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Lower extremity arterial disease Diagnostic aspects

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The prevalence of peripheral arterial disease (PAD) continues to increase, with recent data suggesting that almost 30% of patients in at-risk populations have PAD [1]. Interest in the management of PAD has increased, partly secondary to the technologic advancement of devices and procedures capable of treating a wide array of vascular disorders via endoluminal techniques. A thorough clinical evaluation and accurate noninvasive testing remain the cornerstones of successful patient management and will promote improved outcomes through better patient selection. The utility of physiologic tests for determination of the presence and severity of PAD and more sophisticated imaging studies will allow the cardiovascular specialist to make appropriate decisions about management options. The currently accepted methods for determining the presence of peripheral arterial disease include a historic review of patient symptoms and atherosclerotic risk factors, physical examination, and the appropriate use of noninvasive modalities including duplex ultrasound and magnetic resonance arteriography, and x-ray digital subtraction angiography (x-ray DSA).

Noninvasive vascular testing

The ankle-brachial index

The most important first test after the history and physical examination is the ankle-brachial index (ABI). This simple, painless, highly reproducible test may be performed in a physician's office and requires a blood pressure apparatus and a hand-held, continuous-wave Doppler probe. This test compares the blood pressure obtained with the hand-held Doppler in the dorsalis pedis or posterior tibial artery (whichever is higher) with the blood pressure in the higher of the two brachial pressures. Generally, an ABI $\geq$0.9 is considered normal, $>$0.4 to $\leq$0.9 reflects mild to moderate PAD, and $\leq$0.4 suggests severe lower extremity arterial disease (Fig. 1). The ABI has emerged as one of the most potent markers of diffuse atherosclerosis, cardiovascular risk, and overall survival in many patient populations. For example, in a study of 2023 middle-aged men screened with the ABI, the relative risks of mortality from all causes, cardiovascular causes, and coronary causes was significantly higher in patients with an ABI $<$ 0.90 than in patients with a normal ABI [2]. In a population of 1492 women over the age of 65, the relative risk of all-cause mortality, heart disease, and cardiovascular disease was significantly greater when the baseline ABI was $\leq$0.90 [3]. Finally, in a study of more than 5000 men and women over 65 years of age, it was found that the lower the ABI, the greater the incidence of cardiovascular risk factors and clinical cardiovascular disease [4].

The ABI may be normal or high ($>$1.3) in patients (especially diabetics) with extensive medial vascular calcification, which renders the vessel relatively incompressible. In such cases, a toe brachial index (TBI) may be of value because digital arteries are much less susceptible to medial calcification. Digital arterial pressures are normally less than the brachial pressure, and a normal TBI is 0.7. A TBI $<$0.7 is consistent with claudication, and an index less than 0.2 correlates with rest pain. Table 1 reviews the potential limitations of the ABI.

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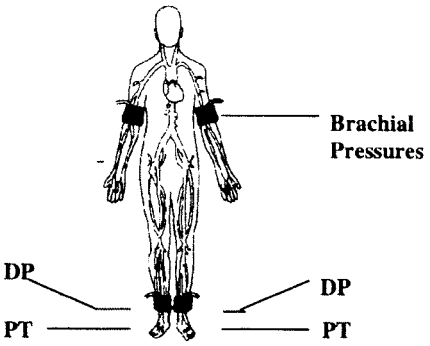

Rest ABI	Interpretation
0.90-1.30	Normal
0.70-0.89	Mild
0.40-0.69	Moderate
<0.40	Severe
>1.30	Non-Compressible Vessels

Pointers in Rest ABI Measurement

- Use higher of two brachial pressures if different
- Use higher of two ABI's (at DP or PT levels) if different
- Request a Toe Brachial Index if vessels non- compressible

Fig. 1. Interpreting ABIs.

Table 1
Limitations of common vascular laboratory tests

Test	Limitations
ABI	May be normal in patients with aorto-iliac disease and in well collateralized patients at rest May be artifactually normal (or "supernormal") in patients with arterial calcification (diabetes mellitus, end-stage renal disease) Does not define location of disease or stenosis versus occlusion
Segmental limb pressures	Pressures inaccurate when arteries are calcified (similar to ABI) Thigh cuff may sometimes produce an artifactual high pressure and may miss aorto-iliac/femoral lesions Does not discern between stenosis or occlusion Thigh pressures may be uncomfortable for some patients
Pulse volume recording or Doppler waveform analysis	Qualitative indices of disease NOT quantitative
Arterial duplex ultrasonography	Requires expensive equipment and trained technologist and tends to be operator dependent Examination times may be >60 minutes Calcified arteries limit visualization of arterial lumen and determination of stenosis No functional information
MRA (3D contrast)	Expensive equipment Bolus timing is a problem in patients with vascular disease Signal to noise ratio lower in small-caliber vessels at ankle Post-processing techniques are complicated and time consuming No functional information unless combined with other studies, such as phase-contrast MRA

Abbreviations: ABI, ankle-brachial index; MRA, magnetic resonance arteriography.

Segmental limb pressures and pulse volume recordings

Once the ABI has been performed, providing objective evidence of the presence and overall severity of PAD, more specific information can be obtained to localize the disease process by the addition of segmental limb pressures (SLP). A series of limb pressure cuffs are placed on the thigh, calf, ankle, transmetatarsal region of the foot, and digit. The ABI is calculated, and the pressure is sequentially inflated in each cuff to approximately 20 to 30 mm Hg above systolic pressure. Using a continuous-wave Doppler probe placed on a pedal artery, the pressure in the cuff is gradually released, and the pressure at each segment is measured. A decrease in pressure between two consecutive levels of >30 mm Hg suggests arterial disease of the artery proximal to the cuff. In addition, when comparing the two limbs, a 20- to 30-mm Hg discrepancy from one limb to the other at the same cuff level suggests significant arterial disease proximal to the cuff [5].

Pulse volume recordings (PVR) are plethysmographic measurements that detect changes in the volume of blood flowing through a limb. Using similar equipment as described for segmental pressures, limb cuffs are inflated to ~65 mm Hg, and a plethysmographic tracing is recorded at various levels [6]. The normal PVR is similar to the normal intra-arterial pulse wave tracing and consists of a rapid systolic upstroke and rapid downstroke, with a prominent dicrotic notch. With increasing severity of disease, the waveform becomes more attenuated, with a wide downslope, and, ultimately, virtually absent waveforms.

Doppler waveform analysis

Doppler waveform analyses can be used in lieu of pulse wave recordings, although they tend to be more operator dependent than PVRs. Used in conjunction with SLP, the waveform analysis provides additional information in assessing the extent and location of disease. The normal waveform is triphasic and includes forward and reverse (diastolic) components. With progression, the reverse component is lost, and the waveform becomes biphasic. When forward flow becomes continuous, the waveform is considered monophasic. With severe disease, the waveform amplitude is attenuated (Fig. 2). Patterns of arterial flow may be recorded using a continuous Doppler over the femoral, popliteal, posterior tibial, and the dorsalis pedis arteries.

Ankle-brachial indices in conjunction with SLPs and PVR/Doppler waveform analysis are useful objective tests in the evaluation of a patient with suspected PAD or limb discomfort without an obvious cause as methods for evaluating the success of an intervention and as parameters for longitudinal follow-up (Figs. 3 and 4). The test is inexpensive, painless, reproducible, and relatively easy to perform. The equipment required to perform these examinations is significantly less expensive than modern color-flow duplex ultrasound units. There are some limitations associated with ABIs, SLP, and PVR/Doppler waveform analysis, which are detailed in Table 1.

Treadmill exercise arterial studies

Treadmill exercise arterial studies measure the lower extremity arterial circulation's response to exercise. The normal response to exercise is a slight increase or no change in the ankle systolic pressures compared with resting pressures. If ankle systolic pressure decreases by at least 20 mm Hg, the test is considered positive. Constant-grade testing (2 miles per hour at a 12% incline to a maximum of 5 minutes) and variable-grade testing (0% at start, increased by 2.0% every 2 minutes) are acceptable. Exercise arterial studies are helpful in making the diagnosis in patients with unclear

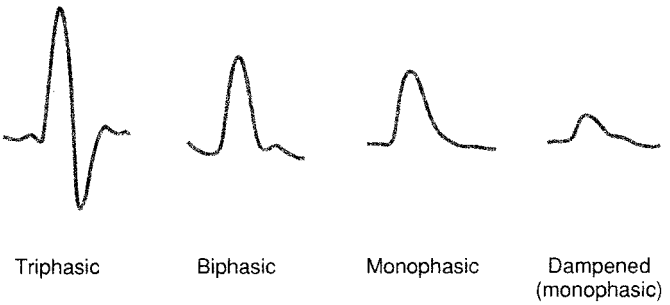

Fig. 2. Doppler waveform analysis.

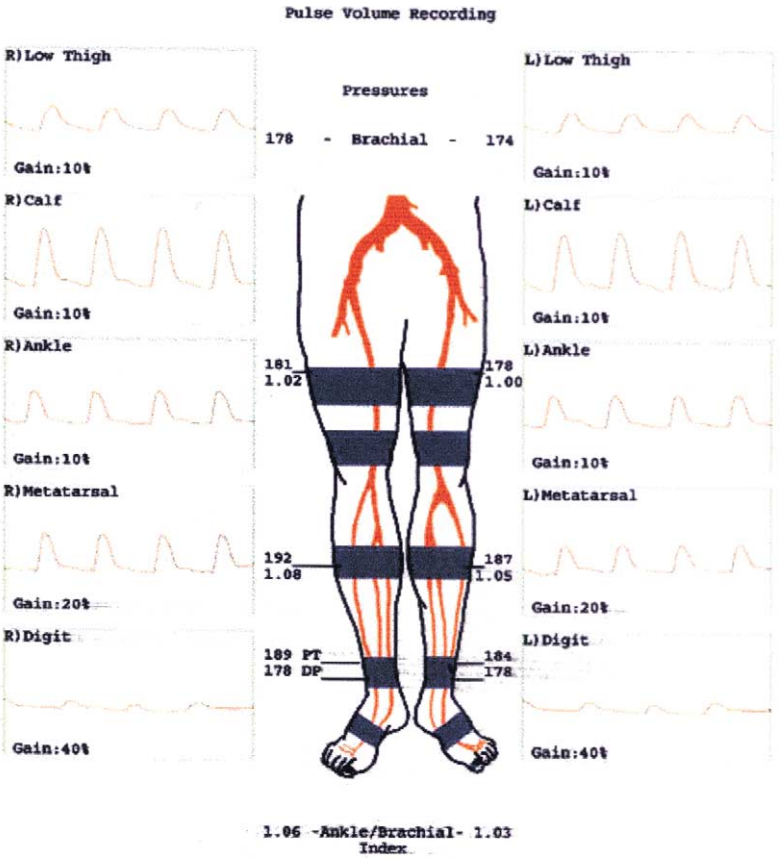

Fig. 3. Normal lower extremity physiologic study. The ABIs are 1.06 on the right and 1.03 on the left—both normal. The segmental limb pressures and pulse volume recordings are normal bilaterally. The patient had a normal response to exercise on a graded treadmill test despite having exertional limb symptoms, suggesting a neurogenic etiology for limb discomfort.

history and an ABI at rest that is normal or mildly reduced (Fig. 5). They may also serve as a useful index of disease severity, to assess response to an intervention, and to serially follow patients. Exercise studies also provide functional information and should be considered in all patients in whom the diagnosis of peripheral arterial disease has been made. Two components of the response to exercise are evaluated: (i) the magnitude of the immediate decrease in ankle systolic pressure and (ii) the time for recovery to resting pressure. The initial and absolute claudicating distances (ICD, ACD) are easily calculated from the treadmill test and are useful as objective measures of treatment effect.

Arterial duplex ultrasonography

Arterial duplex ultrasonography is performed in most modern vascular laboratories and is widely accepted as a precise method for defining arterial stenoses and occlusions. The sensitivity of duplex ultrasonography to detect occlusions and stenoses has been reported to be 95% and 92%, respectively, with specificities of 99% and 97%, respectively [7]. Limitations have included tandem stenoses [8], tibial vessel imaging [9], and difficulty imaging the inflow arteries [10] (see Table 1).

Using a 5.0- to 7.5-MHz transducer, imaging of the supra- and infrainguinal arteries is performed. The vessels are studied in the sagittal plane, and Doppler velocities are obtained using a 60° Doppler angle. Vessels are classified into one of five "stenosis severity" categories: normal, 1% to 19% stenosis, 20% to 49% stenosis, 50% to 99% stenosis, and occlusion. The categories are determined by alterations in the Doppler waveform and by comparing increasing peak systolic velocities within the stenosis and the normal artery proximal

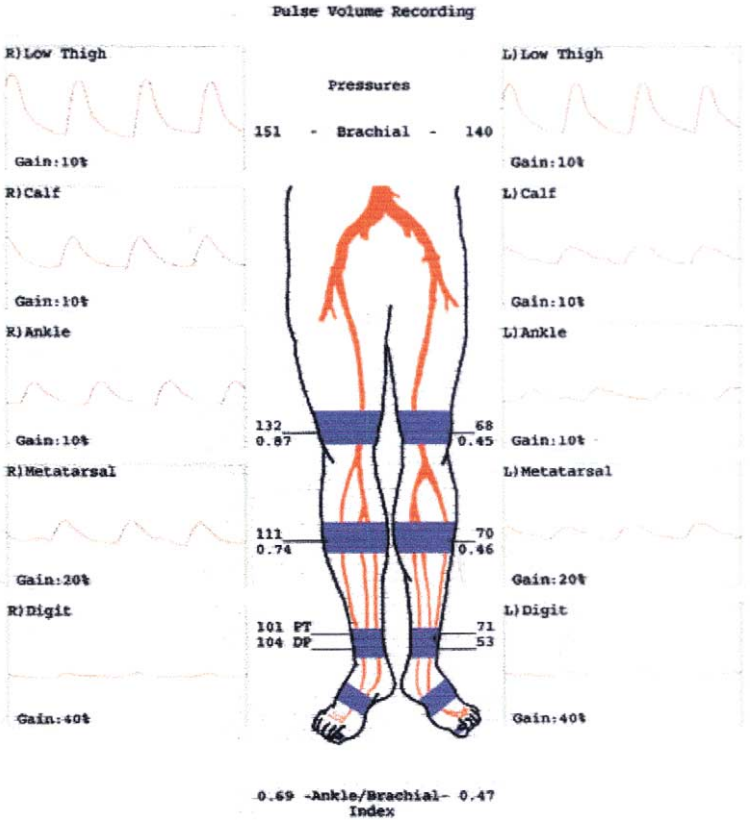

Fig. 4. Abnormal lower extremity physiologic study. The ABIs are markedly abnormal at rest (0.69 right; 0.47 left). The segmental limb pressures and PVRs suggest bilateral femoropopliteal disease. This patient was able to ambulate for 1 minute, 40 seconds on a graded treadmill and had a dramatic reduction in limb pressures after exercise.

to the stenosis. For a stenosis to be classified as 50% to 99%, for example, the peak systolic velocity must increase by 100% in comparison to the normal segment of artery proximal to the stenosis [11].

Arterial duplex ultrasonography can reliably demonstrate stenoses in deep abdominal arteries (Fig. 6) and has been used to guide endovascular therapy [12] and to determine technical success [13] and durability of endovascular procedures [14] (Fig. 7). There are data to suggest that duplex ultrasonography within 30 days of balloon angioplasty may overestimate the residual stenosis and may be a limitation of this technology soon after endovascular therapy [15].

Graft surveillance

Patients who have undergone surgical bypass graft revascularization, particularly with saphenous vein, are at increased risk of developing stenoses, which increase the risk of graft failure. Once the graft thromboses, secondary patency rates are dismal. If the stenosis is detected and repaired before graft thrombosis, it is estimated that 80% of grafts will be salvaged [16]. A well organized graft surveillance program is crucial in preserving patency of bypass grafts. In one series of 170 saphenous vein bypass grafts, 110 stenoses were detected over a 39-month period. Grafts that underwent surgical revision once a stenosis was detected demonstrated a 4-year patency of 88%, whereas grafts that did not undergo revision despite the detection of a stenosis demonstrated a 4-year patency of 57% [17]. The use of an intensive surveillance program has been less beneficial in prosthetic grafts [18].

The procedure for graft surveillance is performed in a similar manner to that used in native vessel arterial duplex ultrasonography. The inflow artery to the bypass graft is initially imaged using a 5.0- to 7.5-MHz transducer and a Doppler angle of 60°. Subsequently, the proximal anastomosis; proximal, mid, and distal graft; distal anastomosis;

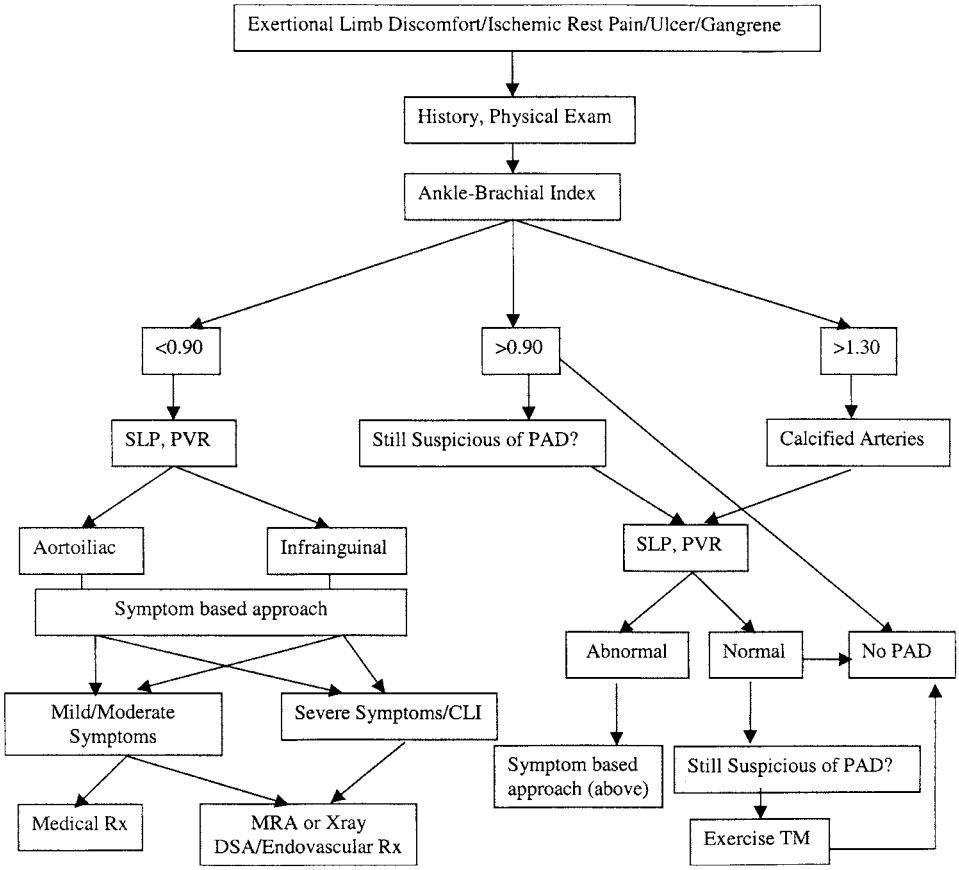

Fig. 5. Suggested diagnostic algorithm for the evaluation of lower extremity arterial disease.

and outflow artery are interrogated. Peak systolic and end-diastolic velocities are obtained at each segment and compared with the segment of graft proximal to the area being studied. If the ratio of the peak systolic velocity within a stenotic segment relative to the normal segment proximal to the stenosis is >2, this suggests 50% to75% diameter reduction. The additional finding of end-diastolic velocities >100 cm/s suggest >75% stenosis (Fig. 8) [19].

Vein bypass grafts should be studied within 7 days of surgery and then in 1 month and every 3 months for the first year. If the graft ultrasonography remains normal after 1 year, follow-up surveillance should be performed every 6 months thereafter. Ankle pressures and waveforms should be performed at the time of each surveillance study. The development of a stenosis during a surveillance examination should prompt consideration of further evaluation with arteriography (contrast or using magnetic resonance technology) [20].

Duplex ultrasonography is helpful in identifying areas of vascular trauma, specifically iatrogenic. Pseudoaneurysms occur in up to 7.5% of femoral artery catheterizations [21] and can result in significant complications, including distal embolization into the native arterial system; expansion; and extrinsic compression on neurovascular structures, rupture, and hemorrhage. Duplex ultrasonography can rapidly and accurately identify these lesions. In addition, direct ultrasound-guided compression [22] or, more recently, ultrasound-guided thrombin injection [23] can repair these lesions without the need for more invasive surgical procedures.

Magnetic resonance arteriography

The single greatest advance in diagnosis of peripheral arterial disease in the last 10 years has been magnetic resonance arteriography (MRA).

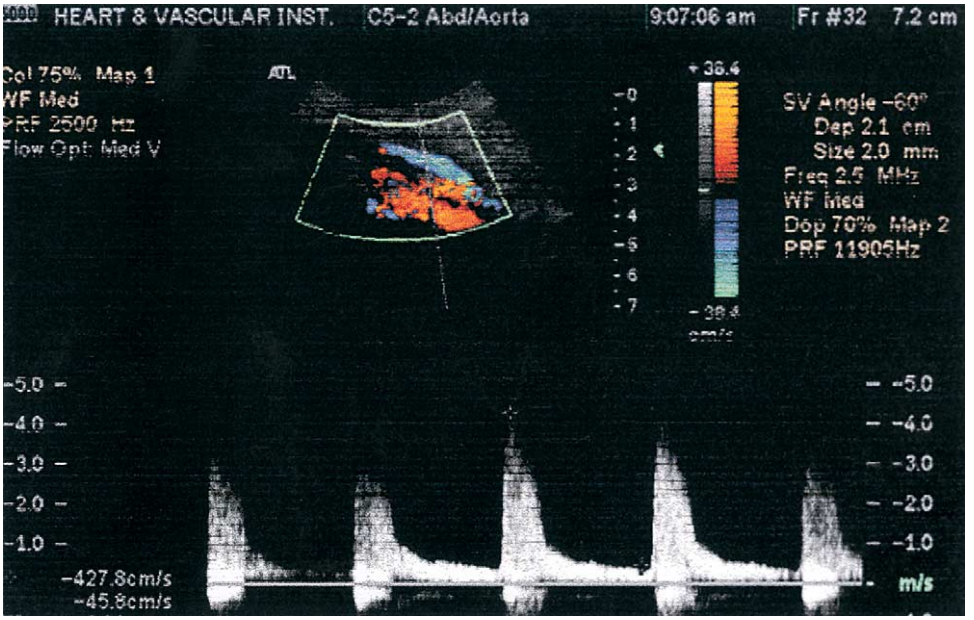

Fig. 6. Arterial duplex ultrasound examination demonstrating a 50% to 99% right common iliac artery stenosis. The image is technically adequate and reveals a peak systolic velocity of 427.8 cm/s. The peak systolic velocity of common iliac artery just proximal to this stenosis was 88.2 cm/s.

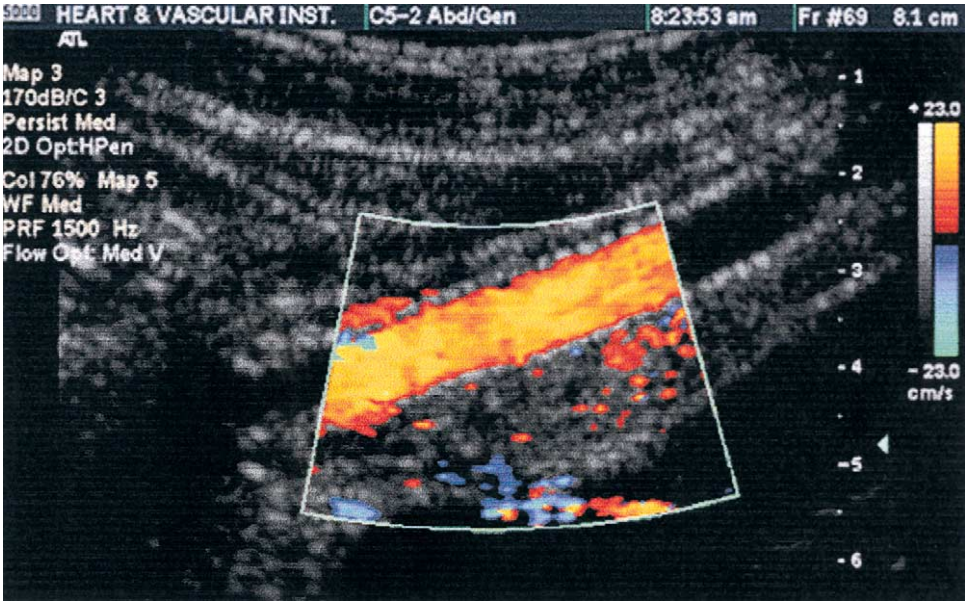

Fig. 7. Arterial duplex ultrasound examination performed after placement of an endoluminal stent in the left external iliac artery. Note the smooth color flow within the stent. The struts of the stent are easily visible.

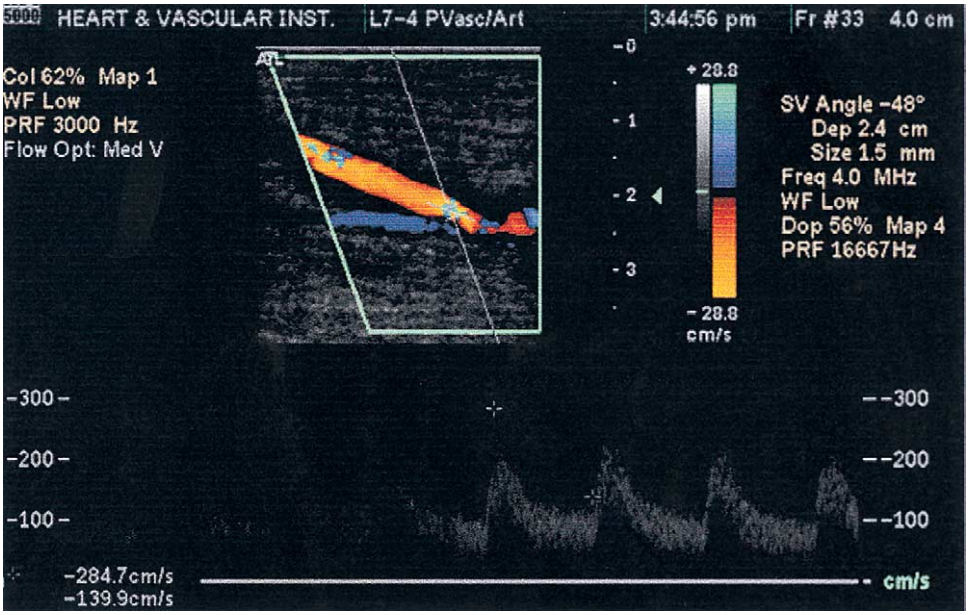

Fig. 8. Arterial duplex ultrasound image of the distal anastomosis of a bypass graft. The peak systolic and end-diastolic velocities are 284.7 and 139.9 cm/s, respectively, correlating with a >75% stenosis.

MRA is capable of imaging flowing blood with and without the administration of gadolinium-based MR contrast agents (3D-contrast MRA). 3D contrast MRA takes advantage of the T1 relaxation properties of gadolinium. By shortening the T1 relaxation time of blood, it is possible to acquire MR arteriograms in which image contrast is based on differences in T1 relaxation between blood and surrounding tissues. Unlike conventional MRA techniques that do not require contrast (eg, phase contrast MRA [PC-MRA] and e2D-time of flight [2D-TOF], which depend on phase or velocity shifts and are therefore susceptible to flow and motion artifacts), 3D contrast MRA is devoid of such issues and provides high-resolution in-plane imaging. Gadolinium is non-nephrotoxic and is administered via an intravenous infusion in a small forearm vein. With a 3D imaging pulse sequence (spoiled gradient echo sequences), it is possible to obtain entire 3D data sets in less than 1 minute. Post-processing of these images on an independent workstation can yield multi-planar reformations that enable one to view the 3D data set in multiple views. Additional reformation techniques include maximum intensity projections (MIPs) and subvolume MIPs that appear no different than conventional arteriographic images (Fig. 9). Multiple studies have evaluated the accuracy of 3D MRA and have found that this technique is as accurate as conventional contrast angiography [24]. 2D-TOF is generally too time consuming and inaccurate in the patient with PAD with multiple stenosis and is of limited utility. PC-MRA techniques additionally may provide data on the hemodynamic severity of stenosis. This and other concepts in peripheral MRA techniques are discussed further in the article on MRA (see the article elsewhere in this issue) and in other excellent reviews [25].

Invasive vascular testing

X-Ray digital subtraction angiography

X-ray DSA is widely used for the diagnosis of peripheral arterial disease because the resolution obtained with 3D contrast MRA at most centers is not adequate to visualize smaller, diffusely diseased "run-off" arteries. However, ideally X-ray DSA should be performed only in patients in whom the decision has been made to intervene to relieve symptoms and/or salvage the limb. In the patient with critical limb ischemia (CLI), it is the procedure of choice in centers that are not adept at performing routine high-quality 3D contrast MRA (bolus chase/floating table MRA), provided there are no contraindications to receiving con-

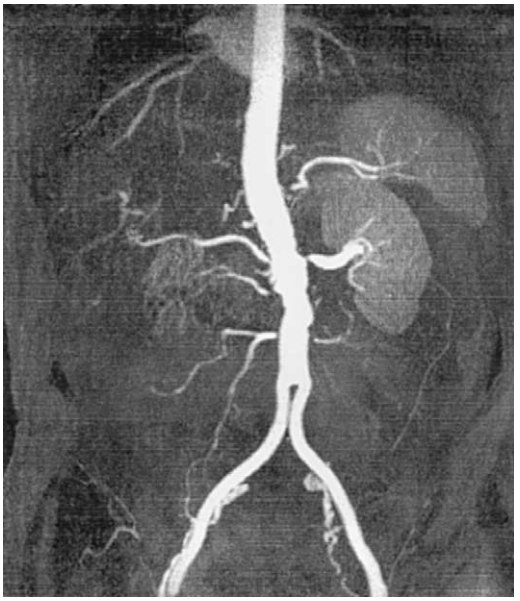

Fig. 9. Magnetic resonance arteriogram with gadolinium demonstrating a patent infrarenal abdominal aorta and iliac arteries. Incidentally noted is a focal ostial left renal artery stenosis.

trast media (eg, advanced renal insufficiency or contrast allergy).

Current diagnostic algorithms in PAD

The evaluation of a patient with PAD begins with an accurate history and physical examination followed by an ABI (Fig. 5). If the symptoms are strongly suggestive of intermittent claudication, physiologic limb studies (segmental pressures and PVRs) with exercise treadmill testing are appropriate. If the patient has symptoms consistent with limiting (moderate to severe) intermittent claudication and physical findings suggestive of aorto-iliac disease where endovascular methods of revascularization (percutaneous transluminal angioplasty) may be appropriate, proceeding to MRA or directly to contrast arteriography with plans for intervention are valid approaches. If the patient's symptoms (claudication) and physical findings are suggestive of infrainguinal disease, medical therapy may be attempted in conjunction with a vigorous exercise program. If the patient's symptoms are progressive and not responsive to these measures, MRA or x-ray DSA are reasonable strategies in determining revascularization strategies, depending on the center's expertise in these techniques. In patients with CLI, directly proceeding to x-ray DSA is the most commonly accepted practice.

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