

# Diagnosis of Peripheral Arterial Disease

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*Prevalence of peripheral arterial disease (PAD) increases with age. PAD is not only associated with disability (e.g., claudication, limb loss), but also with increased mortality from cardiac and cerebrovascular events. A thorough assessment of symptoms, risk factors and physical signs—including ankle-brachial indices—can be sufficient to determine whether PAD is present. Further testing—such as Duplex examination, magnetic resonance imaging and conventional arteriography—is often required to determine progression and accurate localization of lesions, as well as to direct therapeutic intervention. Early detection of PAD can help prevent functional impairment and death in the elderly.*

**Key words:** atherosclerosis, peripheral arterial disease, ankle-brachial index, diabetes, claudication.

Atherosclerotic disease is the leading cause of death and disability in the industrialized world. Progressive occlusion of the arterial lumen, thrombosis and embolism are the causes of tissue ischemia, which can manifest as acute events or as progressive, chronic changes.<sup>1,2</sup>

The term peripheral arterial disease (PAD) is used commonly in reference to occlusive disease of lower extremities. This disease also involves the aorta and visceral arteries and, less commonly, upper-extremity arteries. Coronary and carotid occlusions usually are studied separately from PAD because of differences in pathophysiology, manifestations and management. Given the generalized nature of atherosclerosis, patients with PAD are at increased risk not only for limb loss, but also for visceral gangrene, stroke and myocardial infarction. Such complications are associated with severe morbidity and high mortality rates. Patients with PAD have increased mortality even when asymptomatic.<sup>2,3</sup>

Its high prevalence and adverse impact on functional status and quality of life make PAD a major public health concern. Emerging diagnostic and therapeutic methods are increasingly becoming more available, safer and more

effective. Minimally invasive methods are particularly beneficial in the management of PAD in the elderly.<sup>3,4</sup>

## Pathogenesis and Natural History

Advanced age is a major risk factor for atherosclerosis and PAD; other established risk factors include hypercholesterolemia, hypertension, smoking and diabetes mellitus. Elevated blood levels of homocysteine, fibrinogen and C-reactive protein, as well as an elevated hematocrit, also have been associated with PAD. Infectious agents (e.g., *Chlamydia pneumoniae*) may be implicated in some cases. Cigarette smoking and diabetes are considered the strongest risk factors for PAD.<sup>2,5,6</sup>

Atherosclerotic lesions tend to occur in the arterial tree in areas of bifurcation, turbulence or decreased flow. Complex interactions between endothelial and blood-borne mediators occur during plaque formation and progression to advanced lesions. This process involves platelet adhesion, thrombus formation and inflammation, as well as activation of cytokines, growth factors and adhesion molecules. Macrophages transformed into foam cells contribute to arterial wall inflammation and further accumulation of fat, cholesterol crystals and smooth

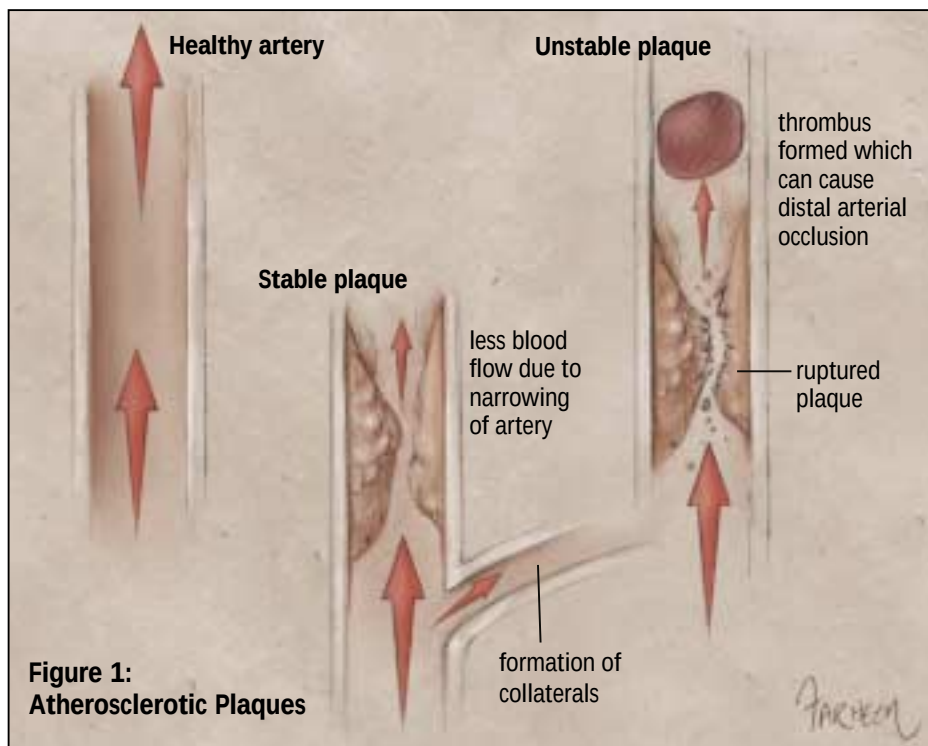
muscle cells, the main components of advanced atherosclerotic lesions.<sup>1,7</sup>

Risk factors can be present alone or in combinations, and can contribute to PAD by different mechanisms. Hypercholesterolemia is known to promote recruitment of mononuclear leukocytes to the vessel wall. Smoking may cause endothelial activation and chronic inflammation. Through poorly understood mechanisms involving insulin resistance and hyperinsulinemia, patients with diabetes have twice the risk of developing ischemic symptoms, and 10 times the risk of developing extremity gangrene requiring amputation.<sup>6</sup>

“Stable” atherosclerotic plaques are fibrotic and calcified, and cause narrowing or occlusion of vessel lumen by growth over long periods, allowing gradual development of collaterals. “Unstable” plaques have complex composition, are rich in foam cells and cholesterol crystals and are prone to rupture, causing thrombosis and acute arterial occlusion (Figure 1).<sup>1,7</sup> Plaques of the stable type usually are found in arteries of elderly patients.

Advanced age correlates with higher prevalences of comorbid conditions that may contribute to PAD. Endothelial damage—caused by hemodynamic, shear-related forces, primarily around arterial bifurcations or areas of turbulence—accumulates over time. This chronic, lifetime damage represents a yet uncontrollable risk factor, and is considered part of the inexorable aging process.

PAD progresses over a period of years or decades. Acute symptoms usually result from thrombosis or embolism. Although such events—recognizable as syndromes of acute limb ischemia—occur in a relatively small percentage of patients with PAD, they are frequently encountered in clinical practice, which reflects the high prevalence of PAD in the general population. Most patients with PAD are asymptomatic. Although manifestations of PAD are uncommon before the fifth decade of



**Figure 1:**  
**Atherosclerotic Plaques**

life, atherosclerotic lesions can be present in major arteries of even children and adolescents. Patients aged 60 years and older have a 15–20% prevalence of clinically detectable PAD, and up to 5% have claudication. The one-year mortality rate (from all causes) is 25% for those with severe, limb-threatening disease.<sup>2,3,7</sup>

## Diagnosis

Intermittent claudication (IC)—pain on exertion, relieved by rest—is the classical manifestation of PAD. Patients may have IC that is stable or that progresses to pain at shorter distances for months or years before onset of rest pain, ulceration or gangrene. Atypical exertional leg pain and other leg symptoms also are common in patients with PAD.<sup>8</sup> Patients who do not walk or who maintain low levels of activity (e.g., use wheelchairs, are bedridden) cannot be evaluated for IC. Mental impairments—such as dementia or inability to verbalize—in elderly patients may preclude obtaining an adequate history. Non-specific reactions, such as agitation or a confusional state, may indicate discomfort (e.g., urinary retention), leg pain or hypoxemia. Patients with rest pain may be observed dangling the ischemic foot over the side

of the bed. Ischemic ulceration (typically over calcaneus, lateral malleolus, dorsum of the foot) or gangrene can be the initial manifestations of PAD in patients with dementia or inactivity. Onset of manifestations tends to be sudden in cases of embolism, and gradual (over a period of hours to days) in thrombosis.

Signs and symptoms of acute and chronic ischemia of lower extremities are summarized in Table 1. Following physical examination, the ankle-brachial index (ABI) should be calculated. Using a Doppler, systolic pressure at the malleolar level is determined, and divided by the higher pressure of the two arms (brachial artery). Clinical correlations with ABI values are summarized in Table 2. An ABI > 1.3 suggests non-compressible vessels secondary to calcification (common in diabetic patients), an indication for further testing (e.g., pulse-volume recordings [PVR], duplex scanning [DS]). If the index is between 0.9 and 1.3 and the patient has claudication or strong risk factors, ABI should be determined following an exercise (treadmill) test.

In the presence of calcified vessels, the ABI may be falsely elevated, above 1.3. In this case, a toe pressure with toe-brachial index can determine the pres-

ence of significant PAD—as indicated by a toe-brachial index below 0.6. Transcutaneous oxymetry (TcPO<sub>2</sub>) also can be utilized for determining tissue ischemia in the extremities. TcPO<sub>2</sub> assesses macro- and microcirculation simultaneously, and may be particularly useful in diabetic patients. Normal TcPO<sub>2</sub> is above 40mmHg; critical hypoxia is associated with values between 10 and 30mmHg; and a TcPO<sub>2</sub> below 10mmHg indicates poor tissue viability, likely requiring revascularization.

Initial assessment of PAD should aim to determine whether the limb is “viable”, “threatened” or “irreversibly damaged”. Viable limbs have adequate capillary refill, preserved muscle strength and no sensory loss; Doppler-measured distal arterial pressures are > 30mmHg, with audible venous flow. Further testing or treatment can be done electively. Threatened limbs have decreased capillary return and muscle strength, and mild or incomplete sensory loss; arterial Doppler signals are not detectable but venous flow is audible. Immediate treatment offers the best opportunity for limb salvage. Irre-

**Table 1**

## Clinical Manifestations of Acute and Chronic Ischemia of Lower Extremities

| Acute<br>(the five “P”s) | Chronic                      |
|--------------------------|------------------------------|
| Pulselessness            | Decreased pulses             |
| Pallor                   | Bruit over area of stenosis  |
| Paresthesia              | Pallor of foot on elevation  |
| Pain                     | Dependent “rubor” (erythema) |
| Paralysis                | Muscle atrophy               |
|                          | Hair loss                    |
|                          | Thin skin                    |
|                          | Nail deformities             |
|                          | Ulceration                   |
|                          | Gangrene                     |

**Table 2**  
**Approximate ABI Values and Corresponding Clinical Implications**

| ABI     | Clinical Features               |
|---------|---------------------------------|
| > 1.3   | Non-compressible vessels        |
| 1.0–1.3 | Normal                          |
| 0.8–1.0 | Asymptomatic PAD                |
| 0.4–0.8 | Intermittent claudication       |
| 0.2–0.4 | Rest pain, ulceration, gangrene |
| < 0.2   | Limb-threatening ischemia       |

ABI: ankle-brachial index; PAD: peripheral arterial disease

versible changes, reflecting tissue loss, include absence of capillary return, paralysis and severe sensory loss, with inaudible arterial and venous Doppler signals; amputation is the only alternative.

DS is well established as a non-invasive method for evaluation of aortoiliac and femoropopliteal arterial disease. Hemodynamic characteristics of lesions can be determined by calculation of peak systolic velocity (PSV) ratios. DS data can be sufficient to guide therapy, and is particularly helpful in determining the need for arteriography in patients with severe lower-extremity ischemia. DS can be used to exclude significant aortoiliac lesions before selective intra-arterial digital subtraction angiography (iaDSA) is performed. Although colour duplex imaging incorporates real-time B-mode imaging and pulsed and colour Doppler, operator-dependent variability remains a concern in cases of borderline stenoses.<sup>9,10</sup>

Hemodynamic tests (e.g., segmental-limb-pressure, PVR) can help localize arterial lesions non-invasively. Newer, non-invasive imaging tools, however, can provide more accurate information while maintaining a minimal risk for the patient.

Magnetic resonance (MR) angiography is gradually replacing invasive contrast studies. MR studies not only avoid arterial puncture and the risk of contrast-induced renal failure, but also can be

more sensitive for vessel identification. High-resolution MR techniques may help to further determine the composition of atherosclerotic plaques based on lipid and water contents. MR angiography has been established as an accurate method to detect PAD of aorta, iliac, femoral and popliteal arteries; further technical improvements also should allow adequate imaging distal to the trifurcation. Contrast-enhanced MR angiography is likely to become the primary means for non-invasive imaging of lower-extremity arteries, and should be particularly useful for evaluation of elderly patients with impaired renal function.<sup>11,12</sup>

Conventional angiography—iaDSA is the most common technique used currently—remains helpful, particularly in the preoperative assessment of PAD. Other invasive tests such as angioscopy and intravascular ultrasound have limited use in clinical practice.

## Management

Diagnosis of PAD should be pursued using the least-invasive methods first. Despite availability of a number of non-invasive tests, accurate history and physical examination remain essential for diagnosis and management of PAD. Invasive tests (e.g., conventional arteriography) are reserved for patients who require surgery or endovascular intervention. In general, interventional or surgical treatments are not required if symptoms or signs of ischemia are not present.

Even severe stenoses or complete occlusions can be asymptomatic or amenable to medical management, including control of risk factors (e.g., diabetes, smoking) and use of prophylactic, antiplatelet drugs (e.g., Aspirin, ticlopidine). This approach is somewhat different from the management of coronary and carotid occlusive diseases, or aneurysmal disease of the aorta and its branches; in such instances, decision-making often is based on anatomy and morphology of lesions, degree of stenosis or size of an aneurysm, rather than symptomatology. In most patients with PAD, limb viability is maintained by collaterals. Risk factor modification,

antiplatelet drugs and exercise are often sufficient to control symptoms.<sup>3</sup>

Localization studies are indicated for patients with severe disability who do not improve with conservative measures and, therefore, become candidates for revascularization. In addition, patients with ABI < 0.3 (critical limb ischemia) should undergo localization studies to determine whether lesions amenable to surgical or endovascular treatment are present. ♦

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