

Review

The Significance of Lower Extremity Peripheral Arterial Disease

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Summary: The role of the cardiologist is expanding and involves the management of patients with lower extremity atherosclerotic occlusive arterial disease. Peripheral arterial disease (PAD) remains an underdiagnosed and undertreated disease. The purpose of this review is to educate the clinician on the significance of lower extremity atherosclerotic occlusive arterial disease. Pathophysiology and anatomy are briefly reviewed. The definition of PAD is based upon both anatomic and functional considerations. Risk factors for PAD include traditional atherosclerotic risk factors. There is a considerable overlap between coronary and cerebrovascular diseases and PAD. Diagnosis is made mainly by history and physical examination. Noninvasive and invasive tests help diagnosis and localize disease. Expanded therapies to improve outcomes include lifestyle changes, medical treatment, interventional cardiovascular procedures, or surgical intervention.

Key words: atherosclerosis, peripheral arterial disease, morbidity, mortality, lower extremity, occlusive arterial disease, review, intermittent claudication, prognosis

Introduction

Atherosclerotic disease is diffuse in nature. As cardiologists, we tend to focus upon atherosclerosis of the coronary arteries and the resultant complications; however, atherosclerosis of the peripheral arterial system contributes to significant morbidity and mortality in our patients. As the role of the cardiologist becomes increasingly broader and encompasses cardiovascular diseases in general, it is imperative that we learn the significance of lower extremity peripheral arterial disease (PAD).

This review will discuss the importance of PAD. Anatomic and physiologic definitions of lower extremity atherosclerotic occlusive arterial disease as well as its pathophysiology will be discussed. The prevalence of PAD in various populations as well as risk factors for the development of atherosclerotic disease will be presented. The natural history, including morbidity and mortality concerns of PAD, will be reviewed. Treatment options will be reviewed only in brief. The intent of this review is to develop a greater appreciation for PAD and update cardiovascular medicine specialists on this disease.

Some readers may ask, “if PAD is generally from atherosclerosis and most of our patients have coronary artery disease (CAD), what is the rationale of looking for PAD if our recommendations will not be changed?” By being educated in lower extremity PAD, the clinician will be able to increase the quality of life of the patient and substantially reduce the associated morbidity and mortality of this disease. The role of the cardiologist is expanding into that of a cardiovascular medicine specialist due to many advances in preventive, medical, rehabilitative, and interventional therapies.

Atherosclerotic PAD affects nearly 10% of men 65 years of age, increasing to 20% of men and women ≥ 75 years.¹ In North American patients with systolic hypertension aged > 60 years, approximately 25% have ankle-brachial indices (ABIs) ≤ 0.90 .² The incidence of intermittent claudication increases with age, but by the age of 55 years, there are approximately five cases per 1000 patients per year. The overall prevalence of intermittent claudication for those aged > 55 years is 4.5%.³ Examination for femoral arterial atheroscle-

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Received: February 27, 2001

Accepted with revision: August 8, 2001

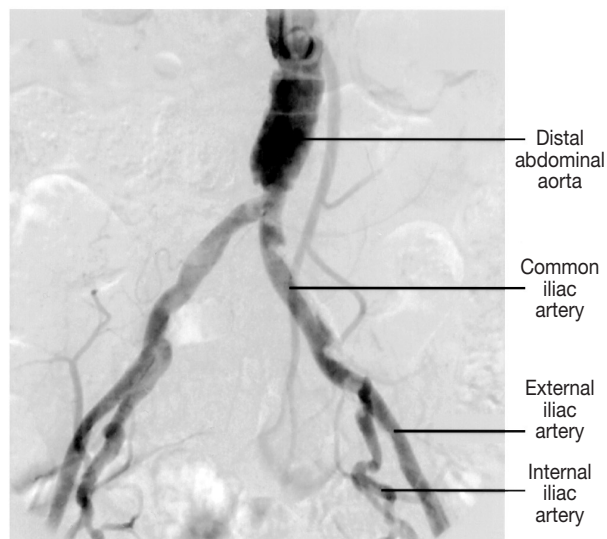


FIG. 1 Aortic bifurcation with occlusive disease.

rotic plaque has yielded a significantly higher prevalence of this disease.⁴ In absolute terms, this translates into several million Americans with either asymptomatic or symptomatic atherosclerotic PAD.

It is difficult to estimate directly the cost caused by PAD. Not only are there direct and indirect costs of treating PAD, but many of these patients eventually succumb to various forms of cardiac disease. Annually, over 50 billion dollars are spent on cardiac disease in the United States.⁵ Furthermore, as the mean age of the population increases, the direct and indirect costs of PAD are expected to continue to increase.

Despite better awareness of coronary arterial disease, PAD is still underdiagnosed—only 20% of patients with PAD have been told that they have the disease.⁶ Various studies have

demonstrated that patients with PAD are not getting proper medical care. In a study by McDermott *et al.*, among 349 consecutive patients with CAD or PAD diagnosed by cardiac catheterization or blood flow studies, only 46% of the patients with PAD with hypercholesterolemia were on lipid-lowering therapy compared with 58% of hypercholesterolemic patients with CAD. Regarding exercise, 71% of the patients with CAD exercised compared with only 50% of the patients with PAD; 74% of the patients with CAD but only 46% of the patients with PAD were told to exercise.⁷ Furthermore, the role of the cardiologist is expanding into that of a cardiovascular medicine specialist.

Peripheral Arterial Anatomy

The abdominal aorta bifurcates into bilateral common iliac arteries (Fig. 1). The common iliac arteries divide into the internal iliac arteries, which supply the pelvis, and continue on as the external iliac arteries. The external iliac arteries, after passing under the inguinal ligament, become the common femoral arteries (Fig. 2). The profunda femoris artery branches off the common femoral artery as the superficial femoral artery continues. As the superficial femoral artery passes into the popliteal fossa, it is renamed the popliteal artery. Upon exit from this fossa, the popliteal artery trifurcates into the anterior tibialis artery, which distally is the dorsalis pedis artery, the posterior tibialis artery, and the peroneal artery (Fig. 3).

Definition and Classification of Peripheral Arterial Disease

Lower extremity occlusive PAD can be defined on the basis of anatomical or functional considerations. Anatomically it is defined as atherosclerotic arterial disease, while functionally it is defined as arterial narrowing, causing a mismatch between

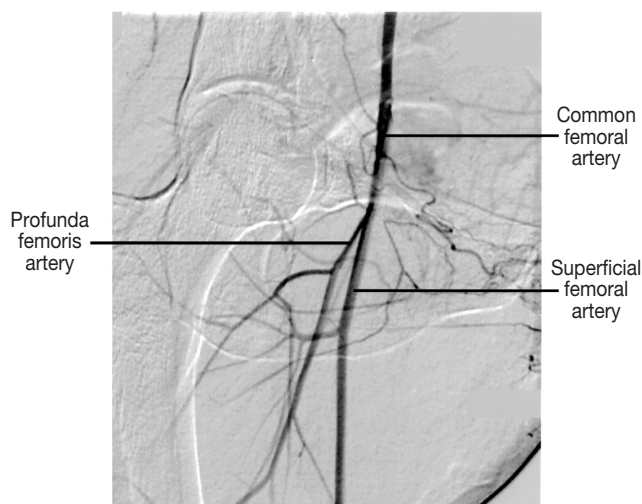


FIG. 2 Femoral artery bifurcation.

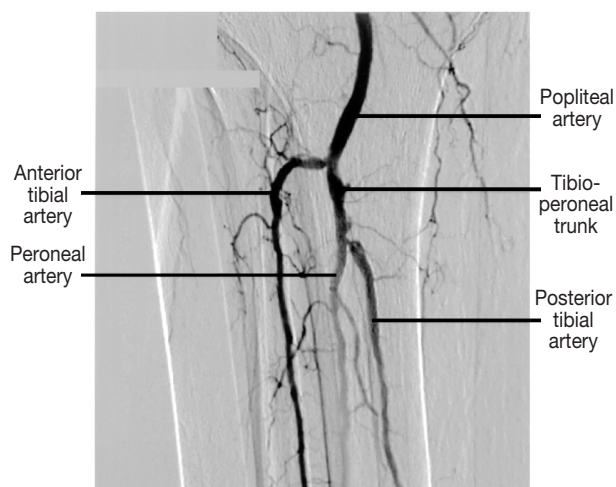


FIG. 3 Popliteal artery trifurcation with occlusive disease.

TABLE I Asymptomatic versus symptomatic peripheral arterial disease

	Asymptomatic	Symptomatic
Ankle-brachial index	<0.9	<0.9
Frequency	1–6× more common	4.5% (≥ 55years)
Functional capacity	Reduced	Reduced
Classification	Fontaine I/ Rutherford 0	Fontaine IIa or higher, Rutherford I or higher

the oxygen supply and demand resulting in symptoms of intermittent claudication, exercise limitations, or tissue loss. These two definitions help divide PAD into asymptomatic and symptomatic disease states.

For every symptomatic patient with PAD, it is estimated that there are at least one to six asymptomatic patients (Table I).^{3, 8} In a study of patients with PAD, Schroll and Munck reported that only 18 of 95 (19%) of patients with PAD were symptomatic.⁸ Using ultrasonographic examination of the femoral artery for atherosclerotic plaque and a questionnaire for intermittent claudication in men and women 56–77 years of age, Leng *et al.* found that although overall 64% of the patients had femoral artery plaque, <15% were symptomatic.⁴ The prevalence of plaque increased with age, as did intermittent claudication. Of the patients <60 years of age, 51% already had established femoral artery plaque.⁴

Based upon the degree of PAD, ranging from asymptomatic to ischemic ulceration, gangrene, and tissue loss, two major classifications of PAD have been developed. The Fontaine classification uses four stages. Fontaine I represents those who are asymptomatic; IIa and IIb are mild and moderate-severe intermittent claudicants, respectively; those with ischemic rest pain are Fontaine IIIs; and ulcerations and gangrene represent Fontaine IV.³ A similar classification scheme has been developed by Rutherford. The Rutherford classification has four grades, 0–III, and six categories, with grade I having three categories. This classification system is similar to Fontaine's, except claudicants have four categories and tissue loss is subdivided into two categories, minor and major.³

Pathogenesis of Atherosclerosis

Although atherosclerosis has been known for over a century, an understanding of the cellular and molecular mechanisms has only been recently elucidated. The atherosclerosis process in peripheral arteries is thought to be similar to that described in the coronary and cerebral circulation, although the flow dynamics and stimulants may be different.

There is a correlation between the degree of atherosclerosis in the brachial artery, carotid artery, and coronary arteries (correlation coefficient, r , 0.4–0.7).⁹ However, advanced lesions, especially in adults >50 years of age, are more likely found in the coronary arteries than in the brachial artery, and the correlation is not as significant in this age group. Certain vascular

territories, including the mesenteric arteries, appear to be less susceptible.⁹ Within an individual there may be a wide variation in the distribution and severity of atherosclerosis.⁹ Likely explanations for this disparity include different flow characteristics, shear stress, and other local factors.¹⁰

Atherosclerosis results from an excessive inflammatory and fibroproliferative response to numerous vascular insults, which leads to alteration of the normal homeostatic properties of the endothelium.^{10, 11} The earliest changes preceding the formation of atherosclerosis lesions occur in the endothelium, which include increased endothelial permeability to lipoproteins and other plasma constituents, upregulation of leukocyte adhesion molecules, upregulation of endothelial adhesion molecules, and migration of leukocytes into the artery wall. The above processes are mediated by numerous vasoactive molecules, cytokines, and growth factors.¹¹ Subsequently, if the inflammatory response cannot neutralize or remove the insulting agents, the inflammatory response will stimulate migration and proliferation of smooth-muscle cells which participate in the formation of fatty streaks in atherosclerosis along with lipid-laden monocytes, macrophages (foam cells), and T lymphocytes.¹¹ Continued inflammation leads to increased amounts of macrophages and lymphocytes, which can emigrate from the blood and multiply in the lesion. Activation of these cells results in release of many factors that induce further damage and eventually lead to focal necrosis. This pathologic process causes further enlargement and restructuring of the lesion, so that it becomes covered by a fibrous cap that overlies a core of lipid, a mixture of leukocytes, and necrotic tissue. The necrotic core represents the results of apoptosis and necrosis, increased proteolytic activity, and lipid accumulation.¹¹ Finally, thinning of the fibrous cap is caused by continuing influx and activation of macrophages, which release metalloproteinases and other proteolytic enzymes. Rupture of the fibrous cap or ulceration of the fibrous plaque can rapidly lead to thrombosis or accelerated plaque growth and usually occurs at sites of thinning of the fibrous cap (e.g., at the edge of the cap) that covers the advanced lesion.¹¹

Therefore, atherosclerosis is a multistaged, multigenic, and very complicated inflammatory disease. During atherogenesis, growth factors, cytokines, lipids, and enzymes modulate critical cell functions by inducing lipid accumulation and oxidation, cell-mediated inflammatory response, smooth-muscle proliferation, vasoconstriction, and a prothrombotic environment within the artery wall.^{10, 11} In the past few years, other probable atherosclerotic risk factors in addition to conventional risk factors have been discovered. These include elevated homocysteine and fibrinogen; impaired fibrinolysis; increased platelet reactivity; hypercoagulability; lipoprotein (a), small dense low-density lipoprotein cholesterol; and inflammatory and infectious markers.^{12, 13} As we know, hypercholesterolemia is one of the principal risk factors for atherosclerosis, but only about 50% of atherosclerosis can be attributed to this condition.¹¹ Therefore, identification of other risk factors may allow better insight into the pathophysiology of atherosclerosis and facilitate the development of preventive and therapeutic measures.¹²

Comorbidities and Risk Factors for Peripheral Arterial Disease

In the vast majority of patients, PAD is a disease of atherosclerosis. Analysis of data from Aronow and Ahn¹⁴ and the Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events (CAPRIE) study¹⁵ demonstrate that there is considerable overlap between cerebral, coronary, and peripheral atherosclerotic disease. It is estimated that 40% of patients with CAD have symptomatic PAD. This finding is not well defined and varies based upon the diagnostic criteria. Of those patients with more severe PAD, there is a 60% incidence of significant CAD (>70% stenosis of at least one coronary artery), and almost one third have severe, correctable, triple-vessel CAD with depressed left ventricular function.^{5,16} The interrelation between PAD and CAD is striking.

Numerous studies have elucidated the risk factors for lower extremity atherosclerotic occlusive arterial disease (Table II).^{3,4,17,18} Traditional risk factors include age, possibly gender, smoking (remote and current, personal and secondhand), diabetes and impaired glycemic control, hypertension, fibrinogen, hyperlipidemia with an elevated low-density lipoprotein (LDL), low high-density lipoprotein (HDL), homocysteine, lipoprotein (a), and potentially many other minor factors. Both exercise and alcohol intake are negative risk factors for PAD.¹⁷ Analysis of the Framingham Heart Study for risk factors and intermittent claudication risk demonstrates that male gender is a significant risk factor for the development of symptomatic PAD, although not all studies have found a similar association.¹⁹ Age is a consistent risk factor for PAD.^{1,3} In the Bogalusa study, Berenson *et al.*, using autopsy data, showed convincing evidence that atherosclerosis may begin at a very young age and is not unique to middle-aged and older individuals with other risk factors.²⁰ The incidence of symptomatic PAD in subjects aged >70 years is approximately 5%, with asymptomatic disease several times higher.^{1,21}

Intermittent claudication is 3.4 times more frequent among men with diabetes mellitus and 5.7 times more frequent among women with diabetes.³ In subjects with type 2 diabetes mellitus, the UKPDS study clearly showed that the risk of ampu-

tation or death from peripheral vascular disease was closely associated with the glycosylated hemoglobin A_{1c} level,²² although intensive treatment did not seem to reduce this risk significantly.²²

As with CAD, tobacco smoking is closely linked to PAD. The severity of PAD is directly proportional to the number of cigarettes smoked. On average, the diagnosis of PAD is made 10 years earlier in smokers than nonsmokers. Overall, PAD is three times more prevalent in smokers.³

The degree of hypertension is also closely linked to the development of PAD.¹⁹ Atherosclerotic PAD itself may contribute to hypertension, thus establishing a cycle of PAD and hypertension. Indeed, the treatment of hypertension may unmask previously asymptomatic PAD, presumably by decreasing the pressure gradient across the diseased vessel. However, there have been no trials that convincingly demonstrate that the use of adrenergic beta-blocking agents is detrimental in patients with PAD.

Natural History of Lower Extremity Peripheral Arterial Disease

Lower extremity PAD is associated with significant morbidity and mortality. Compared with patients without PAD who walk at 3.3 mph, intermittent claudicants can only walk at an average of 1–2 mph.^{23–25} In a study of 933 elderly women in the Baltimore area, McDermott *et al.* found 35% with an ABI <0.9. Only 6.7% were told that they had PAD, and 63% had no exertional leg pain.⁶ Examining only those with asymptomatic PAD (i.e., those without claudication), these subjects had slower walking capacity, poorer standing balance score, a slower time to arise five times from a seated position, and they walked fewer blocks in a week than did those with an ABI >0.9.⁶ Thus, PAD—either symptomatic or asymptomatic—results in significant physical limitations.

Weitz *et al.* analyzed the outcomes of individuals with PAD aged >55 years.²⁶ At 5 years, the majority of those with intermittent claudication had stable claudication (73%), 16% had progression of their intermittent claudication, and only 7% required leg bypass surgery, with an additional 4% undergoing an amputation.²⁶ However, the 5-year mortality is 30% and the incidence of nonfatal events (myocardial infarctions or strokes) was 20%.²⁶ At 1-year follow-up, 20% of patients with critical limb ischemia were dead, 35% had undergone an amputation, and 45% were alive without an amputation.³

The mortality for asymptomatic PAD is similar to that of mild to moderately symptomatic subjects.²⁷ The mortality rate for patients with PAD correlates well with the ABI.^{27–29} All-cause mortality is approximately 30% at 5 years, 50% at 10 years, and 70% at 15 years.³ The majority of these patients die of cardiac, cerebrovascular, or other vascular causes. The 5-year mortality is roughly similar to that of patients with breast cancer or colorectal cancer.^{27,30} It is evident that the majority of patients do not require surgical intervention; they rather need medical care from the cardiovascular medicine specialists.

TABLE II Risk factors^{3,4,17,18}

Positive risk factors	Negative risk factors
Advancing age	Regular physical activity
Smoking	Moderate alcohol intake
Diabetes (level of glycemic control) and impaired glucose tolerance	
Hypertension	
Fibrinogen	
Hyperlipidemia (elevated LDL, low HDL, elevated LP[a])	
Homocysteinemia	

Abbreviations: LDL = low-density lipoprotein, HDL = high-density lipoprotein, LP(a) = lipoprotein(a).

Diagnosis

The diagnosis of PAD is made based upon a focused history and physical examination, and is aided by noninvasive and invasive studies. Intermittent claudication is classically evoked by exercise, with the patient usually being able to give almost the precise distance as to its onset. Claudication pain is promptly relieved by rest in the majority of claudicants. Most claudicants describe their pain as dull, aching, cramping, or a heaviness.³¹ The differential diagnosis for intermittent claudication includes venous claudication (history of deep venous thrombosis), chronic compartment syndrome (generally seen in athletes), spinal stenosis, osteoarthritis of the hip, as well as some less common pathologic states such as rheumatologic/connective-tissue diseases (Table III). In the elderly population, spinal stenosis is a common comorbid condition. The pain of spinal stenosis is more variable in onset and may occur with prolonged standing; the pain is relieved gradually by leaning forward with flexion of the lumbar spine.

The Rose/WHO questionnaire was developed to detect symptomatic PAD. The questionnaire consists of eight questions with predictable answers in patients with intermittent claudication.³² The sensitivity is estimated at 60–68% and the specificity at 90–100%.^{3,31} The Edinburgh modification of the Rose/WHO questionnaire was developed in order to increase the sensitivity and specificity and to make the questionnaire easier to administer.³¹ The final Edinburgh modification of the Rose/WHO questionnaire consists of six questions with a diagram to indicate the location of the pain; the sensitivity of this questionnaire is 91.3% and the specificity 99.3%.³¹

Careful physical examination of the patient suspected of PAD should concentrate on the arterial system. The abdomen should be auscultated for bruits and palpated for an aneurysm. Femoral, popliteal, posterior tibialis, and dorsalis pedis pulses should be palpated and graded. Peripheral pulses should be graded as 0–2, with normal pulsations being 2, diminished 1, and absent 0.³ The feet and lower extremities should be inspected for ulcers, fissures, calluses, tinea, or tendinous xanthomas.³ It is worth mentioning that the dorsalis pedis pulse is congenitally absent in approximately 10% of the population and that the posterior tibialis pulse is congenitally absent in < 1% of the population.^{31,33} Congenital absence of these pulses is more common in Caucasians than in blacks.³¹ An abnormal posterior tibialis pulse is 71.2% sensitive and 91.3% specific for PAD, whereas an abnormal dorsalis pedis pulse is only 50% sensitive and 73.1% specific.³⁴

TABLE III Differential diagnosis for intermittent claudication^{3,5,6,37}

Spinal stenosis
Venous claudication
Chronic deep venous thrombosis causing venous claudication
Chronic compartment syndrome
Osteoarthritis
Rheumatologic/connective-tissue diseases

Noninvasive measurements are invaluable in the diagnosis and management of PAD. Noninvasive studies include the ABI, segmental limb systolic pressure measurements, arterial plethysmography/pulse volume recordings, ultrasound and Doppler velocity waveforms, tissue oxygenation, magnetic resonance imaging (MRI) and computerized tomography (CT).

The ankle systolic blood pressure should be greater than the brachial systolic blood pressure; thus, the ratio of ankle to brachial pressures should be greater than one. If this ratio (ABI) is < 0.9, it is up to 95% sensitive and specific for detecting angiographic arterial disease.³⁵ An ABI of < 0.4 represents severe arterial occlusive disease with a high potential for tissue loss; an ABI > 1.3 indicates a noncompressible calcified artery. In patients with a normal resting ABI, an exercise ABI or reactive hyperemia ABI may be performed to provide objective evidence for intermittent claudication and lower extremity occlusive arterial disease.³⁵ Segmental limb systolic pressure measurements may be combined with an ABI to help localize the area of stenosis. Segmental plethysmography (pulse volume recording) measures the changes in the volume of each limb, in different segments of the leg, with each cardiac cycle. Used in combination with segmental limb systolic pressure measurements, the segmental plethysmography can be up to 95% accurate in detecting and localizing angiographic disease.³⁶

Doppler velocity waveform analysis uses continuous-wave Doppler ultrasound to record arterial pulsations in various lower extremity arteries. The normal wave form is triphasic. Loss of the triphasic pattern and analysis of the peak velocity can localize the area of stenosis.³⁷ Other noninvasive imaging modalities (MRA and CT angiography) can help further define the anatomy and differentiate between tightly localized disease and well collateralized long occlusions.

Angiography is considered the standard of reference for anatomic definition. The use of digital subtraction angiography has allowed better diagnosis and image definition. For patients with renal insufficiency, carbon dioxide angiography is available which does not have the risk of nephrotoxicity that traditional iodinated contrast agents do. However, angiography is not benign; the overall rate of contrast reaction is 0.1%, major complications occur in 0.7% of the cases, with a 0.16% mortality rate.^{38,39}

Treatment

The goal of this article was to outline the importance of PAD to cardiovascular medicine specialists. However, a brief discussion of treatment options for patients with PAD will be made.

Treatment of PAD can be broadly classified into four categories: risk factor modification, exercise and cardiovascular rehabilitation, pharmacologic intervention, and invasive strategies. All patients with atherosclerotic occlusive PAD need to be made aware of their diagnosis and the associated morbidity and mortality, especially from cardiovascular diseases.

Patients with PAD require aggressive risk factor modification. A systematic review of the patient's risk factors is neces-

sary and appropriate interventions must be made. Modifiable risk factors such as hypertension, hyperlipidemia (including hyperhomocysteinemia), sedentary lifestyle, smoking status, diabetes, and glycemic control all need to be evaluated. Smoking cessation for these patients is paramount. Smoking cessation reduces the likelihood of amputation and may increase the ABI and walking distance.⁴⁰⁻⁴² Thus, a smoking cessation program should be a vital component to PAD treatment. Arguably, first-line treatment of hypertension should be with either an adrenergic beta-receptor blocker (beta blocker) or an angiotensin-converting enzyme inhibitor (ACE-I). Although some patients treated with beta blockers may experience a worsening of their claudication, there are no compelling trials showing a significant detrimental effect, while there are numerous studies demonstrating the efficacy of beta blockers in associated coronary disease. In the Heart Outcomes Prevention Evaluation (HOPE) trial, patients with documented cardiovascular disease or those at high risk for cardiovascular disease benefited significantly from the use of ramipril, demonstrating an absolute risk reduction of 3.8% in the composite primary outcome of myocardial infarction, stroke, or death.⁴³

In addition to risk factor modification, a regular exercise program is central to the treatment of PAD.²⁶ Exercise rehabilitation should be at least of 3–6 months' duration, and ideally be supervised and lifelong. Patients are instructed to walk until claudication develops, at which point they should stop until the pain resolves, then begin walking again. Regular exercise has been shown to increase on average the initial claudication distance by 179% and the maximal walking distance to 122%.³

Apart from the necessary drugs to modify risk factors (e.g., antihypertensives, cholesterol lowering medications, etc.), pharmacologic therapy for PAD includes antiplatelet agents and agents that increase the distance to claudication (e.g., pentoxifylline and cilostazol). If the patient has known CAD, then aspirin therapy is indicated. The CAPRIE trial compared clopidogrel, a thienopyridine derivative, with aspirin in patients with atherosclerotic cardiovascular disease (recent ischemic stroke, recent myocardial infarction, or symptomatic PAD). Overall, patients randomized to clopidogrel showed a small but significantly different reduction in the endpoint of ischemic stroke, myocardial infarction, or vascular death.¹⁵ Patients generally tolerate clopidogrel well; however, cases of severe neutropenia and thrombotic thrombocytopenic purpura (TTP) have been noted in patients taking clopidogrel.^{15, 44, 45} Both cilostazol and pentoxifylline are designed to limit the symptoms of intermittent claudication. The efficacy of pentoxifylline beyond that of placebo, however, has been questioned. In a comparison of cilostazol, pentoxifylline, and placebo among patients with stable, moderate to severe symptoms of intermittent claudication, cilostazol showed significant improvement in walking distance compared with the other two groups.⁴⁶ The pentoxifylline group did not differ significantly from the placebo group.⁴⁶ Other studies have shown conflicting results with pentoxifylline.³ Because cilostazol is a phosphodiesterase inhibitor, it is contraindicated in those patients

with a low left ventricular ejection fraction or subjective congestive heart failure.⁴⁷ Vascular endothelial growth factor, basic fibroblast growth factor, and rFGF-2 are being studied to improve collateral vessel growth.³ Single intra-arterial rFGF-2 has shown promise, at least for short term management of intermittent claudication.⁴⁸

Comprehensive evaluations of pharmacologic interventions in PAD can be found elsewhere.⁴⁹

Invasive interventions for PAD are required in some patients who fail to improve or who deteriorate despite aggressive risk factor modifications, exercise programs, and pharmacologic interventions. Therapeutic options include percutaneous as well as surgical revascularization. Reviews of endovascular treatments of PAD can be found elsewhere.^{50, 51} Few patients with PAD require surgical interventions.

Conclusion

Lower extremity peripheral arterial occlusive disease is common, especially in patients with cardiovascular disease. Despite the prevalence of PAD, it is still underdiagnosed and undertreated. Risk factors for PAD are readily identified and include traditional atherosclerotic risk factors. Morbidity and mortality are significant in patients with PAD. Diagnosis is made by both history and physical examination, as well as by various noninvasive and invasive modalities. Treatments include lifestyle changes, aggressive medical management, rehabilitation, and possibly cardiovascular interventions. The majority of these patients do not require surgical intervention. Proper treatment of PAD requires a knowledgeable clinician with a strong emphasis on cardiovascular disease prevention.

Addendum

Since the acceptance of this manuscript, the results of the Peripheral Arterial Disease Detection, Awareness, and Treatment in Primary Care (PARTNERS) study has been published.⁵² Among other endpoints, this study evaluated the prevalence of PAD in patients who were over the age of 70, or were between the age of 50 and 69 years with a history of cigarette smoking or diabetes. Peripheral arterial disease was defined as an ABI < 0.9, prior documentation of PAD, or limb revascularization. A modification of the Rose questionnaire, the San Diego Claudication Questionnaire, was used to assess leg symptoms and allowed for lateralization of leg pain, and classification as either classic, atypical, or no pain. This study confirmed the relative lack of awareness of PAD by patients and their physicians (83% of patients with prior PAD were aware of their condition, although only 49% of physicians were aware of their patient's diagnosis). Furthermore, classic claudication, as defined by the Rose questionnaire, was uncommon in those with PAD, ranging from 5.5 to 15.3% depending on group characteristics. Finally, the PARTNERS study confirmed the lack of treatment for patients with PAD, overall and in comparison with those patients with other car-

diovascular disease. The treatment of hypertension, hyperlipidemia, and the use of antiplatelet medications was less in patients with new or prior PAD than in patients with cardiovascular disease only (hypertension: 84%, 88 vs. 95%; hyperlipidemia: 44%, 56 vs. 73%; antiplatelet medications: 33%, 54 vs. 71%, respectively).

Acknowledgment

The authors would like to thank Dr. Valentin Fuster for his assistance with sections of this manuscript.

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