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# WHAT THE PRIMARY CARE PROVIDER NEEDS TO KNOW FOR LIMB SALVAGE

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## Abstract

Primary care providers are often the first providers to evaluate a patient for peripheral arterial disease (PAD). Understanding the various presentations of PAD symptoms can prevent the disease from progressing to critical limb ischemia and eventual limb loss. This article provided the primary care provider with information needed to prevent limb loss and promote limb salvage, including risk factor management, clinical presentation, physical exam findings, and treatment options.

## PAD Incidence and Presentation

Peripheral arterial disease (PAD) is the term used to describe atherosclerotic disease of the aorta and arteries supplying the lower extremities and abdominal aortic aneurysms (AAAs) that can progress to stenosis or occlusion of the affected vascular beds. It is also a marker of systemic atherosclerosis such as coronary artery disease or cerebrovascular disease. PAD is estimated to affect approximately 8 million Americans and is associated with significant morbidity and mortality due to ischemic events involving cerebral, coronary, or peripheral arterial circulation. The prevalence of PAD is approximately 12% in the adult population and increases drastically with age. It affects men slightly more than women and disproportionately affects blacks.<sup>1</sup> PARTNERS (PAD Awareness, Risk and Treatment: New Resources for Survival), a national cross-sectional survey, found that PAD affects 29% of adults who are  $\geq 70$  years, those 50 to 69 years of age with at least a 10 pack-per-year history of smoking, or those age 50 to 69 years with a history of diabetes. Furthermore, this study found that of the patients screened for PAD, more than 70% of their primary care physicians were unaware that they had the diagnosis.<sup>2</sup> So despite the incidence of PAD, the disease is widely under-diagnosed since patients often present with atypical symptoms or no symptoms of leg pain at all.

The presentation of PAD ranges from intermittent claudication to limb-threatening ischemia. Intermittent claudication is the most common manifestation and is described as consistent and reproducible calf muscle pain causing exercise-induced ischemia. Symptoms of claudication should subside when the exercise is ceased. The diagnosis of intermittent claudication is fairly subjective. Generally, these symptoms occur in a muscle group one level beyond the level of the disease.<sup>3</sup> For example, solitary calf claudication indicates superficial femoral artery disease, which may manifest as a reduced popliteal pulse, while pain in the buttocks or thighs indicates aorto-iliac disease, which may manifest as a weak femoral pulse.

Despite its significant impact on life expectancy, functional status, and quality of life, approximately 75% of patients with intermittent claudication are undiagnosed.<sup>3</sup> Therefore, it is essential that primary care physicians be proactive in identifying this symptom. Recognition is critical as intermittent claudication is an indicator of other more serious vascular events. If the condition is managed vigilantly, only 5–10% of patients with

claudication will require a primary amputation of an extremity due to disease progression in 5 years.<sup>4</sup> Early identification for risk factor modification is vital to prevent progression of systemic atherosclerosis.<sup>5</sup>

Limb-threatening ischemia can present in a variety of ways and should be identified as a high potential risk for a major amputation. Usually the first symptom of severe limb ischemia is rest pain. Rest pain is described as sharp, localized pain in the forefoot below the ankle and the foot and is commonly associated with dependent rubor and elevation pallor. Patients often describe that this pain occurs at night and is relieved by dangling their foot from the bed. Nearly 95% of patients with ischemic rest pain will lose their limb within a year unless they undergo revascularization. Rest pain is associated with a minimum of two hemodynamically significant arterial occlusive lesions.<sup>4</sup> The most common lesions are combined aorto-iliac and superficial femoral arterial occlusive disease, or femoropopliteal arterial occlusion with distal tibial occlusive disease. These patients require an urgent referral to a vascular specialist.

On the other hand, limb-threatening ischemia may not be associated with symptoms of pain but may present with tissue loss. Nonhealing ulcers of the distal foot can result from ischemia, but this is not the only cause. There may be adequate arterial perfusion to the foot, yet ulcers have developed secondary to ill-fitting footwear, osteomyelitis, infections of the soft tissue, foot malformations, or diabetic neuropathy — all of which cause initial skin breakdown that leads to a nonhealing ulcer. The typical sign of ischemia in the soft tissue is gangrene. Without infection, gangrene looks like mummified tissue while wet gangrene is moist with a foul odor and has a combination of necrotic tissue and infection. Once a patient has progressed to gangrene, the possibility of limb loss rises significantly. It is well documented that at 1 year 25% of patients will be dead, 30% will have undergone amputation, and only 45% will remain alive with both limbs.<sup>4</sup> These patients require an immediate referral to a vascular specialist.

## Physical Examination

Given the varied symptoms that are associated with PAD, the diagnosis is based upon a thorough history and physical. The physical examination, regardless of the patient's complaints, should include the entire arterial system in order to discover

underlying atherosclerotic disease. The examination should include the following:

- Measurement of bilateral upper extremity blood pressures
- Neck auscultation for carotid bruits
- Cardiac auscultation for murmurs or gallops
- Abdominal palpation to assess for pulsatile masses (e.g., abdominal aortic aneurysms)
- Abdominal auscultation for bruits
- Palpation of all lower extremity pulses (femoral, popliteal, dorsalis pedis, and posterior tibial)
- Inspection of the lower extremities and feet to assess for ulcers, gangrene, or evidence of previous amputations
- Palpation of the lower extremities and feet to assess skin temperature or tenderness

When assessing patients who have identified risk factors for atherosclerotic disease, an ankle-brachial pressure index (ABI) is an effective screening tool for PAD. Obtaining an ABI is simple and can be easily performed in an office setting or at the bedside. The ABI is calculated by dividing the ankle systolic pressure, measured with a blood pressure cuff at the malleolar level, by the higher of the two brachial pressures. The brachial, posterior tibial, and dorsalis pedis pressures are measured using an appropriately sized blood pressure cuff on the arms and legs above the ankles. Using a hand-held Doppler probe, the systolic pressure in each artery is determined when the flow returns after gradual cuff deflation. A normal ABI is greater than 0.9 mm Hg. An ABI less than 0.9 mm Hg serves as a marker for systemic atherosclerosis. An ABI between 0.4–0.9 mm Hg is a definite sign of PAD and chronic claudication. An ABI less than 0.4 mm Hg is indicative of limb-threatening ischemia. Most commonly, the setting of diabetes mellitus or renal failure can lead to medial calcinosis and poor compressibility of the tibial vessels, which can make the ABI unreliable. ABI values greater than 1.25 mm Hg are considered falsely elevated and must be considered nondiagnostic. Patients with falsely elevated ABI values should be referred for toe pressure measurements to quantify their distal perfusion.<sup>4</sup>

### Risk Factor Modification

Once a patient is diagnosed with atherosclerotic disease, risk factor modification is vital to prevent progression of PAD as well as cardiovascular mortality. Many providers believe that PAD is a disease process best approached from a surgical standpoint; however, it must begin with an aggressive medical approach. A large volume of literature supports prompt and comprehensive risk factor management to improve survival, reduce recurrent vascular events, decrease the need for interventional procedures, and, above all, improve the quality of life of these patients. The American Heart Association guidelines for secondary prevention outlines the risk factor modifications required for patients with PAD.<sup>5</sup> The strongest risk factors are diabetes mellitus and tobacco abuse; however, other risk factors to address include hypertension, hyperlipidemia, sedentary lifestyle, and lack of antiplatelet therapy.

The risk factors associated with PAD include the following:

1. **Diabetes Mellitus.** Diabetes has both microvascular and macrovascular effects and is a strong independent predictor for stroke, myocardial infarction (MI), and PAD.<sup>6</sup> The need for amputation in diabetics with lower extremity arterial occlusive disease is ten times that for nondiabetic patients. In patients with diabetes, for every 1% increase in hemoglobin A<sub>1c</sub> there is a corresponding 26% increased risk of PAD.<sup>7</sup>

Therefore, the goal for hemoglobin A<sub>1c</sub> should be <7%, and hypoglycemic agents should be administered to achieve this goal. Tight glycemic control of blood glucose level should maintain a level of 100–126 mg/dL.<sup>5</sup> Patients should also be educated on the importance of proper foot care to prevent problems associated with diabetes.

2. **Tobacco Abuse.** Cigarette smoking has been identified as an independent predictor of vascular disease and the reason why vascular procedures and interventions fail. More than 80% of patients with PAD are current or former smokers.<sup>1</sup> Smoking increases the risk of stroke at least two-fold and the risk of lower extremity occlusive disease four- to six-fold.<sup>8</sup> Continued tobacco abuse is responsible for vascular disease progression, while smoking cessation mitigates these effects. Therefore, it is imperative that patients with atherosclerotic disease receive counseling on the importance of smoking cessation, and they should be provided pharmacotherapy focused on nicotine replacement.<sup>9</sup>
3. **Hypertension.** The management and control of hypertension diminishes the development and progression of PAD and the risk of adverse perioperative cardiac events such as stroke, myocardial infarction (MI), and cardiovascular death. The target blood pressure for the general population is 140/80 mmHg and <130/80 mmHg for patients with chronic kidney disease and diabetes. Beta-receptor blockers and angiotensin-converting enzyme inhibitors have been proven to reduce the incidence of MI and cardiovascular death in patients with coronary artery disease and have been shown to reduce these same adverse outcomes in patients with PAD.<sup>5</sup>
4. **Hyperlipidemia.** Control of high serum lipids slows the progression of atherosclerosis. Lipid-lowering therapy is effective in reducing the cardiovascular mortality and morbidity associated with PAD and likely improves the most common symptom of PAD, intermittent claudication.<sup>4</sup> The goal for hyperlipidemia management is to maintain an LDL level of <100 mg/dL in the general population and <70 mg/dL in patients with atherosclerotic disease.<sup>5</sup> When the target of <70 mg/dL is chosen for a patient, an HGM-CoA reductase inhibitor, commonly known as a statin, should be initiated. Healthcare providers should increase statin therapy in a graduated fashion to adequately determine the patient's response and tolerance. Since statins are cleared hepatically, it is recommended that liver enzymes be tested before initiating the medication, 12 weeks following initiation of therapy, upon any elevation of the medication dose, and semiannually. Statins should be used with caution in patients who consume substantial quantities of alcohol and/or have a history of chronic liver disease. Other side effects of HGM-CoA reductase inhibitors include myopathy and rhabdomyolysis with acute renal failure secondary to myoglobinuria. Therefore, statins should be prescribed with caution in patients with predisposing factors for myopathy (e.g., age ≥65 years, inadequately treated hypothyroidism, and renal impairment), and they should be discontinued if markedly elevated creatine kinase levels or myopathy is diagnosed or suspected. All patients should be advised to promptly report unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever.

5. **Sedentary lifestyle.** Regular exercise is important for a patient's overall cardiovascular health and has a positive impact on hypertension, hyperlipidemia, and diabetes. Regular lower extremity exercise in the form of a structured or supervised walking program is critical for patients with PAD. Ambulation can lead to the development of collateral blood flow and in time may lead to resolution or improvement of intermittent claudication. A minimum of 30 minutes of moderate activity at least three times per week is beneficial.<sup>10</sup> As the lower extremity adapts to the performed exercise, the patient should consider increasing the duration and frequency of their exercise.

6. **Antiplatelet therapy.** A significant cardiovascular benefit is achieved when patients with PAD take antiplatelet medications. Platelets are an important mediator in the initiation and propagation of thrombus formation, and antiplatelet medications are key in preventing ischemic and recurrent ischemic events. Aspirin is the most common antiplatelet agent and the most cost-effective therapy.<sup>5</sup>

Other pharmacological agents such as pentoxifylline and cilostazol have shown to modestly improve walking distances, primarily in patients with intermittent claudication only. Cilostazol has significant antiplatelet, vasodilatory, and vascular antiproliferative properties. The estimated effect of cilostazol 50 mg and 100 mg was improved walking distances of 35- and 70-meters, respectively.<sup>11</sup> While it has a significant positive effect on health-related quality of life, it is contraindicated in patients with either systolic or diastolic heart failure. Pentoxifylline had a diminished estimated effect when compared to cilostazol, with an improvement of only 60 meters with a 100 mg dose, and its impact on quality of life has not been evaluated. The role of these agents remains controversial.<sup>11</sup>

## Conclusion

Primary care providers serve as portals to direct patients through the healthcare system and, more importantly, act as implementers of cardiovascular preventive guidelines. They are also custodians of the long-term management of patients with peripheral vascular disease and systemic atherosclerotic disease. An enhanced ability to identify patients with PAD, as described in the PARTNERS study, and prompt referral of patients with significant disease to a vascular specialist will improve patient outcomes, limb preservation, and quality of life.<sup>2</sup> The primary care provider plays a vital role in preventing the progression of atherosclerotic disease to a cardiovascular event and mortality by being proactive in the patient's care.

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