2 Noninvasive Diagnostic Evaluation of Peripheral Arterial Disease

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INTRODUCTION

The pathogenesis of arterial stenosis or occlusion may be secondary to a wide spectrum of etiologic factors including atherosclerosis, thrombosis, embolic events of various etiology, fibromuscular dysplasia, vasculitidies, dissection, trauma, external compression, and vasospastic syndromes. Atherosclerosis is by far the most common cause of arterial stenosis.

Atheromatic plaques have been identified as early as the first two decades of life, but usually become hemodynamically significant after the age of 50. They can develop in most of the arteries in the body, and are most commonly located in the area of arterial bifurcations. A hemodynamically significant arterial stenosis reduces blood flow in the capillary bed distal to it. The extent of this interference is related to the severity of the stenosis and is determined by strict hemodynamic principles. Tissue perfusion distal to an arterial stenosis can be maintained by development of a network of collateral vessels around the stenosis,

From: *Clinical Hypertension and Vascular Diseases: Lower Extremity Arterial Disease*
Edited by: D. G. Caralis and G. L. Bakris © Humana Press Inc., Totowa, NJ

increase of the cardiac performance, and dilatation of the local arterioles and precapillary sphincters.

There are three levels of occlusive disease in the lower limb arteries: aortoiliac, femoropopliteal, and infrapopliteal disease. Disease confined to one level may be asymptomatic or it can present with intermittent claudication. The presence of two or three levels of disease are symptomatic, and patients usually present with severe claudication or rest pain. Three levels of disease are often seen in patients with skin damage and critical limb ischemia. Without an intervention most limbs with critical ischemia will be amputated within 1 year. In patients with diabetes mellitus the disease is usually confined in the infrapopliteal vessels. Such patients may develop critical limb ischemia with one level of disease because this is the most distal of the three. Usually, multiple stenoses and/or occlusions are found in at least two of the run-off arteries. Although it is known that atherosclerosis develops most often in bifurcations, in the lower extremities the most frequently involved site is the superficial femoral artery. Other common sites are the aortoiliac, iliac, femoral popliteal, and tibioperoneal trunk bifurcations.

DIAGNOSTIC EVALUATION

History and Physical Examination

The evaluation of a patient with lower extremity arterial occlusive disease starts with a detailed history and a complete physical examination *(1).* A thorough pulse exam of both upper and lower extremities is of outmost importance. Absence of palpable pulses at any level indicates hemodynamically significant lesion(s) to the main artery proximal to that level. Thus, absence of palpable femoral pulses is suggestive of severe stenosis or occlusion of the ipsilateral iliac artery *(2).*

Physiological Testing

Hemodynamic testing of the lower extremity includes noninvasive methods that evaluate the dynamic function of the circulation. Various techniques have been developed for noninvasive assessment including segmental pressures, ankle-brachial indices, continuous-wave Doppler waveform analysis, pulse volume recordings, transcutaneous oximetry, treadmill testing, and duplex scanning. Inexpensive equipment and a short learning curve have made hemodynamic testing widely used for the diagnosis of lower extremity arterial disease.

Systolic pressures can be taken at different locations in the lower extremities to help identify the location of arterial disease. Most commonly, pressures are taken at the high thigh, lower thigh, calf, and ankle.

A pressure gradient > 20 mmHg between cuffs is considered indicative of significant arterial disease. For example, a pressure difference of >20 mmHg between the high and low thigh cuffs indicates the presence of a hemodynamically significant superficial femoral artery stenosis. Segmental pressures can give a general idea of the location of the disease, but cannot ascertain the exact site, extent, or severity of a lesion *(3)*.

The ankle-brachial index (ABI) is the best screening test to evaluate the presence or absence of arterial disease in the lower extremities. It is a ratio between the systolic pressure at the ankle in the arms (Fig. 1). In a person with normal arterial circulation, the ankle pressures should be equal or greater than the brachial pressures. Therefore, the normal ABI value is one or higher. Any patient with an ABI <0.9 has lower extremity arterial occlusive disease. The ABI is an important tool in diagnosing and following up arterial disease *(4)*. It is helpful in the follow-up of patients who have undergone revascularization procedures such as angioplasty or bypass grafting. Success of these procedures and progression of disease can be monitored using the ABI. For example, during follow-up of patients who underwent infrainguinal bypass grafting, a drop of >0.15 in the ABI would indicate the development of significant stenosis either in the graft or in the native arteries. In patients with calcified noncompressible arteries, the ABI is of no value because erroneously high pressures are measured in the lower limb. In these occasions a toe pressure is taken instead *(1)*.

Continuous-wave (CW) Doppler waveforms are commonly used in conjunction with segmental pressures or ABIs. Waveforms can help in identifying the location of arterial disease in the lower extremity. Waveforms are usually taken from the common femoral, superficial femoral, popliteal, dorsalis pedis, and posterior tibial arteries and recorded on a strip chart recorder. Qualitative analysis of the waveforms is performed to identify abnormalities in the arterial circulation. The presence of triphasic waveforms at any level indicates absence of a hemodynamically significant arterial lesion proximal to that level. Attenuated waveforms that have lost their triphasic appearance indicate an arterial stenosis proximally.

Pulse volume recordings (PVRs) are similar to the waveforms obtained by CW Doppler and can be used to identify location of disease in the lower extremity. Blood pressure cuffs are placed on the high thigh, low thigh, calf, and ankle of the lower extremity. Cuff pressure changes reflect a change in cuff volume, which reflects changes in limb volume. Pulse volume recordings from each site can be recorded on a strip chart recorder. Differences in the PVR waveforms can be used to determine the location and severity of arterial disease.

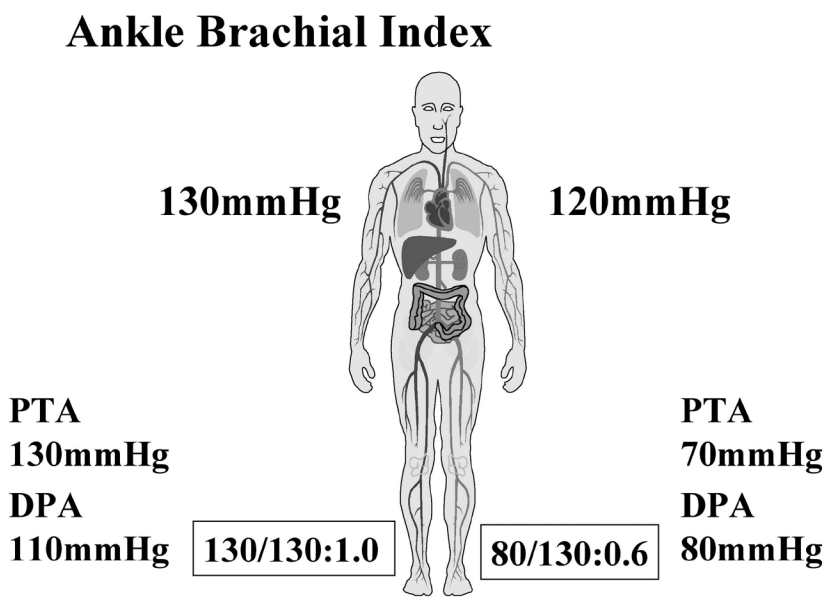

Fig. 1. The measurement of ABI involves bilateral arm pressure measurements. The highest arm pressure is used in the estimation of the ABI. Of the arteries at the ankle level the highest pressured is used.

Transcutaneous oximetry (TCPO2) can be used in the lower extremity to evaluate the oxygen supply to the skin. This procedure is used most often in patients with severe arterial disease requiring surgical reconstruction or amputation. TCPO2 values are obtained by placing an electrode on several areas in the lower extremity. Most commonly, values are taken at the chest (control) above the knee, below the knee, and at several areas on the foot. A measurement can also be taken on the dorsum of the foot with a 30 degree elevation. TCPO2 values can be helpful in patients who have nondiagnostic ABIs (falsely elevated pressures as a result of calcification of vessels). Values obtained from TCPO2 measurements can aid the surgeon in decisions regarding amputation site and healing potential.

Segmental pressures (ABIs) and CW waveforms at rest can be normal in patients with significant arterial lesions. This can be caused by collateral circulation providing adequate flow without significant reduction in pressure. CW waveforms can appear normal if the sample is taken distal to a lesion, where the flow has had a chance to normalize. By exercising a patient on a treadmill, the working muscles require increased blood flow. Symptoms and their severity can be reproduced and walking time

can be documented. In the event of a significant arterial lesion, pressures will drop after exercise. *Treadmill testing* can provide a baseline for patients who have undergone interventional or reconstructive procedures. Improvement or progression of disease can be followed with exercise testing.

Toe pressures can be taken using a photoplethysmography (PPG) probe. A small cuff (2.5 cm) is placed around the digit and the PPG probe is attached with double-stick tape to the pad. Toe pressures can be used in patients with nondiagnostic segmental pressures resulting from calcific vessels. A toe pressure >80 mmHg is normal. Pressures from 80–30 mmHg indicate mild to moderate disease and those <30 mmHg indicate critical disease.

Skin perfusion pressure measurements are taken with laser Doppler. Skin perfusion pressure is used in patients with critical limb ischemia requiring surgical reconstruction or amputation. Like the toe pressures, it is useful in patients with falsely elevated pressures caused by arterial wall calcification.

Color Flow Duplex Scanning

Duplex scanning (with or without color flow) combines a B-mode image with Doppler spectral waveform analysis. Unlike segmental pressures or continuous-wave Doppler waveforms, duplex scanning allows direct visualization of the arterial segment. Location and severity of the disease can be documented with high accuracy. Duplex scanning can also differentiate between different types of disease such as stenosis, occlusion, or thrombosis. Using velocity criteria, the degree of stenosis can be documented *(5).* Color flow can be helpful in identifying changes in velocity resulting from an arterial stenosis. These changes are used to calculate the severity of stenosis *(5).* Thus, duplex scanning provides a combination of anatomic and physiologic information that other imaging or physiologic testing modalities cannot offer.

Basic Principles

Inertial losses depend on the kinetic energy of the blood ($DP = K\ 1/2pv^2$). Because p is a constant changes occur only in the velocity. These changes are significant across a severe stenosis *(6).* According to the equation of continuity, flow (cross-sectional area x velocity) is the same at any point along a tube segment with no branches

$$A1V1 = A2V2 \qquad \text{or} \qquad A1/A2 = V2/V1$$

The V2/V1 from the equation, where V2 is the peak systolic velocity (PSV) at the stenotic segment and V1 the PSV at the normal diameter

segment proximal to the stenosis, is being used to detect significant stenosis in peripheral arteries *(7)*. This ratio is not applicable in the internal carotid artery because the carotid bulb diameter is usually 1.2 times larger than the common carotid diameter, and therefore other complex flow phenomena occur *(8)*. This is one of the main reasons for which different laboratories have to establish their own criteria to detect carotid artery stenosis.

Blood flow in large vessels at rest is laminar with relatively uniform velocities. Narrowing or obstruction causes disruption of the laminar flow, creating vortices and whirls of different velocities and directions. This flow is called turbulent and generally characterizes flow across an area of stenosis (*6*).

Critical Stenosis

A stenosis is hemodynamically significant when a reduction in the blood pressure or flow is being observed. In an experimental setting it has been shown that pressure or flow decrease when a lesion produces at least 75% *area reduction*. This decrease in the luminal area corresponds to a 50% *axisymmetric diameter stenosis (6,9–12)*.

The energy loss across a stenosis is inversely proportional to the fourth power of the minimal radius at the stenosis, and to the ratio of the fourth power of the radius at the prestenotic and stenotic site. It also depends on the blood flow velocity. In a low resistance high-flow artery, flow reduction occurs at a lesser degree of narrowing than in a low-flow (high resistance) artery. Therefore, the resistance of the vascular bed distal to the lesion also affects the energy loss across the stenosis. This phenomenon is well illustrated in the lower extremity arteries where at rest *(high-resistance low-flow system)* may be nonsignificant, but during exercise *(low-resistance high-flow system)* may become significant *(6)*.

The length of the stenosis accounts for viscous energy loss as shown by the Poiseullie's equation. However, such energy loss is less significant compared to that occurring from further reduction in the vessel's diameter. The amount of resistance offered by a stenosis depends largely upon entry and exit blood flow phenomena. This explains why a 2 cm long stenosis in an artery would produce much less resistance than two separate 1 cm long stenoses with the same degree of narrowing *(6)*.

Diagnostic Criteria for Arterial Stenosis by Duplex Scanning

Criteria for detecting significant stenosis have been developed for peripheral arteries. These criteria have been derived by correlating the ultrasound parameters to angiography, pressure measurements across the stenosis, and measurements on operative specimens. For peripheral

arteries and grafts a V2/V1 ratio >2.0 *(7,13,14)* indicates the presence of significant stenosis; this is the most widely recommended diagnostic criterion (Fig. 2). However, few centers are using as a cut-off value a ratio >2.5 for better specificity and a very small reduction in sensitivity. A pooled analysis using the above criteria showed that the sensitivity and specificity for detecting aortoiliac stenosis were 86%, 95% CI 80–91 and 97%, 95% CI 95–99, respectively *(14)*. A V2/V1 ratio >5.5 and/or an end-diastolic velocity >60 cm/s indicates that the diameter reduction is >75%. A DPSV (PSV difference across a stenosis) >160 cm/s at rest has shown a sensitivity of 85% and a specificity of 88% in the aortoiliac segment. After exercise a DPSV >160 cm/s has a sensitivity of 100% and a specificity of 82% *(15)*.

The waveform pattern obtain by duplex scanning can also be used for diagnosing proximal or distal disease *(16,17)*. A triphasic waveform in the common femoral artery indicates that the ipsilateral proximal vessels are normal. A biphasic waveform would indicate stenosis that is not significant, and a monophasic waveform would signify the presence of significant stenosis or occlusion (Fig. 3). A low-end diastolic velocity indicates a tight stenosis or occlusion distal to the measurement (Fig. 4).

Presently, there are no standards by which hemodynamic testing is used. Initially, a clinical examination is performed in an outpatient setting. Depending on the signs and symptoms of arterial insufficiency, any of the earlier discussed tests may be performed. It should be noted that in many centers, the decision to perform a noninvasive test may be linked to the type of treatment the patient will receive. For example, a physician who plans to treat a claudication patient with an angioplasty or a bypass procedure might request a duplex scan. On the other hand, a duplex scan would not be considered in a patient where no intervention is planned. The following are basic algorithms that can be helpful in deciding which method of testing is most beneficial in patients presenting with claudication and rest pain.

In a patient presenting with symptoms of an acute arterial occlusion, time is critical. If the limb is threatened on physical exam, the patient should proceed to angiography/surgery without noninvasive testing. In a nonthreatened limb with suspected occlusion, ABIs can be performed along with a duplex scan. A duplex scan can help to identify the source of occlusion or confirm a thrombotic event, such as in the territory of a peripheral aneurysm or a stenosis (Fig. 5).

Traditionally, arteriography has been the *gold standard* for diagnosis of arterial disease. The recent advancement of duplex scanning has enabled some centers to perform lower extremity revascularization procedures without angiography. Several studies in the last decade have shown

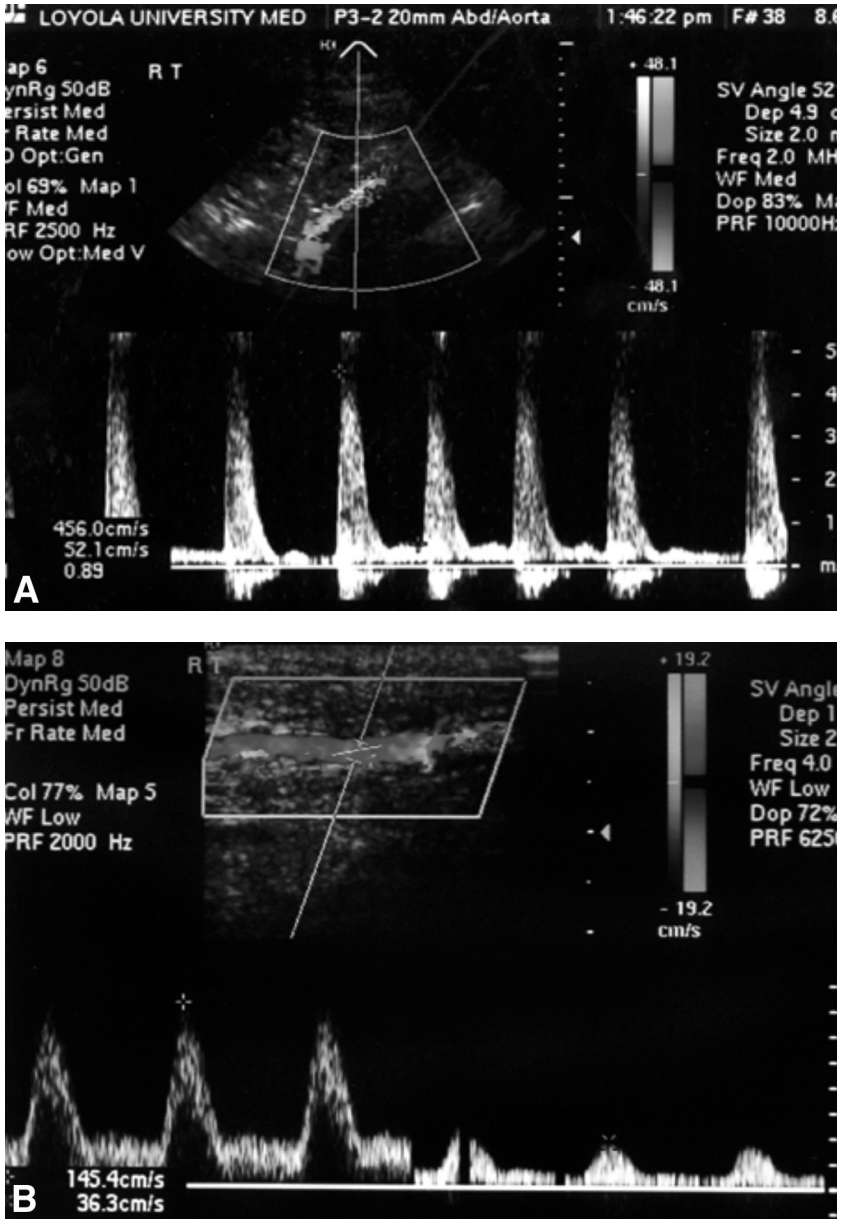

Fig. 2. Significant stenosis in peripheral arteries. **(A)** Stenosis in the common iliac artery. Both the peak systolic and end diastolic velocities are significantly increased. The V2/V1 was 3.9 (456/117) indicating a >50% diameter stenosis. **(B)** Stenosis in the anterior tibial artery. The prestenotic (36 cm/s) and the poststenotic (145 cm/s) velocities are obtained to estimate the V2/V1 ratio (4.0).

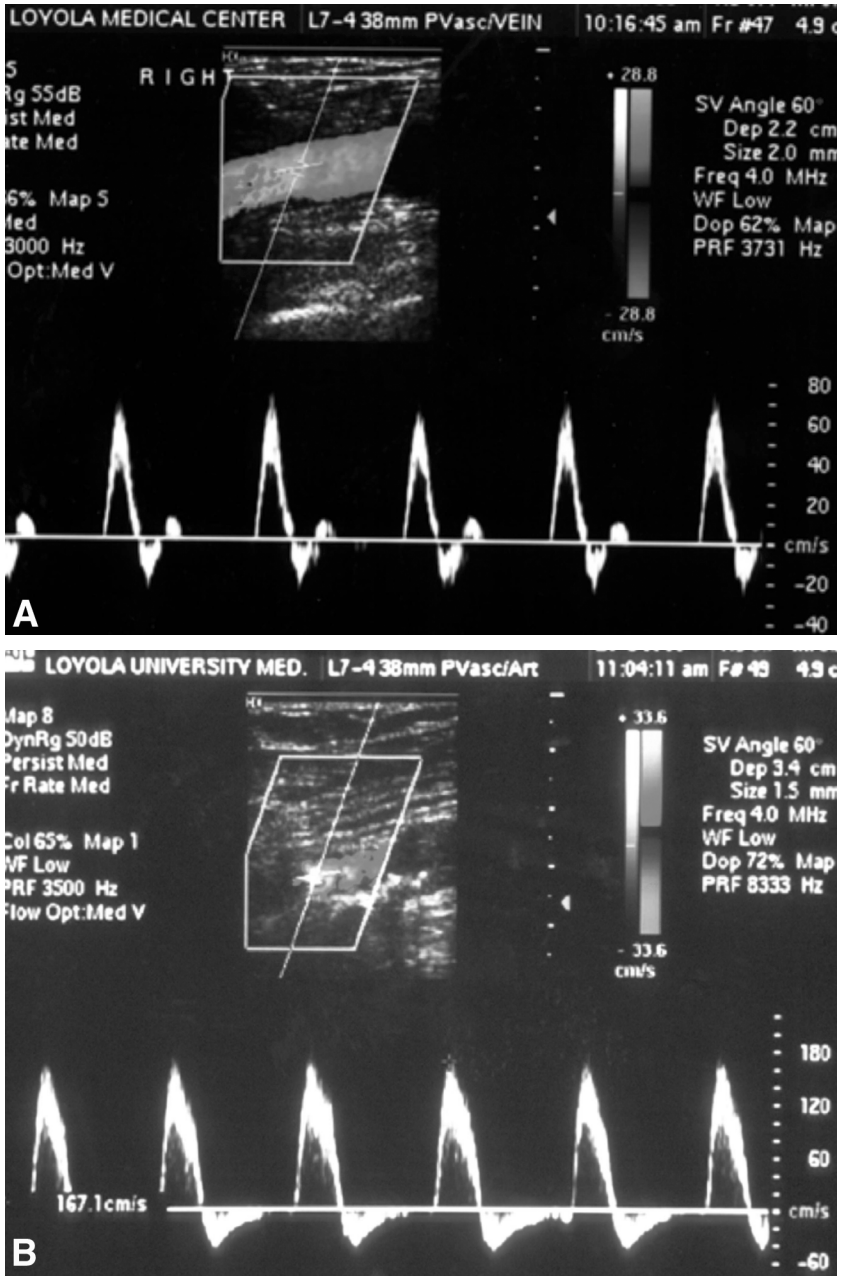

Fig. 3. Prediction of iliac stenosis from the common femoral artery (CFA) waveform. **(A)** triphasic waveform in the CFA indicates normal ipsilateral iliac arteries. **(B)** Biphasic waveform indicates mild to moderate (*continued on page 32*)

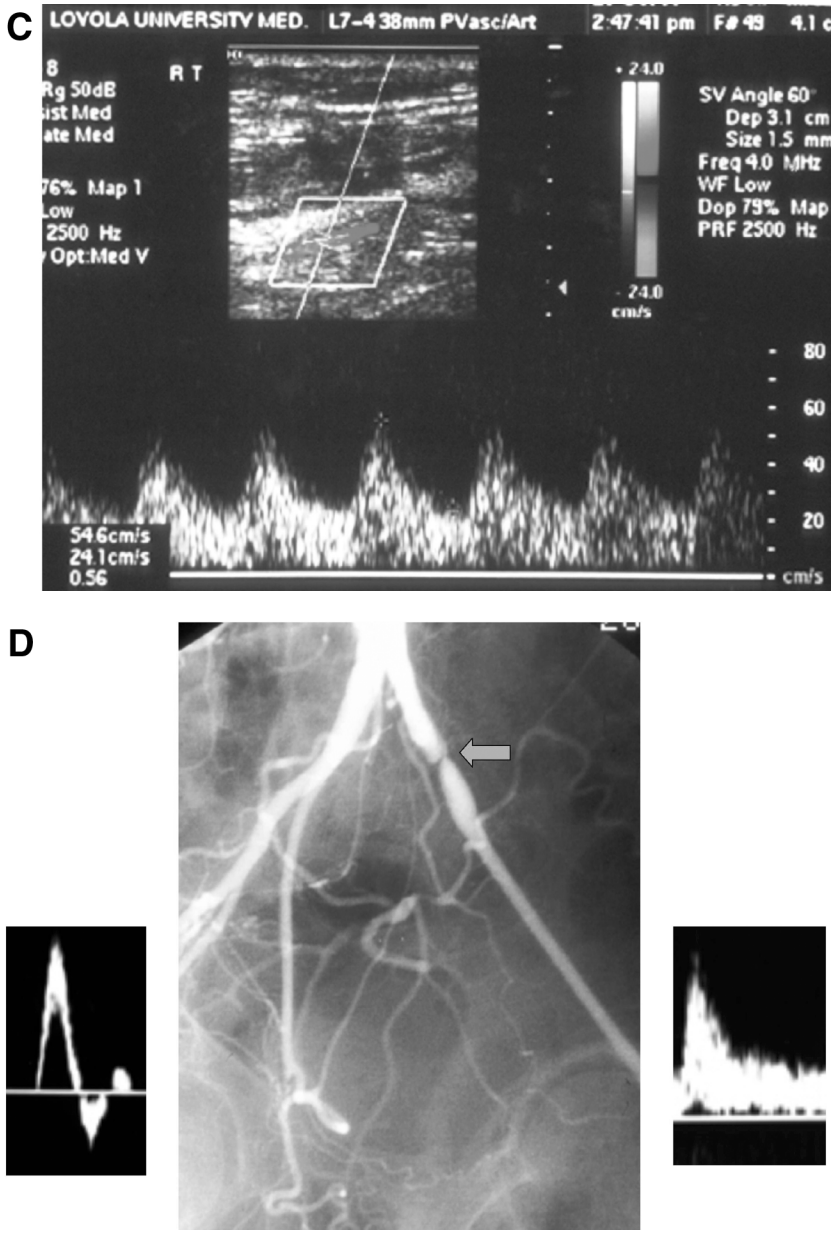

Fig. 3. (*continued from page 31*) stenosis. **(C)** Monophasic waveform denotes the presence of significant stenosis or occlusion. **(D)** Angiography and duplex scanning in a patient with intermittent claudication in the left lower extremity. In the right lower extremity the waveform is triphasic and the ipsilateral iliac artery in the angiogram is normal. In the contralateral limb the waveform is monophasic and a significant stenosis is present in the ipsilateral iliac artery (solid arrow).

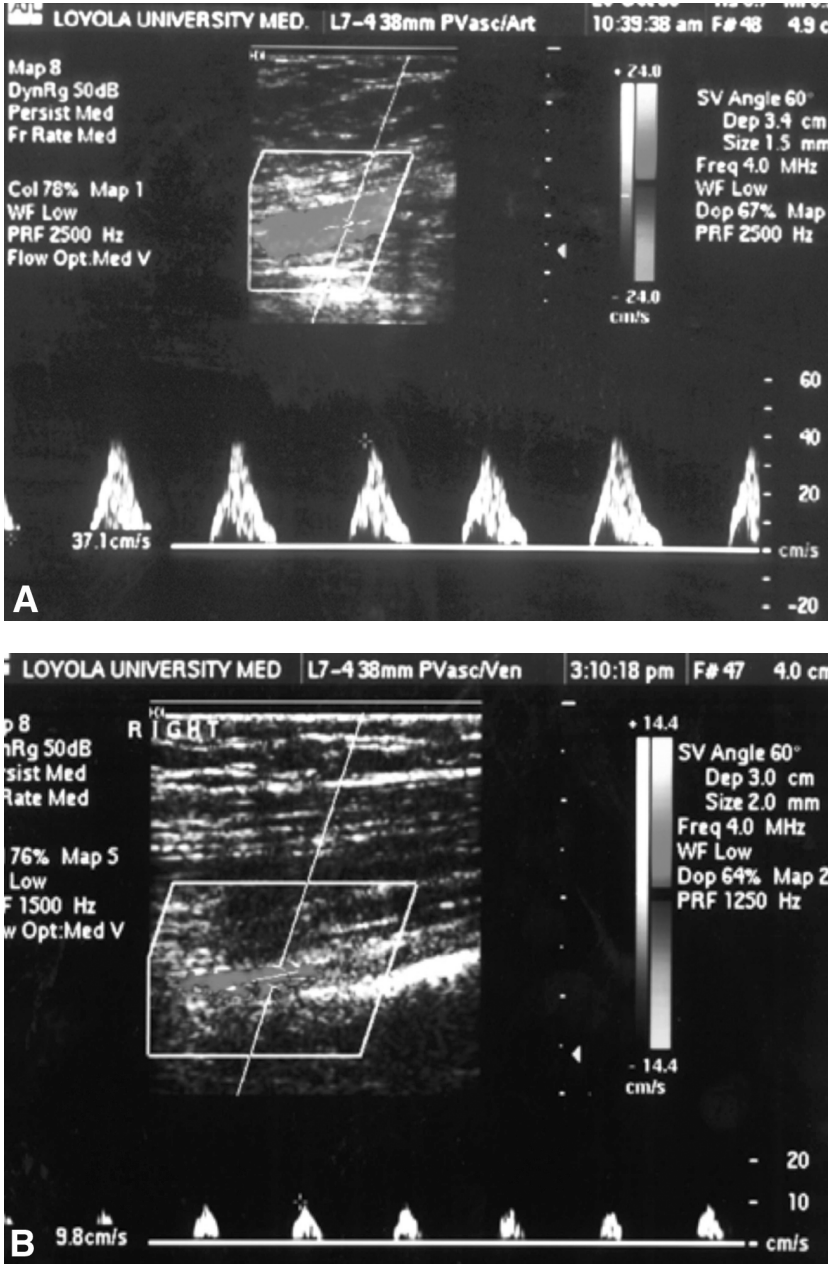

Fig. 4. Low amplitude waveform with absence of end diastolic velocity is common in patients with occluded arterial segments above and below the segment under investigation. **(A)** Low amplitude and absence of end diastolic velocity in the superficial femoral artery in the mid-thigh in a patient with common iliac significant stenosis and distal superficial femoral artery occlusion. **(B)** Very low velocities and a monophasic waveform in the posterior tibial artery of a patient with multiple stenoses and occlusions proximal and distal to the site of measurement.

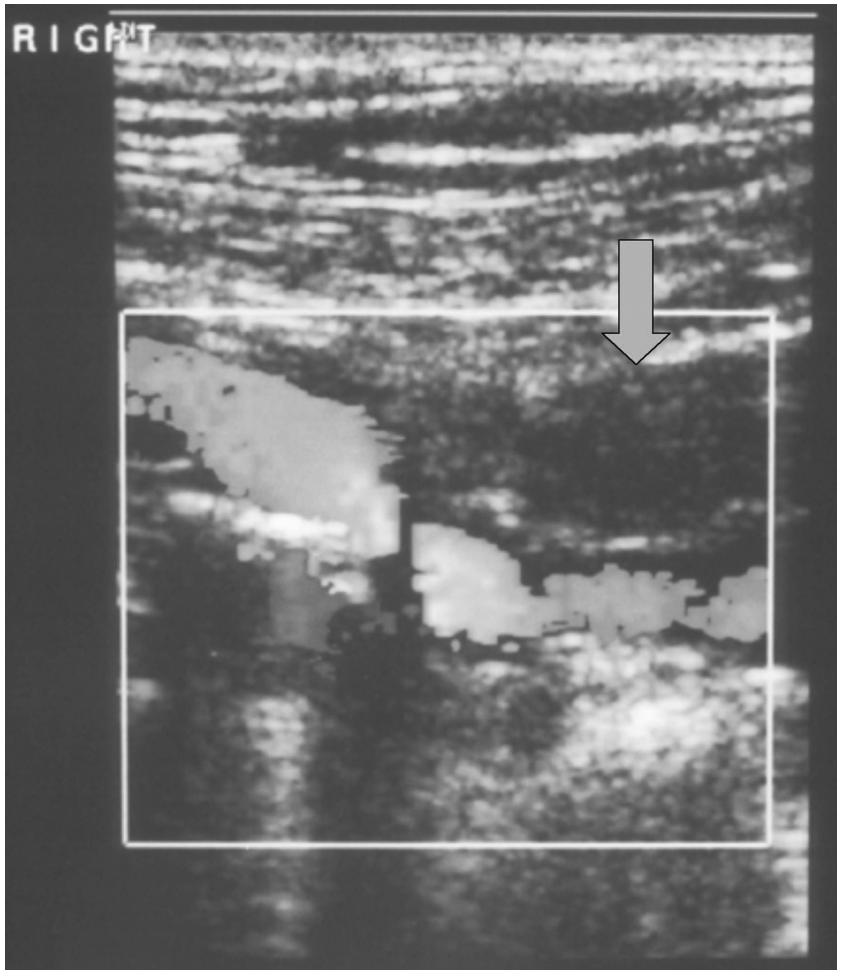

Fig. 5. Acute thrombosis of the right external iliac artery (solid arrow) in a patient with atrial fibrillation. The common iliac and internal iliac arteries are patent. The patient presented with acute lower ischemia. A thrombectomy was performed and the symptoms were resolved.

very promising results on that application. Duplex scanning can also be used with great accuracy in determining whether an iliac lesion is a good target for percutaneous intervention. The length of the lesion, degree of stenosis, and amount of calcification can all be accurately evaluated, giving the physician valuable information for decision making. In addition, duplex can be used to determine the presence of distal targets for revascularization procedures when none are visible by angiography (Fig. 6).

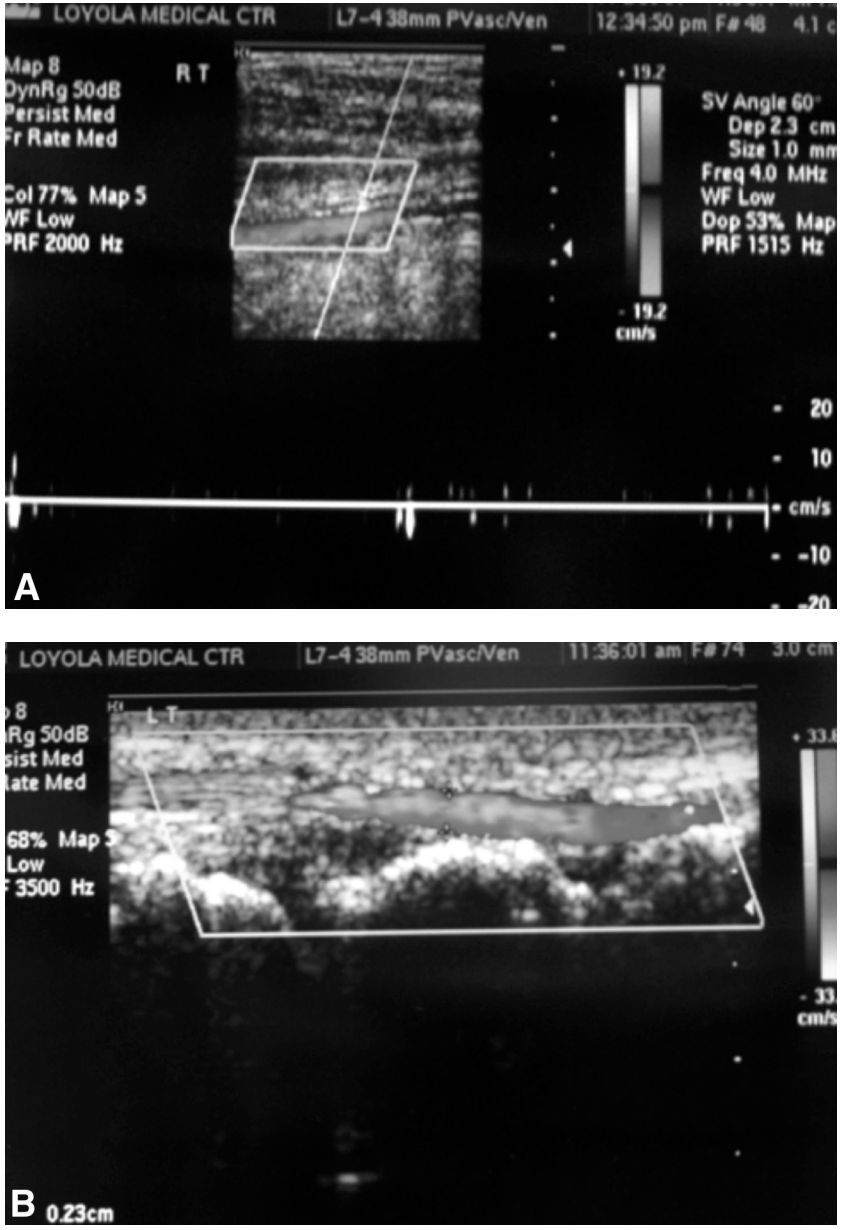

Fig. 6. Target arteries for surgery can be selected with the duplex scanning. Arterial segments with stenosis, diffused disease and heavy calcification are not selected for the distal anastomosis. **(A)** Occluded, calcified posterior tibial artery. **(B)** The dorsalis pedis artery in this patient had no significant abnormality and it was the best artery for the bypass placemet. This was a diabetic patient with typical infrapopliteal disease that underwent a popliteo-tibial by-pass with a saphenous vein.

Magnetic Resonance Angiography

In recent years, magnetic resonance imaging (MRI) and magnetic resonance arteriography (MRA) have been employed with increased frequency as diagnostic tools in the management of peripheral arterial disease *(18).*

Basic Principles

MRI is based on the reactions of various tissues to a magnetic field followed by a radiofrequency radiation pulse. MRA imaging is generated by taking advantage of blood flow-related effects relative to the stationary surrounding soft tissues. Two techniques are currently used for MRA:

Time of flight (TOF) angiography: TOF MRA relies on signal difference between stationary protons in the vessel wall and the surrounding soft tissues, compared to moving protons (flowing blood).

Phase contrast (PC) angiography: Protons undergo a change in the phase of their rotation as they move through a magnetic field. PC MRA uses gadolinium that shortens the T1 relaxation of blood protons, thereby increasing the intravascular signal.

Background can be eliminated by subtraction protocols and its suppression is greater for PC than for TOF MRA. Because of inherent limitations, TOF MRA has never become a real alternative to contrast angiography except in very few highly experienced centers. Currently, PC MRA is considered the best alternative to contrast angiography.

Clinical Applications

MRA has evolved as a noninvasive, sensitive accurate, and cost-effective method of imaging of the peripheral arterial circulation. Although contrast angiography is still considered the gold standard, it carries an overall (major and minor) complication rate of approximately 8%. Local complications related to the arterial puncture (bleeding, hematoma, infection, thrombosis, stenosis, pseudoaneurysm, etc.) and systemic complications (contrast-induced allergic reactions or renal insufficiency) are not uncommon. MRA is an alternative noninvasive imaging method for the peripheral vessels that avoids the risk of these complications. Its sensitivity in and specificity in detecting patent segments, hemodynamically significant stenoses and/or occlusions approaches 100%. In a recent review of the existing literature, TOF MRA was found to have sensitivity and specificity of 82% and 84%, respectively, whereas PC MRA had a 96% sensitivity and specificity compared to conventional angiography *(18).* The latter was also reported to be more sensitive in detecting patent distal run-off vessels in patients

with severely compromised distal circulation. This advantage is inherent to the mechanism of image formation in MRA, which requires only the presence of local flow with velocity as low as 2 cm/s. Presently, MRA is considered the imaging modality of choice for the diagnosis of vascular arterio-venous malformations and popliteal entrapment syndrome. In several centers, MRA is used as the sole pre-operative imaging technique for distal revascularization procedures with great success. It is currently considered to be more cost-effective compared to contrast angiography.

Nevertheless, not all patients are suitable for MRI/MRA exams. Individuals with implanted metal devices (pacemakers, cerebral vascular clips, etc.) should not be considered for such imaging. Claustrophobia remains a relative contraindication. The exam may also be limited by respiratory movements, but with contrast-enhanced MRA the acquisition time has significantly decreased (approximately 20 seconds for a complete limb exam), making *breath-hold images*possible.

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