

Contemporary Management of Peripheral Arterial Disease – A Review

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“Peripheral arterial disease” (PAD)

refers to disease of the aorta and its branches, excluding the coronary and cerebral arteries. This review will focus primarily on the recognition, evaluation and management of atherosclerotic lower extremity arterial disease, an important subset of PAD. In 2005, Hirsch et al published the most recent ACC/AHA guidelines for the management of PAD.¹ This important document should serve as a helpful reference for all clinicians. This review will attempt to highlight the most important recommendations from this document.

EPIDEMIOLOGY

The prevalence of PAD rises with advancing age, increasing sharply after age 40. In the National Health and Nutrition Examination Survey (NHANES), the prevalence was 0.9% between the ages of 40-49, 2.5% between the ages of 50-59, 4.7% between the ages of 60-69, and 14.5% above 70.² Overall prevalence in the study was

4.3% (over 5 million adults in the United States). The prevalence is likely to rise as the proportion of elderly patients in the population increases. Also, in an age and gender-adjusted analysis, patients of non-Hispanic black ethnicity were approximately 3 times more likely to have PAD than their non-Hispanic white counterparts.

RISK FACTORS

The major risk factors for PAD are: cigarette smoking, diabetes mellitus, hypertension, dyslipidemia, renal insufficiency, family history and hyperhomocysteinemia. Age greater than 70 years, post-menopausal state and non-hispanic black ethnicity are also considered risk factors for PAD, as well as for concomitant coronary artery and cerebrovascular disease. Indeed, these diseases very frequently coexist. Management of all relevant risk factors is a critical component in the optimal care for patients with PAD.

PRESENTING SIGNS AND SYMPTOMS

The vast majority of PAD is asymptomatic. This disease is frequently overlooked, and often goes undiagnosed. Among patients diagnosed with PAD, 20-50% are asymptomatic at the time of their initial diagnosis. These patients deny ischemic leg symptoms, but often report significant functional impairment. 40-50% of patients with PAD present with atypical leg pain. 10-35% of patients present with typical claudication, which usually reflects the presence of advanced disease. 1-2% of PAD patients present with critical limb ischemia, defined as the presence of ischemic pain at rest, ulceration and/or gangrene. This small subset is at very high risk of morbidity and mortality within the next 6 months. Another common presentation is Leriche’s syndrome, related to bilateral occlusive aorto-iliac disease. (Image 1) This syndrome consists of buttock and hip claudication, which may be accompanied by weakness in these muscle groups when walking. In men, this syndrome almost always leads to erectile dysfunction. With sufficient vigilance on the part of health care providers, many PAD patients can be identified before the development of any symptoms. This early recognition will allow many patients to avoid the more severe morbidity associated with advanced PAD.

DIAGNOSIS

All patients with risk factors for PAD should undergo a thorough vascular assessment. This includes taking a careful history and review of systems, focusing on the presence of intermittent claudication, ischemic rest pain, non-healing wounds and any functional limitations. These components of a thorough review of systems are particularly important in patients greater than 50 years of age with cardiovascular risk factors, and in all individuals 70 years of age or older. The classic description of intermittent claudication is that of reproducible exertional discomfort or weakness in the buttock,



Image 1: Aorto-iliac occlusive disease, in a patient with Leriche’s syndrome.

Table #1: Differential Diagnosis of Lower Extremity Discomfort

Cause	Description	Effect of Activity	Other Features
Vascular			
Intermittent Claudication (Arterial)	Discomfort or weakness in the buttocks, hip, thigh, calf or foot	Provoked by a predictable amount of exertion, alleviated promptly with rest (usually within 5 minutes)	Symptoms typically occur one segment below the level of stenosis
Venous Claudication	Tightness or squeezing sensation, usually in the calf	Worsens with walking, gradually resolves with rest; relief often accelerated with limb elevation	Signs of DVT and/or chronic venous insufficiency may be present
Lymphedema	Tension, pressure, non-pitting edema within calf, foot and toes	Present at rest and with activity	"Peau d'orange" appearance of thickened skin
Spinal			
Spinal stenosis	Weakness, pain and/or sensory changes	Worse upon standing or walking, may be positional, may be alleviated by sitting, flexion at the waist or squatting	Usually related to arthritis of the spine impinging on the spinal column; may have history of back pain
Radiculopathy	Sharp or burning pain along the posterior or lateral aspect of the leg, often with associated tingling sensation	Worsens with postural changes, cough, sneezing, Valsalva maneuver, not relieved with rest; may be relieved by changes in posture	May be related to degenerative spinal arthritis or herniated nucleus pulposus
Musculoskeletal			
Arthritis	Aching discomfort, often continuous; severity related to intensity of activity	Worse with activity and weight-bearing, often not relieved by rest	Few symptoms in non-weight-bearing activities; symptoms may be sensitive to changes in weather
Chronic Compartment Syndrome	Aching or cramping pain in the area of the affected compartment	Episodic, usually occurring following strenuous activity	Compartment pressure > 20 mmHg confirms Dx; Treatment is surgical
Baker's Cyst	Tenderness and swelling in the popliteal fossa	Worsens with activity, not relieved with rest	Signs of inflammation in the popliteal fossa
Other			
Benign Nocturnal Cramps	Cramping pain, usually in calves, most often at night	Occurs at rest, usually resolves spontaneously	Very common, usually idiopathic; may be related to electrolyte disturbances

A detailed physical examination should also be performed, including a careful evaluation of pulses and an evaluation of the legs and feet. PAD may present with a unilateral cool extremity with significant pallor. Poor wound healing, hair loss, and skin atrophy may occur distal to the point of occlusion. Auscultation of the corresponding arteries should be performed, to identify and localize any bruits.

thigh or calf muscles, which resolves promptly with rest. The amount of exercise which produces symptoms is usually reproducible. Atypical presentations are common, and differentiating claudication from other causes of lower extremity pain can be challenging. (Table #1)

DIAGNOSTIC TESTING

The ankle-brachial index (ABI) is a simple, easily reproducible and widely available test for the diagnosis of PAD. The ABI is a ratio of the blood pressure measured in the ankle, to the blood pressure measured in the brachial artery. This test is usually accompanied by pulse volume recording (PVR) or by assessing Doppler waveforms at sequential locations along the extremities. (Image #2) These techniques greatly enhance the

diagnostic yield of the ABI study by allowing for the determination of the approximate level of disease. This may help differentiate "inflow" disease, (referring to disease of the aorta or iliac arteries), from disease in more distal arteries. The use of PVR or Doppler techniques may also allow for an estimate of the severity of disease. Finally, PVR may assist with diagnosing PAD in patients with stiff, non-compressible vessels, in whom the ABI may be falsely elevated.

The ABI (with PVR or Doppler) should be performed in all patients with claudication or other symptoms suggesting PAD.

This test is also helpful in establishing the initial diagnosis of patients with asymptomatic PAD. The American Diabetes Association, in a consensus statement

from 2004⁴, recommends obtaining screening ABI in diabetic patients greater than 50 years of age. If normal, they recommend repeating the test every 5 years. They also recommend obtaining ABI in diabetic patients younger than age 50 who have other PAD risk factors (e.g. smoking, hypertension, hyperlipidemia, or duration of diabetes greater than 10 years)

In patients with high risk features for PAD, but with a normal or near-normal resting ABI (and PVR or Doppler), additional diagnostic yield can be obtained via measurement of ABI following exercise. (Figure #1) Post-exercise ABI may also help differentiate true claudication from pseudoclaudication, and also helps objectively document the magnitude of any functional limitations.

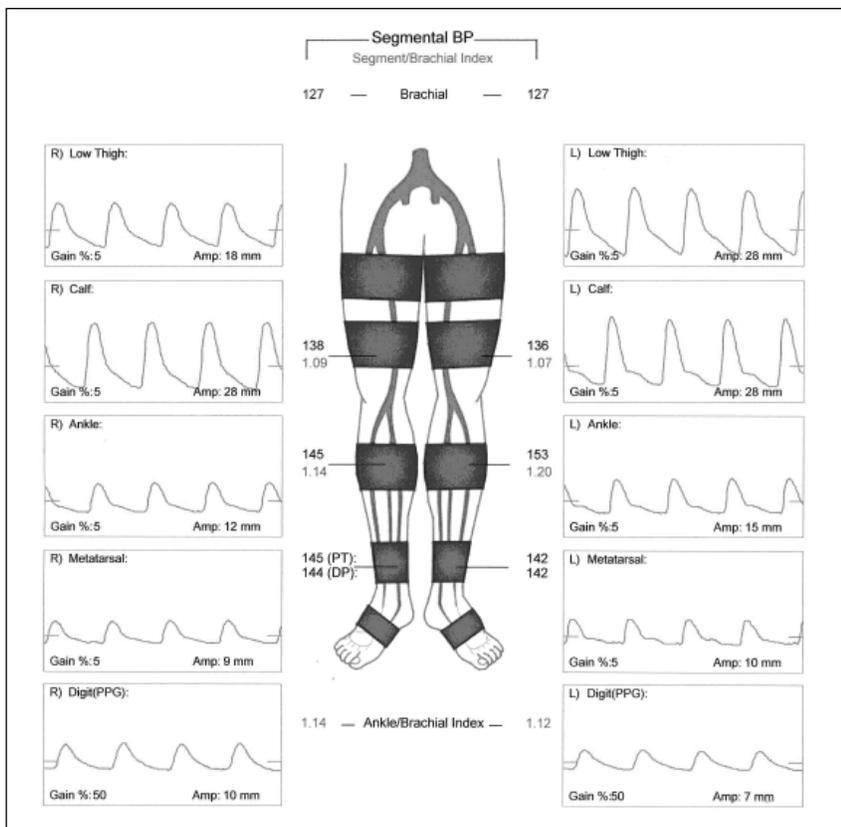


Image #2: Ankle-brachial index (ABI) with pulse volume recording (PVR).

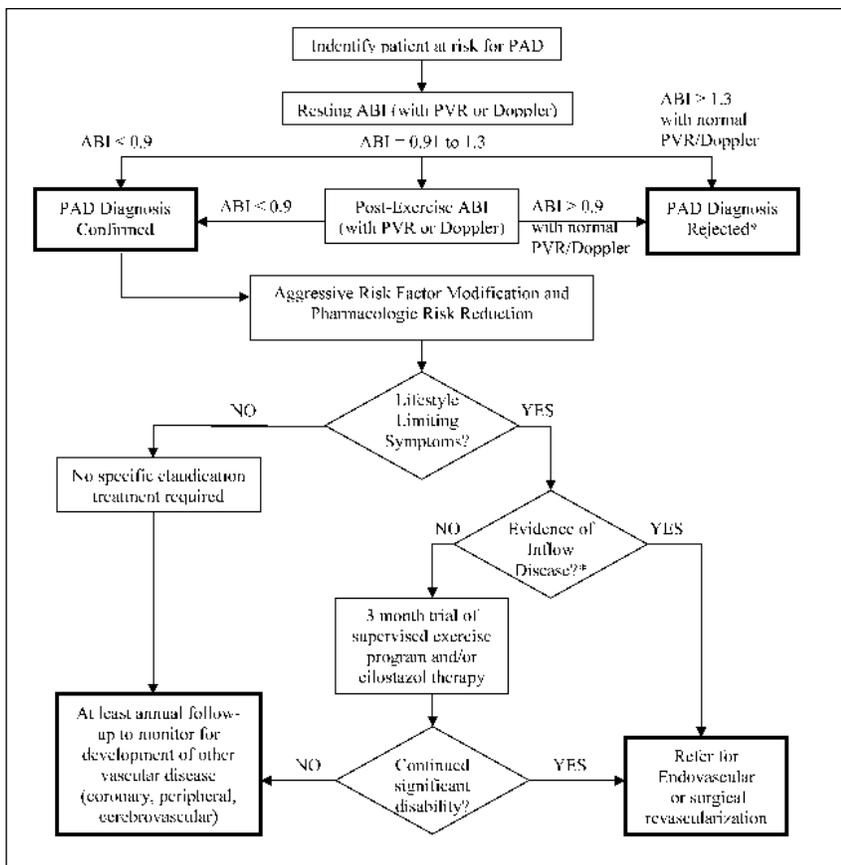


Figure 1: Algorithm for the initial evaluation and management of PAD

For some patients with a high likelihood of PAD, but in whom ABI and post-exercise ABI (with PVR or Doppler) are normal, more advanced imaging techniques may be necessary to allow for a more thorough evaluation for PAD.

Other advanced imaging techniques such as Duplex ultrasonography, Magnetic resonance angiography (MRA), Computed tomography angiography (CTA) and contrast angiography can be very useful for a detailed evaluation of PAD patients. Usually such studies would be ordered by a vascular medicine or surgery specialist, after the initial diagnosis has been established by a primary care physician.

Duplex ultrasonography provide a detailed assessment of PAD, including determining the precise location and severity of any PAD. It is helpful in following patients for progression of disease, and may be helpful in assessing patients with stiff, non-compressible vessels. This technique is often useful in providing quantitative data following revascularization procedures. Duplex ultrasonography is limiting in its ability to assess very proximal vessels, and may be limited by dense arterial calcifications.

MRA, using Gadolinium enhancement is very useful in determining the details of peripheral arterial anatomy including the degree and severity of obstruction, and may assist in selecting patients who may benefit from revascularization. CTA may have benefits similar to that of MRA, particularly in patients with contraindications to MRA. Contrast angiography is still considered to gold standard for assessment of PAD, and is typically reserved for patients undergoing revascularization procedures.

MANAGEMENT

All PAD patients should undergo aggressive risk factor and lifestyle modification, including smoking cessation, an exercise program, as well as careful control of diabetes, hypertension and dyslipidemia.

In the absence of contraindications, all PAD patients (regardless of the presence or absence of symptoms) should receive anti-platelet therapy for primary prevention of adverse cardiovascular events including myocardial infarction (MI), stroke and vascular death. Aspirin

(75 to 325mg daily) is recommended in this setting, and has been shown to reduce adverse cardiovascular events by up to 32% in PAD patients. Clopidogrel (75mg daily) is considered a reasonable alternative therapy in this setting, particularly in patients with symptomatic PAD or who are unable to tolerate aspirin. No supports the use of a combination of aspirin and clopidogrel in this setting. Warfarin therapy is not indicated for the reduction of adverse cardiovascular events in PAD patients.

Cilostazol (100mg twice daily) is an effective agent for improving symptoms and increasing walking distance in patients with PAD and intermittent claudication. Although no trials have found a significant increase in major cardiovascular events with this agent, it is contraindicated in patients with heart failure. Pentoxifylline (400mg three times daily) may be considered as a second-line agent to Cilostazol, but the clinical effectiveness of this agent is not well established.

Exercise rehabilitation has been well documented to reduce symptoms of claudication. Multiple trials have shown that exercise increases maximum walking time and peak oxygen consumption. Some studies have also suggested that exercise rehabilitation improves survival in PAD patients. Stable PAD patients should be referred to an exercise rehabilitation program before being considered for any revascularization procedures.

Revascularization should be reserved for patients with lifestyle-limiting symptoms related to their PAD, a reasonable likelihood of success of the revascularization procedure, and preferably a low risk associated with such a procedure. There are a wide variety of procedures which have been developed to establish revascularization to the lower extremities. In recent years, percutaneous options have begun to supplant many surgical options. However, in some cases, surgical revascularization remains the best options to obtain a satisfactory revascularization.

Critical limb ischemia is a subset of PAD which is characterized by particularly high morbidity and mortality. This is usually defined as the presence of ischemic rest pain, ulceration or gangrene. These patients usually present with resting leg pain which is worse when in a supine position, improving somewhat when the limb is maintained in a dependent position. If left untreated, a large proportion of these patients will require amputation within 6 months. If the clinical course of these patients suggests rapid progression, an expedited evaluation and prompt revascularization should be considered.

Acute limb ischemia represents another subset of PAD with high morbidity and mortality. This occurs when a sudden decrease in limb perfusion threatens limb viability. Patients who present with evidence of acute limb ischemia who are determined to have a salvageable limb should undergo an emergent evaluation to determine the anatomic level of obstruction, and should undergo a prompt revascularization procedure.

OUTCOMES

PAD is a cause of significant morbidity and mortality. The PAD leads directly to major functional impairments and decreased quality of life. The diffuse atherosclerotic disease that accompanies PAD also leads to significant morbidity and mortality from myocardial infarction and stroke.

CONCLUSIONS

PAD illness places a large financial burden on the healthcare system, and will increase in prevalence with the aging population in the United States. The prompt recognition, diagnosis and management of PAD should improve the quality of life of patients with PAD and reduced the overall morbidity and mortality of this serious entity.

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The authors have no financial interests to disclose.

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