition to an anterior approach.

Differential diagnosis

Atherosclerosis. FMD can be distinguished from atherosclerotic disease due to the younger age and lack of traditional atherosclerotic risk factors in some patients. In addition, atherosclerosis occurs at the ostium or proximal portion of the renal and carotid arteries, whereas FMD occurs in the middle or distal portion of these arteries. Because FMD is now being recognized in elderly persons, it is not uncommon to encounter patients with both atherosclerosis and FMD.[5,48-50]

Vasculitis. FMD is a noninflammatory process, whereas there is marked inflammation of the blood vessel in vasculitis. Measurements of acute-phase reactants, such as erythrocyte sedimentation rate and C-reactive protein, are usually within normal reference ranges in FMD unless there is infarction of the kidney or bowel. FMD may be confused with a vasculitis because it can occur in multiple vascular territories and cause accelerated hypertension, kidney impairment, TIA, stroke, and abnormalities such as stenosis, aneurysm, or dissection.

Segmental arterial mediolysis. Segmental arterial mediolysis is a poorly understood condition characterized by spontaneous dissection(s), occlusion, or aneurysm formation, or both, and is often difficult to differentiate from FMD. It is unclear whether segmental arterial mediolysis is a distinct vascular abnormality or a subtype of FMD.[51-53]

Histopathologic findings include mediolysis, which begins in the outer media as a result of vacuolization. There is separation of the media from adventitia that may result in dissection, and arterial gaps that result in loss of intima and media and in subsequent repair, which can result in an appearance resembling FMD. Unlike vasculitis, there is no inflammation or fibrinoid necrosis.[51]

A typical presentation may include severe abdominal or flank pain due to infarction of the visceral organs. In a review of 24 published cases, the distribution of visceral involvement was as follows: celiac artery or branches (50%), superior mesenteric artery or branches (29%), inferior mesenteric artery or branches (9%), and renal arteries (12%).[51] There is no sex predilection, and segmental arterial mediolysis often presents in the fourth to the eighth decade.[52,54]

Other associated diseases. An association has been noted of FMD with other arterial diseases such as Marfan syndrome,[55] Takayasu arteritis,[56,57] neurofibromatosis type I,[58-60] and Ehlers-Danlos syndrome type IV (vascular type).[61]

There is an interesting finding of severe tortuosity in the distal carotid arteries in patients with FMD (Fig 4). This may occur in the absence of other findings such beading.[15] The cause of this tortuosity is not known; however, tortuosity of the carotid arteries occurs frequently in patients with typical renal artery FMD (Fig 4). Further study is required to determine if this type of ultrasound or angiographic picture represents another manifestation of FMD.

MANAGEMENT

Renal artery FMD. The primary goal in treating patients with renal artery FMD is the control of blood pressure to prevent the sequelae of long-standing poorly controlled hypertension.[62] In patients in whom the high blood pressure is newly diagnosed and secondary to renal artery FMD, the initial treatment may be percutaneous transluminal balloon angioplasty (PTA).[4,63] The chance of cure (normal blood pressure on no antihypertensive medications) is the highest when the patient is young, the duration of hypertension is short,[32,64] and the gradient is completely obliterated at the time of angioplasty[40,41,63,65] (Table I).

For patients in whom FMD was not diagnosed at the onset of high blood pressure and the hypertension was present for more than several years, antihypertensive medications should be continued as long as the hypertension is well controlled and the patient does not experience undesirable side effects from the medication. These patients should be monitored clinically every 6 months with assessment of blood pressure and renal function (serum creatinine and estimated glomerular filtration rate).[66] Renal artery DUS imaging should also be obtained every 6 to 12 months to assess renal length and cortical thickness[3,67,68]

If the blood pressure becomes difficult to control, intolerable side effects develop secondary to the medications, or the patient's renal size or function decreases, PTA should then be performed. Balloon angioplasty alone is very effective treatment for renal artery FMD; therefore, there is no need for stent implantation under most circumstances. Because FMD occurs in the middle and distal renal artery and its branches, if surgical revascularization is required in the future, previous stenting may make that revascularization much more difficult. There are two indications for stenting in renal artery FMD: if the gradient cannot be obliterated with angioplasty alone[29] and to treat a dissection. The primary role for surgical revascularization is to treat aneurysms in patients in whom endovascular therapy is not an option[27,69] or if PTA fails.[30]

PTA has replaced surgery as the preferred treatment of renal artery FMD.[30,63] Angioplasty has a number of advantages over open surgical revascularization: it can be performed with a high degree of technical and clinical success

Table II. Results of percutaneous transluminal angioplasty in patients with renal artery fibromuscular dysplasia and hypertension[a]

Study	*Year*	*Patient No.*	*Technical success rate %*	*Effect on blood pressure, %*			*Follow-up, mon Mean (range)*	*Complication rate %*
				Cured	*Improved*	*Unimproved*		
Sos et al	1983	31	87	59	34	7	16 (4-40)	6
Baert et al	1990	22	83	58	21	21	26 (6-72)	NR
Tegtmeyer et al	1991	66	100	39	59	2	39 (1-121)	13
Bonelli et al	1995	105	89	22	63	15	43 (0-168)	11 (major)
Jensen et al	1995	30	97	39	47	14	12 (NR)	3 (major)
Davidson et al	1996	23	100	52	22	26	NR	12 (minor)
Klow	1998	49	98	26	44	30	9 (1-96)	0
Birrer et al	2002	27	100	74[b]		26	10 (NR)	7.4
Surowiec et al	2003	14	95	79[b]		21	NR	28.5
De Fraissinette et al	2003	70	94	14	74	12	39 (1-204)	11
Kim et al	2008	15	79	13	80	7	24 (1-60)	16
Davies et al	2008	29	100	72[b]		18	24[c]	8 (minor)

NR, Not reported.
[a]Modified and updated from Slovut DP, Olin JW. Current concepts: fibromuscular dysplasia. N Engl J Med 2004;350:862-71.
[b]The percentage shown is the total for cured and improved.
[c]Median value.

with minimal complications; it is less invasive, has a markedly shorter recovery time, is less expensive, and may be performed as an outpatient. PTA results in blood pressure reduction in most patients and can be used to treat every type of lesion in the main and branch arteries (Table II).[63,70-82] In an effort to determine the rate of cure of hypertension after angioplasty or surgery, Trinquart et al[64] performed a systematic review and meta-analysis of 47 angioplasty studies (1616 patients) and 23 surgery studies (1014 patients). Cure of hypertension, defined according to the criteria in each study, was estimated to be 46% (95% confidence interval, 40%-52%) after angioplasty and 58% after surgery (95% confidence interval, 53%-62%). There was considerable heterogeneity across studies.

Most instances of recurrence of disease after PTA are related to inadequate angioplasty the first time. Usually a second PTA results in cure or improvement in blood pressure.[63,80] It is important to measure pressure gradients both before and after angioplasty to be certain that all of the webs have been disrupted and the pressure gradient has been obliterated.[40,41,65] IVUS imaging may be a useful adjunct to demonstrate not only the type of FMD involved[29] but also the disruption of the webs after the intervention.[40,42]

It has become our practice to get a baseline DUS image at the first office visit after angioplasty. Patients are then put into a surveillance program of DUS imaging every 6 months to assess kidney size, velocity elevations in the region of previous stenosis, and any changes in cortical thickness. If restenosis develops without resultant hypertension, the patient is monitored serially without reintervention. If, however, hypertension recurs and there is an area of stenosis in the renal artery, angioplasty is repeated. All patients with renal artery FMD are empirically prescribed aspirin (81 mg daily).

Cerebrovascular FMD. The overall prognosis for medial fibroplasia of the carotid or vertebral arteries is quite good.[35,83,84] Patients with asymptomatic carotid or vertebral artery FMD should be monitored medically and prescribed aspirin (81 mg daily) for primary stroke prevention. PTA is the first line of treatment for those with *symptomatic* extracranial cerebral vascular FMD.[4,85-88] There is no role for the older technique of open graduated intraluminal dilatation.[89] Surgical therapy or endovascular therapy with stents or coils is reserved for patients with aneurysms. If the patient experiences amaurosis fugax, TIA, or stroke, balloon PTA should be performed if feasible. If a dissection develops during intervention, a stent should be placed.

Patients with FMD may present with a carotid or vertebral artery dissection. Angiographic changes of FMD are found in about 15% of patients with a spontaneous dissection of the carotid or vertebral artery.[90] If a dissection is present, anticoagulation with heparin should be started, followed by warfarin. If the patient has no further TIA or stroke, the anticoagulation should be continued for 3 to 6 months, allowing for the dissection to heal.[90] However, a stent should be placed if the patient experiences recurrent symptoms while on anticoagulation.[90,91]

There are a host of nonspecific symptoms that patients with FMD experience. A common symptom is an abnormal swishing (swooshing, whooshing) sound in one or both ears. Some of these patients may be so debilitated because of the constant noise in their ear that they seek support and help with others who are similarly afflicted (http://www.whooshers.com).

Another common and quite bothersome symptom is headache. Mettinger et al[10,18] recognized that headaches were common in individuals with FMD. The pathogenesis of headaches in patients with FMD is not known. Most with carotid or vertebral FMD suffer from headaches, and

in some patients, the headaches are debilitating and refractory to treatment. We have now performed internal carotid artery balloon angioplasty on four patients with severely debilitating headaches. All patients underwent a formal neurologic evaluation by a headache specialist to exclude other treatable causes for the headaches. These patients were extremely debilitated by their headaches and frustrated that nothing could be done to help them. All experienced complete relief of headaches after angioplasty. The first patient treated has now been free of headache for nearly 3 years. Clearly, this needs to be studied in a formal manner and reserved for only the most severely debilitated patients. Most of our patients with headaches are not offered angioplasty because their lesions are too diffuse, other causes of headaches (sinus, post-traumatic) are possible, or the headaches are not severely debilitating and usual headache therapy is helpful.

A neurosurgeon should evaluate patients with carotid or vertebral FMD and associated intracranial aneurysms to determine if the aneurysm needs to be observed or be treated with surgery or endovascular stent/coiling.

Patients with carotid artery FMD should be put into a surveillance program of DUS imaging every 6 to 12 months basis to follow the course of the disease. It is not known how often a patient needs to be imaged for intracranial aneurysms after the first negative MRA.

FMD in other locations. Even less information is available about the most effective treatment for FMD in locations other than the renal and extracranial carotid and vertebral arteries. Patients with claudication or acute limb ischemia can be effectively treated with angioplasty (Fig 5).[92] Those with intestinal ischemia can be treated with angioplasty or surgery.[93,94] Most patients with visceral aneurysms will require surgical treatment. Pate et al[38] described the clinical and angiographic features of coronary artery FMD. The disease was distal in all cases, and revascularization was not possible. Therefore, symptomatic patients with coronary disease should be treated medically. Occasionally, the coronary arteries may have a moth-eaten (beaded) appearance that could be treated with angioplasty.[95]

UNRESOLVED ISSUES

Virtually no new information about FMD has been published in the last 40 years. Small case series and single case reports continue to be published. In 2009, 20 single case reports were published in patients with FMD. This indicates that there is virtually no significant research on pathogenesis, genetics, imaging, or treatment. This lack of research is largely due to the perception that FMD is a rare disease and thus no funding has been made available by the National Institutes of Health, other funding organizations, or industry.

A group of individuals who have FMD or who have a close relative with FMD founded the Fibromuscular Dysplasia Society of America (http://www.fmdsa.org). The mission of this nonprofit organization is to (1) increase awareness of FMD, (2) educate health care providers about FMD so that the diagnosis will not be overlooked or delayed and thus complications of FMD prevented, (3) educate patients with FMD and provide a resource for information and support with others with this disease, and (4) raise money for research and education. This organization has succeeded in all four of these goals.

The Fibromuscular Dysplasia Society of America has funded the International Registry for Fibromuscular Dysplasia. This registry will provide observational data on a large number of patients with FMD so that we can better understand the natural history of the disease, the most accurate method for diagnosis, and most effective treatment strategy. These data will allow for the formation of important questions and goals for future research. The registry started with seven centers in the United States (see Appendix, online only). There are plans to add more centers this year. The ultimate goal is to raise enough money so that genetic studies can be undertaken to better understand the pathogenesis of the disease. Most centers working on various research aspects of FMD are doing so with virtually no funding.

Many unanswered questions remain, among them:

- What is the prevalence of FMD in the community?
- What is the prevalence of FMD in asymptomatic first-degree relatives?
- What causes FMD?
  - Genetics?
  - Environmental influences?
  - Hormones?
- Are most patients with FMD asymptomatic?
- What is the natural history of symptomatic and asymptomatic FMD?
- Why are women affected more commonly than men?
- Why do some patients develop aneurysms? Or dissection?
- Why are headaches so common in patients with extracranial cerebrovascular FMD?
- Are there genetic markers associated with FMD? Transforming growth factor-β? Collagen type III α1 (*COL3A1*)?
- What is the diagnostic accuracy of DUS imaging, MRA, and CTA for carotid and renal FMD?
- What are the ultrasound criteria for renal artery and carotid artery stenosis in patients with FMD?
- Why is there such severe arterial tortuosity in some patients with FMD?

CONCLUSIONS

There are a large number of patients with FMD who are either not diagnosed or for whom there is a significant delay in diagnosis and thus treatment. Once patients are diagnosed, they are often told that nothing can be done for them.[96] Many patients with FMD do not accept this as an answer and often seek out information on the Internet. Misdiagnosis or a delay in diagnosis will not occur if the health care provider thinks of FMD under the following circumstances:

1. A young person with a cervical bruit; be certain the vascular laboratory images the middle and distal internal carotid artery
2. A patient describing a "swishing" (swooshing, whooshing) sound or pulsatile tinnitus in the ear(s)
3. Any patient (especially those aged <60 years) with a TIA or stroke
4. Any patient with a dissection of any artery other than the aorta
5. Onset of hypertension in individuals aged ≤35 or difficult to control hypertension in anyone aged <55

REFERENCES

1. Leadbetter WF, Burkland CE. Hypertension in unilateral renal disease. J Urol 1938;39:611-26.
2. McCormack LJ, Hazard JB, Poutasse EF. Obstructive lesions of the renal artery associated with remediable hypertension. Am Jr Pathol 1938;34:582.
3. Slovut DP, Olin JW. Fibromuscular dysplasia. N Engl J Med 2004;350: 1862-71.
4. Olin JW, Pierce M. Contemporary management of fibromuscular dysplasia. Curr Opin Cardiol 2008;23:527-36.
5. Pascual A, Bush HS, Copley JB. Renal fibromuscular dysplasia in elderly persons. Am J Kidney Dis 2005;45:e63-6.
6. Stanley JC, Zelenock GB, Messina LM, Wakefield TW. Pediatric renovascular hypertension: a thirty-year experience of operative treatment. J Vasc Surg 1995;21:212-26.
7. Cragg AH, Smith TP, Thompson BH, Maroney TP, Stanson AW, Shaw GT, et al. Incidental fibromuscular dysplasia in potential renal donors: long-term clinical follow-up. Radiology 1989;172:145-7.
8. Blondin D, Lanzman R, Schellhammer F, Oels M, Grotemeyer D, Baldus SE, et al. Fibromuscular dysplasia in living renal donors: still a challenge to computed tomographic angiography. Eur J Radiol 2009; 75:67-71.
9. Neymark E, LaBerge JM, Hirose R, Melzer JS, Kerlan RK Jr, Wilson MW, et al. Arteriographic detection of renovascular disease in potential renal donors: incidence and effect on donor surgery. Radiology 2000; 214:755-60.
10. Mettinger KL, Ericson K. Fibromuscular dysplasia and the brain. I. Observations on angiographic, clinical and genetic characteristics. Stroke 1982;13:46-52.
11. Stanley JC, Gewertz BL, Bove EL, Sottiurai V, Fry WJ. Arterial fibrodysplasia. Histopathologic character and current etiologic concepts. Arch Surg 1975;110:561-6.
12. Harrison EG Jr, Hunt JC, Bernatz PE. Morphology of fibromuscular dysplasia of the renal artery in renovascular hypertension. Am J Med 1967;43:97-112.
13. Altit R, Brown DB, Gardiner GA. Renal artery aneurysm and arteriovenous fistula associated with fibromuscular dysplasia: successful treatment with detachable coils. J Vasc Interv Radiol 2009;20:1083-6.
14. Kincaid OW, Davis GD, Hallermann FJ, Hunt JC. Fibromuscular dysplasia of the renal arteries. Arteriographic features, classification, and observations on natural history of the disease. Am J Roentgenol Radium Ther Nucl Med 1968;104:271-82.
15. Begelman SM, Olin JW. Fibromuscular dysplasia. Curr Opin Rheumatol 2000;12:41-7.
16. Stanley JC, Fry WJ, Seeger JF, Hoffman GL, Gabrielsen TO. Extracranial internal carotid and vertebral artery fibrodysplasia. Arch Surg 1974;109:215-22.
17. So EL, Toole JF, Dalal P, Moody DM. Cephalic fibromuscular dysplasia in 32 patients: clinical findings and radiologic features. Arch Neurol 1981;38:619-22.
18. Mettinger KL. Fibromuscular dysplasia and the brain. II. Current concept of the disease. Stroke 1982;13:53-8.
19. Cloft HJ, Kallmes DF, Kallmes MH, Goldstein JH, Jensen ME, Dion JE. Prevalence of cerebral aneurysms in patients with fibromuscular dysplasia: a reassessment. J Neurosurg 1998;88:436-40.
20. Stanley JC, Fry WJ. Renovascular hypertension secondary to arterial fibrodysplasia in adults: criteria for operation and results of surgical therapy. Arch Surg 1975;110:922-8.
21. Luscher TF, Lie JT, Stanson AW, Houser OW, Hollier LH, Sheps SG. Arterial fibromuscular dysplasia. Mayo Clin Proc 1987;62:931-52.
22. Stanley JC, Gewertz BL, Renal FWJ. Systemic renin indices and renal vein renin ratios as prognostic indicators in remedial renovascular hypertension. J Surg Res 1976;20:149-55.
23. Rushton AR. The genetics of fibromuscular dysplasia. Arch Intern Med 1980;140:233-6.
24. Perdu J, Boutouyrie P, Bourgain C, Stern N, Laloux B, Bozec E, et al. Inheritance of arterial lesions in renal fibromuscular dysplasia. J Hum Hypertens 2007;21:393-400.
25. Harrison EG Jr, McCormack LJ. Pathologic classification of renal arterial disease in renovascular hypertension. Mayo Clin Proc 1971;46: 161-7.
26. McCormack LJ, Poutasse EF, Meaney TF, Noto TJ Jr, Dustan HP. A pathologic-arteriographic correlation of renal arterial disease. Am Heart J 1966;72:188-98.
27. Olin JW. Recognizing and managing fibromuscular dysplasia. Cleve Clin J Med 2007;74:273-82.
28. Olin JW. Syndromes that mimic vasculitis. Curr Opin Cardiol 1991;6: 768-74.
29. Weiner RB, Kiernan TJ, Yan BP, Rosenfield K, Jaff MR. Images in cardiovascular medicine. Adventitial fibromuscular dysplasia of the renal artery: management challenges of nonatherosclerotic renal artery stenosis. Circulation 2009;120:e157-8.
30. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, et al. ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice guidelines (Writing Committee to develop guidelines for the management of patients with peripheral arterial disease) endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus and Vascular Disease Foundation. J Am Coll Cardiol 2006;47:1239-312.
31. Liu PS, Platt JF. Angiography of the renal circulation. Radiol Clin North Am 2010;48:347-65.
32. Anderson CA, Hansen KJ, Benjamin ME, Keith DR, Craven TE, Dean RH. Renal artery fibromuscular dysplasia: results of current surgical therapy. J Vasc Surg 1995;22:207-15.
33. Goncharenko V, Gerlock AJ Jr, Shaff MI, Hollifield JW. Progression of renal artery fibromuscular dysplasia in 42 patients as seen on angiography. Radiology 1981;139:45-51.
34. Schreiber MJ, Pohl MA, Novick AC. The natural history of atherosclerotic and fibrous renal artery disease. Urol Clin North Am 1984;11: 383-92.
35. Corrin LS, Sandok BA, Houser OW. Cerebral ischemic events in patients with carotid artery fibromuscular dysplasia. Arch Neurol 1981; 38:616-8.
36. Mettinger KL, Soderstrom CE. Pathogenetic profile of TIA before 55. A three-year investigation. J Neurol Sci 1978;36:341-8.
37. de Bray JM, Marc G, Pautot V, Vielle B, Pasco A, Lhoste P, et al. Fibromuscular dysplasia may herald symptomatic recurrence of cervical artery dissection. Cerebrovasc Dis 2007;23:448-52.
38. Pate GE, Lowe R, Buller CE. Fibromuscular dysplasia of the coronary and renal arteries? Catheter Cardiovasc Interv 2005;64:138-45.
39. Das CJ, Neyaz Z, Thapa P, Sharma S, Vashist S. Fibromuscular dysplasia of the renal arteries: a radiological review. Int Urol Nephrol 2007; 39:233-8.
40. Prasad A, Zafar N, Mahmud E. Assessment of renal artery fibromuscular dysplasia: angiography, intravascular ultrasound (with virtual histology), and pressure wire measurements. Catheter Cardiovasc Interv 2009;74:260-4.

41. Olin JW. Misconceptions about the diagnosis and treatment of fibromuscular dysplasia. Catheter Cardiovasc Interv 2009;74:265-6.
42. Gowda MS, Loeb AL, Crouse LJ, Kramer PH. Complementary roles of color-flow duplex imaging and intravascular ultrasound in the diagnosis of renal artery fibromuscular dysplasia: should renal arteriography serve as the "gold standard"? J Am Coll Cardiol 2003;41:1305-11.
43. Rubin GD. MDCT imaging of the aorta and peripheral vessels. Eur J Radiol 2003;45(Suppl 1):S42-9.
44. Rubin GD. 3-D imaging with MDCT. Eur J Radiol 2003;45(Suppl 1):S37-41.
45. Olin JW, Piedmonte MR, Young JR, DeAnna S, Grubb M, Childs MB. The utility of duplex ultrasound scanning of the renal arteries for diagnosing significant renal artery stenosis. Ann Intern Med 1995;122: 833-8.
46. Leung DA, Hoffmann U, Pfammatter T, Hany TF, Rainoni L, Hilfiker P, et al. Magnetic resonance angiography versus duplex sonography for diagnosing renovascular disease. Hypertension 1999;33:726-31.
47. Carman TL, Olin JW, Czum J. Noninvasive imaging of the renal arteries. Urol Clin North Am 2001;28:815-26.
48. Jayawardene S, Reidy J, Scoble J. Clinical picture: ipsilateral atherosclerotic and fibromuscular renal artery stenosis. Lancet 2000;356:2138.
49. Aqel R, Gupta R, Zoghbi G. Coexistent fibromuscular dysplasia and atherosclerotic renal artery stenosis. J Invasive Cardiol 2005;17:572-3.
50. Aqel R, AlJaroudi WW, Hage FG, Nanda NC. Renal artery fibromuscular dysplasia is a cause of refractory hypertension in the elderly. Echocardiography 2009;26:109-10.
51. Slavin RE. Segmental arterial mediolysis: course, sequelae, prognosis, and pathologic-radiologic correlation. Cardiovasc Pathol 2009; 18:352-60.
52. Slavin RE, Inada K. Segmental arterial mediolysis with accompanying venous angiopathy: a clinical pathologic review, report of 3 new cases, and comments on the role of endothelin-1 in its pathogenesis. Int J Surg Pathol 2007;15:121-34.
53. Slavin RE, Saeki K, Bhagavan B, Maas AE. Segmental arterial mediolysis: a precursor to fibromuscular dysplasia? Mod Pathol 1995;8:287-94.
54. Inada K, Maeda M, Ikeda T. Segmental arterial mediolysis: unrecognized cases culled from cases of ruptured aneurysm of abdominal visceral arteries reported in the Japanese literature. Pathol Res Pract 2007;203:771-8.
55. Schievink WI, Bjornsson J, Piepgras DG. Coexistence of fibromuscular dysplasia and cystic medial necrosis in a patient with Marfan's syndrome and bilateral carotid artery dissections. Stroke 1994;25:2492-6.
56. Janzen J, Vuong PN, Rothenberger-Janzen K. Takayasu's arteritis and fibromuscular dysplasia as causes of acquired atypical coarctation of the aorta: retrospective analysis of seven cases. Heart Vessels 1999;14:277-82.
57. D'Souza SJ, Tsai WS, Silver MM, Chait P, Benson LN, Silverman E, et al. Diagnosis and management of stenotic aorto-arteriopathy in childhood. J Pediatr 1998;132:1016-22.
58. Bol A, Missault L, Dewilde W. Renovascular hypertension associated with neurofibromatosis: a case report. Acta Clin Belg 2007;62:61-3.
59. Nopajaroonsri C, Lurie AA. Venous aneurysm, arterial dysplasia, and near-fatal hemorrhages in neurofibromatosis type. 1. Hum Pathol 1996;27:982-5.
60. Vuong PN, Le Bourgeois P, Houissa-Vuong S, Martin P, Berrod JL. [Intimal muscular fibrodysplasia responsible for an ischemic gastric ulcer in a patient with a von Recklinghausen's disease: a case report]. J Mal Vasc 2001;26:65-8.
61. Schievink WI, Limburg M. Angiographic abnormalities mimicking fibromuscular dysplasia in a patient with Ehlers–Danlos syndrome, type. IV. Neurosurgery 1989;25:482-3.
62. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. The seventh report of the Joint National Committee on Prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. JAMA 2003;289:2560-71.
63. Davies MG, Saad WE, Peden EK, Mohiuddin IT, Naoum JJ, Lumsden AB. The long-term outcomes of percutaneous therapy for renal artery fibromuscular dysplasia. J Vasc Surg 2008;48:865-71.
64. Trinquart L, Mounier-Vehier C, Sapoval M, Gagnon N, Plouin PF. Efficacy of revascularization for renal artery stenosis caused by fibromuscular dysplasia: a systematic review and meta-analysis. Hypertension 2010;56:525-32.
65. Mahmud E, Brocato M, Palakodeti V, Tsimikas S. Fibromuscular dysplasia of renal arteries: percutaneous revascularization based on hemodynamic assessment with a pressure measurement guidewire. Catheter Cardiovasc Interv 2006;67:434-7.
66. Sperati CJ, Aggarwal N, Arepally A, Atta MG. Fibromuscular dysplasia. Kidney Int 2008;75:333-6.
67. Mounier-Vehier C, Lions C, Jaboureck O, Devos P, Haulon S, Wibaux M, et al. Parenchymal consequences of fibromuscular dysplasia renal artery stenosis. Am J Kidney Dis 2002;40:1138-45.
68. Mounier-Vehier C, Haulon S, Devos P, Lions C, Jaboureck O, Gaxotte V, et al. Renal atrophy outcome after revascularization in fibromuscular dysplasia disease. J Endovasc Ther 2002;9:605-13.
69. De Martino RR, Stone DH. Repair of multiple right renal artery aneurysms with associated fibromuscular dysplasia in a solitary kidney. J Vasc Surg 2009;49:497.
70. Sos TA, Pickering TG, Sniderman K, Saddekni S, Case DB, Silane MF, et al. Percutaneous transluminal renal angioplasty in renovascular hypertension due to atheroma or fibromuscular dysplasia. N Engl J Med 1983;309:274-9.
71. Baert AL, Wilms G, Amery A, Vermylen J, Suy R. Percutaneous transluminal renal angioplasty: initial results and long-term follow-up in 202 patients. Cardiovasc Intervent Radiol 1990;13:22-8.
72. Tegtmeyer CJ, Selby JB, Hartwell GD, Ayers C, Tegtmeyer V. Results and complications of angioplasty in fibromuscular disease. Circulation 1991;83(2 Suppl):I155-61.
73. Bonelli FS, McKusick MA, Textor SC, Kos PB, Stanson AW, Johnson CM, et al. Renal artery angioplasty: technical results and clinical outcome in 320 patients. Mayo Clin Proc 1995;70:1041-52.
74. Jensen G, Zachrisson BF, Delin K, Volkmann R, Aurell M. Treatment of renovascular hypertension: one-year results of renal angioplasty. Kidney Int 1995;48:1936-45.
75. Davidson RA, Barri Y, Wilcox CS. Predictors of cure of hypertension in fibromuscular renovascular disease. Am J Kidney Dis 1996;28:334-8.
76. Klow NE, Paulsen D, Vatne K, Rokstad B, Lien B, Fauchald P. Percutaneous transluminal renal artery angioplasty using the coaxial technique. Ten years of experience from 591 procedures in 419 patients. Acta Radiol 1998;39:594-603.
77. Birrer M, Do DD, Mahler F, Triller J, Baumgartner I. Treatment of renal artery fibromuscular dysplasia with balloon angioplasty: a prospective follow-up study. Eur J Vasc Endovasc Surg 2002;23:146-52.
78. Surowiec SM, Sivamurthy N, Rhodes JM, Lee DE, Waldman DL, Green RM, et al. Percutaneous therapy for renal artery fibromuscular dysplasia. Ann Vasc Surg 2003;17:650-5.
79. De Fraissinette B, Garcier JM, Dieu V, Mofid R, Ravel A, Boire JY, et al. Percutaneous transluminal angioplasty of dysplastic stenoses of the renal artery: results on 70 adults. Cardiovasc Intervent Radiol 2003;26:46-51.
80. Kim HJ, Do YS, Shin SW, Park KB, Cho SK, Choe YH, et al. Percutaneous transluminal angioplasty of renal artery fibromuscular dysplasia: mid-term results. Korean J Radiol 2008;9:38-44.
81. Mouse M, Sabri SS, Park A, Saad WEA, Angle JF, Matsumoto AH. Treatment of renal artery fibromuscular dysplasia. Technol Vascul Intervent Radiol 2010;13:126-33.
82. Barrier P, Julien A, Guillaume C, Philippe O, Herve R, Francis J. Technical and clinical results after percutaneous angioplasty in nonmedial fibromuscular dysplasia: outcome after endovascular management of unifocal renal artery stenoses in 30 patients. Cardiovasc Intervent Radiol 2010;33:270-7.
83. Wells RP, Smith RR. Fibromuscular dysplasia of the internal carotid artery: a long term follow-up. Neurosurgery 1982;10:39-43.
84. Stewart MT, Moritz MW, Smith RB III, Fulenwider JT, Perdue GD. The natural history of carotid fibromuscular dysplasia. J Vasc Surg 1986;3:305-10.
85. Belan A, Vesela M, Vanek I, Weiss K, Peregrin JH. Percutaneous transluminal angioplasty of fibromuscular dysplasia of the internal carotid artery. Cardiovasc Intervent Radiol 1982;5:79-81.
86. Wilms GE, Smits J, Baert AL, De Wolf L. Percutaneous transluminal angioplasty in fibromuscular dysplasia of the internal carotid artery: one

year clinical and morphological follow-up. Cardiovasc Intervent Radiol 1985;8:20-3.
87. Welch EL, Lemkin JA, Geary JE. Gruntzig balloon dilation for fibromuscular dysplasia of the internal carotid arteries. N Y State J Med 1985;85:115-7.
88. Tsai FY, Matovich V, Hieshima G, Shah DC, Mehringer CM, Tiu G, et al. Percutaneous transluminal angioplasty of the carotid artery. AJNR Am J Neuroradiol 1986;7:349-58.
89. Olin JW. Carotid artery fibromuscular dysplasia. Am J Surg 2007;194: 419.
90. Schievink WI. Spontaneous dissection of the carotid and vertebral arteries. N Engl J Med 2001;344:898-906.
91. Edgell RC, Abou-Chebl A, Yadav JS. Endovascular management of spontaneous carotid artery dissection. J Vasc Surg 2005;42: 854-60.
92. Yoshida T, Ohashi I, Suzuki S, Iwai T. Fibromuscular disease of the brachial artery with digital emboli treated effectively by transluminal angioplasty. Cardiovasc Intervent Radiol 1994;17:99-101.
93. Yamaguchi R, Yamaguchi A, Isogai M, Hori A, Kin Y. Fibromuscular dysplasia of the visceral arteries. Am J Gastroenterol 1996;91: 1635-8.
94. Guill CK, Benavides DC, Rees C, Fenves AZ, Burton EC. Fatal mesenteric fibromuscular dysplasia: a case report and review of the literature. Arch Intern Med 2004;164:1148-53.
95. Camuglia A, Manins V, Taylor A, Hengel C. Case report and review: epicardial coronary artery fibromuscular dysplasia. Heart Lung Circ 2009;18:151-4.
96. Burton TM. The 'rare' disease that isn't. Wall Street J June 27, 2009: A-1.

Submitted Oct 5, 2010; accepted Oct 7, 2010.

Additional material for this article may be found online at www.jvascsurg.org.

APPENDIX (online only)
International Registry for Fibromuscular Dysplasia

Jeffrey W. Olin
Study Chair and Principal Investigator
Mount Sinai School of Medicine
New York, NY

James Froliech and Kim Eagle:
Data Coordinating Center: MCORP
University of Michigan
Ann Arbor, Mich

Initial participating centers and principle investigators:

Michael Bacharach
North Central Heart Institute
Sioux Falls, SD

James Froliech
University of Michigan
Ann Arbor, Mich

Heather Gornik
Cleveland Clinic
Cleveland, Ohio

Bruce Gray
Vascular Health Alliance
Greenville, SC

Mark Grise
Ochsner Clinic
New Orleans, La

Robert McBane
Mayo Clinic
Rochester, Minn

Jeffrey W. Olin
Mt Sinai School of Medicine
New York, NY