Vascular Diseases

The rehabilitation professional is often asked to evaluate the patient with a painful, swollen, or ulcerated limb. A thorough understanding of the pathophysiology, available diagnostic testing, and clinical evaluation help practitioners to make the vascular diagnosis and choose the appropriate treatment program.

Arterial Diseases

Arterial diseases include those acute and chronic disorders that result in partial or complete, functional or anatomic occlusion, or aneurysmal dilatation of the arteries. An example of functional occlusion is abnormal vascular reactivity of the arteries supplying a given tissue, such as vasospasm. Recognition of the broad differential diagnosis of lower extremity arterial disease is important to optimize management.

Peripheral arterial disease (PAD) has increased in prevalence and put a severe burden on patients and the economy. PAD affects more than 8 million adults in the United States alone. PAD is a disease of aging with an increase in disease prevalence from 10% in individuals age 65 years to more than 30% in octogenarians. Patients with PAD commonly present with symptoms of intermittent claudication or critical limb ischemia. In general, symptoms occur distal to the level of stenosis. If the patient is active, intermittent claudication is the typical presenting complaint. If the patient is inactive, then rest pain, ulceration, dependent rubor, or gangrene may be the presenting finding (Fig. 25.1).

Patients with intermittent claudication have a significantly higher mortality than age-matched controls, approximately 12% per year. Of these deaths, 66% are caused by heart disease and 10% by strokes. Only one in four patients with intermittent claudication will develop critical limb ischemia. Longitudinal studies have shown that the amputation rate in this group of patients is only 1% to 7% at 5 to 10 years.

Arteriosclerosis Obliterans

The clinical presentation of acute arterial occlusion is described as the “6 P’s”: pain, pallor, paresthesias, paralysis, pulselessness, and polar (cold). Some or all of these findings may be present. The limb with acute arterial occlusion is at risk if blood flow is not restored quickly.

Historically, it has been thought that 4 to 6 hours (following the onset of symptoms) is the maximal length of tolerable ischemia. However, patients with previous chronic limb ischemia tend to tolerate longer periods of acute ischemia. The physiologic state of the limb, determined mainly by a balance between metabolic supply and demand, rather than the elapsed time from the onset of occlusion, is actually the best predictor of limb salvage.

Intermittent claudication indicates an inadequate supply of arterial blood to contracting muscles. It occurs primarily in chronic arterial occlusive disease or severe arteriospastic disease. Intermittent claudication is brought on by walking and is relieved promptly by rest without change of position of the affected limb. Patients describe claudication as leg numbness, weakness, buckling, aching, cramping, or pain. It may change in character as the underlying lesions progress. Claudication occurs at a predictable distance or time. When the workload is increased (rapid pace, walking up hills, or walking over rough terrain), the time to claudication decreases. Claudication may worsen over a period of inactivity (when the patient is hospitalized) but usually returns to baseline with reconditioning. When claudication abruptly increases, one must consider thrombosis in situ or an embolic event. Claudication at the arch of the foot suggests occlusion at or above the ankle; claudication at the calf suggests occlusion at or above this region. Claudication is less frequent above the knee (probably because of the rich collateral circulation in the thigh); however, occlusion of the iliac arteries or aorta may cause thigh, lumbar region, and buttock claudication.

Although many other disorders can cause symptoms of lower extremity arterial insufficiency (thromboangiitis obliterans [TAO], arterial thromboemboli), these conditions account for only a small percentage of lower extremity arterial disease.

Vasculitic Syndrome

Vasculitis or angiitis is an inflammatory disease of blood vessels. It often causes damage to the vessel wall, stenosis, or occlusion of the vessel lumen by thrombosis, and progressive intimal proliferation. Vasculitic symptoms reflect systemic inflammation and the ischemic consequences of vascular occlusion. The distribution of the vascular lesions and the size of the blood vessels involved vary considerably in different vasculitic syndromes and in different patients with the same syndrome. Vasculitis can be transient, chronic, self-limited, or progressive. It can be the primary abnormality or secondary to another systemic process. Histopathologic classification does not distinguish systemic illness or secondary from primary insult.

Rheumatoid Vasculitis

Rheumatoid vasculitis manifests almost exclusively in patients with rheumatoid autoantibodies and often occurs in the context of other extraarticular manifestations. The vasculitis is mediated
by the deposition of circulating immune complexes on the blood vessel wall with activation of complement. Proliferation of the vascular intima and media causes an obliterative endarteropathy. Leukocytoclastic or small vessel vasculitis produces palpable purpura or cutaneous ulceration. The presence of human leukocyte antigen-C3 (HLA-C3) and smoking are independent predictors of vasculitis in patients with rheumatoid arthritis. Smoking, rheumatoid factor, and antinuclear antibodies are all associated with severe extraarticular disease manifestations.84

Cryoglobulinemia
Cryoglobulins are immunoglobulins that reversibly precipitate at reduced temperatures. Type I consists of monoclonal immunoglobulin, generally immunoglobulin M (IgM) or IgG. Type II cryoglobulins are a mixture of monoclonal IgM and polyclonal IgG. Type III cryoglobulins are a mixture of polyclonal IgM and IgG. Cryoglobulinemia is associated with many illnesses, which can be broadly grouped into infections (hepatitis C), autoimmune diseases, and malignancy. More than 90% of cases of cryoglobulinemia have a known underlying cause; treatment is focused on the cause of the disorder rather than merely symptomatic relief.65

Polyarteritis
Polyarteritis occurs by itself (polyarteritis nodosa [PAN]) or in association with another disease (secondary polyarteritis). PAN is an acute necrotizing vasculitis that affects primarily medium-sized and small arteries. It is a systemic disorder that may involve the kidneys, joints, skin, nerves, and various other tissues. The prognosis of PAN is heavily dependent on the severity and organ distribution at the time of diagnosis. PAN has a tendency to involve medium-sized muscular arteries. It spares the aorta and its major branches, as well as capillaries and small arterioles that lack muscular coats. PAN also spares the venous system. Vasculitis of medium-sized arteries usually produces one of the following: livedo reticularis, nodules, ulcerations, and digital ischemia.81 For cases of idiopathic PAN, corticosteroids and cytotoxic agents remain the cornerstone of treatment.31

Other Vasculitides
A wide variety of other vasculitides may affect small- and medium-sized vessels. These include allergic angiitis (Churg-Strauss syndrome), Henoch-Schönlein purpura, various forms of hypersensitivity vasculitis, and numerous nonspecific necrotizing and nonnecrotizing vasculitides.

Thromboangiitis Obliterans (Buerger Disease)
TAO or Buerger disease is a nonatherosclerotic segmental vasculitis that affects small- and medium-sized arteries and veins of the extremities and is strongly associated with tobacco exposure. The immunopathogenesis of TAO remains largely unknown.40 The first manifestation of Buerger disease may be superficial phlebitis. TAO occurs predominantly in young adult male smokers. Few cases, if any, occur in the absence of tobacco use. If smoking is discontinued, the process is frequently arrested.

Raynaud Syndrome
Raynaud syndrome is characterized by episodic attacks of vasospasm in response to cold or emotional stress. The fingers and hands are most often affected. In certain patients, the toes and feet may be involved. Classic episodes of vasospasm cause an intense pallor of the distal extremity followed by cyanosis and rubor on rewarming. Most patients do not experience this complete triple color response. Typically, only pallor or cyanosis is noted during attacks. In general, the attacks are over within 30 to 60 minutes, and these episodes are usually bilateral. Attacks may occur infrequently; for example, some may have symptoms only during the winter. However, other patients may have a significant impairment/disability with multiple daily episodes. Digital ulcerations are rare but may occur. Females are affected more commonly than males.

Raynaud disease refers to a primary vasospastic disorder where there is no identifiable underlying cause. Raynaud phenomenon refers to vasospasm, secondary to another underlying condition or disease. Predisposing factors include atherosclerosis, arteritis, cancer, collagen vascular disease, thoracic outlet syndrome, embolic occlusion, occupational disease, and certain medications.77 Secondary Raynaud phenomenon is occasionally unilateral and may produce skin breakdown.

Vibration Syndrome
Vibratory tools, such as chainsaws, grinders, and jack hammers, can induce hand dysesthesias and Raynaud phenomenon when used for several years. Symptoms initially occur during use of the instrument. Subsequently, dysesthesias and cold sensitivity persist when the vibratory tool is not being used. During exposure to vibration, there is a reduction in finger blood flow in both vibrated and nonvibrated fingers. The acute vascular responses during and after exposure to vibration may not be separate independent effects of vibration frequency, magnitude, and duration; there may be complex interactions between the effects of these variables.9
Vascular diagnostic laboratories can use segmental pressures, Doppler waveform analysis, pulse volume recordings, or ankle-brachial index (ABI) with duplex ultrasonography (or some combination of these methods) to document the presence and location of PAD. Segmental pressure analysis in this manner can be indexed relative to the brachial artery pressure which makes the toe-brachial index (TBI) useful. To calculate the TBI, blood pressures are obtained at the brachial artery and at the toe. The toe systolic pressure requires a photoplethysmograph distal to the cuff instead of a stethoscope. Normal TBI values are 0.65 to 0.7 and greater. The incidence of noncompressible (artifactually high), calcified conduit arteries is highest in patients with diabetes, patients with chronic renal failure, and elderly patients. Despite high recorded systolic pressure, these patients may have severe disease. The TBI should be used to establish the lower extremity PAD diagnosis in patients in whom lower extremity PAD is clinically suspected but in whom the ABI test is not reliable as a result of noncompressible vessels (usually patients with long-standing diabetes or advanced age). Other diagnostic tests (arterial duplex studies, segmental pressure measurement, Doppler waveform analysis, pulse volume recording, or transcutaneous oximetry [TcPO2]) may also be performed to rule out significant arterial occlusive disease.

**Ankle-Brachial Index**

The ABI is known to be unreliable in patients with vascular stiffness and fails to detect the early phase of atherosclerotic development. The toe vessels are less susceptible to vessel stiffness, which makes the toe-brachial index (TBI) useful. To calculate the TBI, blood pressures are obtained at the brachial artery and at the toe. The toe systolic pressure requires a photoplethysmograph distal to the cuff instead of a stethoscope. Normal TBI values are 0.65 to 0.7 and greater. The incidence of noncompressible (artifactually high), calcified conduit arteries is highest in patients with diabetes, patients with chronic renal failure, and elderly patients. Despite high recorded systolic pressure, these patients may have severe disease. The TBI should be used to establish the lower extremity PAD diagnosis in patients in whom lower extremity PAD is clinically suspected but in whom the ABI test is not reliable as a result of noncompressible vessels (usually patients with long-standing diabetes or advanced age). Other diagnostic tests (arterial duplex studies, segmental pressure measurement, Doppler waveform analysis, pulse volume recording, or transcutaneous oximetry [TcPO2]) may also be performed to rule out significant arterial occlusive disease.

### Table 25.1 Ankle-Brachial Index

<table>
<thead>
<tr>
<th></th>
<th>Resting</th>
<th>Post Exercise</th>
<th>Treadmill Time (Expected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noncompressible</td>
<td>&gt;1.40</td>
<td>&gt;0.90</td>
<td>Complete 5 min</td>
</tr>
<tr>
<td>Normal</td>
<td>1.00–1.40</td>
<td>&gt;0.90</td>
<td>Complete 5 min</td>
</tr>
<tr>
<td>Borderline</td>
<td>0.90–0.99</td>
<td>&gt;0.90 or ≥10% drop from baseline</td>
<td>Complete 5 min</td>
</tr>
<tr>
<td>Mild</td>
<td>0.80–0.89</td>
<td>0.51–0.90</td>
<td>Complete 5 min</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.50–0.79</td>
<td>0.15–0.50</td>
<td>Greater than half</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;0.50</td>
<td>&lt;0.15</td>
<td>Less than half</td>
</tr>
</tbody>
</table>

**Hypothemar Hammer Syndrome**

Occlusive disease in the hands can result from trauma to the hypothenar area caused by using the palm of the hand as a hammer in an activity that involves pushing, pounding, or twisting. This results in intimal injury to the ulnar artery as it crosses the hamate bone. Such injuries of the ulnar artery may lead to severe vascular insufficiency in the hand with thrombosis and distal embolization of the digital arteries.

**External Iliac Syndrome in Cyclists**

Exercise-induced external iliac artery endofibrosis is rare and has been described primarily in endurance male cyclists. Clinically, it presents as claudication during maximal exercise with quick resolution after exercise. Most patients have fibrotic changes within the external iliac artery. Vasospasm may be more important than wall thickening for the reduction of blood flow during extreme exercise in affected athletes.

**Arterial Evaluation**

Vascular diagnostic testing is typically performed to confirm a clinical diagnosis and document the severity of disease.

**Noninvasive Arterial Studies**

Vascular diagnostic laboratories can use segmental pressures, Doppler waveform analysis, pulse volume recordings, or ankle-brachial index (ABI) with duplex ultrasonography (or some combination of these methods) to document the presence and location of PAD.

**Ankle-Brachial Index**

The ABI provides objective data about arterial perfusion of the lower limbs (Table 25.1). Pressures are obtained with a blood pressure cuff placed around the patient’s lower calves or ankles. A handheld Doppler detects systolic blood pressure in the dorsalis pedis and the posterior tibial arteries. The brachial (arm) pressure is often used to determine the location of arterial stenosis. Arterial pressure can be measured with blood pressure cuffs placed at various levels (upper thigh, lower thigh, upper calf, and lower calf above the ankle) sequentially along the limb. The presence of a significant systolic pressure gradient (greater than 10 to 15 mm Hg) between the brachial artery pressure and the upper thigh systolic pressure usually signifies the presence of aortoiliac obstruction. A pressure gradient located between the upper and lower thigh cuffs signifies obstruction in the superficial femoral artery. A gradient between the lower thigh and upper calf cuffs indicates distal superficial femoral or popliteal artery obstruction. A gradient between the upper and lower calf cuffs identifies infrapopliteal disease. Gradients of 10 to 15 mm Hg between adjacent sites may represent physiologically important obstruction.

**Resting Post Exercise Treadmill Time (Expected)**

- ≥10% drop from baseline: Complete 5 min
- >0.90 or ≥10% drop from baseline: Complete 5 min
- 0.90: Complete 5 min
- 0.90 or ≥10% drop from baseline: Complete 5 min
- 0.51–0.90: Complete 5 min
- 0.15–0.50: Greater than half
- <0.15: Less than half

**Hypothenar Hammer Syndrome**

Occlusive disease in the hands can result from trauma to the hypothenar area caused by using the palm of the hand as a hammer in an activity that involves pushing, pounding, or twisting. This results in intimal injury to the ulnar artery as it crosses the hamate bone. Such injuries of the ulnar artery may lead to severe vascular insufficiency in the hand with thrombosis and distal embolization of the digital arteries.

**External Iliac Syndrome in Cyclists**

Exercise-induced external iliac artery endofibrosis is rare and has been described primarily in endurance male cyclists. Clinically, it presents as claudication during maximal exercise with quick resolution after exercise. Most patients have fibrotic changes within the external iliac artery. Vasospasm may be more important than wall thickening for the reduction of blood flow during extreme exercise in affected athletes.

**Arterial Evaluation**

Vascular diagnostic testing is typically performed to confirm a clinical diagnosis and document the severity of disease.

**Noninvasive Arterial Studies**

Vascular diagnostic laboratories can use segmental pressures, Doppler waveform analysis, pulse volume recordings, or ankle-brachial index (ABI) with duplex ultrasonography (or some combination of these methods) to document the presence and location of PAD.

**Ankle-Brachial Index**

The ABI provides objective data about arterial perfusion of the lower limbs (Table 25.1). Pressures are obtained with a blood pressure cuff placed around the patient’s lower calves or ankles. A handheld Doppler detects systolic blood pressure in the dorsalis pedis and the posterior tibial arteries. The brachial (arm) pressure is also obtained. In a healthy individual, because of peripheral amplification of the pulse pressure, the ankle pressure should be higher than the brachial arterial systolic pressure. A normal ankle to arm systolic blood pressure ratio is 1.0 to 1.4. ABI values are considered to be borderline low when they are between 0.91 and 0.99 and abnormally low when less than or equal to 0.90. Values greater than 1.4 indicate noncompressible arteries. An ABI identifies individuals who are at risk for developing rest pain, ischemic ulcerations, or gangrene, and it is a marker of generalized atherosclerosis. The risk of death, usually from a cardiovascular event, increases dramatically as the ABI decreases. The 5-year mortality rate in patients with an ABI less than 0.85 is 10%. When the ABI is less than 0.40, the 5-year mortality rate approaches 50%.

The ABI is known to be unreliable in patients with vascular stiffness and fails to detect the early phase of atherosclerotic development. The toe vessels are less susceptible to vessel stiffness, which makes the toe-brachial index (TBI) useful. To calculate the TBI, blood pressures are obtained at the brachial artery and at the toe. The toe systolic pressure requires a photoplethysmograph distal to the cuff instead of a stethoscope. Normal TBI values are 0.65 to 0.7 and greater. The incidence of noncompressible (artifactually high), calcified conduit arteries is highest in patients with diabetes, patients with chronic renal failure, and elderly patients. Despite high recorded systolic pressure, these patients may have severe disease. The TBI should be used to establish the lower extremity PAD diagnosis in patients in whom lower extremity PAD is clinically suspected but in whom the ABI test is not reliable as a result of noncompressible vessels (usually patients with long-standing diabetes or advanced age). Other diagnostic tests (arterial duplex studies, segmental pressure measurement, Doppler waveform analysis, pulse volume recording, or transcutaneous oximetry [TcPO2]) may also be performed to rule out significant arterial occlusive disease.

**Segmental Pressure Measurements**

Segmental pressure is the arterial closing and opening pressure at a specific anatomic location. Systolic blood pressure obtained in this manner can be indexed relative to the brachial artery pressure in a manner analogous to the ABI. Segmental pressure analysis is often used to determine the location of arterial stenosis. Arterial pressure can be measured with blood pressure cuffs placed at various levels (upper thigh, lower thigh, upper calf, and lower calf above the ankle) sequentially along the limb. The presence of a significant systolic pressure gradient (greater than 10 to 15 mm Hg) between the brachial artery pressure and the upper thigh systolic pressure usually signifies the presence of aortoiliac obstruction. A pressure gradient located between the upper and lower thigh cuffs signifies obstruction in the superficial femoral artery. A gradient between the lower thigh and upper calf cuffs indicates distal superficial femoral or popliteal artery obstruction. A gradient between the upper and lower calf cuffs identifies infrapopliteal disease. Gradients of 10 to 15 mm Hg between adjacent sites may represent physiologically important obstruction.
Continuous Wave Doppler (See Videos 25.1–25.3)
A normal continuous wave Doppler is triphasic, with a rapid upstroke or forward flow, a downstroke to below baseline as flow reverses, and finally a short period of forward flow is seen again. When stenosis is present, and as it increases, the reversal of flow is lost, and the upstroke may be delayed. With greater stenosis, the upstroke becomes smaller, further delayed, sinusoidal, and eventually absent. A change from triphasic to monophasic waveforms provides reasonable, accurate information about the location and extent of specific lower extremity lesions. Doppler waveform analyses are reliable even in highly calcified vessels that are not amenable to pressure determinations (Table 25.2).

Transcutaneous Oximetry
TcPO₂ determinations provide a very sensitive means to assess skin perfusion and the potential for cutaneous healing at a specific site. TcPO₂ values less than 20 to 30 mm Hg suggest inadequate perfusion for healing. A decrease in the TcPO₂ value of 10 mm Hg with leg elevation also suggests tenuous perfusion (Table 25.3).

Duplex Scanning
Duplex scanning with B-mode imaging combined with directional Doppler can visualize and assess arterial aneurysms and detect flow velocity changes at sites of localized stenosis or occlusion. Duplex scanning is particularly helpful in assessing proximal iliofemoral stenosis that may be amenable to angioplasty, providing follow-up data to assess continued patency of both venous and prosthetic arterial grafts, and evaluating the patency of previous angioplasty sites or intravascular stents.

Imaging Techniques
Advances in technology are enabling computed tomography angiography (CTA) and magnetic resonance angiography (MRA) to replace conventional angiography as a means of identifying arterial stenoses and occlusions.

Computed Tomography Angiography
CTA has become a standard noninvasive imaging modality for vascular anatomy and pathology (Fig. 25.2). With continued improvement in spatial resolution, CTA is currently a mainstay for preoperative imaging of abdominal aortic aneurysms. It provides accurate information not only of the size of an aneurysm but also the exact location and critical measurements needed for repair.

Magnetic Resonance Angiography
MRA can be used to determine the morphology of blood vessels, assess blood flow velocity, evaluate the lumen for the presence of thrombosis, and evaluate for the presence of hemorrhage, infection, or the status of the end organ. Unlike ultrasound, MRA is not compromised by overlying bone, bowel gas, or calcification. MRA is relatively expensive, and its use is limited in situations in which metallic instrumentation may be required. MRA is the optimum imaging alternative in patients who are pregnant and patients with severe iodinated contrast allergy. Magnetic resonance studies using gadolinium have a long safety record with little nephrotoxicity at the doses used. Reports that gadolinium may play a role in inducing nephrogenic systemic fibrosis (NSF) are a concern. Although rare, NSF can be catastrophic. Caution is recommended in patients with reduced glomerular filtration rate (GFR) (definitely a GFR less than 30, possibly less than 60).

### Table 25.2 Doppler Signals of the Patient in Fig. 25.1 Showing Right Multilevel Popliteal and Infrapopliteal and Left Infrapopliteal Arterial Occlusive Disease

<table>
<thead>
<tr>
<th></th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common femoral</td>
<td>Biphasic</td>
<td>Biphasic</td>
</tr>
<tr>
<td>Superficial femoral</td>
<td>Biphasic</td>
<td>Biphasic</td>
</tr>
<tr>
<td>Popliteal</td>
<td>Reduced biphasic</td>
<td>Biphasic</td>
</tr>
<tr>
<td>Posterior tibial</td>
<td>Monophasic</td>
<td>Monophasic</td>
</tr>
<tr>
<td>Dorsalis pedis</td>
<td>Monophasic</td>
<td>Monophasic</td>
</tr>
</tbody>
</table>

### Table 25.3 Transcutaneous Oximetry Values of the Patient in Fig. 25.1 Showing Severely Reduced Perfusion by Transcutaneous Oximetry Criteria at the Left Foot

<table>
<thead>
<tr>
<th>Electrode Site</th>
<th>Supine</th>
<th>Elevated</th>
<th>Dependent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest (reference)</td>
<td>58</td>
<td>66</td>
<td>65</td>
</tr>
<tr>
<td>R foot</td>
<td>58</td>
<td>58</td>
<td>64</td>
</tr>
<tr>
<td>L above knee</td>
<td>60</td>
<td>59</td>
<td>64</td>
</tr>
<tr>
<td>L below knee</td>
<td>38</td>
<td>35</td>
<td>44</td>
</tr>
<tr>
<td>L foot proximal</td>
<td>2</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>L foot distal</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

L, Left; R, right.
There are currently techniques available to allow angiographic imaging without the use of contrast.\textsuperscript{62}

**Catheter Arteriography**

Catheter angiography has been the traditional “gold standard” for lower extremity arterial evaluation.\textsuperscript{87} Angiography remains the definitive approach for perioperative evaluation in patients requiring open revascularization if noninvasive axial imaging is inconclusive. Angiography is helpful to evaluate the tibial and pedal arteries, which are difficult to assess on axial imaging. Preprocedure arteriography is an essential part of endovascular procedures (Fig. 25.3).

**Management**

The goals of management in patients with PAD should be to reduce cardiovascular risk and alleviate symptoms. Medical therapies can effectively modify both the natural history of atherosclerotic lower extremity arterial occlusive disease and significantly reduce the morbidity of this disorder.

On average, an age-matched control group has an all-cause mortality rate of 1.6\% per year. This rate increases to 4.8\% per year for patients with PAD. Cardiovascular mortality rates are similarly affected with an overall event rate of 0.5\% per year in controls and 2.5\% per year in patients with PAD. The presence of PAD is an independent risk factor for mortality even when other known risk factors are controlled.\textsuperscript{66} Treatment needs to focus on both the effects of atherosclerosis in the peripheral circulation and...
the systemic nature of the disease. Appropriate therapy should be instituted to decrease the risk for both peripheral progression and cardiovascular mortality. The increased cardiac event rate in patients with PAD underscores the importance of intensive medical management to reduce the risk for cardiovascular morbidity and mortality.

**Risk Factor Management**

A transition in the pattern of atherosclerotic risk factors in the United States and worldwide is being witnessed. Certain traditional atherosclerotic risk factors are on the wane (as a result of decreased rates of smoking, antihypertensive medications, statins). The astounding increase in obesity in the US population has led to a significant increase in the prevalence of the components of the clustered risk factors often referred to as the metabolic syndrome. The metabolic syndrome is characterized by a constellation of interrelated pathologic conditions of a metabolic or hemodynamic nature (abdominal obesity, atherosclerosis, impaired glucose control, or hypertension) that appear to directly promote the development of cardiovascular disease.

All patients presenting for treatment of PAD should have their risk factors rigorously assessed. Patients with known PAD should be treated aggressively with a combination of an HMG-CoA (3-hydroxy-3-methylglutaryl-coenzyme A) reductase inhibitor (statin), an angiotensin-converting enzyme (ACE) inhibitor, an antiplatelet agent, and a β-blocker (if there is a history of coronary disease). Blood pressure and glucose control is imperative and aggressive smoking cessation counseling is recommended for every medical interaction.

Diabetes is a strong independent predictor for stroke, myocardial infarction (MI), and PAD. The need for amputation in patients with diabetes for lower extremity arterial occlusive disease is 10 times that for patients who do not have diabetes. In patients with diabetes, for every 1% increase in hemoglobin A1c, there is a corresponding 26% risk of PAD.

Cigarette smoking has been identified as an independent predictor of vascular disease and the reason why vascular procedures and interventions fail. More than 80% of patients with PAD are current or former smokers.

Patients with PAD consistently have higher levels of homocysteine when compared with controls. The data suggest that hyperhomocysteinemia may either be a marker of PAD or etiologically implicated in the development of PAD. Elevated homocysteine levels can be lowered by folic acid and other vitamin supplementation. Randomized trials that have used vitamin treatments to lower homocysteine levels have not documented improvement in cardiovascular outcomes.

**Lipid Management**

Effective lipid management should be considered a mandatory component of the medical therapy of patients with objective evidence of atherosclerotic peripheral arterial occlusive disease. Statins have favorable effects on multiple interrelated aspects of vascular biology important in atherosclerosis. In particular, they have beneficial effects on inflammation, plaque stabilization, endothelial function, and thrombosis.

Lipid-lowering therapy is effective in reducing the cardiovascular mortality and morbidity associated with PAD and likely improves the most common symptoms of PAD, intermittent claudication. The goal for hyperlipidemia management is to maintain a low-density lipoprotein (LDL) level of less than 100 mg/dL in the general population and less than 70 mg/dL in patients with atherosclerotic disease.

Health care providers should increase statin therapy in a graduated manner to adequately determine the patient’s response and tolerance. Side effects of HMG-CoA reductase inhibitors include myopathy and rhabdomyolysis with acute renal failure secondary to myoglobinuria. Statins should be prescribed with caution in patients with predisposing factors for myopathy, and they should be discontinued if markedly elevated creatine kinase levels or myopathy is diagnosed or suspected.

**Angiotensin-Converting Enzyme Inhibitors**

The Heart Outcomes Prevention Evaluation (HOPE) study showed that ACE inhibitors reduce cardiovascular events by 25% in patients with symptomatic PAD. In addition, treatment with ACE inhibitors improves walking ability in patients with intermittent claudication. This was not associated with any significant improvement in the ABI. Patients with intermittent claudication may benefit from treatment with a high tissue affinity ACE inhibitor for a period of 6 months. The overall treatment effect achieved by ACE inhibitors is more than that of other therapeutic agents for intermittent claudication, such as cilostazol and pentoxifylline, but less than that of a supervised exercise program.

**Antiplatelet Therapy**

Antiplatelet therapy may decrease the rate of atherosclerotic disease progression, decrease the incidence of thrombotic events in the limbs, and decrease the rate of adverse coronary and cerebrovascular ischemic events. Aspirin in doses of 80 to 325 mg is recommended as safe and effective platelet therapy to reduce the risk of MI, stroke, or vascular death in individuals with atherosclerotic lower extremity PAD.

Antiplatelet therapy is indicated to reduce the risk of MI, stroke, and vascular death in individuals with symptomatic atherosclerotic lower extremity PAD, including those with intermittent claudication or critical limb ischemia, previous lower extremity revascularization (endovascular or surgical), previous amputation, or lower extremity ischemia. Long-term administration of clopidogrel in patients with atherosclerotic vascular disease has been reported to be more efficient than aspirin in reducing the combined risk for ischemic stroke, MI, or vascular death. More intense antiplatelet treatment strategies might provide additional benefit in patients with PAD.

**Agents for Intermittent Claudication**

Cilostazol and pentoxifylline have been shown to modestly improve walking distances in patients with intermittent claudication. Cilostazol has significant antiplatelet, vasodilatory, and vascular antiproliferative properties. It is contraindicated in patients with either systolic or diastolic heart failure. Cilostazol (100 mg orally two times per day) is indicated as an effective therapy to improve symptoms and increase walking distances in patients with lower extremity PAD and intermittent claudication (in the absence of heart failure). Pentoxifylline has diminished estimated efficacy when compared with cilostazol. Minimal efficacy and caffeine-like side effects limit use of this medication.
Rehabilitation

Patients with PAD should be instructed to wear protective footwear at all times (never walk barefoot or in socks) and monitor their extremities carefully for redness or skin breakdown. Temperature extremes should be avoided. The feet should be washed carefully with mild soap and warm water. Drying is best performed by blotting or patting with a soft clean towel (rubbing should be avoided because it may injure the skin). The skin between the toes should be carefully dried to avoid maceration. Emollients without preservatives or perfume should be used to prevent cracking of the skin (avoid between the toes). Proper footwear, which does not produce areas of point pressure, should be used. Whenever new shoes are purchased, the patient should gradually (over a period of a week) wear-in shoes to make sure that there are no areas of point pressure with the new footwear. Warm outer footwear should be used in the winter to protect against thermal injury. Decreased activity secondary to symptomatic lower extremity arterial occlusive disease can result in deconditioning, which further contributes to disease impairment. Deconditioning may also be “iatrogenic” as a result of a prolonged period of limited mobility to avoid trauma to ischemic wounds.

Regular lower extremity exercise in the form of a structured or a supervised walking program is critical for patients with PAD. Ambulation can help to develop collateral blood flow and in time may lead to resolution or improvement of intermittent claudication. A minimum of 30 minutes of moderate activity at least three times per week is beneficial.38 Regular training has been shown to improve oxygen extraction from blood, muscle enzyme activity, and hemorheology.80 Regular exercise training produces a reduction in the inflammatory markers associated with endothelial damage.34 Evidence suggests that patients following an exercise regimen improve both their claudication distance and cardiovascular risk profile. Exercise improves maximal walking ability by an average of 150%.47 Remarkably, increased walking capacity increased further 6 months after supervised exercise training cessation, suggesting an ongoing benefit of the intervention.71

In summary, current recommendations are that all patients with PAD should receive antiplatelet therapy, stop smoking, exercise, and be screened and treated for hyperlipidemia, hypertension, diabetes, and hypercoagulability in accordance with national guidelines and community standards.16

Gene Therapy

Molecular therapies to induce angiogenesis are appealing in the claudicant population because ischemia is subacute, time is available for angiogenesis to occur, and collateral development is associated with increased walking distance.

Revascularization

Ischemic rest pain and tissue necrosis, including ischemic ulcerations or gangrene, are well-accepted indicators of advanced ischemia and threatened limb loss. Without treatment, most limbs with these symptoms experience disease progression and require major amputation. Previously, surgical revascularization was considered for patients with rest pain, impending tissue loss, or significant limitations of lifestyle who failed medical treatment. Endovascular intervention coupled with aggressive proactive medical management is replacing this conventional paradigm. The multicenter Bypass Versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial found no significant difference between surgical and endovascular revascularization in amputation-free survival or overall survival. A bypass surgery first approach was associated with a significant increase in overall survival of 7.3 months and a trend toward improved amputation-free survival of 5.9 months for those patients who survived for at least 2 years after randomization.10 If early and long-term patency is to be achieved, it is important that the site for vascular reconstruction has a relatively unobstructed inflow and a patent distal runoff.

Attempts at revascularization should be avoided in the presence of life-threatening sepsis, chronic flexion contracture, and paralysis and in patients with markedly reduced life expectancy. Revascularization should be delayed in most individuals with a significant acute comorbidity (recent MI), unless the limb is imminently threatened and high perioperative morbidity is acceptable.68

Intermittent Pneumatic Compression

Intermittent pneumatic foot and calf compression has been shown to improve walking distance comparable with supervised exercise.38 External compression briefly raises the tissue pressure, emptying the underlying veins and transiently reducing the venous pressure without occluding arterial blood flow. The proposed mechanism to explain the increased flow is analogous to the pumping action of the calf muscle during walking. The transient inflation (quick impulse) imitates the effects of normal gait by generating a vigorous hemodynamic impulse throughout the veins each time the lower extremity is compressed. An increase in the hydrostatic pressure gradient is thought to be a major mechanism for the enhancement of arterial leg inflow. In addition, the altered flow and shear forces generated by the inflation of the pneumatic cuff may mediate the release of endothelial and humeral factors having local and systemic effects. A direct reduction in the peripheral resistance is also postulated via release of nitrous oxide secondary to shear stress across the vessel wall.17

Venous Disease

Venous disease includes acute or chronic occlusion of the systemic venous or pulmonary arterial system, usually as a result of thromboembolism. Chronic venous disease is a spectrum of diseases and disorders of the limbs with spider veins and varicosities on one end of the spectrum and edema, skin changes (stasis, hyperpigmentation), and ulceration on the other end (Fig. 25.4). The cause is either primary valvular incompetence or postphlebitic/postthrombotic syndrome secondary to previous deep venous thrombosis (DVT).

Venous Thromboembolism

The disease burden from venous thromboembolism (VTE) is major. Each year there are an estimated 900,000 patients with clinical evidence of VTE in the United States resulting in an estimated 300,000 deaths from pulmonary embolism.32 When a patient presents with the possibility of a DVT, predisposing risk factors, such as prolonged immobilization during car or plane trips, use of estrogen, previous DVT, or family history of thrombosis, should
Upper extremity DVT is most often the result of intravenous catheters causing trauma to the endothelium. A much rarer occurrence is venous thoracic outlet syndrome (Paget-Schroetter syndrome), which is thrombosis due to compression of the subclavian vein at the costoclavicular junction.

**Phlegmasia Cerulea Dolens**

Phlegmasia cerulea dolens is a rare complication of DVT, characterized by rapid and massive edema, severe pain, and cyanosis. Distal cyanosis may indicate extensive blockage to venous return. Phlegmasia cerulea dolens most commonly occurs with proximal, iliofemoral obstruction with extensive distal thrombus of deep and superficial veins. In phlegmasia, the arterial pulses may not be palpable, although anatomically the arteries are patent. In severe cases, gangrene, which may necessitate amputation, occurs. Urgent treatment, including placing a caval filter, heparinization, and surgical thrombectomy or thrombolysis if possible, is essential to minimize loss of life or limb.

**May-Thurner Syndrome**

May-Thurner syndrome is defined as isolated left lower extremity swelling caused by compression of the left common iliac vein by the right common iliac artery. Treatment of May-Thurner syndrome has historically involved anticoagulation therapy. Advances in interventional management have allowed relief of the associated mechanical compression by open surgical or endovascular repair. Endovascular stents are the most common treatment.

**Chronic Venous Insufficiency**

Chronic venous disease is an important cause of discomfort and disability and is present in a significant percentage of the population worldwide. A clinical score of Clinical-Etiologic-Anatomic-Pathophysiologic (CEAP) has been developed as a standard for reporting venous disease. Many factors can result in the development of venous insufficiency, including heredity, local trauma, thrombosis, and intrinsic defects in the veins or valves themselves. Venous flow is based on a force that pushes the blood proximally, an adequate outflow, and the presence of competent valves limiting reflux. Any disruption of these components results in chronic venous hypertension. Normally, the pressure in the leg veins is equal to the hydrostatic pressure from a vertical column of blood extending to the right atrium of the heart. At the ankle level, the hydrostatic pressure is approximately 90 mm Hg. The pumping action of the calf muscles during exercise reduces this venous pressure by two-thirds. Even slight muscular movements during normal standing will lower the pressure. Patients with venous insufficiency might fail to reduce ankle pressure or show a rapid return of venous pressure to resting levels at the end of the exercise. The time required for the ankle vein pressure to return to resting levels after exercise is an indicator of the degree of reflux in the limb. Elevated ambulatory venous pressure is associated with an increased incidence of ulceration. When ambulatory, venous ankle pressure is less than 30 mm Hg and the incidence of ulceration is close to 0%. The incidence of ulceration increases linearly when ankle pressure is greater than 30 mm Hg, reaching 100% when the ambulatory venous pressure is greater than 90 mm Hg. The superficial leg veins normally carry 10% to 15% of the venous return. Incompetent valves in the superficial veins alone rarely cause serious venous hypertension, although 10% of patients with venous ulcers have superficial venous incompetence alone.
Primary deep venous reflux is more often observed in patients who are obese and is more persistent following eradication of the superficial reflux than observed for patients who are of normal weight.86

A quarter of patients with a first, unprovoked, unilateral, proximal DVT who were free of clinically significant primary venous insufficiency showed postthrombotic syndrome 5 to 7 months after the index event. Obesity, mild contralateral venous ectasia, poor international normalized ratio (INR) control, and the presence of ultrasonographic residual venous obstruction significantly increased the risk of postthrombotic syndrome in this population.24 Venous insufficiency may present up to 5 to 10 years after resolution of the acute episode of thrombosis. Postphlebitic damage in the deep veins is an important cause of chronic venous insufficiency. Advanced venous insufficiency develops when the valves in the perforator or deep veins are also incompetent. Ultimately, venous hypertension is the result of valve damage and retrograde venous blood flow to the superficial veins.

**Venous Evaluation**

**Continuous Wave Doppler**

Continuous wave Doppler (described earlier) is portable, inexpensive, and used clinically as a screening tool to test the integrity of the venous system. This method can identify the presence of venous obstruction or incompetence, quantify the severity of the venous disease, and localize these abnormalities to a particular segment of the limb. The venous flow signal is obtained at several sites in the limb. The patency, spontaneous flow, phasicity, augmentation, competency, and pulsatility of the venous flow are determined and graded. Normal venous flow is spontaneous and phasic with respiration. Obstruction of a vein is characterized by the absence of normal spontaneous venous flow or by the loss of phasic variation with respiration. If the Doppler probe is placed directly over an obstruction, there is absence of spontaneous flow. If the probe is placed below the site of obstruction, there is a loss of phasic change in the venous flow with respiration (a monophasic low-frequency signal). Several maneuvers (deep breathing,Valsalva, and distal compression of the calf or forearm) can produce augmentation of venous flow. Continuous wave Doppler provides subjective information. If positive for obstruction, findings should be followed by an objective test. Because of this and other limitations, continuous wave Doppler ultrasound has largely been replaced by venous duplex scanning for the diagnosis of DVT (combines Doppler principles with real-time B-mode and color-flow ultrasound imaging).

**Duplex Ultrasound**

Duplex scanning has become the method of choice for testing veins of the superficial, deep, and perforating systems. Duplex ultrasound directly visualizes and locates intraluminal obstruction; assesses the characteristics of venous flow distal to the inguinal ligament; identifies the presence of collateral veins around an obstructed venous segment; permits direct detection of valvular reflux; allows visualization of specific venous valves and valve leaflet motion; quantifies the degree of incompetence; locates and assesses veins before harvest for bypass procedures; evaluates venous perforator incompetence; and evaluates conditions that may mimic venous disease.

**Computed Tomography and Magnetic Resonance Venography**

Early venous disease rarely requires advanced imaging studies other than duplex ultrasonography. Computed tomography (CT) and magnetic resonance imaging (MRI) have progressed tremendously in the past decade. Both modalities are suitable to identify pelvic or iliac venous obstruction in patients with lower limb varicosities when proximal obstruction or iliac vein compression (May-Thurner syndrome) is suspected. Gadolinium-enhanced MRI is especially useful in evaluating patients with vascular malformations including those with congenital varicose veins.46

**Contrast Venography**

Lower extremity contrast venography remains a powerful, but decreasingly used, tool in the evaluation of both acute and chronic DVT. With advances in duplex ultrasonography, venography has been largely replaced by duplex scanning to evaluate patients with suspected deep venous obstruction or incompetence. In chronic venous disease, ascending venography demonstrates the location and extent of postthrombotic disease (Fig. 25,5), as manifested by occlusion, venous recanalization, collateral channels, and superficial varicosities. Ascending venography may also help with planning of endovascular and open surgical procedures, such as iliac and inferior vena cava recanalizations and venous bypass grafts. Ascending contrast venography is performed primarily in patients with significant chronic deep venous occlusive disease who are candidates for endovascular treatment with stents, surgical venous bypass, venous valve repair, or valve transplantation. Descending venography is used in concert with ascending venography to distinguish primary valvular incompetence from thrombotic disease. Descending venography identifies the level of deep vein reflux and evaluates the morphology of the venous valve.

**D-Dimer**

Fibrin D-dimer is the final product of the plasmin-mediated degradation of cross-linked fibrin. The plasma concentration of D-dimer depends on fibrin generation and subsequent degradation by the fibrinolytic system.64 D-dimer levels have a high sensitivity for patients with acute venous thrombosis.67 However, the specificity for acute thrombosis is rather poor.65 D-dimer levels can be elevated in other clinical conditions that are associated with enhanced fibrin (malignancy, trauma, increased age, disseminated intravascular coagulation, inflammation, infection, sepsis, postoperative states, and preeclampsia).

**Management**

**Compression**

Compression therapy is the mainstay of treatment for chronic venous insufficiency. Because venous hypertension in the upright position and during ambulation is the physiologic cause of the damage in chronic venous insufficiency, the first step of treatment should be to reduce the ambulatory venous pressure.

Compressive dressings aid venous return by compressing the leg and increasing the interstitial tension. Compression of dilated, engorged, superficial, and intramuscular veins indirectly increases the efficiency of the calf pump mechanism.48 After the volume
stabilizes, the patient can be measured for stockings. Typically, knee-length graduated compression stockings with a pressure of 30 to 40 mm Hg (at the ankles) are prescribed. Graduated compression providing decreasing pressure from distal to proximal has been the standard of care for both thromboprophylaxis and management of venous and lymphatic disorders. One study showed that a negative graduated compression bandage applied with higher pressures over the calf than the ankle showed significant hemodynamic superiority in patients with severe venous incompetence. Bandages exerting a higher pressure over the calf compared with the ankle were more effective in increasing the venous pump function in patients with venous insufficiency compared with graduated compression. The superior effect of stronger compression over the calf could be explained by more intense squeezing on the venous blood pooled in the calf or a more complete hindrance to venous reflux during walking. To prevent postthrombotic syndrome, compression stockings should be used routinely following diagnosis of a proximal DVT and continued for a minimum of 1 year.

Elevation

When elevation is used for edema control, the extremity is typically elevated above the level of the heart. The patient should lie on a sofa or sit in a recliner to elevate the legs appropriately. The correct duration and frequency of leg elevation should be tailored to the severity of disease. The leg should be elevated whenever possible and long periods of standing or sitting with the legs dependent should be avoided. In patients with concomitant arterial disease, lower compression and modified elevation is used to avoid further compromise of arterial inflow.

Intermittent Pneumatic Compression

With no history of congestive heart failure and no evidence of venous obstruction (on noninvasive studies), lower extremity volume can be stabilized with an intermittent pneumatic compression pump (40 to 50 mm Hg). Compression wraps should be used between pumping sessions.

Exercise

The value of exercise in the management of chronic venous insufficiency has not been conclusively demonstrated. Exercises involving the leg musculature, such as walking, bicycling, or swimming, promote muscle tone in the calf and enhance venous return. However, exercise produces variable reductions in venous hypertension. Patients with chronic venous stasis as a result of incompetent deep vein valves generally do not obtain as much reduction in venous pressure as do those in which the primary defect is caused by incompetent perforator valves.

Lymphatic Disease

Lymphatic diseases result from congenital or acquired disorders that cause obstruction, incompetence, or destruction of lymphatic vessels or the lymph-conducting elements of lymph nodes. The most frequent form of obstructive lymphatic disease is lymphedema.

Lymphedema

The lymphatic system is a vascular system composed of endothelial-lined channels that parallel the arterial and venous systems.
The lymphatics originate in the tissue interstitium as specialized capillaries. These capillaries are porous and readily permit the entry of even large macromolecules such as albumin. The distribution of fluid between the peripheral vascular system and the tissues depends on the transcapillary balance between hydrostatic and protein osmotic pressure gradients. Normally, there is a slight hydrodynamic imbalance favoring a small amount of excess capillary filtrate (fluid, salt, and macromolecules) into the tissue spaces. This filtrate or lymph is collected by the lymphatics and returned to the venous circulation.

Lymphedema is the result of protein-rich interstitial volume overload, secondary to lymph drainage failure in the face of normal capillary filtration. This occurs whenever there is an imbalance between capillary filtration and lymph drainage no matter the etiology. Lymphedema may be characterized as either high-lymph-output failure or low-lymph-output failure. High-lymph-output failure results from an overproduction of capillary filtrate (congestive heart failure, ascites, nephrotic syndrome) and leads to a greatly expanded extracellular fluid space. Low-lymph-output failure (decreased lymph absorption) occurs with deficient or obliterated lymphatics.

When lymphatic blockage occurs (e.g., after lymphadenectomy or radiation-induced lymph node fibrosis), intralymphatic pressure distal to the site of the blockage increases. As lymphatic vessels dilate, their valves become incompetent. Increased intra-lymphatic pressure also decreases lymph formation and increases tissue fluid volume.

Edema that resolves after elevating the affected area overnight is likely secondary to an overproduction of capillary filtrant (e.g., congestive heart failure, chronic venous insufficiency/high-lymph-output failure). Edema that does not improve much with overnight elevation often indicates lymphedema with failure of the lymph-conducting pathways (deficient or obliterated lymphatics/low-lymph-output failure). Edema does not improve much with overnight elevation often indicates lymphedema with failure of the lymph-conducting pathways (deficient or obliterated lymphatics/low-lymph-output failure). Edema that does not improve much with overnight elevation often indicates lymphedema with failure of the lymph-conducting pathways (deficient or obliterated lymphatics/low-lymph-output failure). Fibrosis may result from the inability of local macrophages to digest the excessive protein load. The accumulation of protein promotes chronic inflammation and scar formation. Although the exact mechanism of this scarring is unknown, interstitial fibrosis results in the brawny, nonpitting soft tissue swelling seen in chronic lymphedema.

Classification of Lymphedema

Clinical lymphedema is classified as either primary or secondary. Primary lymphedema occurs with aplasia, hypoplasia, or abnormal development of the lymphatic system. In addition, primary fibrosis of the lymphatics during puberty or at a later age also results in primary lymphedema. Several forms of heritable primary lymphedema are presently recognized. Congenital lymphedema is usually observed at birth with asymmetric presentation in a lower extremity. Lymphedema praecox, which typically appears in the peripuberlal period, can occur anytime from after birth into the third decade. Lymphedema tarda is primary lymphedema occurring after the age of 35 years.

Secondary lymphedema occurs much more commonly. Disrupted lymphatic flow may occur because of infection, trauma, tumor, obstruction, surgery, or radiation. Secondary lymphedema from filariasis, usually affecting the lower extremities, is the most common cause of lymphedema worldwide. Breast cancer–associated lymphedema is the most common form of lymphedema in the United States. High body mass index, axillary surgery, radiation therapy (particularly the breast and axilla), and the number of positive lymph nodes are risk factors for developing upper limb lymphedema. Secondary lymphedema commonly presents within the first year after surgery but can also present many years later.

Lymphedema may also be classified into clinical stages. Grade I edema easily pits in response to pressure and is reduced in response to elevation. There is no evidence of thickened spongy fibrosis on examination. Grade II edema does not easily pit with pressure and does not reduce with elevation. Some degree of fibrosis may be present. Grade III edema is irreversible with fibrosis and sclerosis of the skin and subcutaneous tissues. This severe, organized tissue stage is often not responsive to mechanical treatment measures.

Evaluation

The differential diagnosis for new-onset unilateral limb edema is important. Acute DVT must be ruled out whether the edema is presenting in the upper or lower extremity. Other possibilities for diagnosis include postphlebitic syndrome, chronic venous insufficiency, tumor obstruction, chronic infection, and lipidemia. Edema secondary to deep vein thrombophlebitis usually develops suddenly. Chronic venous insufficiency is generally associated with slowly progressing edema. Lymphedema may develop with either of these presentations. Unlike venous edema, there is often involvement of the foot and toes with loss of dorsal vascular and joint markings. Systemic reasons for edema accumulation, such as congestive heart failure, liver or renal disease, and fluid-retaining medications (antiinflammatory drugs and some antihypertensive drugs), should be considered.

Imaging Techniques

Lymphoscintigraphy

Lymphoscintigraphy performed by injecting a radioactive colloid and observing uptake into the lymphatic system has become the standard evaluation tool to establish lymphatic flow patterns. This test can be performed in both upper and lower extremities by injecting the colloid between the digits of the hands or toes, respectively. Lymphoscintigraphy assesses the most basic function of the lymphatic system, mainly the clearance of interstitial macromolecules that are too large to reenter the blood capillaries. When lymphedema is present, the images often show a highly characteristic dermal backflow pattern or rerouting of tracer away from the main lymphatic trunks and into fine collateral lymphatic vessels of the skin. Images may also suggest distal or proximal lymphatic obliteration, hyperplasia, or aplasia/hypoplasia of the lymphatic vessels. Because lymphatic disease occurs so rarely, the skills for administration and accurate interpretation of this test are often available only in larger medical centers where higher volumes of testing occur.

Computed Tomography Imaging

The studies described earlier help to distinguish venous disease from lymphatic disease. CT scan of the abdomen is helpful to discover the underlying obstructive pathology and should be part of an evaluation of new edema in the lower extremity.

Magnet Resonance Imaging

MRI is useful in studying the swollen limb without obvious etiology. Fluid, fat, soft tissue, and tumor can all be identified.
**Lymphangiography**

Lymphangiography should not be considered unless specific surgical intervention is being contemplated. It is invasive and may damage the (remaining) lymphatic vessels.

**Treatment of Lymphedema**

Lymphedema treatment is directed at minimizing the swelling, restoring normal function, and avoiding infection of the affected region. Often a patient is offered a diuretic for lymphedematous edema. Short-term diuretic use, during hospitalization for acute edema reduction, accompanied by elevation and compression bandaging may be useful. Diuretics are usually not helpful for chronic management of lymphedema because the effect is temporary and the diuresis leaves behind large protein molecules that create a concentrated state in the interstitium.

Antibiotic therapy is indicated in the management of infection associated with lymphedema (focal cellulitis). Inflammatory destruction of remaining lymphatics secondary to repeated infections can worsen the clinical problem. As a result, a program of 1-week-per-month prophylaxis of Pen VK 250 mg or 500 mg four times daily has been advocated for patients with several episodes of cellulitis per year. For those with a penicillin allergy, a first-generation cephalosporin, clindamycin, or erythromycin can be considered.

Comprehensive treatment regimens for lymphedema (complex decongestive therapy) have become the standard of care. This includes the following:

1. Skin care management and treatment of infection
2. Specialized massage techniques to promote the movement of lymph
3. Compression of the lymphedematous regions
4. Elevation and exercises to reduce swelling and supplement the massage

After an active reduction phase (phase I), an ongoing maintenance phase (phase II) includes daily use of compression garments (and often nocturnal compression) to maintain reduction. One study compared the effects of applying manual lymph drainage (MLD) and postural drainage techniques to lower extremity edema of patients after bariatric surgery. Although both interventions were efficient in reducing the edema resulting from the surgery, MLD achieved the best results.

General contraindications to aggressive lymphedema management include acute infection, cardiopulmonary edema, and ongoing malignant disease. Conditions such as pregnancy, recent abdominal surgery, radiation fibrosis, DVT, and aortic aneurysm may preclude some portions of the treatment. Palliative lymphedema management is appropriate.

**Compression**

Compression of a lymphedematous region causes increased total tissue pressure, decreases the hydrostatic pressure gradient from the blood to the tissues, and increases the hydrostatic pressure gradient from the tissues to the initial lymphatics. The pressure gradient along the lymphatic trunk is also increased. Compression of the affected region is necessary to maintain reductions in edema during and after the treatment. Lymphedematous regions may be compressed with bandages (elastic or low stretch) or graduated compression garments.

There are two basic types of compression bandages. Elastic high-stretch compression bandages have a high resting pressure (from elastic recoil) and low working pressure because they stretch in response to muscle contraction. Low-elastic or low-stretch compression bandages have low resting pressure and a high working pressure, which increases the total tissue pressure when muscles contract. Lymphatic vessels are compressed between the muscles and the bandages enhancing transport. Bandages can be used with various types of padding beneath to reshape the limb.

In patients with moderate to severe lymphedema of the legs, adjustable compression wraps (Velcro closure) achieved more pronounced reduction in volume after 24 hours than inelastic multi-component compression bandages. Patients were able to apply and adjust the device after being instructed in its use after an initial 2-hour period of wear. Autonomous handling of adjustable compression wraps seems to improve the clinical outcome and is a promising step toward effective self-managed compression.

Once reduced, stable limb volume is achieved, graduated compression garments are necessary to prevent fluid reaccumulation. Similar to compression bandages, compression garments enhance the pumping action of lymphatics and veins and decrease the hydrostatic pressure gradient from the blood to the tissues. Compression garments are available in various levels of compression. For lymphedema, pressures of 30 to 40 mm Hg often suffice. Recalcitrant edema may require 40 to 50 mm Hg of support. Appropriate compression and fit of the garment along with instruction in donning and doffing are critical to a successful management program.

**Elevation**

Elevation of a lymphedematous limb can decrease the hydrostatic pressure gradient from the vasculature to the tissues and reduce the amount of fluid and protein moving out of the capillaries. Elevation can also increase the lymphatic flow by increasing the hydrostatic pressure gradient along lymphatic trunks. Patients are encouraged to elevate the involved limb periodically through the day.

**Exercise**

Exercise improves mobility and muscular activity and lead to the internal compression of lymph vessels. Lymph drainage is stimulated by intermittent pressure changes between muscles and external compression (bandages or compressive garments). Resistance exercises seem to increase strength and decrease the exacerbation of lymphedema, as well as decrease symptoms associated with lymphedema.

**Vasopneumatic Compression Therapy**

Vasopneumatic compression pumps increase the total tissue pressure in edematous limbs and push tissue fluid back into blood capillaries. Because excess protein is not removed from the tissues, the concentration of tissue protein may increase and theoretically lead to the reoccurrence of edema. Other limitations of compression pumps in the management of lymphedema are that they cannot apply pressure to the areas of the trunk adjacent to draining lymph nodes and may exacerbate genital edema or produce a collection of high-protein fluid proximal to the site of pumping, which can exacerbate inflammation and fibrosis. When compression pumps are used for lymphedema management, pressures of 40 to 50 mm Hg are sufficient for fluid removal and to lessen the risk for tissue damage. Compression pumps are more...
helpful in the management of chronic venous insufficiency than in
the management of chronic stage II or III lymphedema.

Surgery

Excisional Debulking
Excisional debulking procedures have occasionally been recom-

mended for patients with significant functional impairment due
to excessive lymphedema.42 This may decrease the volume of the
affected extremity when irreversible changes in skin and subcuta-
neous tissues have occurred.

Reconstruction of Lymphatics
Surgical reconstruction of obstructed lymph vessels and lymph
nodes has been performed using lymphovenous anastomoses5,29,59
or lymphoymphatic anastomoses (lymphatic grafting).13,36
Although clinical benefit has been reported by a few surgical
groups, the long-term potency and function of such Anastomo-

ses is still uncertain. Currently, surgical treatment is reserved for
those patients who have lymphanagiectasia and primary chylous
disorders (lymphedema, chylous effusions, and chylous fistula).
Reconstruction of dilated lymph vessels in these patients is done
with saphenous vein grafts.57 At present, lymphatic reconstruc-
tions are not considered a first line treatment for chronic obstruc-
tive lymphedema.

Conclusion
The patient with vascular disease poses a significant challenge to
the rehabilitation professional. Arterial, venous, or lymphatic dys-
function may be the primary issue or a critical comorbidity in
many patients who present to rehabilitation. A detailed vascular
history and examination and selected diagnostic tests should be
inherent in the rehabilitation evaluation. When identified, early
interventions including exercise, appropriate compression, posi-
tioning, protection, and proper footwear may ameliorate the need
for more aggressive medical and surgical treatments in patients
with vascular disease.

Key References
factors for systemic and limb ischemic events in patients with symp-
tomatic peripheral artery disease: insights from the REACH Regis-
studies including transcutaneous oxygen pressure measurements
with the limbs elevated or dependent to predict healing after par-
3. Armer JM: The problem of post-breast cancer lymphedema: impact
of chronic venous disease in the lower limbs. A consensus statement,
5. Bellis A, Trimarco B: Pharmacological approach to cardiovascu-
lar risk in metabolic syndrome, J Cardiovasc Med 14:403–409,
2013.
manual lymphatic drainage for lower limb edema in women with
morbid obesity after bariatric surgery: a randomized controlled trial,
in Severe Ischaemia Of The Leg (BASIL) trial: an intention to treat
analysis of amputation free and overall survival in patients random-
ized to a bypass surgery-first or a balloon angioplasty-first revascular-
8. Brooks B, Dean R, Patel S, et al.: TBI or not TBI: that is the ques-
tion. Is it better to measure toe pressure than ankle pressure in dia-
9. Damstra R, Parstch H: Prospective, randomized, controlled trial
comparing the effectiveness of adjustable compression Velcro wraps
versus inelastic multicomponent compression bandages in the ini-
tial treatment of leg lymphedema, J Vasc Surg: Venous and Lym Dis
10. Davies MG, Waldman DL, Pearson TA: Comprehensive endovas-
tular therapy for femoral popliteal arterial atherosclerotic occlusive
11. Delis KT, Nicolaides AN: Effect of intermittent pneumatic compres-
sion of foot and calf on walking distance hemodynamics and quality
of life in patients with arterial claudication: a prospective random-
ized controlled study with one-year follow up, Ann Surg 214:431–
441, 2005.
12. Dornandy JA, Murray GD: The fate of the claudicant—a prospective
evidence for linkage and genetic heterogeneity, Hum Mol Genet
thrombotic syndrome in a population with a first deep vein throm-
busis and no primary venous insufficiency, J Thromb Haemost
15. Gazzano JM: Fifth phase of epidemiologic transition: the age of obe-
line on the management of patients with lower extremity peripheral
artery disease: executive summary: a report of the American college
of cardiology/American heart association task force on clinical prac-
17. Heit JA, Silverstein MD, Mohr DN, et al.: The epidemiology of
venous thromboembolism in the community, Throm Haemost
the management of patients with peripheral arterial disease (lower
extremity, renal, mesenteric, and abdominal aortic): a collaborative
report from the American Associations for Vascular Surgery/Society
for Vascular Surgery, Society for Cardiovascular Angiography and
Interventions, Society for Vascular Medicine and Biology, Society of
Interventional Radiology, and the ACC-AHA Taskforce on Practice
19. Hoyer C, Sandermann J, Petersen IJ: The toe-brachial index in the
20. Keilin SS, Cooper LT: The role of autoimmunity in thromboangiitis
21. Khandanpour N, Locke YK, Meyer FJ: Homocysteine and periph-
eral arterial disease: systematic review and meta analysis, Eur J Vasc
22. Kullo IJ, Rooko Tj: Clinical practice. Peripheral artery disease, N
23. Kwan ML, Darbinian J, Schmitz KH: Risk factors for lymphedema
in a prospective breast cancer survivorship study: the pathway study.
24. Leng GC, Fowler B, Ernst E: Exercise for intermittent claudication,
25. Mosti G, Parstch H: High compression pressure over the calf is more
effective than graduated compression in enhancing venous pump
TASC II working group. Inter-society consensus for the management
eral arterial disease and risk factors in persons age 60 and older: data