Vascular Assessment and Reconstruction of the Ischemic Diabetic Limb
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Atherosclerosis obliterans complicates the medical and surgical treatment of the diabetic foot. The systemic and local manifestations of the disease have profound effects on wound healing, symptom control, and, ultimately, foot salvage and patient longevity. The medical and surgical treatment of diabetic foot disorders can be drastically effected by the presence or absence of occlusive disease secondary to atherosclerosis and the absolute and relative ischemia induced by such involvement. Before treatment of any lesion involving a diabetic foot, the clinician should consider the degree of involvement of the limb with atherosclerosis and the effects of such treatment and should anticipate the problems and probabilities of success before any incision is actually made on the affected foot. This article discusses the epidemiology, anatomic features, clinical presentation, and treatment of the dysvascular diabetic foot. In addition, an attempt is made to present a rational diagnostic and therapeutic strategy to avoid the common pitfalls associated with the treatment of diabetic foot lesions in limbs affected with atherosclerosis and to maximize the success of any intervention.

Atherosclerosis and peripheral artery disease

Atherosclerosis is a progressive systemic disease that can involve any artery within the body. The common perception is that atherosclerosis represents a continuum of disease initiated through an abnormal response to endothelial injury. The loss of the functionally and physically important barrier of the intima of an artery leads to the increased susceptibility of the endothelium to oxidative injury, lipid accumulation, and inflammatory cell adherence, accumulation, and activation, ultimately leading to
a proliferative, progressive accumulation of cellular and noncellular material within the media of an artery. This results in the development of occlusive lesions and thrombotic events [1].

Manifestations of atherosclerosis are largely related to the end organs involved and the degree of ischemia induced by the occlusive disease involving their respective feeding vessels. Typically, the territories affected by atherosclerosis are divided into three regions: (1) the coronary circulation, (2) the cerebrovascular circulation, and (3) the peripheral circulation. By definition, peripheral arterial disease (PAD) involves occlusive or aneurysmal disease involving the arteries outside of the heart and intracranial vessels [2]. Although several medical conditions can affect the peripheral arterial circulation, the most common etiology, by far, is atherosclerosis. Approximately 12 million Americans are affected by symptomatic PAD [3]. For every patient diagnosed with PAD in an office, there are likely three to four patients afflicted by the disease that are not diagnosed, representing a significant proportion of the population [4,5].

Beyond the local effects of such lesions on the end organs supplied by the diseased arteries, the systemic manifestations are germane and profound. Depending on the sensitivity of the diagnostic testing, the prevalence of concomitant coronary artery disease and cerebrovascular disease is 14% to 90% and 25% to 72%, respectively, among patients diagnosed with PAD [6]. In fact, the diagnosis of intermittent claudication, a local manifestation of PAD, is a more profound marker for cardiovascular death than it is for limb loss [7,8]. Patients with known symptomatic coronary disease diagnosed with PAD have been shown to have an increased risk of recurrent myocardial infarction, stroke, and vascular death when compared with patients without PAD [2]. In addition, 25% of patients with PAD who underwent routine coronary angiography before PAD treatment were found to have significant surgically correctable coronary artery disease involving three coronary vessels [9]. Clearly, PAD represents one manifestation of atherosclerosis that has profound implications on long-term survival as well as limb salvage.

**Diabetes and atherosclerosis**

*Epidemiology and pathophysiology*

The association between diabetes and atherosclerosis is significant. The prevalence of PAD in the United States among diabetic persons has been estimated to be 9.5% [10]. Matched for age, this is twice the prevalence found among non-diabetic persons. When examining cardiovascular risk factors, the presence of diabetes is associated with a threefold to fourfold greater risk of PAD than in non-diabetic patients; this association is second only to active smoking as a risk factor for PAD [2,7,8]. The American Diabetes Association [3] has gone as far as recommending PAD noninvasive
arterial testing with ankle-brachial indices (ABIs) for all patients with diabetes who are 50 years of age or older, for those younger than 50 years if they have other atherosclerotic risk factors, and for subjects who have sustained diabetes for more than 10 years.

Patients who have diabetes have profound abnormalities in arterial physiology and biology that may explain the significant association between the two diagnoses. Patients with diabetes have been shown to have abnormal endothelial-mediated contraction and relaxation through nitric oxide–dependent mechanisms [11]. Nitric oxide is produced by the endothelial cell and is a critical marker for vascular health [12]. Its profound role in endothelial vascular reactivity, platelet and monocyte adherence and activation, and smooth muscle migration and transformation are well known, and dysfunction has been suggested as a precursor for occlusive atherosclerotic plaque development [13]. In addition, diabetes-associated insulin resistance and hyperglycemia have been shown to affect non-endothelial–dependent abnormalities in oxidative metabolism and platelet function, coagulation, and thrombosis [3,11].

Anatomic involvement

An unfortunate nomenclature has developed to describe arteries in diabetic patients affected by atherosclerosis. The blood vessel lesions are typically divided into two groups—large vessel disease and small vessel disease. The implications of such a grouping are profound and have led to the misplaced perception that “small vessel disease” in the foot obviates revascularization as an option for the ischemic diabetic foot. It should be reinforced that “microvascular disease” refers to the important, but separate, obliterative effects at the arteriolar level seen in the retina (diabetic retinopathy), the renal parenchyma (diabetic nephropathy), and, to some degree, the peripheral nervous system (diabetic ischemic neuropathy). The microvascular arteriolar lesion is distinct from atherosclerosis and represents a process involving the basement membrane of the microvasculature on the arteriolar level in these specific end organs. Although this accumulation of matrix within the basement membranes of the nutrient cutaneous vessels within the foot is evident on biopsy in diabetic patients, it is rarely an obliterative process, and the lumen of these vessels is usually preserved [14,15]. Some evidence suggests that this microvascular process leads to abnormalities in nutrient delivery and even hypoxia to the tissues supplied by these nutrient vessels, but the process is not atherosclerosis [15,16]. A recent study noted that the only standard cardiovascular risk factor that contributes to the progression of small vessel PAD in the foot is the presence of diabetes [17]. The risk factors for small vessel PAD are distinct from those contributing to large vessel atherosclerosis [16,17].

Although PAD in diabetic patients tends to be more prevalent and malignant, the peripheral atherosclerosis involving the large vessels of the
dysvascular diabetic limb is histologically no different from that affecting non-diabetic patients; however, the distribution of the lesions is significantly different. PAD in the non-diabetic patient is typically seen in the more proximal vessels of the lower extremity, specifically, in the aortoiliac and femoral-popliteal system. The distribution of atherosclerotic PAD in the diabetic patient will often be isolated to the infrapopliteal tibial and pedal segments with a relative sparing of the proximal vessels (Fig. 1) [18,19]. An exception to proximal vessel involvement is seen in the predilection for atherosclerotic involvement of the internal iliac arteries and the deep femoral arteries in diabetic patients [19]. Such involvement may influence the ischemic reserve of a diabetic limb because these vessels represent important collateral pathways to the main axial arteries of the limb. Infrapopliteal artery involvement has been shown to be more frequent than pedal involvement, but there remains a strong association between the two levels [20].

Some researchers have suggested that involvement with atherosclerosis of the named vessels of the foot often spares the dorsal vessels, whereas others have suggested that the plantar vessels are more often spared [18,21]. The author’s group has not been able to demonstrate any predilection for sparing of a dorsal versus plantar system in atherosclerotic affected diabetic feet [20]. This observation does not mean that the pedal circulation always offers some suitable vessel for revascularization in the foot (Fig. 2). The “microvascular disease” represents microangiopathy seen in the eyes, kidneys, and nerves of diabetic patients and should not be confused with “small vessel” involvement in the foot. The effects of this real phenomenon on patient care and prognosis are discussed further in the section on noninvasive testing.

A separate pathologic entity distinct from atherosclerosis that is often seen in the limbs of diabetic patients is the typical semilunar medial calcinosis of the tibial vessels. This calcification can be seen on plain radiographs in many patients [22]; however, it does not lead to luminal encroachment. The effects of medial calcinosis are largely related to changes in external vessel compressibility and are seen on diagnostic imaging and physiologic testing. Nevertheless, recent investigations suggest that cardiovascular event-free survival in patients with an abnormally elevated ABI (>1.40) may be significantly worse than in patients with normal indices regardless of the presence or absence of diabetes [23].

Fig. 1. Contrast-enhanced MRA demonstrating the typical pattern of occlusive disease in the diabetic patient, notable for internal iliac artery involvement with sparing of the aorta, common, and external iliac arteries (A). Relatively disease-free common femoral and superficial femoral arteries, with disease noted in the deep femoral arteries (B). (C) Severe infrapopliteal disease.
Clinical manifestations of peripheral arterial disease

The clinical presentation of PAD is variable. The complaints and symptoms associated with PAD represent a continuum ranging from asymptomatic resting arterial insufficiency to profound limb-threatening ischemia. The Fontaine and Rutherford classification systems for chronic lower extremity ischemia have been well described in other publications [2,7]. In brief, the continuum of presentation is as follows: 1—asymptomatic resting ischemia, 2—intermittent claudication, 3—ischemic rest pain, 4—ischemic ulceration, and 5—gangrene. A large subset of “asymptomatic patients” may not complain of classic intermittent claudication but may have other less definable complaints [24].

The asymptomatic patient manifests no overt symptoms of ischemia but has an abnormal examination with or without evidence of ischemia on non-invasive testing. The prognosis for such a diagnosis regarding the involved extremity is good. The likelihood of progression of local disease may be high, but the development of worsening symptoms or limb loss is rare in non-diabetic patients [8]. In stark contrast, the systemic implications of even asymptomatic PAD in a limb are profound. The systemic manifestations of atherosclerosis in these patients lead to an increased long-term risk of cardiac-related events and cardiac death [6,25]. The emphasis of treatment in these patients should be on systemic risk factor modification and anti-platelet therapy as a means of preventing cardiac-related morbidity, rather than on improving the perfusion of an affected limb.

Intermittent claudication is a relatively benign condition from a limb health standpoint. This fairly common condition affects 3% to 6% of patients over the age of 60 years [7]. Typically, the symptoms are described as a cramping, muscular discomfort involving the calf muscles initiated by a reproducible distance of walking that is relieved by a brief period of rest (typically 5 to 10 minutes). The affected muscle group is usually immediately distal to the level of occlusive disease; however, this is not a uniform finding. More than an occasional patient suffering from iliac occlusive disease will
present with calf claudication rather than an expected involvement of the hip, buttock, or thigh.

In the patient who has calf claudication, the condition is secondary to the inability of a compromised artery (iliac or superficial femoral artery) above the gastrocnemius muscle group to deliver the increased blood flow required to meet the increased metabolic demands of the muscle associated with exercise. The muscle group is rendered ischemic, leading to the development of symptoms. The symptoms resolve with resting of the muscle group and the subsequent decrease in metabolic demands associated with rest. Hip, thigh, and buttock claudication usually result from proximally located occlusive disease involving the aortoiliac system. The constellation of symptoms related to aortoiliac occlusive disease may include a more frequent complaint of muscular weakness and tiredness, rather than the cramping discomfort usually attributed to vasculogenic claudication in the calf. In addition, males with severe bilateral aortoiliac occlusive disease may manifest vasculogenic impotence because of involvement of the pelvic arterial circulation and the more proximal aorta or common iliac arteries. Likewise, involvement of the buttocks in the ischemic syndrome is an indication of similar pelvic or more proximal arterial involvement. In the absence of hip or buttock complaints, external iliac artery involvement may elicit symptoms of claudication only in the thigh muscle groups.

The diagnosis of foot claudication bears special attention. It is an uncommon finding in which the affected foot suffers from walking-induced cramping, midfoot aching, or pain that is often accompanied by a feeling of numbness. Foot claudication is seen with diffuse infrapopliteal and tibial artery involvement. It is a frequent complaint in patients suffering from Buerger’s disease; however, as an independent symptom, the diagnosis of foot claudication is often treated with some skepticism, because it is very uncommon to find a patient with a limb with enough disease present to cause foot claudication who does not suffer from rest pain or tissue loss as the dominant presenting complaint.

The natural history of a particular limb with claudication is good, with only about 5% of limbs progressing to amputation or requiring revascularization for limb salvage over a 5-year period [7]. As noted previously for the asymptomatic limb, intermittent claudication is a marker for overall cardiac morbidity and mortality and should be treated as a risk equivalent for coronary artery atherosclerosis [6]. Although the discomfort associated with claudication can be treated with risk factor modification, exercise therapy, and, in select patients, revascularization, the bulk of counseling and treatment should be directed at reducing the risk of concomitant cardiac death.

The symptoms of ischemic rest pain, ischemic ulceration, and gangrene are distinct from the prior two categories. These clinical syndromes fall into the category of critical ischemia or limb-threatening ischemia. Although they are part of a continuum of complaints seen with arterial insufficiency, distinguishing between claudication and critical ischemia is paramount.
Critical ischemia is usually related to atherosclerotic occlusive disease involving multiple levels within a limb. Although other etiologies such as autoimmune vasculitides, thromboangiitis obliterans (Buerger’s disease), or atheroembolism can lead to similar ischemic damage in a particular foot, these entities are much more infrequent. Critical ischemia due to atherosclerosis carries a grave prognosis for the life and limb of the patient, with each condition (rest pain, ulceration, gangrene) associated with increasing risk. The natural history of patients who have symptoms of chronic critical limb ischemia with ankle pressures less than 40 mm Hg is dismal when they are treated conservatively. Almost 95% of these subjects will require a major amputation or die within 1 year of diagnosis [26].

The typical patient with ischemic rest pain complains of intermittent or continuous forefoot pain unrelated to activity. The pain is often described as an “aching” discomfort deep within the foot that is difficult to relieve with any measures including non-steroidal analgesics or narcotics. The stereotypic description of nocturnal pain occurring while recumbent that requires dangling the foot over the side of a bed, or sleeping in a reclining chair with the affected foot dependent, is surprisingly consistent. As would be expected, the advent of tissue loss or gangrene represents the absolute limits of the foot’s ability to compensate for resting arterial insufficiency, with the foot literally dying while still attached to the patient. Intervention in the form of revascularization is imperative if the limb is to be saved.

As is true for most manifestations of atherosclerotic PAD, the systemic consequences for critical lower extremity ischemia are profound. Twenty percent of patients will be dead within 12 months of diagnosis, and 32% will be dead within 2 years [26,27]. The most frequent cause of demise in these patients (as would be expected) is a cardiovascular complication, such as acute coronary syndrome, stroke, or catastrophic peripheral vascular events. In fact, these end-game manifestations of lower extremity PAD are reminiscent of metastatic cancer in terms of the dismal prognosis associated with the diagnosis. Although somewhat nihilistic, the treatment of limb-threatening ischemia should be directed at palliation and maintaining functionality, because any intervention targeted at revascularization will not prolong life per se. The main goal should be directed at maintaining ambulatory status through limb preservation techniques and freedom from pain.

The presentation of PAD in diabetic patients demands special considerations. The manifestation of chronic ischemia may be much more subtle in diabetic patients when compared with non-diabetic patients. The typical symptoms of intermittent claudication may be absent in diabetic patients for several reasons. First, as mentioned earlier, the atherosclerotic burden in the limbs of diabetic patients often spares the proximal vessels; therefore, as the most often affected muscle group in claudicants during walking, the gastrocnemius gets its primary blood supply from the superficial femoral and popliteal arteries and does not suffer from exercise-induced ischemia. No obstructive lesion is present above the muscle group. Second, the peripheral
diabetic neuropathy present in many patients may alter existing sensory feedback and pain perception in the limb [28]. What may be called “pain” by non-diabetic persons is perceived as fatigue or tiredness in patients sustaining diabetes. Third, the combinations of impaired protective sensation, impaired immune response, and impaired healing provide a fertile ground for unrecognized trauma and progressive invasive infection. The subsequent increased metabolic demands of an infected foot can outstrip the compromised baseline arterial blood supply, leading to a failure of supply compared with demand. The result is a rapidly deteriorating foot secondary to a relative ischemic state brought on by the infection or trauma.

Physical examination findings among diabetic patients with PAD can be unreliable [3]. The traditional approach of “look, listen, and feel” is germane to the vascular examination. Although the presence of a gangrenous toe is quite obvious, other findings may be subtle. The functional sympathectomy associated with diabetic neuropathy may make the usual autoregulatory response of the cutaneous capillary beds to chronic ischemia less pronounced. Dependent rubor, which is associated with the pooling of blood within the maximally dilated subcutaneous areas of an ischemic foot, may not be present. The classic bland, painful, irregular appearing ulceration associated with ischemia continues to be a common finding in diabetic feet. The neuroischemic ulcer may be less apparent because the peripheral neuropathy of diabetes makes the lesion painless [8]. The more usual presentation seems to be a diabetic foot infection requiring rapid debridement and drainage, followed by wound breakdown and progressive involvement of the surrounding tissues with gangrene. It is well known that diabetics with PAD tend to present later and with more profound ischemic complications when compared with their non-diabetic counterparts [3,8,19]. These late presenting ischemic manifestations of PAD present a greater challenge to successful limb salvage.

The absence of or a diminished pulse at a given location suggests an occlusion or stenosis in the artery located proximal to the palpated area. An absent femoral pulse would suggest an aortoiliac lesion. An absent pedal pulse associated with a palpable, more proximal popliteal pulse suggests cural and pedal artery lesions. The latter finding represents a common scenario for a diabetic patient with PAD. Similarly, a bruit heard on auscultation of the femoral artery would suggest occlusive disease at or above the femoral level. The assumption that an absent pedal pulse is diagnostic of a proximal lesion is based on another assumption that the patient actually had the pedal artery present from birth. Pulse examination variability is actually relatively common. Certain hospital-based and community-based studies have noted that the dorsalis pedis artery is absent in 8.1% of patients and the posterior tibial artery in 2.0% [3].

Noninvasive physiologic arterial assessment

Few would question the utility of the Doppler-derived ABI as a diagnostic tool in non-diabetic patients with PAD. The test remains a cheap,
reproducible, and portable screening modality. The interobserver and intra-
observer variability are low, and the sensitivity and specificity are high (95% and 100%, respectively) for detecting the presence of angiographically con-
firmed arterial occlusive disease [8]. In addition, its proportionate decrease is a
useful measure for quantifying the severity of ischemia. The utility of this
study is not only its ability to diagnose the presence of disease but also its
ability to quantify the severity of ischemia as well as serially follow the pro-
gression of ischemia over time. In its simplest manifestation, the calculation
of an ABI requires only a manual blood pressure cuff and a continuous-
wave Doppler probe. The Doppler-derived upper extremity systolic brachial
arterial cuff pressure is measured in both upper extremities. This measure-
ment is followed by a similar cuff systolic occlusion pressure measurement
taken in both feet with the Doppler probe placed over the inframalleolar
posterior tibial and dorsalis pedis arteries. The cuff must be placed with
its lowest margin just above the ankle in the tendinous portion of the leg.
The highest recorded pedal pressure (regardless of the vessel) in a limb is
then divided by the highest upper extremity pressure. The resulting ratio
is referred to as the ABI. In the absence of an available continuous-wave
Doppler probe, Beckman and colleagues [29] have shown that a fairly accu-
rate correlation is noted with systolic pressures derived from automated os-
cillometric blood pressure cuff readings taken in the arms when compared
with those obtained at the ankle level.

Thresholds for the diagnosis of symptomatic and asymptomatic arterial
insufficiency at rest have been described [2]. In normal limbs, the ankle pres-
ures are typically equal to or a little higher than those derived at the bra-
chial level. The difference is probably due to the augmentation of the
systolic pressure that occurs with reflection of the pressure wave as it is
propagated distally. A “normal” ABI is between 0.91 and 1.30. In general,
PAD is present if the ABI is less than 0.90. A decreasing ABI is associated
with more severe arterial insufficiency. Mild obstruction is defined as an ABI
between 0.70 and 0.90, moderate obstruction as an ABI between 0.40 and
0.69, and severe obstruction as an ABI less than 0.40 [2,3].

As alluded to earlier, an ABI greater than 1.30 should be considered fal-
lacious and is due to poorly compressible tibial vessels often seen in patients
with medial calcinosis. In these circumstances, the additional measurement
of a toe pressure or toe-brachial index (TBI) may provide additionally useful
information. The toe pressure is usually obtained with an automated small
inflatable cuff and a plethysmographic tracing. The digital vessels are often
spared of significant medial calcinosis, and their evaluation may prove valu-
able in the presence of noncompressible arteries at the ankle [30]. The toe
pressure is usually 10 mm Hg less than the ankle pressure, with a generally
accepted normal value being greater than 70 mm Hg [7,8]. The TBI is a cal-
culated value similar to the ABI except that the denominator of the ratio is
the toe pressure. A normal TBI is expected to be equal to or greater than
0.70. The TBI has been shown to have a similar variability and
reproducibility as the ABI [17]. The American Diabetes Association [3] has recommended the combination of ABI and TBI measurements whenever noninvasive arterial testing is performed in diabetic patients.

In general, the ABI can be obtained in an office with relative ease; however, additional noninvasive physiologic tests usually require referral to a vascular laboratory. In this facility, more sophisticated testing can be performed. These tests are designed to provide quantitative assessment of the severity of disease, to localize the sight of disease, and to follow disease progression through serial examinations [2]. The recent AHA/ACC Practice Guidelines for the diagnosis and treatment of PAD reinforce the need for referral to accredited and validated vascular laboratories. These laboratories adhere to strict quality control measures and are subjected to significant scrutiny through an intersocietal and interdisciplinary peer review process [2]. Some of the additional tests available through an accredited vascular laboratory may include segmental pressure measurements, pulse volume recording, directional Doppler waveform analysis, and duplex ultrasound. Less frequently, transcutaneous oxygen testing and laser Doppler oximetry may be available. A detailed summary of the aforementioned tests is beyond the scope of this article. Each particular test has unique benefits and drawbacks, especially in diabetic patients.

The author and his colleagues reviewed their experience with 101 diabetic patients undergoing treatment for symptomatic lower extremity PAD [31]. The results of noninvasive multimodality testing with ABI, TBI, pulse-volume recording, segmental pressure measurements, and segmental Doppler waveform analysis were examined to specifically assess the accuracy in predicting the level of significant (>50% stenosis) infrainguinal arterial disease, as well as the effects of multimodality testing compared with single modality testing on accurate diagnosis. Blinded comparisons of tests with contrast angiograms were performed, and associations between noninvasive diagnoses and angiographically confirmed disease were evaluated for significance. In total, 15% of limbs had uninterpretable ABIs (noncompressible), and 15% could not undergo TBI assessment because of lack of toes or extensive tissue loss involving the toes. Segmental pressures were only accurate in half of the patients due to noncompressible vessels and an inability to tolerate the test. These results have been seen by other investigators [32]. The best predictive combination of testing included pulse-volume recording and Doppler waveform analysis. This combination resulted in a sensitivity of 78% and a specificity of 80% with an associated positive predictive value of 84% in predicting angiographically significant disease. As a result, we have abandoned the use of segmental pressures among our diabetic patients with PAD, relying on Doppler waveform analysis and pulse-volume recording for noninvasive screening.

**Imaging techniques**

Generally, in a patient who has PAD, a good history will lead the clinician to the suspected diagnosis. The associated physical examination will
likely confirm the diagnosis and possibly isolate the proximal extent of occlusive disease. The addition of noninvasive physiologic vascular testing provides a quantitative assessment of the degree of resting or exercise-induced ischemia in an affected limb and, to some degree, provides anatomic localization. These quantitative assessments are important in determining the severity of a given condition and the need for intervention. Although these tests provide a safe and inexpensive means of diagnosis, they arguably may not provide enough anatomic detail to satisfy accurate planning of a particular revascularization procedure.

When revascularization of a dysvascular limb is planned, additional imaging is usually necessary to delineate the location of treatment and to define the best modality of treatment for a particular lesion. Usually, imaging tests are reserved for patients in whom the decision to intervene has already been made because these tests carry more risks than physiologic testing methods.

More expensive imaging modalities such as MR digital subtraction angiography (MRA) and multidetector CT angiography (CTA) have proven roles in the evaluation of vascular anatomy before intervention. These imaging techniques provide spatial anatomic detail of vascular anatomy in relationship to surrounding structures, information regarding lesion severity, length, morphology, and composition, and, in the case of MRI, a possible window into physiologic and metabolic activity of a given plaque [33].

MRA has been shown to provide excellent accuracy when compared with the gold standard of contrast digital subtraction angiography in visualizing atherosclerotic occlusive disease [34]. Because imaging uses a magnetic coil, ionizing radiation is avoided. Earlier imaging with time-of-flight acquisition allowed examination of arteries without the use of iodinated contrast and the attendant risks of nephrotoxicity; however, the mainstay of MRA has become contrast-enhanced imaging, typically using gadolinium chelate as a contrast agent. The imaging quality has improved significantly. Currently, contrast-enhanced MRA is somewhat limited by prolonged image acquisition times and the need for significant post-processing with source images. Acquisition times are improving drastically with the new 3.0 T MRI coils, which should improve image quality and the rapidity of scanning. Although MRA represents an excellent method of imaging the aortoiliac and femoral-popliteal systems, imaging of the infrapopliteal segments (the segments most often involved in diabetic patients with PAD) is more difficult. At this level, deep venous enhancement or “venous contamination” can seriously degrade the images and make interpretation difficult (Fig. 3) [34]. The goal of accurate imaging of these vessels is obtained through limiting the venous enhancement. Unfortunately, the highest risk groups for venous contamination are patients with cellulitis and diabetes [34]. Although MRA has become the default imaging study in patients with chronic renal insufficiency in whom the larger doses of nephrotoxic iodinated contrast required for traditional angiography and CTA would induce renal failure, the use of gadolinium has been associated with acute renal failure, possibly related to acute tubular necrosis [35].
Recently, enthusiasm has been building for the use of CTA in lower extremity arterial imaging. CTA has the benefits of low image acquisition time and ready availability and remains cheaper than conventional angiography. The overall accuracy in diagnosing angiographically significant disease is more than 95%, with sensitivities and specificities of more than 95% and 96%, respectively [36]. Volume rendering and curve planar reconstructions provide images that are nothing less than spectacular to look at; however, as is true for any imaging modality, there are limitations. Although direct arterial access is not required, the test requires the use of potentially nephrotoxic intravenous contrast in doses approaching those used in conventional angiography. The sensitivity and specificity of CTA are greater for the detection of arterial occlusions versus stenoses, and CTA has greater accuracy and less interobserver variability for proximal lesions compared with infrapopliteal lesions [37]. These more distal lesions are often found in diabetic patients with PAD. Willmann and colleagues [36] reported 96% sensitivity, 95% specificity, and 96% accuracy in diagnosing significant infrapopliteal occlusive disease with CTA. Another limitation is seen when imaging calcified vessels (prevalent among patients with diabetes), which may preclude an accurate assessment of the luminal diameter in affected segments.

The final imaging modality, conventional digital subtraction angiography, has long been considered the gold standard for imaging the arteries of a dysvascular limb. Although diagnostic conventional angiography is readily available, improved imaging with MRA and CTA has led to the decline of conventional angiography as a primary diagnostic modality. This
diminution is largely the result of its limitations. It is expensive and invasive and provides little information beyond the two-dimensional image of a contrast-filled lumen of an artery. Its utility in imaging diabetic patients sustaining PAD arises from the limitations of newer imaging techniques, specifically, the ability to see the infrapopliteal, calcified segments of diseased tibial and pedal arteries. This visualization often requires superselective cannulation of the distal superficial femoral or popliteal vessels with direct injection at the popliteal level to achieve maximal contrast delivery. This selective imaging proves invaluable in planning for crural and pedal level bypasses.

Revascularization techniques

In general, the decision to attempt revascularization in a critically ischemic limb is based on several factors: (1) Can the patient tolerate an attempt at revascularization? (2) Is the affected foot salvageable? (3) Is the patient ambulatory? (4) What is the patient’s current living status? Regarding the first question, the usual confounding comorbid medical conditions that may prohibit an attempt at revascularization are related to complicated cardiac issues. One should expect coronary artery disease in this population [6,25], and most procedures, whether performed percutaneously or through open surgery, can be carried out with acceptable risk and outcomes [38,39]. Assessment of perioperative cardiac risk would entitle a separate article and is not discussed herein; however, a few conditions do make any intervention exceptionally dangerous, that is, uncontrolled congestive heart failure, severe aortic stenosis, and acute coronary syndrome. These conditions would make the risk of any intervention exceptionally high, and procedures should be avoided.

The second question is also very pertinent. There is an undefined limit to the amount of tissue loss present in a given foot and the utility of attempting revascularization. Despite the use of vacuum-assisted wound devices, free tissue transfer strategies, and skin grafting, a serious assessment of foot functionality should be made before revascularization. The patient needs to understand the residual disability associated with such heroic measures. The expectations regarding functionality of a viable but mangled foot should not be glossed over. In addition, there must be an informed decision made by the patient that such salvage techniques are associated with considerable pain, hospitalization, additional surgeries, and prolonged recovery. When presented with the reality of the situation, a significant minority of patients may opt for primary amputation rather than aggressive revascularization and reconstructive efforts [24,40]. Likewise, as alluded to in the third and fourth questions, if the patient was nonambulatory before the current crisis, or if the patient was living in an assisted living setting or nursing home, there should be no reasonable expectation that the patient will begin ambulating and live independently despite successful limb salvage [41].
The timing of intervention in diabetic patients with tissue loss or active infection requires special consideration. If an aggressive posture toward limb salvage is to be adopted, delay in revascularization is associated with significant morbidity. Sheahan and colleagues [42] studied a large cohort of 670 patients who underwent 920 minor amputations, defined as interphalangeal, ray, or transmetatarsal, performed on 747 dysvascular limbs. All limbs underwent surgical revascularization. Sixty-five percent of these procedures were performed before (<30 days) amputation, 9.8% after (<30 days) amputation, and the rest at the time of amputation. Conversion to a major amputation occurred in 2.9%. Patients who had bypass subsequent to amputation had twice the risk of limb loss when compared with those who underwent concomitant or early revascularization. It is commonly agreed among vascular surgeons that any form of minor amputation in a dysvascular limb should be performed simultaneously or after the limb has been revascularized. To accomplish this mandate, revascularization procedures in patients with tissue loss requiring some form of minor amputation for ulceration, gangrene, or infection are, by necessity, urgent or emergent procedures.

Once the decision to proceed with revascularization is made, the next critical decision should be what methods to adopt. The broad categories are generally considered catheter-based, percutaneous methods (ie, endovascular techniques), open surgical techniques, or a combination of both (ie, hybrid techniques). The method adopted for treatment is usually based on a combination of systemic risk and local anatomic considerations [43–45].

Endovascular interventions may include conventional balloon angioplasty, “cutting balloon” angioplasty, unconventional balloon angioplasty (so-called “cryoplasty”), intraluminal stenting, plaque excision (mechanical atherectomy), or laser atherectomy, among others. The multitude of treatment options makes independent evaluation of each modality difficult; however, in general, shorter focal lesions usually respond well to endovascular interventions regardless of the particular method used. Because most diabetic patients with critical limb ischemia are afflicted with varying degrees of infrapopliteal occlusive disease, the utility of various forms of endovascular therapy in these patients requires further examination. Technical successes are often excellent, with clinical success occurring with less frequency; however, most would agree that failed angioplasty (or other endovascular intervention) does not preclude surgical bypass. Because endovascular procedures generally have a more favorable risk profile when compared with bypass, it would not be unreasonable to proceed with an attempt at endovascular intervention for anatomically favorable disease before surgical revascularization [8,46–49]. That being said, attempted percutaneous revascularization for longer, less favorable lesions in which failure is more frequent may simply delay revascularization. Unfortunately, not enough research has been devoted to the rapidity of clinical response associated with endovascular therapy for critical ischemia. An important
question remains: Do clinical failures of endovascular treatment result in an unacceptable delay before surgical revascularization and a higher risk for limb loss?

Surgical infrainguinal revascularization has been well studied. Several generalities are clear: (1) the complexity of the procedures is increasing, and the patients are getting sicker [50]; (2) autogenous conduits are preferable for all procedures involving infrapopliteal vessels; (3) any artery can serve as a bypass inflow vessel provided the vessels proximal to the anastomotic site are relatively disease free [8]; (4) the distal target of revascularization should be the least diseased vessel that establishes the best continuous runoff to the foot [8]; and (5) pedal artery targets are acceptable [7,15,39]. In patients with diabetes, the bypass graft patency is comparable with that achieved in non-diabetic patients. Although it is generally accepted that limb salvage rates are higher than graft patency rates among patients with critical ischemia, this is less evident among diabetic patients; primary graft failure is associated with substantial limb loss in this population [51].

Although the outcomes of a particular revascularization procedure are generally measured through the patency of a given bypass or intervention and limb salvage rates, the limitations of these survival metrics are seen in their inability to match up with patient satisfaction and well being [44]. Perhaps our traditional measurements of success are becoming more useful for research purposes than as clinically relevant measures of success [24,40,44]. The complex effects of anatomic features of the disease, the clinical presentation, the baseline functional status of the patient, comorbid medical conditions, and various technical considerations may require the use of algorithms guiding therapy in an objective standardized manner to maximize overall success [43,45]. Successful revascularization must always be coupled with successful application of multidisciplinary parallel treatment of local and systemic effects of infection, the systemic manifestations of diabetes, and good foot care [52].

Summary

PAD in diabetic patients is common. Patients with diabetes tend to present with more severe manifestations of the disease and require a more complicated diagnostic and therapeutic strategy for revascularization. Although techniques are rapidly evolving, revascularization remains only one component in the treatment of patients with diabetes and PAD. Because overall cardiovascular morbidity and mortality are high among patients with PAD, treatment to control the systemic atherosclerotic disease cannot be overemphasized. In addition, improvement in arterial perfusion is important, but wound care and pressure point unloading remain vital if more limbs are to be saved. As new treatment paradigms evolve, the assessment of outcomes needs to become more clinically relevant. Traditional measures
of success may prove unreliable in measuring patient satisfaction and the perception of well being. Newer patient-oriented (rather than limb-oriented) measures of success will need to be developed and expanded.

References


