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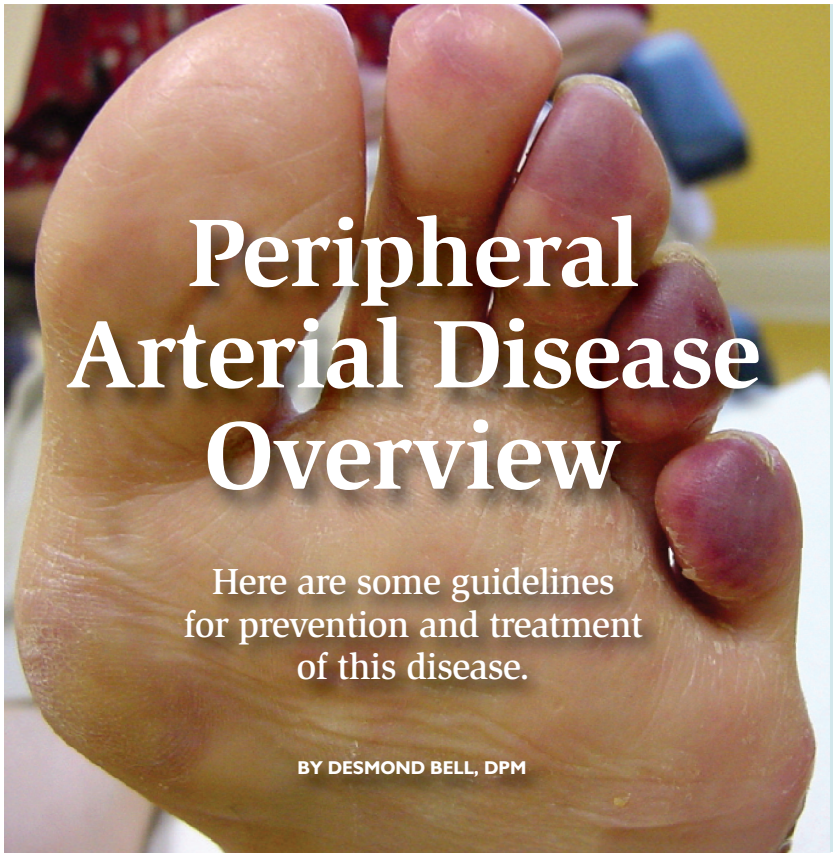

Peripheral Arterial Disease Overview

Here are some guidelines for prevention and treatment of this disease.

BY DESMOND BELL, DPM

Objectives

After completing this CME, the reader should be able to:

1) Define peripheral arterial disease.

2) Comprehend the pathophysiology of peripheral arterial disease.

3) Understand the risk factors for peripheral arterial disease.

4) Differentiate the symptoms of P.A.D. from other conditions that share similar presentation.

5) Encourage early detection of P.A.D. to empower podiatric physicians in the prevention of critical limb ischemia and other catastrophic events, such as heart attack and stroke.

6) Recognize the financial impact of peripheral arterial disease, amputation, and limb preservation

7) Apply knowledge of medical management of peripheral arterial disease into practice.

8) Understand the need of when to refer patients for endovascular or surgical intervention to prevent amputation and to increase chances for limb salvage.

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*Following this article, an answer sheet and full set of instructions are provided (pg. 184).—**Editor***

Introduction

Never as much as now has the team approach to wound management and limb salvage presented the opportunity for podiatric physicians to serve as the gatekeepers in the reduction of lower extremity amputation.

In 2006, Allie reported that a three billion dollar annual saving to the U.S. healthcare system can be realized with a 25% reduction in lower extremity amputations.[1,2]

As podiatric physicians, we are positioned to identify the early and the advanced symptoms of peripheral arterial disease (P.A.D.) in our patients. The link between P.A.D. and coronary arterial disease makes recognition of P.A.D. symptoms not only important for potentially helping to reduce amputation rates, but also for preventing catastrophic events, such as heart attack and stroke. There is an increased risk of myocardial infarction (MI), stroke, and cardiovascular death in patients with lower extremity P.A.D., including a 20% to 60% increased risk for MI and a two- to six-fold increased risk of death due to coronary heart disease events. The risk of cerebral vascular accident (CVA) is increased by 40% in this pa-

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tient population.[3]

Medical-legally, we also find ourselves in the position where recognition of P.A.D. and pro-active intervention will not only be expected, but also necessary for better risk management. An article by Janov entitled "Seven Keys to Preventing Malpractice Lawsuits" included information regarding a case in Michigan where a jury awarded a patient $1.23 million for a podiatrist's failure to refer to a vascular specialist in a timely manner. The patient of the podiatrist was initially treated for an ulcer that deteriorated within approximately a three week period and led subsequently to ischemic gangrene and a below-the-knee amputation. The jury rejected the podiatrist's defense which included "the patient had chronic, but stable symptoms," and "the patient did not need an urgent referral".[4]

The point here is that where P.A.D. is an underlying issue, especially where a wound is present, deterioration is likely to occur. Referral to the appropriate vascular specialist is not only critical, but is a standard of care. Failure to refer a P.A.D. patient to a specialist can have tragic consequences for both patient and provider, whether podiatrist, primary care physician, internist, or nurse practitioner.

Team Approach

As P.A.D. recognition and treatment modalities improve with advances in technology, so does the opportunity to partner with other specialists. "Interventionalists" is a term used to refer to those physicians who can provide revascularization of arteries that are occluded due to P.A.D. Interventionalists include not only vascular surgeons, but also interventional cardiologists and interventional radiologists. The key to not only reduce amputation rates, but also improve wound-healing rates often lies in the amount of perfusion available. Working closely with interventionalists ensures better outcomes, reduced risk, and opportunities to not only increase referrals, but to further advance the importance and role of podiatry in the medical community.

P.A.D. Defined

Peripheral arterial disease is a type of occlusive peripheral vascular disease. P.A.D is the most common type of peripheral vascular disease; P.V.D., as defined, includes disease of both the arteries and veins.

P.A.D. affects the arteries outside the heart and brain and most commonly affects the arteries of the pelvis and legs. It affects 12-20% of Americans age 65 and older.[5] An estimated 12 million people in the U.S. alone suffer from P.A.D.[6] Compare these numbers with those of other common diseases and the fact is that P.A.D. is not only more prevalent, but is more deadly than diseases that have been better publicized.

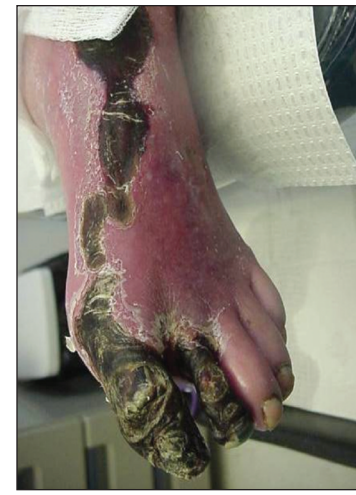

Figure 1: Critical Limb Ischemia in non-diabetic patient with long term tobacco abuse

Consider the fact that there is a three-time greater risk in those persons with diabetes over the age of 50 to have peripheral arterial disease.[7]

The disease prevalence of P.A.D. is approximately 12 million; this is greater than cancer (8.9 million), stroke (5 million), congestive heart failure (4.8 million), and Alzheimer's disease (4 million). The five-year mortality rate of P.A.D. is 30%, compared to colorectal cancer at 39%, stroke at 28%, CAD at 21%, and breast cancer at 14%.[8]

Atherosclerosis is the most common form of P.A.D. and P.A.D. is a systemic marker of atherosclerosis.[3] The word atherosclerosis is derived from the Greek words athero ("gruel" or "paste") and sclerosis ("hardness"). It is a process by which plaque builds up in the wall of an artery leading to varying degrees of reduced blood flow through the vessel, ranging from mild to complete (and often multi-segmental) occlusion. Plaque is made up of deposits of fats, cholesterol and other substances.

P.A.D Risk Factors

The risk factors for P.A.D. can be classified as traditional and non-traditional. Non-traditional risk factors include race/ethnicity, elevated levels of inflammatory markers: (C-reactive protein, fibrinogen, leukocytes, interleukin-6), chronic renal disease, genetics, hypercoagulable states (altered levels of D-dimer, homocysteine, lipoprotein[a]), abnormal waist to hip ratio, and sedentary lifestyle.[3]

Among the traditional risk factors are those that include advanced aging, smoking, diabetes, hypertension and hyperlipidemia.[3]

The prevalence of P.A.D. has been shown to increase with age. The Framingham Heart Study found subjects >65 years old were at increased risk for development of P.A.D., while the National Health and Nutrition Examination Survey, 1999-2000 (NHANES) report found patients >40 years old had a prevalence of 4.3%, while patients who were >70 yearsold had a prevalence of 14.5%.[8,9]

Smoking

Smoking increases the risk of P.A.D. four times and accelerates the onset of P.A.D. symptoms, particularly intermittent claudication, by nearly 10 years. Additionally, a dose-response relationship between pack year history and P.A.D. risk has been established. Smoking is the single most important modifiable risk factor for prevention of P.A.D. (Figure 1)[3]

Diabetes

Diabetes increases the risk of developing P.A.D. whether asymptomatic or symptomatic, by 1.5 to 4 times. Diabetes is also associated with an increased risk of cardiovascular events. Among diabetics, there is an early mortality among those with P.A.D. Diabetics are also at higher risk for developing ischemic ulcerations and gangrene. Diabetics also have more risk factors for developing P.A.D. than do non-diabetics. These risk factors include elevated blood pressure, increased triglycerides and increased cholesterol. Diabetics also appear to have greater vascular inflammation, increased endothelial cell dysfunction,

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abnormalities in vascular smooth muscle cells, increased platelet aggregation, and impaired fibrinolytic function when compared to non-diabetics.[10]

Pathophysiology of P.A.D.

Atherosclerosis frequently occurs at arterial bifurcations and branches where endogenous atheroprotective mechanisms are impaired as a result of disturbed flow on endothelial cells. Atherosclerosis causes the arteries to compensate initially by remodeling vessels which become larger in size. Advanced lesions intrude into the lumen of vessels, resulting in flow-limiting stenoses and chronic ischemia syndromes. Risk factors are involved in the initiation and acceleration of this process.

Atherosclerosis and the evolution of plaque formation may be characterized by four distinct stages that include:

- Lesion initiation
- Formation of fatty streak
- Fibroproliferative atheroma development
- Advanced lesion development

Lesion Initiation

Any mechanical or chemical injury can damage the endothelial cell layer. This alters the normal blood flow and provides sites for the adhesion and aggregation of thrombocytes, leading to the formation of blood clots or thrombi in the arterial wall. Alterations of the endothelial layer cause white blood cells (macrophages) to stick and to migrate into this layer, where they become active macrophages.

Fatty Streaks

The earliest recognizable lesions of the inner arterial layer are called "fatty streaks", which are aggregations of foam cells. Foam cells induce the further replacement of smooth endothelial cells by muscle cells from the medium arterial wall layer. The fatty streak affects the intima of the artery. The lesion consists largely of smooth muscle cells, monocytes, macrophages, T and B cells.

Fibroproliferative Atheroma

Fibroproliferative Atheroma originates from the fatty streak and contains larger numbers of smooth muscle cells filled with lipids.

Advanced Lesion

This highly cellular lesion contains intrinsic vascular wall cells (endothelial and smooth muscle). Advanced lesions also contain inflammatory cells (monocytes, macrophages, T-lymphocytes).

The advanced lesion also contains a lipid core that is covered by a fibrous cap. Acute arterial events can occur if the fibrous cap is disrupted. The resulting exposure of the "prothrombotic" necrotic lipid core and subendothelial tissue leads to thrombus formation and flow occlusion.

P.A.D. Symptoms and Differentiating Leg Pain Symptoms

An understanding of symptoms of P.A.D. may help to isolate the level(s) of the disease, regions of stenosis and, in most severe cases, the level of possible occlusions (Table 1). Since many patients who are afflicted with diabetes also suffer from P.A.D and peripheral neuropathy (among other disease manifestations), it is important to recognize the similarities and overlapping of symptoms. Remember that a patient does not have to be diabetic to have P.A.D., peripheral neuropathy, or both. Neuropathy may mask symptoms of P.A.D. Conversely, symptoms of P.A.D. may be mistaken for those of neuropathy.

Claudication is widely recognized as a dull cramping or pain in muscles of hips, thighs, or calf muscles when walking, climbing stairs, or exercising which is relieved with cessation of activity. Claudication is the most common manifestation of P.A.D.

Claudication may also be characterized by fatigue in the legs, which may require a patient to stop and rest while walking. These persons may also exhibit a slow or antalgic gait and may have difficulty keeping up with others when ambulating.

Rest pain or night pain that occurs when legs elevated in bed, and relieved when placed in dependent position is another common symptom of P.A.D. Pain may typically occur in the distal foot, possibly in the vicinity of an ulcer. Questions that should be asked of patients where P.A.D. is suspected should include: "Do you have pain when you elevate your legs at night? And "Do you ever sleep sitting up with pillows behind your back, or with your legs dangling from the side of the bed?"

Impotence may also be a sign of P.A.D. and patients may see some relief with sildenafil citrate.

Critical Limb Ischemia

Critical limb ischemia is characterized by persistently recurring rest pain requiring regular analgesia. Externally,

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TABLE 1

Differentiating Leg Pain Symptoms

Pain Symptomology	PAD Pain	Pain from Other Causes
Character	Variable. Fatique to severe pain	Same. May have weakness
Location	Buttock, hip, thigh, calf, feet	
Exercise induced	Yes	Same
Distance to claudication	Same each time (may vary with speed)	Variable
Occurs with standing	No	Yes or no
Relief	Stop walking	Often must sit or change body position

CLI may reveal non-healing ulceration or gangrene of the leg, ankle, foot, or toes. These ulcers are typically exquisitely painful, even in cases where patients are afflicted with concomitant decreased sensation due to neuropathy. Threatened limb loss or tissue loss is impending.

The Rutherford-Becker categorization of lower extremity P.A.D. specifies the extent of symptoms from asymptomatic to those seen in critical limb ischemia (Rutherford-Becker Category 4-6).[11] The Rutherford-Becker categories include:

0. asymptomatic
1. mild
2. moderate
3. severe
4. Ischemic rest pain
5. minor tissue loss, e.g. non-healing ulcer, focal gangrene
6. major tissue loss, i.e. above transmetatarsal level

Where vascular shutdown of a lower extremity is occurring as an advanced symptom of critical limb ischemia, the "6 P's of acute limb ischemia" may also be observed (Chart 1).

The 6 P's of acute limb ischemia will be seen in the absence of compensating collateral circulation. Longstanding P.A.D. typically results in the formation of collateralization off the primary arteries; in essence, the body's creation of its own bypassing of the diseased and occluded vessels.

The evolution to paresthesia and paralysis reflects the presence of severe and potentially irreversible ischemia (Figure 2).

Chart 1

The 6 P's of Acute Limb Ischemia

- Pulselessness
- Pain
- Pallor
- Poikilothermy (cold)
- Paresthesia
- Paralysis

Recognition of P.A.D. Symptoms by Anatomical Level

Cerebrovascular Symptoms of P.A.D.

Patients with carotid artery stenosis present with ipsilateral transient ischemic attacks, strokes or amaurosis fugax (transient monocular vision loss). Symptomatic carotid ischemia is caused by:

- Hemodynamic factors relating to the degree of stenosis in the internal carotid artery (usually at least 70%) ipsilateral to the involved hemisphere.
- Degree of collateral flow from both the Circle of Willis and the external carotid artery.
- Degree of intracranial disease.

Embolism from an ulcerated plaque or from the stump of a completely occluded internal carotid artery may also cause a neurological defect.

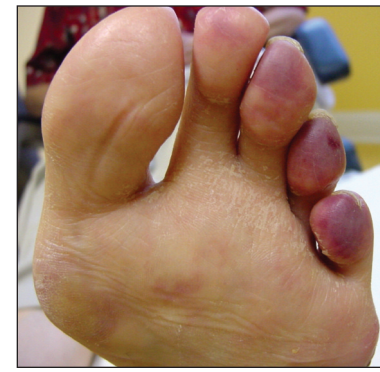

Figure 2: Patient with acute limb ischemia and the 6 P's

Mesenteric Ischemia

Post-prandial abdominal pain begins 30-90 minutes after eating and persists for two to three hours. This may cause patients to avoid food, resulting in weight loss. Acute mesenteric ischemia is caused by thrombosis of a severely diseased supermesenteric artery or by an embolic event originating from the heart.

Aneurysmal Disease

Abdominal aortic aneurysm (AAA) is more commonly recognized than peripheral aneurysm. It is a condition marked by inherent weakening of the arterial wall, and subsequent focal edema. A peripheral aneurysm usually leads to acute thrombosis rather than rupture. Femoral and popliteal athery aneurysms enlarge and compress surrounding venous structures causing unilateral leg edema, venous hypertension, venous thrombosis with occlusion, or pain due to local nerve compression. Ischemia is the most common presentation of peripheral aneurysm. It presents as mild claudication to severe limb threatening ischemia. Urgent reperfusion or revascularization is necessary to avoid limb loss. As in the case of abdominal aortic aneurysm, recognition of the presence of peripheral aneurysm must be detected by obtaining a thorough history and by ordering the appropriate vascular studies.

Aorto-iliac Disease

Manifested by claudication in the buttocks, thigh and calves, isolated aorto-iliac disease is associated with sexual impotence in men and is referred to as Leriche's syndrome. Its symptoms may be relieved with sildenafil nitrate. Aorto-iliac disease of this nature may be seen in patients < 50 years of age.

Lower Extremity Disease

Superficial femoral artery or popliteal arteries occlusion usually begins at Hunter's canal (adductor canal of thigh). P.A.D. at this anatomical level typically occurs in patients over the age of 40. The profunda femoris functions as a bridge between the aortofemoral segment and the femoropopliteal segment. The profunda femoris also provides collaterals to keep the lower leg viable and free of severe ischemia. It is not uncommon for patients with isolated SFA occlusion to have only mild to moderate, stable intermittent claudication.

Femoropopliteal disease is manifested by claudication in the calves and occasionally in the arches of the feet. Walking for consistent distances (example-"2 blocks") where the onset of pain occurs and cessation of ambulation must result, is the hallmark symptom of intermittent claudication.

Pseudoclaudication is a differential diagnosis to intermittent claudication. Pseudoclaudication is caused by lumbar canal stenosis.

Patients with pseudoclaudication experience leg pain with walking or prolonged standing. Calf pain arises when walking variable distances, unlike in cases of intermittent claudication. In cases of pseudoclaudication, relief is obtained from sitting or stooping, which decompresses the lumbar canal stenosis, usually taking at least 20 minutes for symptoms to abate. These patients often experience numbness and tingling in feet.

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Patients with severe chronic lower extremity ischemia manifest pallor on elevating the leg above the level of the heart and reveal dependent rubor or rubor-cyanosis. Many patients experience ischemic rest pain, especially when supine, and often dangle their feet from the side of the bed for relief. They may find additional relief from symptoms by sleeping sitting up with pillows behind their back or in a chair to allow for dependent position of legs. In both scenarios, gravity assists in the perfusion of the lower extremities.

TABLE 2

Vascular Surgical Procedures for Inflow Improvement

Inflo Procedure	Oprerative Mortality (%)	Expectied Patency Rate (%)
Abortobifemoral bypass	3.3	87.5 (5 years)
Aortoliac or aortofemoral bypass	1 to 2	85 to 90 (5 years)
Iliac endarterectomy	0	79 to 90 (5 years)
Fermorofemoral bypass	6	71 (5 years)
Axillofemoral bypass	6	49 to 80 (3 years)
Axxillofemoral-femoral bypass	4.9	63 to 67.7 (5 years)

TABLE 3

Vascular Surgical Procedures for Outflow Improvement

Outflow Procedure	Oprerative Mortality (%)	Expectied Patency Rate (%)
Fem-AK popliteal vein	1.3 to 6.3	66 (5 years)
Fem-AK popliteal prosthetic	1.3 to 6.3	50 (5 years)
Fem-BK popliteal vein	1.3 to 6.3	66 (5 years)
Fem-BK popliteal prosthetic	1.3 to 6.3	33 (5 years)
Fem-Tib vein	1.3 to 6.3	74 to 80 (5 years)
Fem-Tib prosthetic	1.3 to 6.3	25 (3 years)
Composite sequential bypass	0 to 4	28 to 40 (5 years)
Fem-Tib blind segmental bypass	2.7 to 3.2	64 to 67 (2 years)
Profundoplasty	0 to 3	49 to 50 (3 years)

Surgical Management Treatment Options for P.A.D.

Revascularization is indicated where chronic arterial occlusive disease has caused tissue loss, ischemic rest pain, or "lifestyle limiting intermittent claudication." Surgery is not recommended as a prophylactic therapy in asymptomatic patients with lower extremity P.A.D. Revascularization of diseased vessels can be categorized according to the approach of the Interventionalist. The approach of the Interventionalist can be classified in terms of traditional surgical revascularization (by-pass procedures) versus endovascular intervention (angioplasty, atherectomy, stent placement, and thermal devices—i.e. cold laser, etc.).

Claudication does not usually progress to limb-threatening ischemia. Surgery is infrequently used to treat claudicants and should be considered only when atherosclerotic risk factors have been treated and appropriate trials of exercise and pharmacotherapy have been utilized.

Endovascular procedures may be useful where patients suffer from symptomatic focal aorto-iliac disease, iliac and femoropopliteal lesions.

Stenting may be useful where iliacs have had suboptimal or failed balloon dilation, in cases of common and or external iliac stenosis or occlusion.

Stents, lasers, cutting balloons, atherectomy devices, and thermal devices can be useful in femoral, popliteal and tibial artery revascularization as salvage treatments or when failed results are found after balloon dilation.

It should be noted that the improvements in endovascular technology have been dramatic over the past five years and have played a major role in re-perfusion of occluded lower extremity vessels in patients previously presented with no further surgical options for revascularization. There exists a debate as to whether endovascular procedures are worthwhile, as a perception exists among some that re-occlusion rates are high. One can argue that even in cases where re-occlusion may occur, the benefit of increased blood flow in a patient with wounds complicated by ischemia may be enough to allow for the healing of such wounds.

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Evidence to support the use of endovascular procedures is limited to date and can only be established after significant numbers of cases are performed along with follow-up data accumulation. Anecdotal and clinical evidence appears to strongly support the use of endovascular procedures for limb preservation and it is anticipated that further evidence will be forthcoming in the near future.

Surgical bypass data is presented in Tables 2 and 3, for a comparative perspective.

Overall, there is insufficient data to recommend one method of revascularization over another. There is a real

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American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for the Treatment of P.A.D.

‡ 2011 ACCF/AHA Focused Update of the Guideline for the Management of Patients with Peripheral Artery Disease (Updating the 2005 Guideline)

The high prevalence of atherosclerotic risk factors places these patients at a "markedly" increased risk of atherosclerotic ischemic events, including MI and stroke. All patients with lower extremity P.A.D. should achieve risk reduction and specific treatment targets comparable to those of individuals with established coronary artery disease.

Medical Management of P.A.D.:

To reduce adverse cardiovascular events associated with lower extremity P.A.D., lifelong treatment should include:

- Modification or elimination of atherosclerotic risk factors, such as cigarette smoking, diabetes, dyslipidemia, and hypertension
- Promotion of daily exercise
- Non-atherogenic diet

Lipid-Lowering Drugs:

Statins (Hydroxymethyl glutaryl [HMG] co-enzyme Q reductase inhibitors) are recommended to achieve a target LDL of <100 mg / dl in ALL patients with P.A.D.

Statins used with goal of < 70 mg/ dl in patients with very high risk of ischemic events.

Among the statins recommended in the ACC/AHA guidelines are the following:

- Lipitor (atorvastatin),
- Lescol (fluvastatin)
- Mevacor, Altoprev(lovastatin)
- Pravachol (pravastatin)
- Crestor (rosuvastatin)
- Zocor (simvistatin)

Fibric acid derivatives can be useful for patients with P.A.D. and low HDL cholesterol, normal LDL cholesterol and elevated triglycerides. The fibric acid derivatives include:

Antara, Tricor (fenofibrate) and Lopid (genfibrozil).

Anti-hypertensive Therapy:

Anti-hypertensive therapy should be administered to hypertensive patients with lower extremity P.A.D. to achieve a goal of: reducing blood pressure to < 140 / 90 in non-diabetics and <130 / 80 in diabetics to reduce the risk of MI, stroke, CHF and cardiovascular death.

Beta-adrenergic blocking drugs are effective antihypertensive agents and are not contraindicated.

Angiotensin-converting enzyme inhibitors are reasonable for symptomatic patients with lower extremity P.A.D. to reduce the risk of adverse cardiovascular events.

Angiotensin-converting enzyme inhibitors may be considered for patients with asymptomatic lower extremity P.A.D. to reduce the risk of adverse cardiovascular events.

ACE Inhibitors recommended for use in the treatment of patients with P.A.D., both symptomatic and asymptomatic, include: Captopril, Enalapril, Fosinopril, Ramipril, Perindopril, Quinapril, Verapamil, and Trandolapril.

Antiplatelet therapy is indicated to reduce the risk of MI, stroke, or vascular death in patients with symptomatic atherosclerotic lower extremity P.A.D. including those with intermittent claudication or critical limb ischemia, prior lower extremity revascularization (endovascular or surgical), or prior amputation for lower extremity ischemia.

Aspirin, typically in daily doses of 75 to 325 mg, is recommended as safe and effective antiplatelet therapy to reduce the risk of MI, stroke, or vascular death in individuals with symptomatic atherosclerotic lower extremity PAD, including those with intermittent claudication or critical limb ischemia, prior lower extremity revascularization (endovascular or surgical), or prior amputation for lower extremity ischemia.‡

Antiplatelet therapy can be useful to reduce the risk of MI, stroke, or vascular death in asymptomatic individuals with an ABI less than or equal to 0.90.‡

The usefulness of antiplatelet therapy to reduce the risk of MI, stroke, or vascular death in asymptomatic individuals with borderline abnormal ABI, defined as 0.91 to 0.99, is not well established.‡

Clopidogrel (75 mg per day) is recommended as a safe and effective alternative antiplatelet therapy to aspirin to reduce the risk of MI, ischemic stroke, or vascular death in individuals with symptomatic atherosclerotic lower extremity PAD, including those with intermittent claudication or critical limb ischemia, prior lower extremity revascularization (endovascular or surgical), or prior amputation for lower extremity ischemia.‡

The combination of aspirin and clopidogrel may be considered to reduce the risk of cardiovascular events in patients with symptomatic atherosclerotic lower extremity PAD, including those with intermittent claudication or critical limb ischemia, prior lower extremity revascularization (endovascular or surgical), or prior amputation for lower extremity ischemia and who are not at increased risk of bleeding and who are at high perceived cardiovascular risk.‡

In the absence of any other proven indication for warfarin, its addition to antiplatelet therapy to reduce the risk of adverse cardiovascular ischemic events in individuals with atherosclerotic lower extremity PAD is of no benefit and is potentially harmful due to increased risk of major bleeding.‡

Homocysteine-Lowering Drugs:

The effectiveness of the therapeutic use of folic acid and B12 supplements in patients with lower extremity P.A.D. and homocysteine levels of > 14 μ moles/liter is not well established.

- Cilostazol (Pletal) 100mg p.o., b.i.d. is indicated as an effective therapy to improve symptoms and increase walking

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need for standardized reporting of baseline demographic data, severity of disease and outcome reporting in this group of patients. These standards should take into account both the specific characteristics of the PAD and of the wound in these patients. Further efforts are also required to standardize and improve outcome reporting, which should include wound healing, and it is important to move away from procedure-specific outcomes to disease-specific outcomes in this cohort of patients.[12]

Conclusion

Peripheral arterial disease remains virtually unknown among healthcare providers and the general population alike. A basic misunderstanding of PAD persists among healthcare providers. They often under-diagnose PAD or simply do not recognize the disease.

The five-year mortality rate for PAD is approximately 64 percent while breast cancer mortality at five years is between 14 and 18 percent.13 With far more people at risk of having PAD, which is often the underlying reason for lower extremity amputation as well as extensive pain and suffering, why do we not hear more about this disease?

Peripheral arterial disease is also a common complication for those afflicted with diabetes yet many of the ever-growing number of patients with diabetes are unaware of PAD.

Consider that surgeons perform more than 50 percent of lower extremity amputations without even doing a non-invasive vascular test, such as an ankle-brachial index, let alone an arteriogram.[1]

The Sage Group is a for-profit research and consulting company specializing in lower limb vascular disease including PAD, intermittent claudication, critical limb ischemia (CLI), acute limb ischemia and diabetic foot ulcer. According to SAGE Group Co-Founder Mary Yost, the Hallett study, published in 1997, examined more than 20,000 Medicare patients with CLI who had a major amputation.[15]

Researchers found that practitioners made no attempt at either a diagnostic angiogram or revascularization prior to amputation in 71 percent of these patients.[16]

Since the publication of this study, little headway has been made.

Here are some additional facts to consider when examining the impact of PAD from an economic standpoint:

- The estimated total cost of PAD in 2010 was between $164 and $300 billion. The range is based on per patient costs in two large studies: the REACH Registry and a study of managed care patients multiplied times 17.6 million with PAD.[16,17]
- Peripheral arterial disease actually costs more than coronary disease and four times more than costs surrounding strokes.[16]
- Seventy-five percent of those with PAD are asymptomatic. While they do not have leg symptoms, 70 percent most likely have coronary and/or cerebrovascular disease.[16]
- Between 5 and 10 percent of patients requiring below-knee amputations die in the hospital. Approximately 15 to 20 percent of patients who require above-knee amputations die while hospitalized.[16]
- A single in-hospital death from PAD or CLI can cost $12,000.[16]
- There is a high rate of revision amputations. This means the initial amputation did not heal adequately and the patient requires another amputation on that same leg at a higher level. The revision amputation rate is

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distance in patients with lower extremity P.A.D. and intermittent claudication (in the absence of heart failure).

- A therapeutic trial of cilastazol should be considered in all patients with lifestyle-limiting claudication (in the absence of heart failure).
- Pentoxifylline (Trental) 400mg p.o., t.i.d may be considered as a second line alternative therapy to cilastazol to improve walking distance for patients with intermittent claudication.
- The clinical effectiveness of pentoxifylline as therapy for claudication is marginal and not well established.

Other Proposed Medical Therapies:

The effectiveness of L-arginine for patients with intermittent claudication is not well established.

The effectiveness of propionly-L-carnitine as a therapy to improve walking distance in patients with intermittent claudication is not well established.

The effectiveness of ginkgo biloba to improve walking distance is marginal and not well established.

- Oral vasodilator prostaglandins such as beraprost and iloprost are not effective medications to improve the walking distance for patients with intermittent claudication.
- Vitamin E is not recommended as a treatment for patients with intermittent claudication.
- Chelation (e.g. Disodium ethylenediaminetetraacetic acid [EDTA]) is not indicated for treatment of intermittent claudication and may have harmful adverse effects, including hypocalcemia, renal insufficiency, proteinuria, and gastro-intestinal distress.

Additional ACC/AHA Non-surgical Recommendations for the Management of P.A.D.

Patients with lower extremity P.A.D. who smoke or use other forms of tobacco should be advised by each of their clinicians to stop smoking and should be offered comprehensive interventions, including behavior modification therapy, nicotine replacement therapy, or buproprion (Wellbutrin, Zyban).

Proper foot care including use of appropriate footwear, referral to podiatric medicine, daily foot inspection, skin cleansing and use of topical moisturizing creams should be encouraged.

Skin lesions and ulcerations should be addressed urgently in all diabetic patients with lower extremity P.A.D. (e.g. all diabetic patients should be assumed to have lower extremity P.A.D.).

Treatment of diabetes in individuals with lower extremity P.A.D. by administration of glucose control therapies to reduce HbA1C to < 7% can be effective to reduce microvascular complications and potentially improve cardiovascular outcomes.

A program of supervised exercise training is recommended as an initial treatment modality for patients with intermittent claudication.

Supervised exercise training should be performed for a minimum of 30-45 minutes, in sessions performed at least three times per week for a minimum of 12 weeks. The usefulness of unsupervised exercise is not well established as an effective initial treatment modality for patients with intermittent claudication.•

20 percent in patients requiring below-knee amputations and 12 percent in patients who require above-knee amputations.[16]

*Nursing home care after amputation is approximately $100,000 per patient (Figure 3).

Each of these statistics adds to the total national bill for amputation. This is before you consider the adverse patient outcomes such as the 60 to 80 percent of patients who are unable to walk, those suffering from depression, hospital re-admissions for amputation related problems, the necessity for long-term care, etc.[16]

Steps are highlighted to improve P.A.D. treatment and outcomes per the Prevention of Atherothrombotic Disease network (P.A.D. Network).

1) Increase awareness of P.A.D. and its consequences;

2) Identify people with symptomatic P.A.D.;

3) Screen for patients at high risk;

4) Improve treatment for symptomatic P.A.D. cases;

5) Increase early detection of asymptomatic cases.

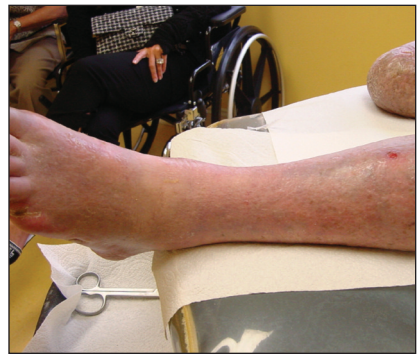

Figure 3: Annual cost of post-amputation care is approximately $49,000 per patient

The P.A.D. network also references the American Diabetes Association's recommendation that people with diabetes who are over 50 years old be regularly screened for P.A.D. as well as recommend that they have an annual foot exam.

In conclusion, the problems associated with peripheral arterial disease are extensive, and the impact of P.A.D. affects millions of patients and their families and costs billions of dollars to our healthcare system. Baby-boomers are aging and the number of diabetics continues to increase. Fortunately, technology is improving to address complications of P.A.D., yet prevention remains the best way to address the overall problem. Greater understanding of P.A.D. by all healthcare providers through greater awareness, early recognition, and knowledge of treatment options can have an enormous benefit to individual patients and society as a whole. **PM**

References

[1] Allie, David E, MD. New Advances in Critical Limb Ischemia. "The Staggering Clinical and Economic Cost of CLI" Lecture. New Cardio Vascular Horizons. CLI Summit. Miami, FL. 2006.

[2] Allie, David E, MD. Podiatry Today. Vol. 20. July 2007. "Emerging Vascular Approaches for Healing Diabetic Foot Ulcers". 44-54.

[3] Hirsch, Alan T., MD; Haskal, Ziv J. MD; Hertzer, Norman R., MD, et al.: ACC/AHA Guidelines for the Management of Patients with Peripheral Arterial Disease (Lower extremity, renal, Mesenteric, and Abdominal Aortic). Journal of the American College of Cardiology. © 2006 by the American College of Cardiology Foundation and the American Heart Association, Inc.American Diabetes Association: Diabetes 1996 Vital Statistics.

[4] Janov, J. Podiatry Today. Seven Keys to Preventing Malpractice Lawsuits. August 2007. 96-106.

[5] Becker, GJ, et al. The Importance of Increasing Public and Physician Awareness of Peripheral Arterial Disease. J Vasc interv Radiol 2002; 13[1];7-11.

[6] "Peripheral Arterial Disease in People with Diabetes", American Diabetes Association Consensus Statement, Diabetes Care, Volume 26, Number 12, December 2003, 3333-3341.

[7] "Diagnosis of P.A.D. is Important for People with Diabetes", American Diabetes Association Consensus Statement, Diabetes Care, November 21, 2003, www.diabetes.org.

[8] American Cancer Society, American Heart Association, Alzheimer's Disease Education/Referral Center, American Diabetes Association, SAGE Group

[9] Framingham Heart Study http://www.framinghamheartstudy.org http://www.americanheart.org/downloadable/heart/1136822690283P.A.D.06%20REVdoc.pdf

[10] American Diabetes Association: National Diabetes Fact Sheet, 2005. Bartholomew, John MD and Olin, Jeffery DO. Cleveland Clinic Journal of Medicine. Vol. 73 Supplement 4. October 2006. "Pathophysiology of peripheral arterial disease and risk factors for its development".

[11] www.tasc-P.A.D..org, TASC Consensus Paper, Outcome Assessment Methodology in Peripheral Arterial Disease—Impetus for Outcomes Research, Page 39, Table IX; Classifications of P.A.D.

[12] Hinchliffe,, RJAndros G, Apelqvist J, et al. A systematic review of the effectiveness of revascularization of the ulcerated foot in patients with diabetes and peripheral arterial disease. http://onlinelibrary.wiley.com/doi/10.1002/dmrr.2249/full

[13] Armstrong DG, Wrobel J, Robbins JM. Guest editorial: Are diabetes related wounds and amputations worse than cancer? Int Wound J. 2007; 4(4):286-287.

[14] Allie DE. How to address vascular complications with lower extremity wounds. Podiatry Today. 2008; 21(7):85-96.

[15] Allie DE, Hebert CJ, Lirtzman MD, et al. Critical limb ischemia: a global epidemic. a critical analysis of current treatment unmasks the clinical and economic costs of CLI. Euro Interventions Journal. 2005; 1(1):75-84.

[16] Hallett JW Jr, Byrne J, Gayari MM, Ilstrup DM, Jacobsen SJ, Gray DT. Impact of arterial surgery and balloon angioplasty on amputation: a population-based study of 1155 procedures between 1973 and 1992. J Vasc Surg. 1997; 25(1):29-38

[17] Yost M. The SAGE Group. Interview, WOKV radio. Jacksonville, FL: July 8th, 2012. Podcast available at www.WOKV.com .

[18] Bhatt D, Steg PG, Ohman EM, et al. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. JAMA. 2006; 295(2):180-189.

‡ Rooke TW, Hirsch AT, et al. 2011 ACCF/AHA Focused Update of the Guideline for the Management of Patients With Peripheral Artery Disease (Updating the 2005 Guideline)A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines J Am Coll Cardiol. 2011;58(19):2020-2045.

Additional References

Strategic Health Resources commissioned by the Spectranetics Corp.

Falanga, Vincent, MD. Editor. Cutaneous Wound Healing. Copyright 2001, Martin Dunitz, Ltd. United Kingdom.

Navarro, Felipe MD. Cleveland Clinic Medicine Index. May 29, 2002. "Peripheral Arterial Disease" www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/cardiology/P.A.D./P.A.D..htm

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SEE ANSWER SHEET ON PAGE 185.

1) Allie reported that a 25% reduction in lower extremity amputations could result in multi-billion dollar annual savings to the U.S. healthcare system. This amount is:
A) $ 3 billion
B) $5 billion
C) $30 billion
D) $50 billion

2) There is an increased risk of myocardial infarction (MI), stroke and cardiovascular death for patients with lower extremity P.A.D. The risk of these patients suffering a heart attack or stroke, respectively, is:
A) 20-30% and 50%
B) 40-60% and 30%
C) 20-60% and 40%
D) 40-60% and 20%

3) An interventionalist is a term used to refer to those physicians who can provide revascularization of arteries that are occluded due to P.A.D. Among those considered interventionalists are:
A) cardiologists, podiatrists, radiologists
B) cardiologists, podiatrists, vascular surgeons
C) cardiologists, radiologists, vascular surgeons
D) podiatrists, radiologists, vascular surgeons

4) The most common type of peripheral vascular disease is:
A) atherosclerosis
B) peripheral arterial disease
C) amaurosis fugax
D) hyperlipidemia

5) Which of the following is not considered a traditional risk factor for the development of P.A.D.?
A) Diabetes
B) Smoking
C) Hypertension
D) Hypercoagulable state

6) Which of the following is not considered a non-traditional risk factor for the development of P.A.D.?
A) advanced age
B) race/ethnicity
C) abnormal waist to hip ratio
D) elevated levels of inflammatory markers: (C-reactive protein, fibrinogen, leukocytes, interleukin-6)

7) The single-most important modifiable risk factor in the prevention of P.A.D. is:
A) diet
B) sedentary lifestyle
C) smoking
D) abnormal hip-to waist ratio

8) Atherosclerosis and the evolution of plaque formation may be characterized by four distinct stages, which include the following, EXCEPT:
A) lesion initiation
B) formation of fatty streak
C) fibroproliferative atheroma development
D) foam cell induction

9) Diabetics have more risk factors for developing P.A.D. than do non-diabetics. Which of the following is not considered among those risk factors?
A) elevated blood pressure
B) increased triglycerides
C) increased cholesterol
D) peripheral neuropathy

10) The most common manifestation of P.A.D. is:
A) Arch pain in feet
B) Claudication
C) Abdominal pain after eating
D) Amaurosis fugax

11) Pseudoclaudication is a differential diagnosis for claudication. Which statement is false regarding pseudoclaudication?
A) Calf pain arises after walking consistent distances.
B) Leg pain is experienced with walking or standing for prolonged periods.
C) Numbness and tingling in feet are common symptoms.
D) Relief is obtained from sitting or stooping, typically for at least 20 minutes.

12) The Rutherford-Becker is a classification system used to identify the degree of symptoms of P.A.D. At what levels of Rutherford-Becker can critical limb ischemia be found?
A) 0,1,2
B) 1,2,3
C) 3,4,5
D) 4,5,6

13) Acute limb ischemia is an advanced form of critical limb ischemia. The 6 P.'s of acute limb ischemia include: pulselessness, pain, pallor, poikilothermy, paresthesia and paralysis. Which two symptoms represent the presence of severe and potentially irreversible ischemia?
A) pain and paresthesia
B) poikilothermy and paralysis
C) paresthesia and paralysis
D) pulselessness and pain

14) Which of the following is manifested by claudication in the calves and occasionally in the arches of the feet?
A) Leriche's syndrome
B) mesenteric ischemia
C) peripheral aneurysm
D) femorpopliteal disease

15) Which is not indicated to reduce the risk of cardiovascular ischemic events in patients with atherosclerotic lower extremity P.A.D.?
A) ACE Inhibitors
B) Statins
C) Coumadin
D) Clopidogrel (Plavix)

16) The following are recommended to reduce the risk of myocardial infarction, stroke, or vascular death in

Continued on page 184

Continuing Medical Education

CME EXAMINATION

patients with atherosclerotic lower extremity P.A.D.:
A) Coumadin
B) Aspirin
C) Clopidogrel (Plavix)
D) B and C

17) Treatment of diabetes in individuals with lower extremity P.A.D. by administration of glucose control therapies can be effective to reduce microvascular complications and potentially improve cardiovascular outcomes. What is the recommended HbA1C level for this patient population?
A) < 8.5%
B) < 8.0%
C) < 7.5%
D) < 7.0%

18) Endovascular intervention to open occluded arteries includes all of the following modalities, except:
A) atherectomy
B) angioplasty
C) chelation
D) stent placement

19) Which of the following statements regarding pentoxifylline (Trental) is false?
A) Pentoxifylline may be considered as a second line alternative therapy to cilastazol (Pletal) to improve walking distance for patients with intermittent claudication.
B) Pentoxifylline may be considered as a first line therapy over cilastazol (Pletal) to improve walking distance for patients with intermittent claudication.
C) The clinical effectiveness of pentoxifylline as therapy for claudication is marginal and not well established.
D) The typical dosing schedule of pentoxifylline is 400mg three times daily.

20) Which of the following statements is false?
A) Less than 50% of all amputees will regain the ability to ambulate (< 50% of below knee and < 25% of above knee amputees).
B) Amputation is still the most common form of treatment for critical limb ischemia.
C) Less than 50% of lower extremity amputees survive past 2-3 years.
D) Amputation should be recommended versus endovascular procedures in cases where patients have been classified as having no further surgical options at revascularization.

See answer sheet on page 185.

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ENROLLMENT FORM & ANSWER SHEET *(continued)*

EXAM #1/13
Peripheral Arterial Disease
Overview
(Bell)

Circle:

1.	A	B	C	D	11.	A	B	C	D
2.	A	B	C	D	12.	A	B	C	D
3.	A	B	C	D	13.	A	B	C	D
4.	A	B	C	D	14.	A	B	C	D
5.	A	B	C	D	15.	A	B	C	D
6.	A	B	C	D	16.	A	B	C	D
7.	A	B	C	D	17.	A	B	C	D
8.	A	B	C	D	18.	A	B	C	D
9.	A	B	C	D	19.	A	B	C	D
10.	A	B	C	D	20.	A	B	C	D

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