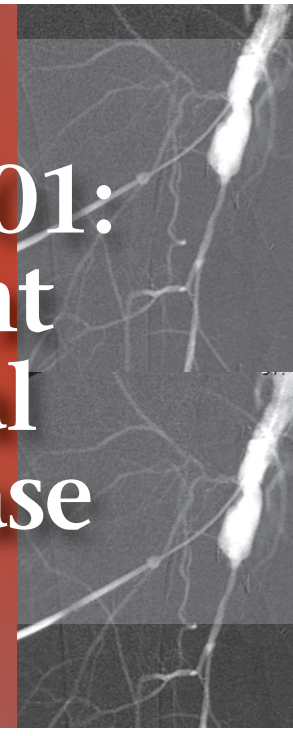
Continuing Medical Education

Vascular Plumbing 101: Management of Peripheral Artery Disease

Here's what to do when the pipes get clogged.



Goals/Objectives

Upon completion of this article, the reader should:

1) Have a strong understanding of the pathophysiology of and risk factors for peripheral artery disease (PAD).

2) Be able to recognize its signs and symptoms in the clinical setting.

3) Be aware of the non-invasive and invasive screening modalities available to practitioners to verify the diagnosis of PAD.

4) Understand the basic rationale behind surgical and interventional indications and options.

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*Following this article, an answer sheet and full set of instructions are provided (p. 186).—**Editor***

By Vicken Pamoukian, MD and Damien De Collibus, R-PAC

In many situations, the podiatrist is in the best position to screen for and diagnose asymptomatic disease. Many disease processes may not be easily elicited on physical exam, however, and it is often necessary to perform less common diagnostic testing, or refer to a specialist. Peripheral artery disease (PAD) is one such disease that may not be readily diagnosed on physical exam, and may require further testing either in the primary care setting, or with a vascular specialist. However, if detected early, appropriate treatment of PAD can have profound effects on a patient's care—including prevention of PAD-related complications and cardiovascular-related co-morbidities, and reduction in the cost of long-term medical management and treatment of these issues. Numerous healthcare professionals make referrals to vascular specialists; but due to its symptomatology, referrals are more often made by primary care physicians, endocrinologists, cardiologists, and podiatrists.

Diagnosis of PAD may also lead to suspicion and early diagnosis of other diseases.

Peripheral artery disease is a disease of the upper and lower extremities that affects over eight million people in the United States.[19] PAD is primarily mediated by atherosclerotic disease, and may manifest as cramping muscle pain, pain at rest,

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tissue loss and gangrene, or may exist entirely symptom-free. Medical costs in the inpatient and outpatient setting are higher for patients with PAD, and even higher in the setting of arterial and diabetic ulcers.

In a meta-analysis performed at the Diabetes Center in Beijing, China, the average medical cost of hospitalized patients with diabetes and PAD-related foot problems was markedly higher than with patients having diabetes alone. Subsets of patients diagnosed with diabetes more than 20 years prior, or subsets including laborers and retired workers, demonstrated obviously higher medical costs than average. As expected, patients with infection, ischemic changes in the feet, or gangrene of the feet had a longer hospital stay with subsequently higher medical costs.[23]

Diagnosis of PAD may also lead to suspicion and early diagnosis of other diseases. Patients with a history of PAD with claudication have a 2.5 times higher risk of experiencing a cardiac event than age-matched subjects without claudication. Similarly, approximately 30% of patients undergoing major peripheral bypass surgeries demonstrate severe triple-vessel coronary disease on pre-operative cardiac catheterization.[2] A near 30% correlation between carotid stenosis and peripheral artery disease has also been documented by numerous meta-analyses.

The tunica intima is the innermost vessel layer lined entirely by endothelial cells that serve to facilitate circulation, prevent unwanted transport of certain materials outside of the vessel lumen, and regulate function of smooth muscle cells.

Surveillance is quickly becoming more readily available to all practitioners, some opting to maintain on-site resources for performing non-invasive vascular screening, such as ankle-brachial index measurements, pulse-volume recording, or peripheral arterial duplex studies. With the advances made in pharmacology, enhanced treatments for hyperlipidemia, diabetes, and anti-platelet therapy to reduce cardiovascular risk have subsequently reduced the risk of PAD-related morbidity. As with any disease process, treatment of PAD must be personalized for each patient, and treatment options are much more varied than they once were. Many hospital centers offer newer treatments for PAD, including endovascular and hybrid endovascular/open surgical treatments, in addition to conventional open surgical revascularizations.

Type 3 lesions constitute the remaining 60-70% of lesions, and demonstrate multi-level disease of aortoiliac, femoral, popliteal, and tibial vessels.

Pathogenesis

Arteries are constructed of three discrete layers, differentiated by both their composition and function. The tunica intima is the innermost vessel layer lined entirely by endothelial cells that serve to facilitate circulation, prevent unwanted transport of certain materials outside of the vessel lumen, and regulate function of smooth muscle cells. The tunica media contains smooth muscle necessary for directed contraction and relaxation of the muscle layer, and subsequent vasoconstriction and vasodilation, respectively; this layer provides structural integrity and strength to the vessel. The tunica adventitia is the thin, outermost layer of loose connective tissue that gives rise to the blood supply for the vessel itself—the vasa vasorum.[10]

Atherosclerotic disease involves the potential space between the tunica intima and the surrounding tunica media. Therefore, prevention of atherosclerotic-related disease requires prevention of migration outside of the tunica intima, and treatment involves repair of the plaque formed at the site of this migration.

Atherosclerosis describes a process in which eccentric lesions develop and progress to become flow-limiting, or may narrow the vessel lumen enough that it becomes thrombosed and, at times, fully occluded. The process itself may be characterized in five phases. Phase 1 involves deposition of macrophage-derived foam cells, or smooth muscle cells containing lipid droplets or extracellular deposits, resulting in a small, usually eccentric lesion. Phase 2 involves destabilization of the initial plaque, now consisting primarily of extracellular lipids and fibrous tissue. Phase 3 and 4 plaques progress from phase 2 to include a partially or fully occlusive mural thrombus in the lumen. Finally, fibrosis of the lesion is demonstrated in phase 5.[10] In addition to smooth muscle cells, the fibrotic cap formed in phase 5 also entraps inflammatory cells and a lipid-rich core of necrotic debris within the plaque, which can lead to chronic vessel inflammation and vasoconstriction. (Zhou)

Atherosclerotic disease normally affects larger vessels at their bifurcations, and other areas where turbulent blood flow and low sheer stress are common. Most commonly, arterial plaque formation develops in three specific sites in the lower extremity vasculature, although lesions could potentially develop anywhere vascular injury and vessel wall inflammation occur. The three sites, first characterized by De Bakey, are the 1. aortic bifurcation, 2. tibial trifurcation, and 3. superficial femoral artery at the adductor hiatus; the disease often spares the internal iliac, profunda femoral, and peroneal arteries.

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Lesion Types

De Bakey went on to classify lesions as Types 1, 2, and 3 lesions. Seen in 10-15% of atherosclerotic lesions, type 1 lesions are found in aortoiliac distribution, most commonly in patients with smoking histories and hyperlipidemia. Type 2 lesions account for approximately 25%, and involve aortoiliac and external iliac vessels. Type 3 lesions constitute the remaining 60-70% of lesions, and demonstrate multi-level disease of aortoiliac, femoral, popliteal, and tibial vessels. Types 2 and 3 are seen more often with more than two PAD risk factors.[2] Commonly, the risk factors associated with atherosclerotic disease is increasing age, hypercholesterolemia, diabetes mellitus, smoking, positive family history, hypertension, sedentary lifestyle, and obesity. Elevated serum marker levels of lipoprotein A, homocysteine, C-reactive protein (CRP), vascular endothelial growth factor (VEGF), and homocysteinuria.[21,26]

In the peripheral arteries, narrowed vessels can lead to symptoms due not only to the degree of narrowing within the vessel, but also to the functional limitations they pose to blood flow and velocity. When blood velocity through the vessel is impeded, blood volume reaching muscle tissue is reduced, and can impair normal aerobic metabolism of the muscle, more evident during times of high oxygen demand, such as during exercise and strenuous physical activity. Oxygen-deprived muscle will revert to anaerobic respiration and metabolism during times of exertion, and can lead to symptoms of cramping pain in the short-term.

Symptomatology

Patients with PAD can present with a multitude of symptoms, sometimes seeming unrelated. They may disclose a history of impotence, lower extremity claudication with exertion, rest pain, gangrene or tissue loss. When patients describe claudication, they should be describing reproducible pain, numbness, or weakness predominantly in the calves, thighs, or buttocks, elicited with exertion of the extremities, completely resolved with rest. In one study, a rapid decline in lower extremity strength and functional performance was seen over a six-year period in women with PAD, although the same decline was not seen in men with PAD over the same period. (Herman)

Symptoms are directly related to the distribution of diseased vessels in an individual—for instance, in the case of iliac artery stenosis, patients may complain of bilateral hip and buttock claudication and erectile dysfunction. These symptoms associated with absent femoral pulses describes Leriche syndrome, and may be an alarm that disease is present elsewhere in the body.[2] Symptoms that do not appear to correlate with actual sites of disease may be attributed to other causes. Therefore, it is important to differentiate symptoms of claudication from neuropathic or radicular pain that originates from the lumbosacral nerve roots, or is isolated to the feet.

Patients should be instructed to refrain from smoking immediately prior to arterial studies, as nicotine can cause vasoconstriction in the upper and lower extremity vessels.

Ischemic rest pain occurs in the absence of exercise or exertion, and is normally isolated to the dorsum of the foot overlying the metatarsal heads. This pain can be elicited with elevation of the extremity or even lying supine, but can be relieved by moving the legs to a dependent position, massaging the affected area, or initiating activity to promote pedal circulation. Potential consequences of chronic lower extremity ischemia include gangrene and soft tissue loss, and infection. These conditions are imminent when rest pain is present. Soft tissue loss can include arterial and diabetic ulcers, and may progress to involve underlying bone and joints, leading to osteomyelitis or septic arthritis if the periostium or joint space is compromised, respectively.

Ulcers

Ulcers of the skin and soft tissue can be characterized by their underlying pathology. Venous stasis ulcers develop in areas where chronic edema results in chronic inflammation, deposition of avascular material under the skin, skin atrophy, and subsequent skin break-through. Arterial and diabetic ulcers result from poor circulation and oxygen delivery to soft tissue, but present differently from each other, in location and quality. Arterial ulcers are normally painful, well-circumscribed lesions located over the extensor surface of joints, commonly over the interphalangeal joints, or at pressure points—at the plantar surface of the metatarsal heads, or the heels, for instance. Arterial ulcers may be treated with conservative therapy and wound care for 6-12 weeks before revascularization should be attempted. If ulcers worsen despite appropriate conservative therapy, percutaneous or surgical revascularization should not be delayed. Diabetic ulcers may develop in the presence or absence of PAD, and most will resolve with improvement in skin hygiene, glycemic control, and daily debridement regimens. Patients with diabetic ulcers and underlying PAD or peripheral artery occlusive disease (PAOD) should be assessed for revascularization procedures to expedite healing, if no improvement is seen with conservative treatment.[22]

Screening for PAD

Screening for PAD can and should be performed well before a patient encounters a vascular surgeon, based on populations demonstrating multiple risk factors for the disease. It can involve a routine physical exam, questionnaires targeting PAD and PAD-related diseases, or can include more selective and specific testing, including ankle-brachial index and arterial Doppler studies, or more invasive imaging including computed tomographic (CT) or magnetic resonance imaging (MRI) stud-

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ies, as will be discussed later.

On interview, all practitioners should be able to elicit a history of PAD or risk factors for the disease, including: symptoms of calf claudication or pain in the foot, history of ulcers, recurrent infection, or gangrene of the feet or legs, documentation of and treatment for related diseases, and previous surgeries or procedures involving the lower extremities.

Proper use of lipid-lowering medication with a correlated drop in total cholesterol and lipid levels resulted in a 40% risk reduction for new onset claudication or progressively worsening claudication.

On physical exam, there should be a thorough evaluation of the lower extremities and feet, assessing skin color for rubor, pallor, or mottling, noting the presence of any irregular lesions, muscle atrophy, and hair distribution over the legs. Size, location, and appearance of ulcers and areas of gangrene should be documented, to help ascertain location of arterial disease, and to monitor progress made in wound healing throughout the treatment course. Extremities should be felt for temperature, as arterial insufficiency could manifest as a cool extremity, referred to in the acute setting as a "cold foot."

A thorough lower extremity peripheral pulse exam can suggest both the location and severity of occlusive arterial lesions. For instance, iliac occlusive disease may be suggested by the absence of an ipsilateral femoral pulse; superficial femoral artery (SFA) occlusion may be suggested when a popliteal pulse is weak or absent, or if an abnormally bounding femoral pulse is noted, creating a "water hammer" effect in the vessel; absent dorsalis (DP) or posterior tibial (PT) pulses may allude to anterior or posterior tibial artery occlusion, respectively. The practitioner should assess the quality and location of all palpable pulses making bilateral comparisons, noting absent pulses, and distinguishing between Dopplerable and non-palpable pulses, if a handheld Doppler is available.

Non-invasive Screening Methods

Non-invasive testing can often validate concerns of PAD after a clinical history and physical is performed. The ankle-brachial index (ABI) measurement is a comparison of occlusive pressures of the upper and lower extremities used to calculate a ratio. In the absence of significant atherosclerotic disease, the external applied pressure required to obstruct flow in the ankle and brachial arteries should be nearly equal, thereby generating a ratio of approximately 1.0 (accepted range for normal is 0.9-1.1); an ABI 0.7—>0.9 is associated with mild arterial insufficiency, can still present with palpable pulses, but may be asymptomatic; an ABI 0.4—>0.7 is associated with moderate arterial insufficiency and commonly presents with claudication; an ABI <0.4 often presents with non-palpable pulses, rest pain, and ulcers, and is associated with severe arterial insufficiency.

Pletal (cilostazol)—increases calcium-mediated vasodilation and inhibits platelet aggregation via phosphodiesterase III (PDE-III) inhibition.

Toe brachial indices (TBI) may be useful in determining the extent of disease when tibial vessels are calcified and non-compliant, and an ABI is unattainable, or inaccurate (usually falsely elevated due to calcification and non-compressibility of the vessel). Such an elevation in ABI may be secondary to chronic diabetes mellitus or renal failure. In populations of new hemodialysis patients, ultrasonography results of the lower extremities were correlated to ABI results to assess for PAD, regardless of signs or symptoms of ischemia. The presence of PAD was noted when significant stenosis or obstruction of lower limb arteries was seen on ultrasound. Of this population, 59.3% showed PAD on ultrasound, but only 22.2% of the population had an ABI<0.9.[15]

While ABI measurements can be sensitive and diagnostic, PAD may be missed in some patients, and additional screening methods may be necessary to make the diagnosis of PAD. Follow-up testing with ABI may be done at scheduled intervals to monitor the progress of disease. Often, ABI testing is performed in correlation with pulse volume recordings, which qualitatively describe vessel compliance at multiple levels of the lower extremities.

Like most non-invasive testing, ABI and TBI testing can be done in most practitioner settings, and does not always need to be performed by a vascular specialist. In many cases, ABI testing can be performed in five minutes, on average, with some additional time to effectively prepare and educate the patient for the test.[19]

Arterial duplex testing screens for PAD, using sound waves that reflect off a column of moving blood, in order to measure absolute velocity and velocity gradients. Often, arterial duplex is performed with Doppler testing, to identify areas of narrowed lumen within the vessel. Such testing is effective in screening patients to determine the presence of any stenotic or flow-limiting lesions in the aorta or lower extremity vessels, based on abrupt changes in blood flow velocity; velocity gradients can translate to estimate degree of stenosis and percent of luminal occlusion.

No special preparation is necessary for testing, but patients should be instructed to refrain from smoking immediately prior to the study, as nicotine can cause vasoconstriction in the upper and lower extremi-

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ty vessels.[11] Duplex testing is also useful as a mode of surveillance of bypass and stent patency after intervention (Figure 3). When performed every six months, duplex ultrasound may identify threats to bypass of stent life expectancy due to restenosis of the vessel, thrombosis, or intimal hyperplasia. If diagnosed early enough, threatened areas may be repaired before the progress to complete occlusion.

Diagnostic X-rays may be used to rule out osteomyelitis as a cause for, or a result of, a non-healing arterial or diabetic ulcer. With severe disease, highly calcified vessels may be seen on X-ray, although the studies are usually non-specific.

Invasive testing such as CTA, MRA, and angiogram can be performed when non-invasive testing is not feasible or inaccurate. These invasive tests are especially useful for pre-operative evaluation of vessels for bypass targets, and are highly sensitive in determining the degree of calcification and patency of most peripheral vessels. Due to the risk of nephrotoxicity of contrast agents, and complications with implanted metal devices, CTA and MRA may not always be appropriate.

In addition, in order to undergo these imaging studies, patients are required to lie supine in a confined space for some time, making some patients too anxious to undergo them. Patients may also resist CTA studies due to exposure to external radiation. Post-operatively, CTA/MRA studies may not be cost-effective for surveillance, but they can be useful in assessing implanted grafts for extravasation at anastomotic sites, or for infection.

Conservative Treatment and Medical Management

As with many diseases, patients with PAD should be evaluated for severity, and management; and treatment should be decided based on all aspects of the patient's health and lifestyle. Treatment can be conservative and may include behavioral and/or lifestyle changes, and pharmacological therapy. Often, these treatment regimens are highly effective in managing the disease, and can avoid or delay the need for surgical intervention. Initially, conservative treatment of PAD requires strict control of associated risk factors, and may employ behavior modification and medical management. Smoking cessation, lowering serum lipid levels, and adherence to a regimented daily exercise program can have significant improvement in patients with PAD.

In fact, proper use of lipid-lowering medication with a correlated drop in total cholesterol and lipid levels resulted in a 40% risk reduction for new onset claudication or progressively worsening claudication.[16] Exercise programs, if carried out over a minimal six month course, can increase pain-free walking by 1.5 times, by increasing the tolerance of anaerobic respiration in lower extremity muscles. It is also believed that via angiogenic factors, continuous oxygen demand can lead to the formation of collateral circulation at areas of high-grade stenosis and occlusion.

Coumadin dosage must be individualized for each patient to maintain an International Normalized Ratio (INR) of 2-3 times the normal prothrombin (PT) level.

Medical Management

Medical management specifically for treatment of PAD symptoms and progression of the disease include, but are not limited to, Vitamin E (although its role is not fully understood), Trental (pentoxyfylline), Pletal (cilostazol), Aspirin (Acetylsalicylic acid), Plavix (clopidogrel), Aggrenox (aspirin/dipyridamole), and Coumadin (warfarin). Research with gene transfer therapy of vascular endothelial growth factor (VEGF), endothelial nitric oxide synthetase (eNOS), angiopoietin-1 is also being considered for treatment.[14] The drug information below is a summarization of compiled data from multiple drug references, primarily the NCI Drug Dictionary:

1) Trental (pentoxyfylline)—previously thought to be effective in reducing the symptoms caused by PAD. Trental is a phosphodiesterase inhibitor that increases levels of cyclic adenosine monophosphate (cAMP) in erythrocytes, endothelium, and surrounding tissues; thereby potentiates vasodilation, improves erythrocyte flexibility, and enhances blood flow by inhibiting cAMP mediated platelet aggregation. In controlled randomized trials, Trental has failed to show any significant improvement in symptoms or quantifiable improvement in ABI or flow rates. Trental is typically dosed at 400mg TID.

2) Pletal (cilostazol)—increases calcium-mediated vasodilation and inhibits platelet aggregation via phosphodiesterase III (PDE-III) inhibition. It is contraindicated in patients with heart failure, but has been shown to improve pain-free ambulation in most patients, especially those who are not candidates for revascularization. Dosing for most patients is 100mg BID, but may be reduced to 50mg BID if new-onset tachycardia is observed as a result of the medication. In one London study, Cilostazol used in patients with critical limb ischemia (CLI) improved signs and symptoms of ischemia in 23% of the population, with 58% of the population stabilizing.[20]

3) Aspirin (acetylsalicylic acid)—a non-selective, reversible cyclooxygenase (COX) inhibitor that decreases synthesis of prostaglandin, reduces inflammation, and inhibits platelet aggregation. Aspirin dosed minimally at 81mg QD is recommended for all patients with PAD except for those with a sensitivity or allergy to the drug, or are at increased bleeding risk. To date, aspirin is the only drug to demonstrate reduction of intimal hyperplasia after surgical or endovascular procedures.

4) Plavix (clopidogrel)—an irreversible modifier of the platelet receptor for adenosine diphosphate (ADP), preventing formation of the ADP-receptor complex, and inhibit-

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ing ADP-mediated activation of the glycoprotein complex GPIIb/IIIa. Inhibition of this pathway ultimately impedes fibrinogen binding to platelets, and platelet adhesion and aggregation. Plavix dosed at 75mg QD is often started in patients in status post-angioplasty and stent deployment to reduce the thrombotic risk of closure.

5) Aggrenox (aspirin/dipyridamole)—a combination medication that reduces platelet aggregation via COX inhibition and inhibition of adenosine uptake by platelets and endothelial cells, thereby increasing cAMP levels. Aggrenox is commonly dosed at 25mg ASA/200mg dipyridamole), and given to patients who cannot tolerate Plavix.

6) Coumadin (warfarin)—inhibits replenishment of Vitamin K1 by inhibiting the activity of Vitamin K reductase. Vitamin K serves as a cofactor for clotting factors II, VII, IX, and X, and anticoagulant proteins C and S. This decrease in clotting factor levels and activities results in delayed clotting time, and is meant to limit stable thrombus formation and progression in the vessels. Dosage must be individualized for each patient to maintain an International Normalized Ratio (INR) of 2-3 times the normal prothrombin (PT) level. This medication may be prescribed for post-arterial bypass patients with high risk of thrombosis, including those with a hypercoagulable state, thrombogenic conduit use for bypass (e.g., polytetrafluoroethylene (PTFE) or Dacron graft), or poor outflow into distal run-off vessels.

Endovascular and Open Surgical Repair for PAD

Revascularization procedures are typically reserved for patients suffering from claudication that significantly impairs activities of daily living and daily functioning. These limitations may be subjectively determined on a patient-by-patient basis, as previous activity levels and expectations of post-procedure functioning may be vastly different among patients. Generally, these procedures are considered when ambulation on flat ground is stopped at a half block to a full block due to claudication, for rest pain, or for tissue loss, ulceration, or gangrene associated with arterial insufficiency, and unresponsive to conservative treatment.

The operative mortality rate for aortic disease is 2-5%, and 1-3% for infrainguinal disease, requiring bypass surgery. Due to these anesthesia- and surgical-risks associated with formal bypass, endovascular procedures are often favored for revascularization. These procedures involve localization of flow-limiting lesions using real-time angiography, followed by dilation of lesions with a balloon catheter (Figures 1 & 2), and often deploying a self-expanding or balloon-expandable stent at the area of repair.

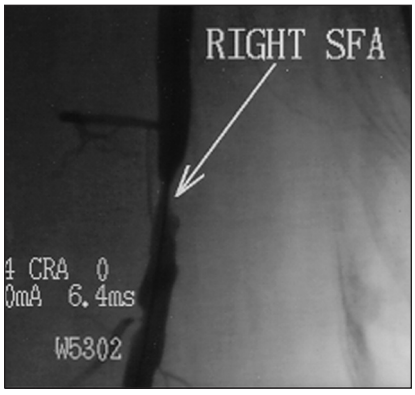

Figure 1a: Wire access obtained in the right superficial femoral artery (SFA) where a focal high-grade stenosis is noted.

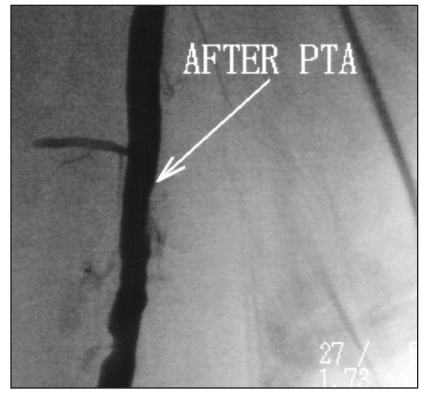

Figure 1b: Balloon angioplasty of the SFA results in full patency of the vessel. Angioplasty can be reinforced with balloon- or self-expanding stents.

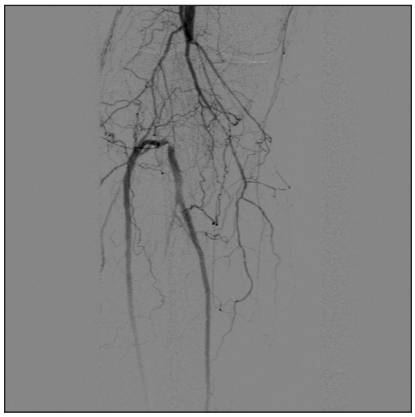

Figure 2a: Occlusion of the distal right popliteal artery proximal to the tibial trifurcation, resulting in reduced blood flow distally; note the poor visualization of the peroneal artery.

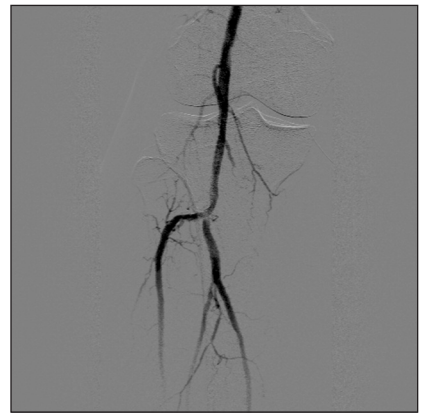

Figure 2b: Balloon angioplasty and stent deployment in the distal popliteal artery increases distal runoff, demonstrating three-vessel runoff into the ankle.

Endovascular Repair

Endovascular repair has greater success for specific types of lesions in key areas of the lower extremities, specifically with stenotic lesions in the common iliac arteries, and with short-segment stenoses and occlusion of most infrainguinal lesions. Angioplasty alone has been associated with higher recurrence rates than angioplasty with stenting, with three-year patency rates improving to nearly 80% with either stent type.[17]

Drug-eluting stents (DES) bonded with drugs such as tacrolimus and sirolimus have demonstrated their effectiveness in reducing post-angioplasty intimal hyperplasia to increase patency rates. Poorer patency rates of up to 60% have been seen with external iliac artery (EIA) stenting, and success with stenting of the tibial arteries is poorer still. In some cases, endovascular procedures can eliminate the need for surgical bypass; in other cases, hybrid procedures can combine open surgical and endovascular techniques at one time to maximize pa-

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tency and minimize surgical risks and length of operating room stay.

Open Surgical Repair

Open surgical repair can be an alternative to endovascular therapy for revascularization, or may be used for those patients with progressive disease that are no longer endovascular candidates. The open repairs are also employed for those patients who failed percutaneous therapy due to thrombosis or restenosis. The preferred conduit for most peripheral bypasses is the autologous greater saphenous vein, as the average five-year patency rates can reach higher than 75-80% for all infrainguinal bypasses; in some cases, where the resources are unavailable, cryogenically frozen harvested vein is used.

Biologic Conduits

Biological conduits have a reduced risk of thrombosis and occlusion than do synthetic conduits, like PTFE and Dacron.[8] However, due to the caliber of the target vessels and high flow rates, certain occlusions benefit from the use of synthetic graft, as is the case of aortoiliac occlusions necessitating aortoiliac or aortobifemoral bypasses, or femoral artery occlusions requiring femoral-femoral artery bypasses. Data measuring patency rates of recent generation modified PTFE graft demonstrated 1-, 2-, and 3-year patency rates approaching that of autologous or cryogenic vein.[13] For high-risk surgical patients, or if local infection at anticipated target anastomotic sites is a concern, extra-anatomical grafts such as axillary-femoral artery or femoral-femoral artery bypasses with graft may be employed, though their 10-year patency rates are lower.

In a true endarterectomy, the two innermost layers of the artery, the tunica intima and tunica media are dissected and resected along with luminal thrombus and intimal plaque.

Due to limited accessibility to the hypogastric artery, disease in this vessel is limited in terms of repair. Options for revascularization of the hypogastric artery include endarterectomy and bypass, often as a SFA-profunda femoral artery (PFA) bypass, or ilio-PFA bypass. In a study of patients with proximal lower limb ischemia, described by the researchers as "a decrease in exercise-transcutaneous oxygen pressure (TcPO2) lower than -15mmHg at the buttock level"-direct versus indirect revascularization of the hypogastric artery was evaluated for prevention of claudication. Direct revascularization was characterized as angioplasty or iliac artery bypass, where inflow was augmented for effect, while indirect revascularization was characterized as aortobifemoral bypass, resulting in retrograde and collateral perfusion into the area of the hypogastric artery.

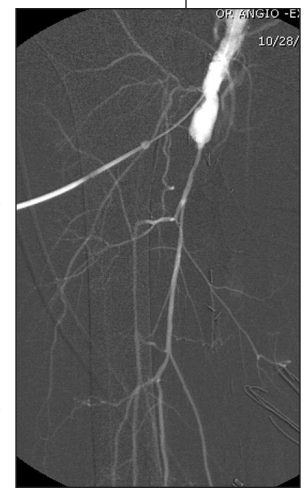

Figure 3a: Near occlusion of right SFA with formation of collateral circulation. Continuation of the angiogram distally revealed reconstitution of the above knee popliteal artery

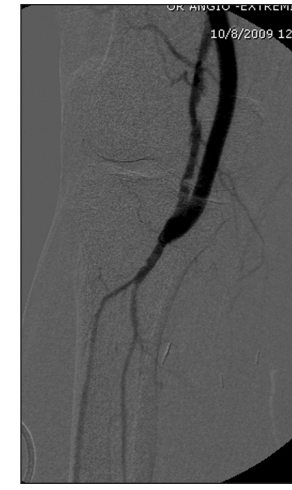

Figure 3b: After right femoral-popliteal artery bypass with PTFE graft, improved blood flow into the tibial arteries is seen, as is improved flow into the popliteal artery via retrograde filling.

Using maximum walking distance (MWD) and ABI as a comparative diagnostic marker to the incidence of claudication post-therapy, it was found that direct revascularization did show improvement over indirect repair for relief of buttock claudication, though no significant improvement was seen in MWD or ABI in those patients.[18] Such studies may provide empiric data to clinicians in determining the indicated surgery for a specific patient.

Surgical Revascularizations

Surgical revascularizations carry risk of occlusion due to conduit material, but also due to three main factors: 1. poor arterial inflow due to upstream lesions and episodes of hypotension can encourage thrombosis within a bypass; 2. poor distal outflow and downstream obstruction which can increase resistance within the bypass leading to complete occlusion; and 3. length of artery segment bypassed and the necessary length of conduit used. As the length of conduit increases, the luminal resistance based on diameter also increases, exponentially. Disease involving the foot is usually a manifestation of extensive tibial disease. If such a patient is a candidate for surgical revascularization, these factors should be considered since a conduit length of 8-10 cm may be necessary, thereby hindering flow rate and outflow both antegrade and retrograde. Therefore, these patients should be thoroughly evaluated with CTA or MRA for anastomotic target sites and predictors for bypass failure.[8]

An alternative to bypass for the lesions in the larger arteries of the lower extremity is endarterectomy and thromboendarterectomy. In a true endarterectomy, the two innermost layers of the artery, the tunica intima and tunica media are dissected and resected along with luminal thrombus and intimal plaque. This method can be highly effective for short segment lesions of the EIA,

Continued on page 184

Plumbing...

common femoral artery (CFA), PFA, and SFA.

Conclusion

Peripheral artery disease affects eight million people in the United States and often goes undetected when patients present without symptoms. Early screening and detection of PAD can also aid in diagnosing cardiovascular-related diseases, like coronary and carotid artery disease, leading to early treatment and improved prognoses. Treatment of PAD should be individualized on a per-patient basis, but is not limited to surgery alone. Advances in pharmacological therapy and endovascular treatment have allowed vascular specialists to reserve surgical procedures for a select group of patients. ■

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Damien De Collibus earned an M.S. in Molecular and Cellular Biology from St. John's University and a post-graduate degree in Physician Assistant studies from Stony Brook University. He has worked as a Physician Assistant in General, Vascular, and Thoracic Surgery, and in Emergency Medicine. Damien is currently employed at Lenox Hill Hospital in the Department of Surgery, and is a clinical lecturer for the Stony Brook University Physician Assistant program.

EXAMINATION

Continuing Medical Education

See answer sheet on page 187.

1) Peripheral artery disease develops as atherosclerotic changes in the peripheral vessels progress, and may present with:
- A) Intermittent claudication
- B) Pain at rest
- C) Gangrene and tissue loss
- D) All of the above

2) Patients with a history of PAD with claudication have a ____ times higher risk of experiencing a cardiac event than those patients without claudication.
- A) 1
- B) 2.5
- C) 5
- D) 10

3) Which of these studies is not considered a non-invasive screening test for PAD?
- A) Ankle-brachial index
- B) Angiogram
- C) Pulse volume recording
- D) Arterial duplex

4) From innermost to outermost, which sequence best describes the layers of the arterial wall:
- A) tunica adventitia—>tunica media—>tunica intima
- B) tunica intima—>tunica adventitia—>tunica media
- C) tunica media—>tunica adventitia—>tunica intima
- D) tunica intima—>tunica media—> tunica adventitia

5) Which atherosclerotic phase involves destabilization of intimal plaque containing extracellular lipids and fibrous tissue?
- A) Phase 1
- B) Phase 2
- C) Phase 3
- D) Phase 4

6) Described by De Bakey, what are the three most common sites of arterial plaque formation in the lower extremity?
- A) Superficial femoral artery at the adductor hiatus
- B) Aortic bifurcation
- C) Tibial trifurcation
- D) All of the above

7) Type 3 lesions are the most common type in the lower extremity, and account for what percentage of lesions?
- A) 10-15%
- B) 25%
- C) 60-70%
- D) 95-100%

8) "Leriche syndrome" describes the presentation of iliac artery occlusion with complaints of hip and buttock claudication, erectile dysfunction, and what finding on physical exam?
- A) Aortic bruit
- B) Pes plantaris
- C) Absent femoral pulses
- D) Gangrene

9) Pain that develops in the absence of exertion, localized to the dorsum of the foot overlying the metatarsal heads is known as:
- A) Intermittent claudication
- B) Colic
- C) Rest pain
- D) Restless legs syndrome

10) What ABI value is typically associated with severe arterial insufficiency/PAD?
- A) <0.9
- B) 0.7—>0.9
- C) 0.4—>0.7
- D) <0.4

11) If ABI measurements are felt to be inaccurate due to changes of diabetes and renal failure, what non-invasive test may be employed to assess for PAD?
- A) Computed tomographic angiography
- B) Magnetic resonance angiography
- C) Toe-brachial index
- D) Angiogram

12) What substance has been shown to cause vasoconstriction in the peripheral arteries, and should be avoided prior to arterial duplex studies, if possible:
- A) Cilostazol
- B) Aspirin
- C) Nicotine
- D) Clopidogrel

13) Controlling which PAD risk-factor has been associated in a 40% risk reduction for new onset claudication or progressively worsening claudication?
- A) Hypertension
- B) Obesity
- C) Hyperlipidemia
- D) Increasing age

14) Pletal (cilostazol) may improve pain-free ambulation for many patients via inhibition of what cellular messenger?
- A) Prostaglandin
- B) Phosphodiesterase-III (PDE-III)
- C) Cyclic Adenosine monophosphate (cAMP)
- D) Vitamin K

Continued on page 186

Continuing Medical Education

EXAMINATION

(cont'd)

15) Effective coumadin dosing is achieved when a patient's INR reaches what range?
- A) 0.5–1.5
- B) 2.0–3.0
- C) 3.5–4.5
- D) 8.0–9.0

16) Indications for endovascular and surgical repair of PAD lesions include:
- A) Intermittent claudication limiting activities of daily living and function
- B) Rest pain
- C) Gangrene or tissue loss
- D) All of the above

17) The bypass conduit of choice for most lower extremity bypass surgeries is:
- A) Autologous greater saphenous vein.
- B) PTFE graft
- C) Dacron graft
- D) Biomodified graft

18) Open surgical revascularizations of the lower extremities include which of the following:
- A) Endarterectomy/thromboendarterectomy
- B) Bypass with autologous greater saphenous vein
- C) Bypass with synthetic graft
- D) All of the above

19) Which factor is NOT believed to increase the risk of thrombosis of a peripheral bypass?
- A) Increased length of bypass material
- B) Poor distal outflow
- C) Hypotension and poor arterial inflow
- D) Use of vein over synthetic graft

20) Endarterectomy involves surgical resection of plaque along with which two layers of the arterial wall?
- A) Tunica media and tunica adventitia
- B) Tunica intima and tunica media
- C) Tunica intima and tunica adventitia
- D) Tunica intima and submucosa

See answer sheet on page 187.

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Vascular Plumbing 101: Management of Peripheral Artery Disease (Vicken Pamoukian, MD and Damien De Collibus, R-PAC)

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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