Contemporary and Optimal Medical Management of Peripheral Arterial Disease

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KEYWORDS

• Peripheral arterial disease • Claudication • Cardiovascular disease risk
• Supervised exercise therapy • Optimal medical therapy

KEY POINTS

- Atherosclerotic lower extremity peripheral arterial disease (PAD) is a highly prevalent condition associated with a significant increase in risk of all-cause mortality and cardiovascular morbidity and mortality.
- PAD is underdiagnosed and undertreated.
- Treatment is focused on 2 primary objectives: (1) lowering cardiovascular risk and cardiovascular disease (CVD) event rates and (2) improvement in symptoms and quality of life.
- Contemporary multidisciplinary and intersociety guidelines exist to optimal medical therapy.
- Substantial evidence supports the implementation of tobacco cessation counseling and pharmacotherapy to help achieve tobacco abstinence, antiplatelet therapy, HMG-CoA reductase inhibitors (statins) therapy and antihypertensive therapy in patients with PAD for the purpose of lowering cardiovascular event rates and improving survival.
- For patients with claudication, supervised exercise therapy and cilostazol improve measures of walking performance and quality of life.

BACKGROUND

PAD refers to the stenosis, occlusion, or aneurysmal change of upper extremity and/or lower extremity arteries.[1,2] Although the term, PAD, can be used to categorize a variety of disease entities and presentations, the acute and chronic conditions associated with atherosclerosis are the most common. The focus of this review is on the epidemiology, risk factors, and medical management of nonacute atherosclerotic lower extremity PAD.

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EPIDEMIOLOGY

PAD affects more than 8 million adults in the United States alone.[3] PAD is a disease of aging, with an increase in disease prevalence from 10% in individuals aged 65 to more than 30% in octogenarians.[4,5] Concomitant PAD is highly prevalent in individuals with new or established cerebrovascular or coronary artery disease, with prevalence rates greater than 30%.[6,7] Many studies have demonstrated equal prevalence among genders but there is a well-described ethnic disparity, with PAD afflicting non-Hispanic African Americans and Mexican Americans at a higher rate than non-Hispanic whites.[4] Even after controlling for traditional risk factors, PAD prevalence is 2-fold higher in non-Hispanic African Americans compared with non-Hispanic whites.[4,8]

PAD is associated with significant morbidity and mortality, with more than 14,000 US deaths attributable to PAD in 2011.[3] Studies have indicated that regardless of symptom status, the presence of PAD or a low ankle-brachial index (ABI) (<0.9) is associated with a more than 2-fold increase in total mortality, cardiovascular mortality, and coronary events.[9–11]

PAD is an under-recognized condition. The classical clinical presentation of PAD is lower extremity claudication. Historically, claudication has been defined using the Rose questionnaire[12]:

- Pain involving 1 or both calves
- Provoked by exertion
- Not present at rest
- Prompts patient to stop exertion
- Must abate within 10 minutes of rest
- No abatement in leg pain during continued exertion

Less than 10% of patients afflicted with PAD, however, present with typical claudication symptoms.[5] A majority of patients with PAD are either asymptomatic or present with atypical leg pain and a minority of patients present with acute or limb threatening conditions:

- Asymptomatic approximately 40%
- Atypical leg pain approximately 50%
- Typical claudication less than approximately 10%
- Critical limb ischemia approximately 1%–3%
- Acute limb ischemia less than 1%

Recent analyses have indicated that the diagnosis of PAD is missed in 85% to 90% of patients when relying only on clinical history or a screening questionnaire.[13]

PATHOPHYSIOLOGY

Claudication symptoms occur due to a mismatch in oxygen demand and delivery in the skeletal muscles. Arterial insufficiency and PAD most often occur due to insidious progression in the severity of atherosclerosis, but other processes can also cause reduced arterial blood flow (**Box 1**). The presence and severity of symptoms are also affected by other physiologic factors (muscle mechanics and energy metabolism, endothelial function, collateral blood flow, oxygen delivery, and carrying capacity) and patient factors (age, weight, and conditioning). Atherosclerotic PAD is a marker of a progressive systemic process; therefore, even asymptomatic disease and borderline reduction in ABI values (0.9–1.0) are associated with a significantly increased risk in all-cause mortality and cardiovascular morbidity and mortality.[5,11,14,15]