Heather L. Gornik, MD

The Cleveland Clinic vascular medicine specialist shares her insights on recent fibromuscular dysplasia research and selecting medical therapy for PAD patients.

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What are your recommendations for diagnostic assessment of critical limb ischemia (CLI)? What tests should be part of a complete vascular lab?

I think the vascular laboratory is the most obvious first stop for the CLI patient. The most basic tool would be the ankle-brachial index (ABI), but in the CLI population, there is a high prevalence of diabetes and end-stage renal disease with associated vascular calcifications. This potentially leads to inaccurate assessment of disease severity. For this reason, in the setting of CLI, I believe that ABIs with plethysmographic waveforms at the ankle (at minimum) are needed, as well as a toe pressure for the toe-brachial index. Beyond these basic tools, microcirculation assessment can be helpful to determine the healing potential and local perfusion environment of a wound, including the use of transcutaneous oximetry and laser Doppler, but not all clinicians have fully embraced this. Segmental pressures and waveforms can be useful to localize disease and get the surgeon or interventionist in the anatomic ballpark (eg, recognition of multilevel disease vs more localized occlusive disease). Complete arterial duplex examination is time-intensive, but can provide extensive arterial mapping for planning revascularization, especially for patients with renal failure in whom computed tomographic or magnetic resonance angiography must be avoided. Of course, arterial duplex (combined with physiological testing, usually the ABI) plays a central role in evaluating the CLI patient after revascularization, whether it is after bypass grafting or stenting.

What is your usual protocol for selecting the best pharmacological option for peripheral arterial disease (PAD) patients?

First and foremost, I start with cardiovascular risk reduction therapies, because what gets most patients who have PAD into trouble in the long haul isn't their claudication or limb threat, but myocardial infarction or stroke. I utilize antiplatelet therapy and a statin for all of my PAD patients and an ACE inhibitor or ARB for the majority of patients without a contraindication. Smoking cessation (including nicotine replacement, varenicline, or bupropion) is an important element of this treatment as well. In terms of medical therapy for claudication, the choices are few and far between—we basically have two FDA-approved drugs. I might try cilostazol for the stable claudicant, and the literature has shown that this does provide modest benefit. I strongly think medical therapy for patients with PAD is an important area of unmet medical need. We just need more tools to work with.

How do you foresee the use of drug-eluting stents for the superficial femoral artery (SFA) affecting the use of dual-antiplatelet therapy in the US?

I am interested in seeing more data on this. I want to see how much they improve long-term patency, and I am, of course, interested to see if there is any signal of delayed stent thrombosis. In some cases, this may be moot, as many of my PAD patients are already on dual-antiplatelet therapy for coronary indications.

In which SFA cases do you not recommend best medical therapy?

Before answering this, I'll emphasize that we really need better data to prove that SFA revascularization improves functional outcomes in patients with stable PAD beyond medical therapy. The world literature on medical/exercise therapy versus SFA revascularization for claudication is very sparse and is overshadowed by the large number of clinical trials that have investigated different interventional strategies and devices for SFA disease.

That being said, I definitely think there is a subset of PAD patients with SFA lesions who need more than medical therapy. Obviously, the patient with CLI falls into this category (who likely has multilevel disease), but also the patient who is highly limited by his/her claudication symptoms, has tried medical therapy but has failed, or who has a vocational limitation. When I see a patient in consultation or follow-up for claudication, I generally spell out the different treatment options, including revascularization. I think it's also important to engage the PAD patient in the decision making.

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What are some of the most important data points from the initial look at the United States Registry for Fibromuscular Dysplasia (FMD) published earlier this year? How do you anticipate these conclusions affecting care for FMD in the future?

My involvement in the FMD registry has been a highlight of my vascular career. In our publication on the first 447 patients in the United States FMD registry, we had a number of important discoveries, including that cerebrovascular FMD is basically as common as renal FMD, the average age of diagnosis of the typical FMD patient is in his or her 50s, and the realization that FMD is a disease that not only causes stenotic lesions and hypertension, but also has potential for major vascular morbidity including transient ischemic attack/stroke, arterial dissection (especially carotid and renal), and significant arterial aneurysm.

The finding that there was a significant family history of aneurysms among family members of the FMD patients supports a strong genetic component of this disorder. The recognition that FMD often presents in multiple vascular beds within the same patient and the association with occult arterial aneurysm are two findings that I foresee having a positive impact on FMD care. I do think FMD patients should undergo brain to pelvis imaging assessment, at least once, to assess for disease extent and aneurysmal disease. Beyond that initial assessment, surveillance can be targeted to the vascular beds involved.

What is the correlation between FMD and Mendelian vascular connective tissue disorders?

With one of our former medical students (Dr. Stacey Poloskey), we recently published our single-center experience in *Vascular Medicine* of genetics testing for vascular

Ehlers-Danlos syndrome (Col3A1 mutation) and Loeys-Dietz syndrome (TGF-beta receptors 1/2 mutations) in a subset of our FMD patients who had a personal or family history of significant aortic or arterial aneurysms or arterial dissection. The yield of clinical genetic testing was quite low—no overlap with vascular Ehlers-Danlos syndrome. We did identify two patients with TGF-beta receptor variants, but the significance of these genetic variants is uncertain. Interestingly, both of these patients had FMD, prior cervical artery dissection, and aortic ectasia. Clearly, there is much work to be done in terms of understanding the genetic underpinnings of FMD, and I don't think the standard clinical connective tissue disorder panel is helpful in most cases.

Which patients benefit most from percutaneous interventional therapies for atherosclerotic renal artery stenosis? How is this determined?

I'm waiting for the CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions) data, but I don't know if it will provide the definitive answer. I have seen a marked dampening of enthusiasm for renal artery stenting at my own institution and others at national meetings, likely on the basis of ASTRAL (Angioplasty and Stenting for Renal Artery Lesion) and other studies. Right now, I really reserve referring patients for renal revascularization for those with severe, drug-refractory hypertension (blood pressure still very high on three or more medications at maximum doses, including a diuretic) or those with bilateral high-grade renal artery stenosis.

The first component of the American College of Cardiology Foundation's appropriate use criteria for peripheral vascular ultrasound and physiological testing was published earlier this year. What were some of the goals of the review, and what can we expect to see in part II?

Mainly, I think the document was an important first step to bring the principles of appropriate use into the vascular laboratory and to bring a multidisciplinary writing and technical panel to review the data regarding testing. The document is not perfect, but I think it did highlight some areas where there really is no indication for testing, but testing is performed anyhow in some labs and other areas where we really need more data (and there are a lot of them, I am afraid). The writing committee identified six key areas in need of clinical and cost-effectiveness research. A few of these were investigation of the cost-to-benefit of screening carotid artery duplex examinations prior to open heart surgery, determination of the optimal frequency of ultrasound surveillance for asymptomatic carotid artery stenosis, and comparative effectiveness of duplex ultrasound versus CT angiography for surveillance following aortic endografting.

I would like to see the document lead to more focused research on the cost effectiveness of vascular lab testing for certain indications versus other modalities. Part II will focus on testing for venous disease.

As a vascular medicine specialist, what do you consider your role to be in the patient care continuum at the Cleveland Clinic?

One of the best parts of my job is that my role in patient care as a vascular medicine specialist varies from day to day. During a typical week at the Clinic, I play many roles. I might be the vascular lab reader for a surveillance study after aortic endografting, I might do a STAT read on a venous duplex with an acute deep vein thrombosis, and I might do a thrombin repair of an arterial pseudoaneurysm. In my clinic, patients come to see me for a first opinion on how to best manage their claudication or FMD, and I might refer that patient for a revascularization procedure or put together a plan for medical therapy and surveillance. I have a good-sized practice of patients with atherosclerotic vascular disease for whom I serve as both cardiologist (for their atrial fibrillation, congestive heart failure, and coronary disease) and vascular doctor (for PAD, abdominal aortic aneurysms, carotid artery disease, and varicose veins), and I follow some patients with isolated venous disease, too. For many of the FMD patients, I serve as the "FMD primary care physician" and engage other members of our multidisciplinary team when I think additional consultation or revascularization/aneurysm repair is needed.

I spend time on our vascular medicine consult service where we assist in the management of venous thromboembolism and anticoagulation primarily, but I am also called in to help out with those "zebra cases" (for example, I recently saw a fascinating inflammatory abdominal aortic aneurysm case). The dynamic nature of my role in patient care, the diversity of diagnoses I encounter, and the large number of terrific colleagues with whom I regularly interact is definitely a big draw for me in terms of this job. It's a really busy place, but I feel fortunate to work here and to be able to practice noninvasive vascular medicine at the highest level. ■

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