Contemporary Diagnosis of Carotid Fibromuscular Dysplasia: Role of Power Doppler and a Review of Other Diagnostic Modalities

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Fibromuscular dysplasia (FMD) is a nonatheromatous, noninflammatory arteriopathy with segmental involvement of medium-sized arteries in multiple vascular beds. It most commonly involves the renal and carotid arteries. The etiology is unknown, although various hormonal and mechanical factors have been suggested. The disease can occur at any age but is usually diagnosed in middle-aged individuals, predominantly women. FMD is much more common than previously thought, perhaps affecting as many as 4% of adult women. Clinical manifestations of the internal carotid artery involvement are transitory ischemic attacks or cerebral infarction, as well as nonspecific symptoms such as headache and vertigo. In cases of cerebrovascular events, endovascular or surgical treatment is recommended; therefore, detection of FMD is of considerable importance. The gold standard for diagnosing FMD is catheter angiography (with the classic "string of beads" pattern), but this invasive procedure is only used for patients in whom it is clinically pertinent to proceed with revascularization. The optimal noninvasive modality for diagnosis and quantification for FMD is not known and little information has been recently published about new diagnostic modalities. Although angiography, computed tomography angiography, and magnetic resonance angiography are excellent in confirming the morphologic diagnosis of FMD, they are less accurate in assessing the hemodynamic significance of the lesions. Ultrasonography is useful in assessing the degree of carotid artery stenosis. Use of power Doppler ultrasound improves the ability to detect the morphologic features of carotid FMD.

[Rev Cardiovasc Med. *2013;14(2-4):e136-e143 doi: 10.3909/ricm0653]*

KEY WORDS

Fibromuscular dysplasia • Duplex ultrasonography • Power Doppler • Internal carotid artery

Fibromuscular dysplasia (FMD) is a nonatherosclerotic, noninflammatory vascular disease that primarily affects women aged 20 to 60 years.[1,2] It most commonly affects the renal and carotid arteries but has been observed in almost every artery in the body.[3] Carotid artery FMD has been considered rare and thus is often underdiagnosed and poorly understood by many health care providers. However, FMD is much more common than previously thought (often overlooked or misdiagnosed), perhaps affecting as many as 4% of adult women.[1,2,4]

The diagnosis is based primarily on noninvasive studies such as duplex ultrasound (US), computed tomography angiography (CTA), magnetic resonance angiography (MRA), or by invasive angiography.[5] The ideal diagnostic modality for FMD is one that not only establishes the morphologic diagnosis of the disease but also accurately assesses the hemodynamic significance of the lesions.[5,6] Further, it should allow for safe, convenient, and accurate follow-up of the disease progression. An added benefit would be if it allowed for identification of associated abnormalities, such as cerebral aneurysms.[1,2] Unfortunately, there is no one perfect imaging modality that can do it all.[7]

This report presents three illustrative cases of asymptomatic carotid artery FMD diagnosed using these various imaging modalities. The relative merits of the different imaging modalities used to diagnose and monitor disease progression are discussed. We particularly discuss the role of power Doppler in improving the diagnostic yield of duplex US in the diagnosis of FMD.

Case 1

A 62-year-old woman with a history of hypertension was referred for evaluation of a left carotid bruit. A standard carotid duplex US showed increased peak systolic velocity (PSV) of 1.52 m/s in the mid right internal carotid artery (ICA) indicating moderate (50%-69%) stenosis; the left mid ICA had a PSV of 2.66 m/s indicating a > 70% stenosis (based on the Society of Radiologist Ultrasound consensus conference; Table 1).[8,9] She had no history of neurologic symptoms. CTA showed the classic "string of beads" appearance of the mid ICAs bilaterally, suggestive of FMD (Figure 1). The stenosis on the left side was 30% by CTA. No intracerebral stenosis or aneurysm was seen. With the CTA showing FMD, we repeated the duplex US using power Doppler to see if the morphologic features of FMD could be identified. Power Doppler was used to evaluate the carotid vessel walls and it revealed clear evidence of a beading appearance (Figure 1). She was started on low-dose aspirin, and will have subsequent follow-up with duplex US to monitor hemodynamic severity.

TABLE 1

Society of Radiologists in Ultrasound Criteria for the Diagnosis of ICA Stenosis

% Stenosis	Velocity
0%-49%	ICA PSV < 1.25 m/s ICA EDV < 0.4 m/s ICA/CCA ratio < 2
50%-69%	ICA PSV 1.25-2.3 m/s ICA EDV 0.4-1.0 m/s ICA/CCA ratio 2:4
≥ 70% (but less than near occlusion)	ICA PSV > 2.3 m/s ICA EDV > 1.0 m/s ICA/CCA ratio > 4
Near occlusion	ICA PSV = high, low, or undetectable ICA EDV = variable ICA/CCA ratio = variable
100%	Occluded, no flow detected

ICA, internal carotid artery; CCA, common carotid artery; PSV, peak systolic velocity; EDV, end diastolic velocity. Data from Grant EG et al.[9]

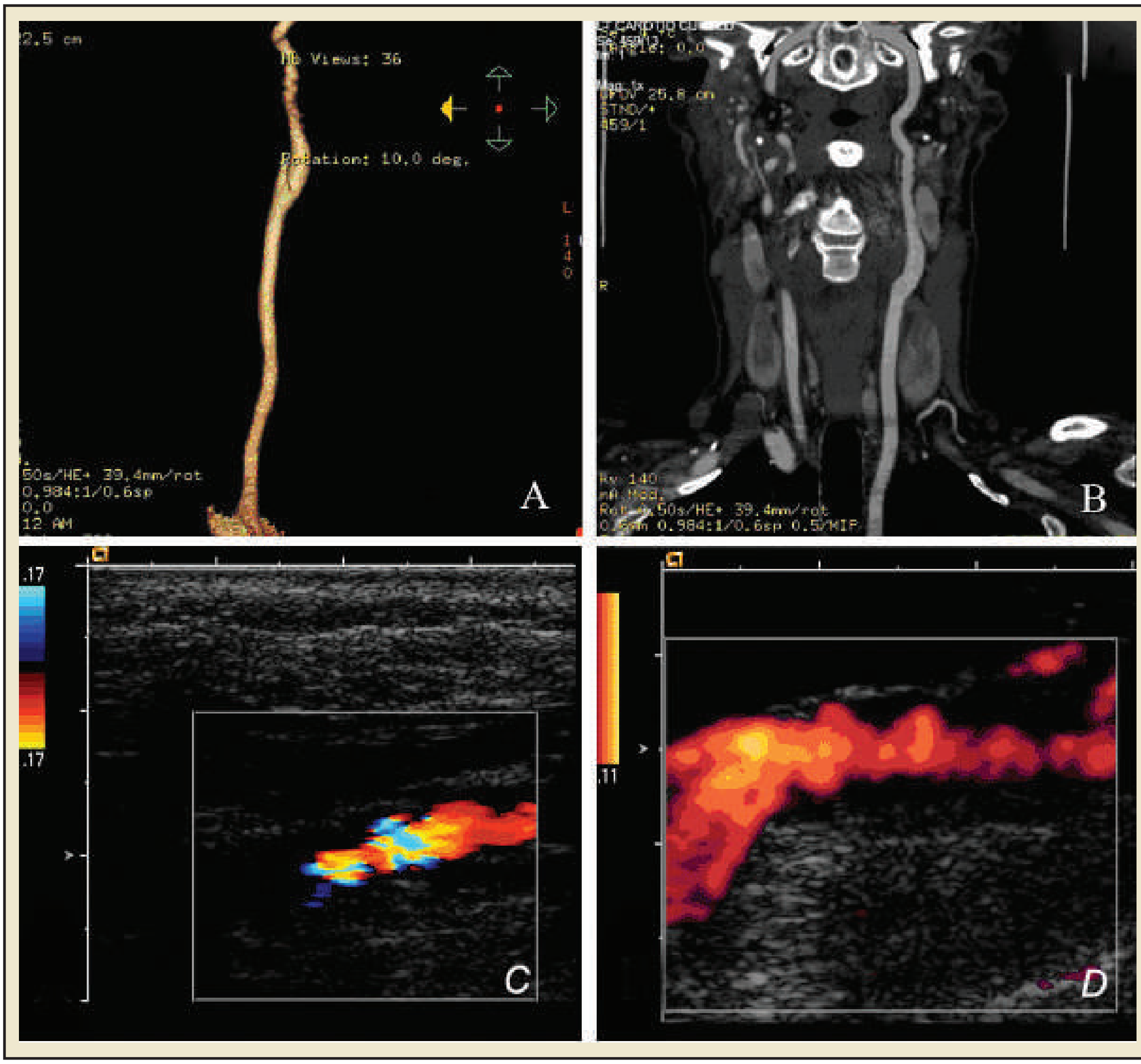

Figure 1. Computed tomography angiogram of the carotid arteries. Three-dimensional reconstruction **(A)** and coronal section **(B)** revealing the classic "string of beads" appearance of the left internal carotid artery (ICA) suggestive of carotid fibromuscular dysplasia (FMD). Doppler ultrasonography of the left ICA with color Doppler **(C)** shows turbulent flow but not the beaded appearance. Power Doppler **(D)** revealing the typical "string of beads" appearance of carotid FMD.

Case 2

A 54-year-old woman was referred for bilateral carotid artery disease. She had been diagnosed with moderate (50%-69%) bilateral distal carotid artery disease 4 years previously using duplex US at our institution. Recently, we repeated a follow-up duplex US of the carotid arteries, revealing worsening disease with an increased PSV of 2.8 m/s of the distal right ICA indicating a > 70% stenosis (Table 1). She was asymptomatic. Her examination was significant for bilateral carotid bruit. Due to the unusual pattern of limited distal carotid artery atherosclerotic disease, a repeat duplex US was performed with power Doppler revealing a clear morphologic pattern of carotid FMD with classic beading appearance (Figure 2). Carotid angiography confirmed the diagnosis of distal bilateral carotid and bilateral vertebral artery FMD (Figure 2). There were no intracerebral findings of FMD or aneurysm. She was started on low-dose aspirin and will have subsequent clinical follow-up for symptoms with duplex US to evaluate for increasing velocities.

Case 3

A 64-year-old asymptomatic woman was referred for bilateral carotid bruits. Her physical examination was unremarkable except for bilateral carotid bruit. She underwent carotid duplex US that showed moderate (50%-69%) mid left ICA stenosis with a PSV of 1.8 m/s (Table 1). CTA of the neck showed undulating luminal irregularities

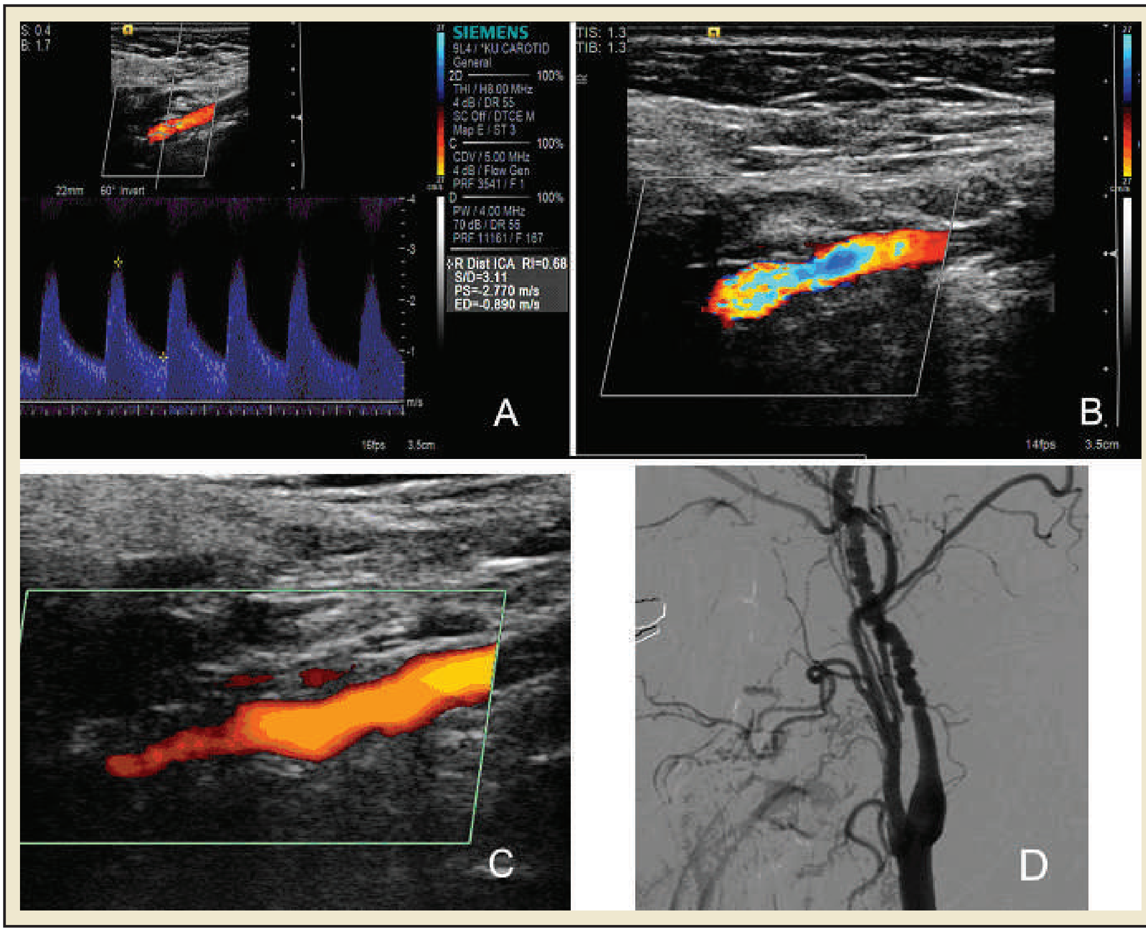

Figure 2. Doppler ultrasonography **(A, B)** of the internal carotid artery with color Doppler shows increased velocities with turbulent flow but not the beaded appearance. Power Doppler **(C)** revealing the typical “string of beads” appearance of carotid fibromuscular dysplasia. Carotid angiography **(D)** with typical fibromuscular dysplasia appearance is shown.

involving the mid and distal ICA, as well as bilateral vertebral arteries that were mostly consistent with a diagnosis of FMD (Figure 3). A repeat duplex US was performed with power Doppler, which also showed a beading appearance of the distal left ICA characteristic of FMD (Figure 3). She will have clinical follow-up with duplex US to assess for increasing velocities.

Discussion

Carotid artery FMD may result in arterial narrowing and aneurysm formation.[1,2] Although the true prevalence of this condition is not known, there appears to be a significant delay from the time symptoms first appear until diagnosis.[10] In addition, carotid FMD is poorly understood and diagnosis is often missed, leading to potential serious sequelae.[4,11] It is most frequently located in the middle and distal part of the ICAs at the level of C1-C2 and is usually bilateral.[3,11] It often presents at a mean age of 50 years, and more often in women.[1,3]

Carotid FMD is primarily asymptomatic and is usually discovered when a cervical bruit is heard or when imaging is performed for another reason.[11] There are a myriad of nonspecific symptoms or signs that frequently occur in patients with carotid FMD, such as headache, pulsatile tinnitus, neck pain, and a swishing sound in the ears. More focal and specific neurologic signs and symptoms that may occur include transient ischemic attack, cerebral infarction, subarachnoid hemorrhage, syncope, Horner syndrome, and cranial nerve palsies. Symptoms may be related to one or more of the following mechanisms: severe stenosis producing hypoperfusion, embolization, thrombosis, dissection, or aneurysm rupture.[2,4,11]

The gold standard for diagnosis of FMD is considered catheter-based angiography showing the classic beading appearance.[3,6] With the advancement of noninvasive diagnostic modalities, the ability to diagnose and monitor carotid FMD

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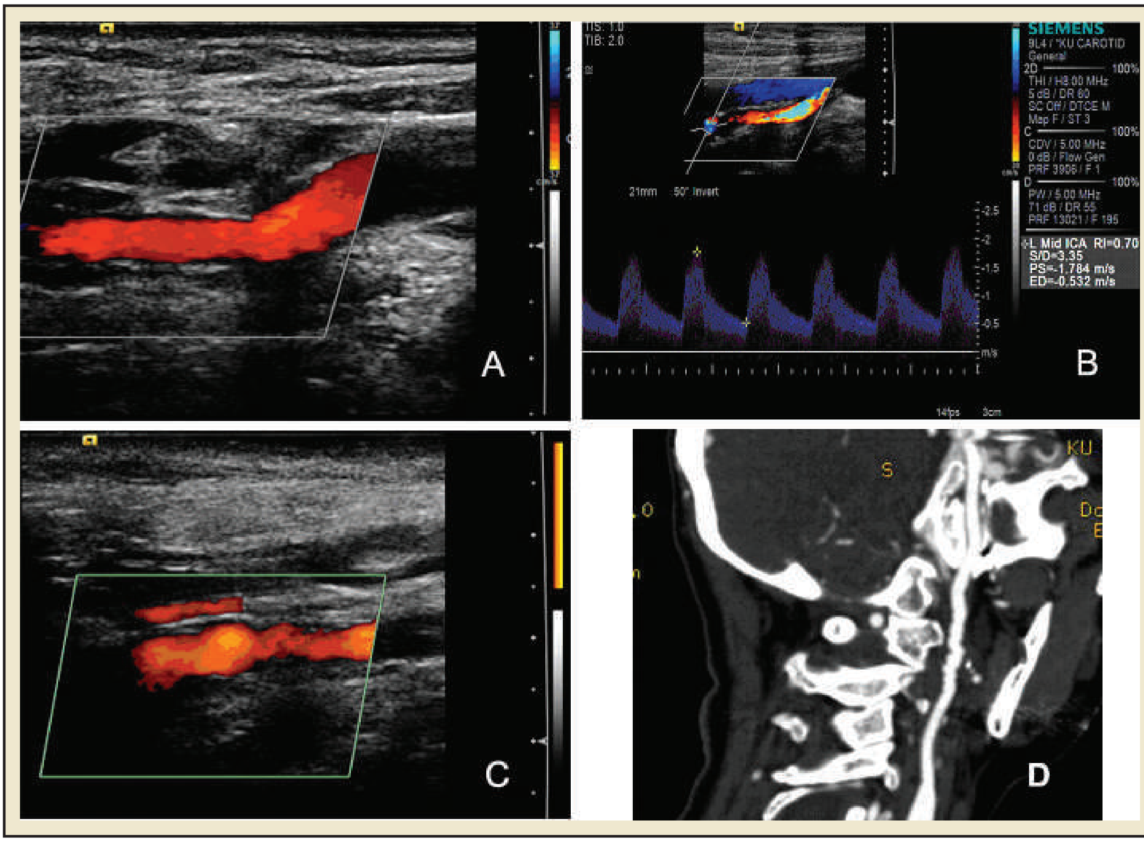

Figure 3. Doppler ultrasonography **(A, B)** of the internal carotid artery (ICA) with color Doppler revealing the increased velocities and mild turbulent flow. Power Doppler **(C)** revealing the typical "string of beads" appearance of carotid fibromuscular dysplasia (FMD) not previously seen on Doppler ultrasonography. Computed tomography angiogram **(D)** of the carotid arteries revealing the classic "string of beads" appearance of the ICAs suggestive of carotid FMD.

has increased significantly. This includes modalities such as duplex US, MRA, and CTA. Each modality has its specific strengths and drawbacks.[4-6] An optimal imaging modality should be able to discern all aspects of carotid FMD. In our opinion, these include the identification of the classic morphologic string of beads/undulating pattern of the most common variety of FMD (medial fibroplasia), definition of the extent of involvement (extra- and intracranial), and categorization of hemodynamic severity of stenosis and ancillary association (presence of intracerebral aneurysm). Further, the imaging modality should not pose significant risk, and should be reproducible and readily available at reasonable cost. Various strengths and weaknesses of these modalities are summarized in Table 2. We especially emphasize the role of power Doppler, as we believe that it is significantly underutilized in the diagnosis of FMD.

TABLE 2

A Comparison of Different Imaging Modalities for the Diagnosis of Carotid FMD

	US	CTA	MRA	Angiography
Morphologic diagnosis	+/++[a]	++/+++	++	+++
Categorization of stenosis	+++[b]	++	+	++
Follow-up	+++	+/++	+/++	+
Intracranial pathology	—	+++	+++	+++

—, no or minimal utility; +, some utility; ++, moderate utility; +++, strong utility.
[a]Increased sensitivity probably with the use of power Doppler due to better wall delineation.
[b]Suboptimal for intracranial lesions.
CTA, computed tomography angiography; FMD, fibromuscular dysplasia; MRA, magnetic resonance angiography; US, ultrasound.

Duplex US

Duplex US is readily available, portable, and the safest imaging modality. It is also the most economical. It has the advantage of being the most common screening modality for carotid artery disease in general. Although highly sensitive for the diagnosis of carotid atherosclerosis, nonatherosclerotic lesions such as FMD are less readily appreciated.[7,12] A study by Arning and Grzyska[12] showed that the sensitivity of color Doppler for diagnosing FMD was significantly less than angiography. Perhaps the greatest difficulty of a duplex US diagnosis of FMD is the limited imaging of the distal region of the ICA and the inability of conventional gray scale and color imaging to identify the morphologic characteristics. However, duplex US can, in most cases, detect flow disturbances in the mid and distal ICA, and has significant value in detecting degree of hemodynamic stenosis. It may be the only modality that can be used to follow the progression of hemodynamic significance of an FMD lesion.[7,12,13] It should be noted, however, that even though most laboratories use the same criteria for grading severity as are used for atherosclerotic carotid disease in the proximal ICA, these have never been validated for FMD.[1,7] In our view, such a validation would be quite difficult because, unlike atherosclerotic disease, angiography itself is not a reliable tool for grading severity of stenosis in FMD.

Lesions, especially those of the distal ICA, may not be well visualized if no hemodynamically significant flow disturbances are found, thus lowering sensitivity compared with angiography.[5,7,12] However, even in the absence of significant stenosis, some flow disturbance is usually noted due to abnormal morphology. The biggest limitation of duplex US in the diagnosis of FMD is that, although it can detect stenosis, it offers poor delineation of the intimal layer.[5,12]

Power Doppler US (also called ultrasound angiography) allows for improved definition of the vessel walls.[13] This may increase the sensitivity of duplex US for the diagnosis of carotid FMD. With power Doppler US, the color map displays the integrated power of the Doppler signal; this power is related to the number of erythrocytes creating the Doppler frequency shift. This method differs from the traditional color Doppler US, in which the mean frequency shift is measured. The advantage of power Doppler US is that noise, which is composed of low-amplitude signals, is assigned a uniform color that remains constant, whereas flow information is assigned a contrasting color. This arrangement allows use of higher color gain settings and improves the sensitivity of color Doppler US without compromising image quality and adversely affecting signal-to-noise ratio.[14] In addition, power Doppler US has been reported to be three to five times more sensitive than conventional color Doppler US, relatively angle independent, and unaffected by aliasing.[14,15]

The benefits of using power Doppler include better visualization of vessel walls as well as flow and is much less dependant of the probe angle when compared with standard color Doppler.[14,15] This is especially useful in FMD, in which the distal ICA location often precludes optimal angle of insonation.[7,14] As demonstrated in all three of our cases, duplex US was able to definitively diagnose FMD on power Doppler images but not on conventional color sonography. To our knowledge, no studies have systematically looked at the use of power Doppler in evaluation of carotid artery FMD. It has, however, been evaluated better in the renal vasculature. Hélénon and colleagues[15] evaluated power and conventional color Doppler in 916 patients suspected of having renal artery FMD. Power Doppler was able to provide superior morphologic diagnostic information in 77% of renal artery stenotic lesions, including 9 of the 49 lesions consistent with FMD. To our knowledge, there are no comparable studies comparing power Doppler versus color Doppler for lesions of the carotid artery. Thus, duplex US is a good modality in the follow-up of progression of the disease and, when combined with power Doppler, may also help confirm the morphologic diagnosis of FMD. However, it is obviously a suboptimal tool for delineating intracranial stenosis and for intracerebral aneurysms.[4,14]

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CTA and MRA

CTA and MRA are the modalities that most commonly detect/confirm the diagnosis of FMD.[7] Most cases are detected incidentally in scans done for neurologic symptoms that may or may not be related to FMD.[5] In addition, CTA and MRA may diagnose FMD when performed to further define a stenosis found during duplex US.[4,5] Unlike duplex US, both these modalities are excellent in the detection of intracranial lesions and intracranial aneurysms (that have a higher incidence in

FMD). Further, they can easily diagnose any associated carotid artery dissections that are also more frequent with FMD.[7,14,16] Although both CTA and MRA can visualize all portions of the carotid arteries, and have a fairly good spatial resolution (CTA better than MRA),[17] they may not detect subtle FMD due to limitations of their resolution.[7,16] Conventional angiography is the gold standard in this regard. There are no good studies comparing their sensitivity or specificity in detecting cerebrovascular FMD with catheter-based angiography.[7,16] In a case series, de Monyé and associates[16] showed that CTA has better sensitivity and specificity than US, especially in the distal ICA. Though quite good in confirming the morphologic diagnosis of FMD, CTA and MRA have limited ability in quantification of the degree of stenosis. Unlike focal stenosis, the diffuse and beaded nature of the disease makes it difficult to accurately quantify the degree of stenosis.[17,18] Thus, CTA and MRA are not optimal modalities for following the hemodynamic progression of FMD disease severity.[1,7]

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Conventional Angiography

This is considered the gold standard for the diagnosis of carotid FMD.[7] Angiography has the best spatial resolution of all the modalities to diagnose FMD. Further, it can fully define the extent of involvement, including intracranial lesions, aneurysms, and dissections. However, even angiography is limited in the assessment of the hemodynamic significance of FMD.[7,19] There are no data in this regard for carotid artery FMD. However, for renal FMD, angiography has been shown to be a poor determinant of stenosis severity and does not always correlate with improved hypertension control after angioplasty. In renal FMD, measurement of translesional pressure gradients using coronary pressure wires has been shown to be a useful method of estimating the true severity of stenosis and has been shown to be more accurate than angiography.[20,21] This technique, however, involves wire manipulation in the affected artery and the risks would be high in the carotid vasculature. We do not believe that wire instrumentation of the carotid with FMD is easily justified for purely diagnostic purposes.

Conclusions

Carotid artery FMD is often underdiagnosed. Invasive angiography is considered the gold standard for diagnosis. However, multiple noninvasive diagnostic modalities such as duplex US, CTA, and MRA are used for the diagnosis and management of patients with FMD. Although angiography, CTA, and MRA are excellent in confirming the morphologic diagnosis of FMD, they are less accurate in assessing the hemodynamic significance of the lesions. Duplex US is less helpful in making a morphologic diagnosis but is useful in assessing the degree of carotid artery stenosis. Use of power Doppler ultrasound improves the ability of ultrasound to detect the morphologic features of carotid FMD. ■

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MAIN POINTS

- Fibromuscular dysplasia (FMD) affects perhaps as many as 4% of adult women, and is frequently underdiagnosed.
- An optimal imaging modality should be able to discern all aspects of carotid FMD. Although no imaging modality is perfect, conventional angiography has the best spatial resolution of all these modalities to diagnose FMD. Further, it can fully define the extent of involvement, including intracranial lesions, aneurysms, and dissections.
- Duplex ultrasonography is helpful in assessing the hemodynamic significance of the FMD lesions. However, unlike for atherosclerotic lesions, stenosis severity criterion have not been validated for FMD lesions.

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