Diabetic Foot

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Introduction

While arterial occlusive disease causing limb ischemia is a major factor in diabetic foot ulceration, it is only part of a complex interaction of multiple factors leading to the serious risks and complications of the diabetic foot.

Diabetes mellitus is among the leading causes of mortality and major morbidity in the United States. According to the National Diabetes Statistics Report for 2014, approximately 1.7 million new cases of diabetes were diagnosed in 2012. In 2012, 29.1 million Americans, or 9.3 % of the population, had diabetes. Eighty-six million Americans age 20 and older had prediabetes and 25.9 % of seniors had diabetes in 2012 [1]. Boulton reports that up to 50 % of older diabetics will be affected by a manifestation of diabetic foot such as neuropathy. The lifetime risk for foot ulcer in diabetic patients may be as high as 25 % and up to 80 % of amputations in diabetics are preceded by a diabetic foot ulcer [2]. In 2010 about 73,000 nontraumatic lower limb amputations were performed in diabetics over the age of 20. About 60 % of nontraumatic lower limb amputations in adults occur in diabetics [1].

It is well accepted that peripheral artery disease (PAD) is common in patients with diabetes. In the EURODIALE Study, approximately 50 % of all patients with diabetic foot ulcers had PAD [3]. The seriousness of social and economic implications of diabetic foot disease on individual patient cannot be overstated. Therefore, an understanding of the pathophysiology, diagnosis, and treatment of the diabetic foot is paramount for any physician involved in the care of patients with diabetes and/or limb ischemia.

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Pathophysiology

Neuropathy, PAD, and infection are generally considered a triad of leading factors in the development of diabetic foot ulceration. However, while neuropathy and PAD are clear risk factors for diabetic foot ulceration, Boulton suggests that infection is a result of, and not a risk factor for, ulceration [2]. Numerous other factors, such as age, prior foot ulcer or amputation, and foot deformity, play a role in foot ulcer formation as well. Understanding the multiple factors leading to diabetic foot ulcer formation can be instrumental in developing strategies to prevent these ulcers.

Diabetic Peripheral Neuropathy

Worldwide, diabetes is the most common cause of neuropathy, and diabetic neuropathies are among the most common long-term complications of diabetes [2, 4, 5]. An international consensus group defined diabetic neuropathy (DN) as the "presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes" [6]. Of the several forms of DN (Table 32.1), chronic sensorimotor diabetic peripheral neuropathy and peripheral sympathetic autonomic neuropathy play the greatest role in diabetic foot ulceration [4, 6]. Neuropathy is a major risk factor for developing foot ulceration, and according to Boulton, "in patients with significant neuropathy without a history of ulceration, the annual risk of developing an ulcer is five to seven times higher than in those without neuropathy" [6].

The clinical features of DN may be best recognized by understanding the "painful painless foot." This term is attributed to Dr. Paul Brand through his work with patients with leprosy. He recognized that neuropathic patients often experience severe painful neuropathic symptoms, but on examination have complete sensory loss to all modalities [6]. Smith describes the clinical features of DN as presenting

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Table 32.1 Clinical classification of diabetic neuropathies

Polyneuropathy	Mononeuropathy
Sensory	Isolated peripheral
Acute sensory	Mononeuritis multiplex
Chronic sensorimotor	
Autonomic	Truncal
Cardiovascular	
Gastrointestinal	
Genitourinary	
Peripheral sympathetic	
Proximal motor (amyotrophy)	
Truncal	

Items in bold type are important in the etiopathogenesis of diabetic foot problems
From Boulton A. Diabetic Neuropathy: Is Pain God's Greatest Gift to Mankind? Semin Vasc Surg. 2012:25:61–65. Reprinted with permission from Elsevier

either "positive" or "negative" sensory symptoms or being asymptomatic. Positive symptoms are described as abnormal excessive sensations such as pricking, tingling, or burning. These sensations may be downright painful. Negative symptoms are characterized by numbness or sensory loss. Some patients are not aware of their sensory loss and may consider themselves as asymptomatic [5].

Typical sensorimotor neuropathy presents with a symmetric stocking distribution sensory loss described by the patients as a feeling of the limb being asleep or numb [4, 6]. Other patients will describe neuropathic painful symptoms such as burning discomfort, electrical sensations, or stabbing pain.

Motor neuropathy is also a component of overall diabetic neuropathy, thus the term sensorimotor neuropathy, and leads to small muscle wasting in the foot and absent ankle reflexes. The clinical presentation of motor nerve dysfunction is wasting of the small muscles in the feet and absent ankle reflexes. This chronic motor denervation results in malfunction of the intrinsic muscles of the foot that distorts foot architecture. Chronic metatarsal flexion, extensor subluxation of the toes, proximal migration of the metatarsal fat pad, and an imbalance in the action of the toe flexors and extensors lead to a "claw foot deformity." More importantly, with dislocation of the metatarsophalangeal joints, the heads of the metatarsals become more prominent, driven downward, and become the striking surface during ambulation. Other bony prominences become abnormal pressure points as well, and combined with a loss of pain sensation, the overlying skin is subject to repeated injury and ulceration. This so-called claw foot as depicted in Fig. 32.1 is characterized by clawing of the toes, prominent metatarsal heads, and a high arch. The "claw foot" deformity represents a high-risk diabetic neuropathic foot and is associated with increased risk of ulcer formation [7, 8].

Charcot foot (CF) is another form of foot deformity associated with diabetic neuropathy. CF can be acute or chronic.

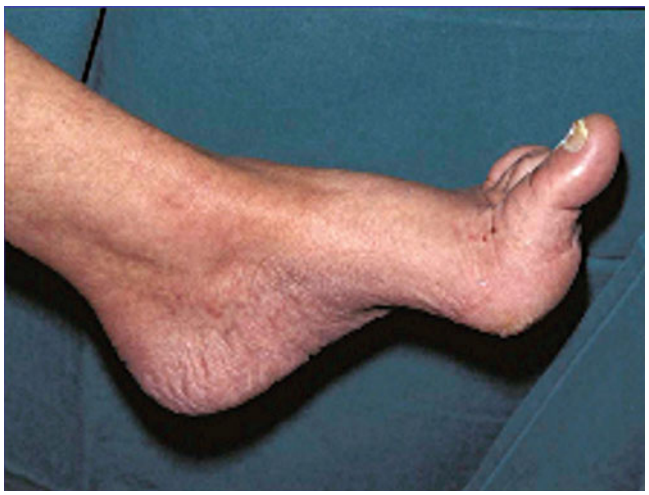

Fig. 32.1 At risk foot. Neuropathic diabetic foot with at risk "claw foot" deformity. From Boulton A. Diabetic Neuropathy: Is Pain God's Greatest Gift to Mankind? Semin Vasc Surg. 2012:25:61–65. Reprinted with permission from Elsevier

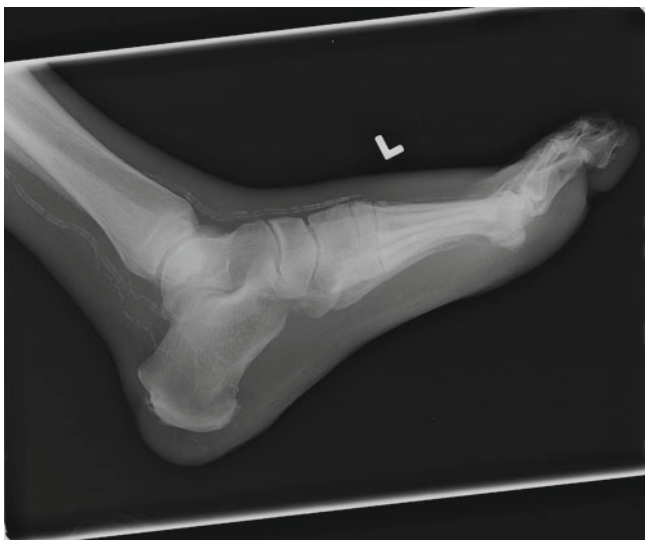

Fig. 32.2 Charcot foot. Radiographic example of a Charcot foot

Acute CF can mimic a foot infection where the foot is markedly red, warm, and swollen. Pain is often minimal or absent. The midfoot is usually most affected. Ongoing mechanical stresses lead to ligament strain, fracture-dislocations of the forefoot bones, midfoot collapse, and severe foot deformity and joint instability [9]. Figure 32.2 shows a radiograph of a Charcot foot.

Peripheral autonomic dysfunction affecting the sympathetic nervous system is also present in diabetic neuropathy. Autonomic dysfunction leads to loss of sweat and oil gland function resulting in dry skin prone to cracking and fissure formation. The cracked skin can breakdown and become a portal of entry for bacteria [2, 8].

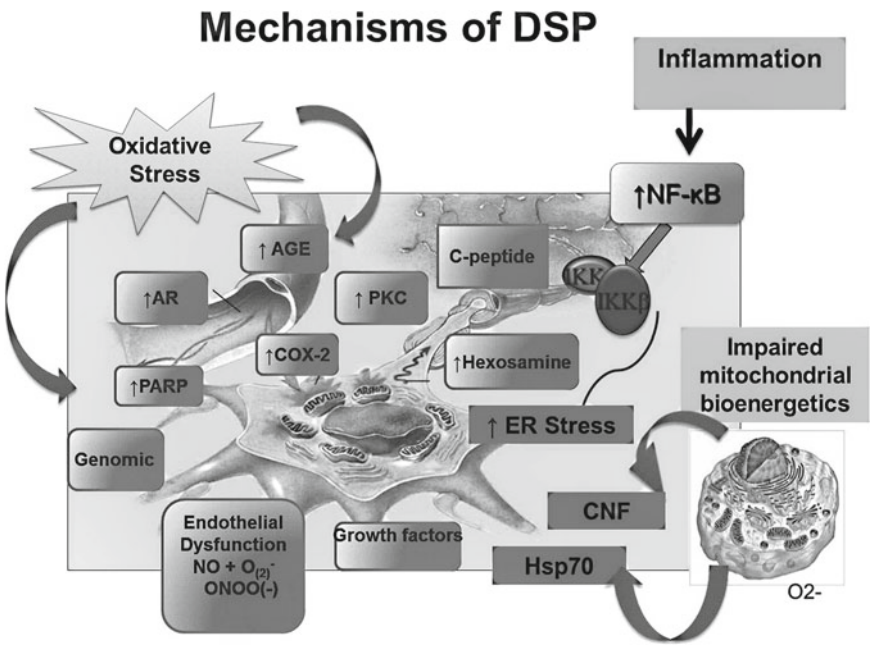

Fig. 32.3 Mechanisms of distal symmetric polyneuropathy (DSP). Proposed mechanisms of diabetic distal symmetric polyneuropathy (DSP). *AGE* advanced glycation end products, *AR* aldose reductase, *CNF* ciliary neurotrophic factor, *COX-2* cyclooxygenase 2, *ER* endoplasmic reticulum, *Hsp70* heat shock protein 70, *IKKβ* inhibitor of nuclear factor, *κB* kinase subunit β, *NF-kB* nuclear factor κB, *PARP* poly(ADP ribose) polymerase, *PKC* protein kinase C. The neuron displayed in the figure was drawn by the Juvenile Diabetes Research Foundation (JDRF) for the University of Michigan Center for Diabetes Complications, and it is reproduced here with permission from Helen Nickerson, PhD, Senior Scientific Program Manager JDRF. Reproduced from Albers JW, Rodica P-B. Diabetic Neuropathy: Mechanisms, Emerging Treatments, and Subtypes. Curr Neurol Neurosci Rep. 2014 Aug;14(8):473. Reprinted with permission from Springer

As one examines diabetic neuropathy, it becomes evident that there is a wide spectrum of presenting symptoms in these patients. Boulton emphasizes that, "neuropathic symptoms correlate poorly with sensory loss and their absence must never be equated with lack of foot ulcer risk." It has been observed that, "any patient that walks into clinic with a foot ulcer but without a limp must have neuropathy because those with normal pain sensation would not be able to put weight on the lesion" [7]. This observation lead Dr. Paul Brand to state that, "Pain is God's greatest gift to mankind" as it pertained to the protective nature of foot pain in the prevention of foot ulcers.

The pathogenesis of diabetic neuropathy is not completely understood and is likely multifactorial involving hyperglycemia, duration of diabetes, age-related neuronal degeneration, and other common factors such as hypertension, hyperlipidemia, and obesity [4]. According to Smith, "neuropathy likely results from a combination of direct axonal injury due to the metabolic consequences of hyperglycemia, insulin resistance, and toxic adiposity, and endothelial injury and microvascular dysfunction leading to nerve ischemia" [5]. The multiple biochemical pathways involved in the development of neuropathy may include increased mitochondrial production of free radicals, increased formation of glycation end products, downregulation of the soluble receptor for glycation end products, increased activity of the polyol or sorbitol pathway with accumulation of protein kinase C, activation of poly(ADP ribose) polymerase, cyclooxygenase 2 activation, endothelial dysfunction, peroxynitrite and protein nitration, and altered Na^+/K^+-ATPase pump function. These pathways alter neuronal activity, mitochondrial function, membrane permeability, and endothelial function. Ultimately these changes promote segmental demyelination, Wallerian degeneration, and microangiopathy and induce neuronal apoptosis leading to axonal and neuronal degeneration [4, 5]. In Fig. 32.3 Smith depicts this complex interaction of multiple pathways leading to neuropathy and the reader is referred to his thorough review of the mechanisms for further details [4].

Peripheral Artery Disease

Initial understanding of PSD in the diabetic population was mistakenly ascribed to the theory of small vessel disease or microvascular occlusion of the arterioles. This led to the assumption that diabetics with arterial insufficiency causing ulcers could not be revascularized and would need amputations. Subsequent decades of experience and research have shown that the predominant cause of ischemia in diabetic patients is macrovascular occlusion of the leg arteries, most commonly the tibial arteries, due to atherosclerosis [8].

PAD in diabetes alters vascular function at the macrovascular and microvascular levels. On a macrovascular level, the formation of standard atheromatous plaques in diabetics is similar to nondiabetics. The pattern of involvement has some unique characteristics in diabetics with the larger iliac and femoral arteries commonly spared of hemodynamically significant disease. However, the popliteal and tibial arteries are more frequently involved compared to nondiabetics. While atherosclerosis affects the femoral and popliteal arteries in both diabetics and nondiabetics, the infragenicular occlusive disease in the anterior tibial, posterior tibial, and peroneal arteries is the classic distribution in diabetic patients (Fig. 32.4). It is not unusual to see diabetic patients with ischemic foot lesions having a palpable popliteal pulse with

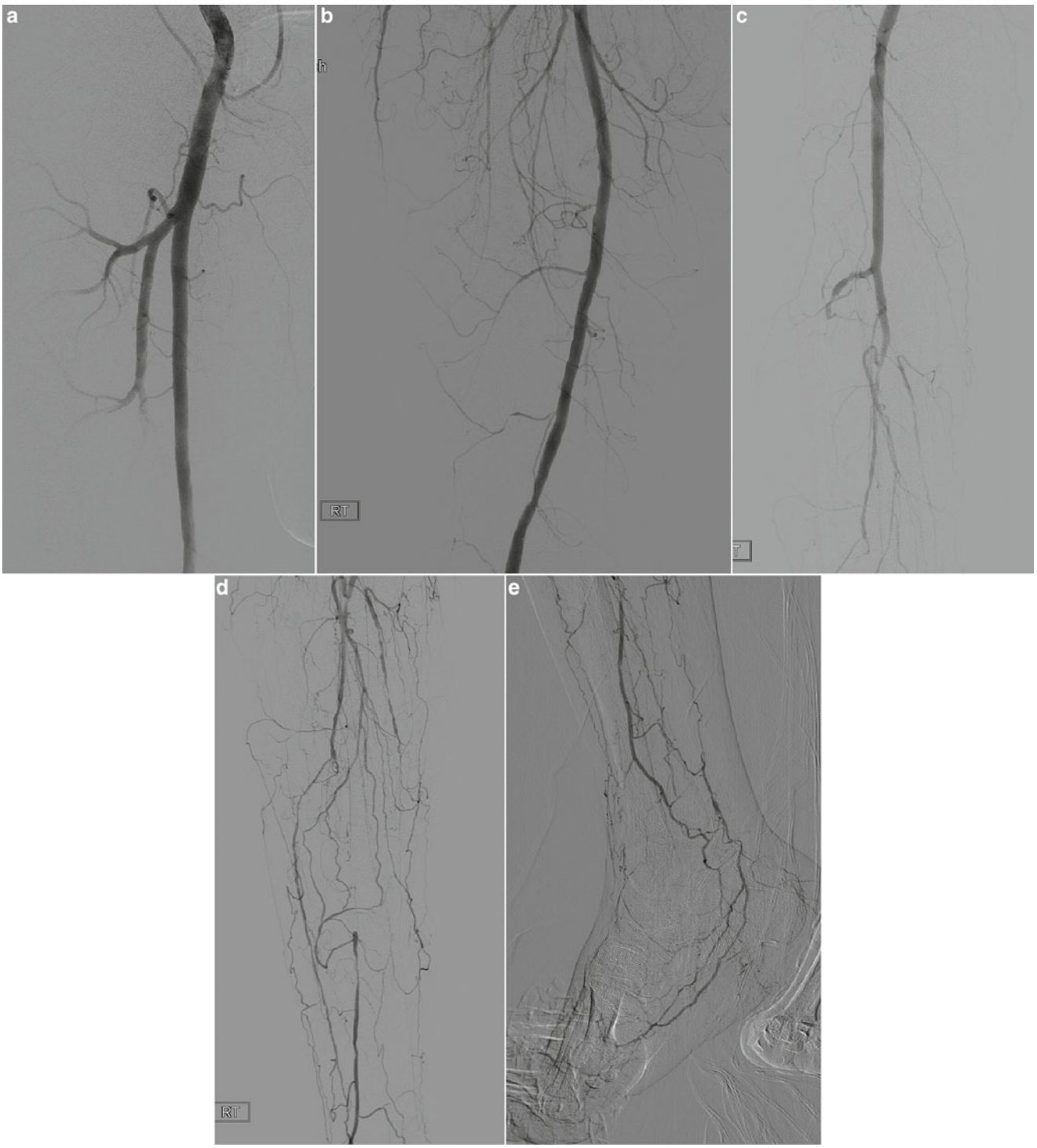

Fig. 32.4 Angiogram of diabetic foot patient. Serial angiograms of diabetic limb patient demonstrating relatively well-preserved femoral and popliteal arteries with severe tibial artery occlusive disease

occlusive disease isolated to the infragenicular arteries. Fortunately, the foot vessels are often spared in diabetics, even in the face of severe tibial level disease, which is important to the success of distal revascularization. A study based on arteriography showed no difference in occlusive disease in the arterial system of the foot when diabetics were compared to nondiabetics [10]. Diabetes can also lead to a hypercoagulable state through alterations in platelet function, coagulation, and blood rheology, thus potentially adding to arterial occlusive disease.

On a microvascular level, the arterial disease in diabetics is best described as nonocclusive microcirculatory impairment. This should not be confused with the term "small vessel disease" that refers to the common misconception of an untreatable occlusive lesion in the microcirculation. The concept of diabetic small vessel occlusive disease often leads to inappropriate management of diabetic patients with nonhealing foot lesions. The formation of these lesions in the presence of normal palpable foot pulses led to the misconception that diabetic patients have microvascular occlusive disease, which causes skin ischemia and formation of foot lesions. Dispelling the notion of "small vessel disease" has been fundamental to diabetic limb salvage, because arterial reconstruction is almost always possible and successful in these patients. In the presence of foot ischemia, the restoration of pulsatile blood flow using vein bypass may be necessary to heal the lesion. In this situation diabetic patients showed the same propensity to healing as nondiabetics. Infrainguinal vein bypasses in diabetics have comparable patency and limb salvage rates to those performed in nondiabetics [11].

Whereas there is no occlusive disease in the microcirculation, multiple structural and physiologic abnormalities result in functional microvascular impairment [12]. Endothelial cell dysfunction as a result of hyperglycemia and hyperinsulinemia plays a major role in this functional defect [13]. Nitric oxide (NO) is the main vasodilator released by the endothelium and causes vasodilation by diffusing into the vascular smooth muscle cells (VSMC) thereby stimulating cyclic guanosine 3′5′-monophosphate-mediated relaxation. NO is synthesized in the endothelial cell through the action of an endothelial-specific NO synthase (ecNOS). The expression of ecNOS is reduced in response to hyperglycemia and hyperinsulinemia [13]. Also, loss of NO homeostasis at the microcirculatory level creates a proinflammatory environment with damaging oxygen-free radical species released into the vasculature and surrounding tissues.

Another effect of hyperglycemia is the nonspecific glycosylation of proteins, so-called advanced glycosylation end products (AGEs). AGEs impair the actions of NO by stimulating the formation of free oxygen radicals that react with NO and convert it to a prooxidant. AGEs also displace disulfide cross-linkages in collagen proteins thereby diminishing the charge in the capillary basement membrane and altering its diffusion properties [14]. These basement membrane alterations contribute to increased vascular permeability and inflammation. AGEs activate and upregulate the expression of endothelial AGE receptors—these add to the local inflammatory state by increasing leukocyte chemotaxis and transformation into foam cells which contribute to increasing local oxidative stress [15]. One result of this increase in inflammation is an increase in C-reactive protein (CRP) which is strongly related to widespread acceleration of atherosclerosis and promotion of endothelial cell apoptosis [16]. These and other mechanisms result in the impaired microvasculature marked by a characteristic thickening of the capillary basement membrane which does not affect arteriolar luminal diameter or blood flow but does impair nutrient and substrate flow into the adjacent tissues. This, coupled with autonomic dysfunction at the capillary level described earlier, severely hinders the hyperemic response to injury, inflammation, and infection.

The macrovascular component of PAD in diabetics is due to atherosclerosis. The atheromatous changes occur in a similar fashion as in nondiabetics, but in an accelerated way. This acceleration could be due to the previously described diabetes-driven increases in inflammation that worsen the course of "normal" plaque pathophysiology, changes in platelet and coagulation system function, and the high coincidence of hypertension among diabetics due to diabetic nephropathy.

Another common finding among diabetics is extensive medial calcification of the arteries. This is a process that can occur either at or separate from sites of atheromatous plaque and in diabetics is characteristically found throughout the arteries of the legs. There are several different disease states and proposed pathways for this abnormal calcification of the media; in diabetics both hyperinsulinemia and hyperglycemia are implicated. Both have been shown to alter gene and protein expression in endothelial and vascular smooth muscle cell (VSMC) that directly result in "osteoblast-like" activity of the VSMC and pericyte cells of the artery [17]. An example is the abnormal expression of proteins like osteopontin by these cells. Osteopontin coupled with chronic inflammation and high presence of oxygen-free radicals and C-reactive protein within the vessel wall leads to the deposition of calcium-phosphate complexes that mineralize within the media. Although this is generally a nonobstructive lesion, it leads to noncompliant arteries unable to augment flow in response to increased demand and, depending on the luminal diameter of the vessel, long segmental stenoses that disturb normal blood flow.

As mentioned before, the formation of atheromatous plaques in diabetics is similar in most regards to nondiabetics, but the pattern of involvement has a unique characteristic in diabetics. Despite sometimes widespread calcinosis, the larger iliofemoral arteries are commonly spared of hemodynamically significant disease. However, in diabetics the popliteal and infra-popliteal vessels are more frequently involved

than the larger arteries and more frequently diseased compared to nondiabetics [18]. The foot vessels are relatively spared in diabetics, even in the face of severe tibioperoneal level disease, which is important to the success of revascularization [19].

In addition to the effects on the endothelium and VSMC, diabetes also leads to a hypercoagulable state through alterations in platelet function, coagulation, and blood rheology. Platelet uptake of glucose is unregulated in hyperglycemia and results in increased oxidative stress which enhances platelet aggregation. These platelets also have increased expression of glycoprotein Ib and IIb/IIIa receptors which are important in thrombosis and platelet adhesion. The coagulation system is affected by diabetic-related increases in tissue factor expression by VSMC and endothelial cells and increases in plasma concentrations of factor VII. Hyperglycemia is also associated with a decreased concentration of antithrombin and protein C, impaired fibrinolytic function, and excess plasminogen activator inhibitor-1 [20]. Blood rheology is altered as a consequence of an increase in viscosity and fibrinogen content due to hyperglycemia.

In summary, the effects of PAD in diabetics confer alterations in the microvascular functioning and macrovascular supply that lead to ischemia. Because of the synergistic consequences of both processes, the actual degree of ischemia can be greater than suspected, and even relatively minor trauma or infection can be made worse due to vascular insufficiency. The contribution of neuropathy with even moderate levels of ischemia is particularly worrisome as these "neuroischemic" feet are more prone to ulceration and infection [21, 22].

Infection

As previously mentioned, infection is more a result of than a true cause of diabetic foot ulceration. The structural and functional alterations of the arteriole and capillary walls, most notably, membrane basement thickening, associated with diabetes add to the likelihood of an ulcer becoming infected. The thickened basement membrane blocks leukocyte migration and hinders hyperemic and vasodilatory response to injury. This may block the normal inflammatory signs associated with infection. Erythema, rubor, cellulitis, and tenderness may be absent. The normal systemic signs of infection like fever, tachycardia, and leukocytosis may be absent as well [8]. Failure by the diabetic patient to recognize the onset of infection in an ulcer can have dire consequences. The risk of amputation correlates directly with increasing severity of infection as confirmed by Lavery in 2007 [23]. This study of 1666 diabetic patients showed increased risk of amputation, higher level amputation, and lower extremity-related hospitalization in patients with increased severity of infection based on the Infectious Disease Society of America (IDSA) classification of wound infection.

Classification of the Diabetic Foot

Discussion of the pathophysiology of diabetic foot ulcers leads into a discussion about classification schemes for the threatened limb. The 2014 Society for Vascular Surgery document details the evolution of classification schemes for critical limb ischemia and the threatened limb. To date, any one of the existing systems failed to include all three major pathophysiologic components of the threatened diabetic foot. In fact, the original 1978 definition of critical limb ischemia actually excluded patients with diabetes altogether. These existing systems tended to concentrate on only one of the causative factors such as perfusion (Fontaine and Rutherford) or foot wound (Wagner and University of Texas) [24]. A complete summary of the previous systems is provided in Table 32.2.

The 2014 SVS document calls the new classification system "The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System." Under this new system, risk stratification is based on wound, ischemia, and foot infection. Shorthand for the system is WIfI (**W**ound, **I**schemia, and **f**oot **I**nfection). It is the intention of this system to, "provide more precise description of the disease burden to allow accurate outcomes assessment and comparison between similar groups of patients and alternative therapies." The system takes into account that, "wound healing depends not only on the degree of ischemia, but also on the extent and depth of the wound and the presence and severity of infection." The entire WIfI system is outlined in Table 32.3.

Assessment of the Diabetic Foot

Screening

Screening patients at risk for diabetic foot ulceration should be based on those factors that may lead a diabetic down the final common pathway to foot ulceration. It is commonly believed that neuropathy, deformity, and trauma interact to ultimately cause ulceration. Therefore, the history and physical examination of the diabetic patient should concentrate on identifying signs and symptoms of these mechanisms.

In 2008, a task force of the American Diabetes Association was assembled to address and construct a comprehensive foot examination for diabetic patients [25]. According to the document, diabetic patients should be assessed for their risk of foot ulceration by exploring key features of their history and following a thorough physical

Table 32.2 Summary and comparison of existing diabetic foot ulcer, wound, and lower extremity ischemia classification systems

Classification system	Ischemic rest pain	Ulcer	Gangrene	Ischemia	Infection	Comments
Rutherford	Yes, category 4/6	Category 5, minor tissue loss, nonhealing ulcer, focal gangrene with diffuse pedal ischemia	Category 6, major tissue loss extending above TM level, functional foot no longer salvageable (although in practice often refers to extensive gangrene, potentially salvageable foot with significant efforts)	Yes, cutoffs for CLI, category 4: resting AP <40 mmHg, flat or barely pulsatile ankle or forefoot PVR; TP <30 mmHg category 5/6: AP <60 mmHg; flat or barely pulsatile ankle or forefoot PVR; TP <40 mmHg	No	Pure ischemia model PAD classification system includes milder forms of PAD (categories 1–3); categories 4–6 based on cutoff values for CLI; no spectrum of ischemia, does not acknowledge potential need for revascularization with <CLI cutoff depending on wound extent/infection; not intended for patients with diabetes; wound classes not sufficiently detailed; omits infection as a trigger
Fontaine	Yes, class III/IV	Class IV/IV, ulcer and gangrene grouped together	Class IV/IV, ulcer and gangrene grouped together	Cutoff values for CLI based on European consensus document: ischemic rest pain >2 weeks with AP <50 mmHg or TP <30 mmHg ulcer and gangrene; AP <50 mmHg, TP <30 mmHg, absent pedal pulses in patient with diabetes	No	Pure ischemia model; no clear definitions of spectrum of hemodynamics; minimal description of wounds; infection omitted
PEDIS	No	Yes, grades 1–3; grade 1: superficial full-thickness ulcer, not penetrating deeper than the dermis; grade 2: deep ulcer, penetrating below the dermis to subcutaneous structures involving fascia, muscle, or tendon; grade 3: all subsequent layers of the foot involved including bone and/or joint (exposed bone, probing to bone)	No	Yes, three grades; CLI cutoff grade 1: no PAD symptoms, ABI >0.9, TBI >0.6, $TcPO_2$ >60 mmHg; grade 2: PAD symptoms, ABI <0.9, AP >50 mmHg, TP >30 mmHg, $TcPO_2$ 30–60 mmHg; grade 3: AP <50 mmHg, TP <30 mmHg, $TcPO_2$ <30 mmHg	Yes, grades 1–4; see IDSA classification (Table 32.3)	Primarily intended for DFUs; ulcer grades validated; includes perfusion assessment, but with cutoff for CLI; gangrene not separately categorized; includes validated IDSA infection categories
UT	No	Yes, grades 0–3 ulcers; grade 0: pre- or postulcerative completely epithelialized lesion; grade 1: superficial, not involving tendon, capsule, or bone; grade 2: penetrating to tendon/capsule; grade 3: penetrating to bone or joint	No	Yes ± based on ABI <0.8	Yes, ± wounds with frank purulence or >2 of the following (warmth, erythema, lymphangitis, edema, lymphadenopathy, pain, loss of function) considered infected	Primarily intended for DFUs; includes validated ulcer categories; PAD and infection included, but only as ± with no grades/spectrum
Wagner	No	Grade 0: pre- or postulcerative lesion; grade 1: partial/full-thickness ulcer; grade 2: probing to tendon or capsule; grade 3: deep ulcer with osteitis; grade 4: partial foot gangrene; grade 5: whole foot gangrene	Ulcer and gangrene grouped together; gangrene due to infection not differentiated from gangrene due to ischemia; also includes osteomyelitis	No	No for soft tissue component; included only as osteomyelitis	Orthopedic classification intended for diabetic feet; no hemodynamics; gangrene from infection not differentiated from that due to ischemia; osteomyelitis included; soft tissue infection not separated from bone infection

(continued)

Table 32.2 (continued)

Classification system	Ischemic rest pain	Ulcer	Gangrene	Ischemia	Infection	Comments
S(AD) SAD system	No	Yes, grades 0–3 based on area and depth; grade 0: skin intact; grade 1: superficial, <1 cm^2; grade 2: penetrates to tendon, periosteum, joint capsule, 1–3 cm^2; grade 3: lesions in bone or joint space, >3 cm^2	No	Pulse palpation only, no hemodynamics	Yes, 1 = no infection; 2 = cellulitis; 3 = osteomyelitis	Intended for DFUs; also includes neuropathy; does not mention gangrene; no hemodynamic information; perfusion assessment based on pulse palpation only
Saint Elian	No	Yes, grades 1–3 based on depth; grade 1: superficial wound disrupting entire skin; grade 2: moderate or partial depth, down to fascia, tendon, or muscle but not bone or joints; grade 3: severe or total, wounds with bone or joint involvement, multiple categories including area, ulcer number, location, and topography	No	Yes, grades 0–3; grade 0: AP >80 mmHg, ABI 0.9–1.2; grade 1: AP 70–80 mmHg, ABI 0.7–0.89, TP 55–80 mmHg; grade 2: AP 55–69 mmHg, ABI 0.5–0.69, TP 30–54 mmHg; grade 3: AP <55 mmHg, ABI <0.5, TP <30 mmHg	Yes, grades 0–3; grade 0: none; grade 1: mild; erythema 0.5–2 cm, induration, tenderness, warmth, and purulence; grade 2: moderate, erythema >2 cm, abscess, muscle tendon, joint, or bone infection; grade 3: severe, systemic response (similar to IDSA)	Detailed system intended only for DFUs; detailed comprehensive ulcer classification system and hemodynamic categories for gradation of ischemia; gangrene not considered separately infection system similar to IDSA
IDSA	No	No	No	No	Yes, uninfected, mild, moderate, and severe (Table 32.3)	Validated system for risk of amputation related to foot infection, but not designed to address wound depth/complexity or degree of ischemia
SVS lower extremity threatened limb classification	Yes, wound/clinical class 0–3	Yes, grades 0–3; grouped by depth, location and size, and magnitude of ablative/wound coverage procedure required to achieve healing	Yes, grades 0–3; grouped by extent, location and size, and magnitude of ablative or wound coverage procedure required to achieve healing	Yes, ischemia grades 0–3; hemodynamics with spectrum of perfusion abnormalities; no cutoff value for CLI; grade 0: unlikely to require revascularization	Yes, IDSA system (Table 32.3)	Includes PAD + diabetes with spectrum of wounds, ischemia, and infection, scaled from 0 to 3; no cutoff for CLI. Need for revascularization depends on degree of ischemia, wound, and/or infection severity; ulcers/gangrene categorized based on extent and complexity of anticipated ablative surgery/coverage

ABI ankle-brachial index, *AP* ankle pressure, *CLI* critical limb ischemia, *DFUs* diabetic foot ulcers, *IDSA* Infectious Disease Society of America, *PAD* peripheral artery disease, *PEDIS* perfusion, extent/size, depth/tissue loss, infection, sensation, *PVR* pulse volume recording, *SAD* sepsis, arteriopathy, denervation, *SVS* Society for Vascular Surgery, *TcPO2* transcutaneous oxygen pressure, *TP* toe pressure, *UT* University of Texas

From Mills JL Sr, et al. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: Risk stratification based on wound, ischemia, and foot infection (WIfI). J Vasc surg. 2014 Jan;59(1):220–34.e1-2. Reprinted with permission from Elsevier Limited

Table 32.3 Society for Vascular Surgery Lower Extremity Threatened Limb (SVS WIfI) Classification System

I. **W**ound
II. **I**schemia
III. **f**oot **I**nfection
WIfI score

W: Wound/clinical category
SVS grades for rest pain and wounds/tissue loss (ulcers and gangrene):
0 (ischemic rest pain, ischemia grade 3, no ulcer), 1 (mild), 2 (moderate), and 3 (severe)

Grade	**Ulcer**	**Gangrene**	
0	No ulcer	No gangrene	
Clinical description: ischemic rest pain (requires typical symptoms + ischemia grade 3), no wound			
1	Small, shallow ulcer(s) on distal leg or foot; no exposed bone, unless limited to distal phalanx	No gangrene	
Clinical description: minor tissue loss. Salvageable with simple digital amputation (one or two digits) or skin coverage			
2	Deeper ulcer with exposed bone, joint, or tendon; generally not involving the heel; shallow heel ulcer, without calcaneal involvement	Gangrenous changes limited to digits	
Clinical description: major tissue loss salvageable with multiple (≥3) digital amputations or standard TMA ± skin coverage			
3	Extensive, deep ulcer involving forefoot and/or midfoot; deep, full-thickness heel ulcer ± calcaneal involvement	Extensive gangrene involving forefoot and/or midfoot; full-thickness heel necrosis ± calcaneal involvement	
Clinical description: extensive tissue loss salvageable only with a complex foot reconstruction or nontraditional TMA (Chopart or Lisfranc); flap coverage or complex wound management needed for large soft tissue defect			

I: **Ischemia**
Hemodynamics/perfusion: measure TP or $TcPO_2$ if ABI incompressible (>1.3)
SVS grades 0 (none), 1 (mild), 2 (moderate), and 3 (severe)

Grade	**ABI**	**Ankle systolic pressure (mmHg)**	**TP**, **TcPO2 (mmHg)**
0	≥0.80	>100	≥60
1	0.6–0.79	70–100	40–59
2	0.4–0.59	50–70	30–39
3	≤0.39	<50	<30

fI: **foot Infection**:
SVS grades 0 (none), 1 (mild), 2 (moderate), and 3 (severe: limb and/or life threatening)
SVS adaptation of Infectious Diseases Society of America (*IDSA*) and International Working Group on the Diabetic Foot (IWGDF) perfusion, extent/size, depth/tissue loss, infection, sensation (*PEDIS*) classifications of diabetic foot infection

(continued)

Table 32.3 (continued)

Clinical manifestation of infection	SVS	IDSA/PEDIS infection severity
No symptoms or signs of infection	0	Uninfected
Infection present, as defined by the presence of at least two of the following items:	1	Mild
• Local swelling or induration		
• Erythema >0.5 to ≤2 cm around the ulcer		
• Local tenderness or pain		
• Local warmth		
Purulent discharge (thick, opaque to white, or sanguineous secretion)		
Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below)		
Exclude other causes of an inflammatory response of the skin (e.g., trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis, venous stasis)		
Local infection (as described above) with erythema >2 cm or involving structures deeper than skin and subcutaneous tissues (e.g., abscess, osteomyelitis, septic arthritis, fasciitis)	2	Moderate
No systemic inflammatory response signs (as described below)		
Local infection (as described above) with the signs of SIRS, as manifested by two or more of the following:	3	Severe[a]
• Temperature >38° or <36 °C		
• Heart rate >90 beats/min		
• Respiratory rate >20 breaths/min or $PaCO_2$ < 32 mmHg		
• White blood cell count >12,000 or <4000 cu/mm or 10 % immature (band) forms		

(32.3 a) Key summary points for use of Society for Vascular Surgery Lower Extremity Threatened Limb (SVS WIfI) Classification System
1. Table 32.3, the full system, is to be used for initial, baseline classification of all patients with ischemic rest pain or wounds within the spectrum of chronic lower limb ischemia when reporting outcomes, regardless of form of therapy. The system is not to be employed for patients with vasospastic and collagen vascular disease, vasculitis, Buerger's disease, acute limb ischemia, or acute trauma (mangled extremity)
2. Patients with and without diabetes mellitus should be differentiated into separate categories for subsequent outcomes analysis
a. Presence of neuropathy (±) should be noted when possible in patients with diabetes in long-term studies of wound healing, ulcer recurrence, and amputation, since the presence of neuropathy (loss of protective sensation and motor neuropathic deformity) influences recurrence rate
3. In the Wound (W) classification, depth takes priority over size. Although we recommend that a wound, if present, be measured, a shallow, 8-cm^2 ulcer with no exposed tendon or bone would be classified as grade 1
a. If a study of wound healing vs. Wound (W) grade were performed, wounds would be classified by depth and could also be categorized by size: small (<5 cm^2), medium (5–10 cm^2), and large (>10 cm^2)
4. TPs are preferred for classification of ischemia (I) in patients with diabetes mellitus, since ABI is often falsely elevated. $TcPO_2$, SPP, and flat forefoot PVRs are also acceptable alternatives if TP is unavailable. All reports of outcomes with or without revascularization therapy require measurement and classification of baseline perfusion
5. In reporting the outcomes of revascularization procedures, patients should be restaged after control of infection, if present, and/or after any debridement, if performed, prior to revascularization
a. Group a patients: no infection within 30 days or simple infection controlled with antibiotics alone
b. Group b patients: had infection that required incision and drainage or debridement/partial amputation to control

From Mills JL Sr, et al. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: Risk stratification based on wound, ischemia, and foot infection (WIfI). J Vasc surg. 2014 Jan;59(1):220–34.e1-2. Reprinted with permission from Elsevier Limited

Patients with diabetes should have TP measurements. If arterial calcification precludes reliable ABI or TP measurements, ischemia should be documented by $TcPO_2$, SPP, or PVR. If TP and ABI measurements result in different grades, TP will be the primary determinant of ischemia grade

Flat or minimally pulsatile forefoot PVR = grade 3

TMA transmetatarsal amputation, *ABI* ankle-brachial index, *PVR* pulse volume recording, *SPP* skin perfusion pressure, *TP* toe pressure, *TcPO2* transcutaneous oximetry, *PACO2* partial pressure of arterial carbon dioxide, *SIRS* systemic inflammatory response syndrome, *ABI* ankle-brachial index, *PVR* pulse volume recording, *SPP* skin perfusion pressure, *TcPO2* transcutaneous oximetry, *TP* toe pressure

[a]Ischemia may complicate and increase the severity of any infection. Systemic infection may sometimes manifest with other clinical findings, such as hypotension, confusion, vomiting, or evidence of metabolic disturbances, such as acidosis, severe hyperglycemia, new-onset azotemia

examination. The major risk factors for diabetic foot ulcer formation are outlined in [25].

The history must consider signs and symptoms consistent with the key issues of prior ulceration, foot deformity, neuropathy, and arterial occlusive disease. While the history is usually very revealing, it must be kept in mind that many patients will describe themselves as asymptomatic. Therefore, a detailed and methodical exam of the feet is paramount [25]. Once the history and physical has been obtained as outlined by the task force document, the risk of developing a foot ulcer can be determined. This risk classification may then be used to determine the timing and extent of referral to members of the treatment team. Details of the risk classification and referral scheme are outlined in [25].

Noninvasive Assessment for PAD

When the diabetic patient has history and physical findings worthy of further assessment for PAD, the noninvasive vascular laboratory offers studies that are well established and easily obtained in most circumstances.

An ankle-brachial index (ABI) is usually the initial step in the objective noninvasive assessment of the patient with suspected peripheral arterial occlusive disease. The study compares the higher of the systolic blood pressure at either the dorsalis pedis or posterior tibial arteries on each limb to the higher of the two brachial artery systolic pressures. A ratio is calculated by placing the ankle pressure value over the brachial pressure value. The generally accepted normal value range is from 1.0 to 1.2. An ABI less than 0.6 generally indicates that a foot ulcer is unlikely to heal without revascularization [26].

In diabetic patients with medial calcinosis, the tibial artery walls may not be compressible. Therefore, the ABI value may be unobtainable or misleading. The noncompressible tibial artery wall usual leads to a supranormal value for the ABI such as 1.3. In such circumstances the clinician must be suspicious that the ABI is not reliable for that patient especially in the absence of palpable pulses and alternative noninvasive measures for arterial occlusive disease should be considered.

The digital arteries usually remain compressible in diabetic patients. Therefore, the measurement of a toe-brachial index (TBI) may be useful when the ABI measurement is unreliable. A TBI greater than 0.75 is generally accepted as normal, while a value below 0.25 suggests critical limb ischemia. An absolute toe pressure greater than 55 mmHg suggests adequate perfusion to heal a foot ulcer [26]. An obvious limitation of the TBI occurs when the toes are absent such as following a transmetatarsal amputation.

If the TBI cannot be obtained due to missing digits, another useful noninvasive study is the pulse volume recording (PVR). In this study blood pressure cuffs are placed at multiple levels along each leg and segmental pressures and pulse waveforms are measured and recorded. As the degree of arterial occlusive disease increases, the waveforms will change from triphasic to biphasic and then monophasic. This study allows measurement and comparison of occlusive disease longitudinally from proximal to distal arterial segments, as well as laterally from one leg to the other leg. A gradient between any consecutive longitudinal segments or from side to side suggests significant arterial occlusive disease between the segments. The PVR is particularly useful in diabetic patients since the study is not affected by medial calcinosis [26].

Duplex ultrasound imaging can provide anatomic and physiologic information with regard to arterial stenosis and/or occlusion. This information may be used to guide selective angiographic imaging or even sometimes may be sufficient enough to guide endovascular intervention or operative therapy [26].

Contrast Imaging of PAD

Historically, most diabetic PAD has been imaged with contrast angiography when planning a revascularization procedure. While catheter-based contrast angiography remains the workhorse of vascular imaging, newer techniques of computerized tomographic angiography and magnetic resonance angiography are becoming more refined and useful for planning vascular reconstruction. Each modality must be examined with regard to its benefits and drawbacks when specifically applied to the diabetic patient.

Catheter-Based Contrast Angiography

Digital subtraction angiography remains the gold standard for lower extremity arterial imaging. The high-resolution images produced on current flat-panel image intensifiers allow for great detail of even the small tibial and pedal artery segments. The flat-panel systems have larger field of view than conventional image intensifiers and can produce the same image acquisition with less radiation and contrast volume. The computer processing techniques of masking and road mapping allow for easier endovascular interventions. One of the greatest benefits of contrast angiography is that it can quickly go from diagnostic to treatment modalities with ease.

The drawbacks of contrast angiography are related to the need to access the vascular system and the use of intravascular contrast agents. The latter issue is particularly problematic in diabetic patients as they often have renal insufficiency along with their vascular disease.

Arterial access can lead to well-known complications of arterial puncture such as hematoma or bleeding, dissection,

pseudoaneurysm formation, and embolism. These mechanical complications can be minimized by the use of ultrasound guidance for arterial puncture and smallest diameter sheaths and catheters for interventions.

A more difficult set of problems comes from the need for iodinated contrast agents for contrast angiography. According to Pompeselli, the typical contrast agents are iodine-containing agents that are ionic or nonionic. The ionic compounds have a higher osmolality than the nonionic compounds. The common side effects of contrast agents like nausea, vomiting, and pain in the artery being studied are related to hyperosmolality. Thus, the use of nonionic agents has mostly supplanted that of ionic agents [27]. Allergic reaction is also more common with ionic agents and might be avoided by combining their use with the administration of steroids and antihistamines prior to angiography [27].

The incidence of contrast-induced nephrotoxicity (CIN) is higher in diabetic patients, particularly in type I diabetics. Preexisting renal dysfunction, which is more common in diabetics, is a significant risk factor for developing nephropathy. The risk of CIN can be reduced by prehydration with intravenous normal saline or sodium bicarbonate solution. The type of contrast agent and volume of contrast are not independent factors in the development of nephrotoxicity [27, 28].

Other strategies to reduce the risk of CIN include the use of half-strength contrast to reduce contrast volume and the use of CO_2 for more proximal larger vessels such as the aorta, iliac, and femoral arteries. The use of gadolinium as contrast for patients with renal insufficiency has mostly been stopped for reasons that will be discussed later. Finally, selective catheterization deep into the vascular tree, such as the distal superficial femoral artery, can be used to better image the popliteal and tibial arteries and reduce contrast volumes.

Computerized Tomographic Angiography

High-speed spiral CT scanners that acquire raw data over continuous volume rather than discontinuous slices allow for collection of major amounts of data that may be reformatted into three-dimensional reconstruction of the vascular system. The benefits of CT angiography (CTA) include rapid acquisition times with the contrast administered intravenously. CTA also provides good resolution of the tibial arteries. According to Schaper, two meta-analyses showed that sensitivity and specificity for detecting a stenosis of at least 50 % per segment were 92–95 % and 93–96 %, respectively. The disadvantages of CTA include the use of relatively high doses of ionizing radiation and ionic contrast agents. Most CTA angiogram protocols require more contrast volume than conventional angiogram and therefore carry risk of nephrotoxicity [27, 28]. Other disadvantages include potential artifacts caused by the artificial reconstruction of the images in postprocessing. The artifacts may include motion artifact, volume averaging, and stair-step artifact. Differentiating calcium in the vessel wall from intravascular contrast can also be difficult. Knowing how to alter the CT image "window" may be crucial to differentiating calcium from contrast, particularly in the small tibial vessels.

Magnetic Resonance Angiography

Magnetic resonance angiography (MRA) is a noninvasive imaging modality that can be helpful in PAD patients. MRA can be done with or without contrast. When done without contrast, the usual MR technique employs time-of-flight (TOF) angiography and rapid sequence T1-weighted images. This technique is designed to, "accentuate the signal from flowing blood and attenuate that from non-moving structures and tissues with signal characteristics different from blood" [27]. Thus the bloodstream appears white or brighter on the displayed images.

Contrast-enhanced MRA is a low invasive imaging method. The contrast agent gadolinium is administered after an unenhanced mask image of the body part under study is obtained. In this way contrast-enhanced MRA is similar to digital subtraction angiography. Contrast-enhanced MRA offers superior image resolution and has mostly replaced noncontrast MRA. However, contrast-enhanced MRA has some drawbacks such as long acquisition times that require proper timing of the image acquisition. The quality of images as a function of time is referred to as temporal resolution. Improper timing of image acquisition can lead to problems such as venous contamination of the arterial images [27].

Much more problematic and limiting to the use of gadolinium for contrast-enhanced MRA is the condition known as nephrogenic systemic fibrosis (NSF). In NSF the skin thickens and contracts on the extremities and trunks. Some cases have reported organ fibrosis as well. As a result of NSF, patients may suffer severe physical limitations and hardships, organ damage, or even death. NSF after gadolinium administration has occurred in patients with all levels of renal insufficiency or failure. NSF has not been reported in patients with normal renal function. It is currently recommended that gadolinium contrast agents not be administered in patients with glomerular filtration rates less than 30 mL/min or acute renal insufficiency [27].

Management of the Diabetic Foot

Treatment selection and timing of treatment for diabetic foot ulcers depend on factors such as the extent of the foot wound, infection, and ischemia. First one should determine if a foot is salvageable. A foot with extensive non-reconstructable tissue loss or advanced sepsis from the foot should be considered for primary amputation. Other individual patient circumstances such as severe medical comorbidities, lower

extremity contractures, and nonfunctional bedridden status must be considered and should likely lead the surgeon to suggest primary amputation.

Medical Management

Medical management of the diabetic foot begins with preventive care. This includes strict glycemic control and modification of other cardiovascular risk factors like hypertension, hypercholesterolemia, and smoking. According to a review by Singh, patient education about proper foot care and hygiene improves short-term knowledge and may modestly reduce risk of foot ulceration and amputation in diabetics. The review also found that when physicians were educated with the LEAP (Lower Extremity Amputation Prevention) project, documented foot care education improved from 38 to 48 % over 9 months, appropriate foot care self-management increased from 32 to 48 %, and there was a trend toward reduced lower extremity amputations [29].

The first active step in treating any diabetic foot ulcer, particularly neuropathic ulcers, is off-loading and weight-bearing restriction. The ulcer must be protected from excessive pressure by special shoes or padding. Cavanaugh reviewed practices for off-loading the diabetic foot for ulcer prevention and healing. He found that standard therapeutic footwear is not effective in ulcer healing. He concludes that the total contact cast is the most effective modality to heal an uncomplicated plantar ulcer in a short time frame [30]. Clearly, input from a podiatrist is paramount at this stage.

When a limb-threatening diabetic foot infection is identified, the patient requires immediate hospitalization and intravenous antibiotics. Empiric broad-spectrum antibiotics should be started as most diabetic foot infections are polymicrobial. Deep wound cultures should be obtained, hopefully, prior to initiating the antibiotics. Table 32.4 summarizes several of the antibiotic trials for treatment of diabetic foot infections. The largest trial by Lipsky in 2005, like the remaining studies, did not show any difference in eradication rates, clinical outcomes, and adverse events between the

Table 32.4 Summary of antibiotic trials for diabetic foot infections

Author	Antibiotic regimens	Design	Patients (no.)	Treatment duration (days)	Reported results	95 % CI	*P*
Grayson 1994	Ampicillin/sulbactam	Randomized, double-blind, single-center	48	13 ± 6.5	81 % cure; 67 % eradication		NS
	Imipenem/cilastatin		48	14.8 ± 8.6	85 % cure; 75 % eradication		
Lipsky 2004	Linezolid IV or PO, ± aztreonam	Randomized, open-label, multicenter	241 (5 % aztreonam)	17.2 ± 7.9	81 % overall cure	–0.1 to 20.1	NS
	Ampicillin/sulbactam, or amoxicillin/clavulanate ± vancomycin or aztreonam		120 (9.6 % vancomycin, 2.5 % aztreonam)	16.5 ± 7.9	71 % overall cure		
Clay 2004	Ceftriaxone + metronidazole	Randomized, open-label, single-center	36	44	72 % treatment success		NS
	Ticarcillin/clavulanate		34	4	76 % treatment success		
Harkless 2005	Piperacillin/tazobactam ± vancomycin	Randomized, open-label, multicenter	155	9 median	81 % cure or improvement	12.9–9.1	0.124
	Ampicillin/sulbactam ± vancomycin		159	10 median	83.1 % cure or improvement		
Lipsky 2005	Daptomycin ± aztreonam or metronidazole	Randomized, open-label, multicenter	47 (38 % aztreonam)	7–14	66 % cure	–14.4 to 21.8	NS
	Comparator (vancomycin or semisynthetic PCN) ± aztreonam or metronidazole		56	7–14	70 % cure		
			(29)				
			(27)				
			(41 % aztreonam)				
Lipsky 2005	Ertapenem ± vancomycin	Randomized, double-blind, multicenter	295 (2.3 % vancomycin)	11.1	87 % favorable clinical response	–6.3 to 9.1	NS
	Piperacillin/tazobactam ± vancomycin		291 (1.7 % vancomycin)	11.3	83 % favorable clinical response		

CI confidence interval, *IV* intravenous, *PCN* penicillin, *PO* oral administration

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Table 32.5 Summary of randomized trials comparing hyperbaric oxygen therapy to standard wound care

Author	Patients	Treatment sessions	Reported results	*P*
Faglia 1996	Five HBOT + standard wound care	38.8 ± 8	8.6 % major amputation (RR, 0.26; 95 % CI, 0.08–0.84)	0.016
	33 standard wound care		33.3 % major amputation	
Abidia 2003	Eight HBOT	30	62.5 % ulcer healing	
			100 % median ↓ wound area 6 weeks	0.027
			100 % median ↓ wound area 6 months	NS
	Eight control (air)	30	12.5 % ulcer healing	
			52 % median ↓ wound area 6 weeks	
			95 % median ↓ wound area 6 months	
Kessler 2003	14 HBOT + standard wound care	20	Ulcer size decrease	
			42 % ± 25 % (day 15)	0.037
			48 % ± 30 % (day 30)	NS
	14 standard wound care		22 ± 17 % (day 15)	
			42 ± 27 % (day 30)	
Duzgun 2008	50 HBOT + standard wound care	60–90	66 % healing without surgery	<0.05
			8 % distal amputation	<0.05
			0 % major amputation	<0.05
	50 standard wound care		0 % healing with surgery	<0.05
			48 % distal amputation	<0.05
			34 % major amputation	<0.05

CI confidence interval, *HBOT* hyperbaric oxygen therapy, *RR* relative risk
From Kalish J, Hamdan A. Management of diabetic foot problems. J Vasc Surg. 2010;51:476–86. Reprinted with permission from Elsevier Limited

study drugs. One should notice the relatively high failure rates of 11–12 % for moderate infections and 19–30 % for severe infections. This highlights the limitation of treating diabetic foot ulcers with antibiotics alone [8].

Hyperbaric oxygen treatment may be an adjunct to facilitate wound healing in diabetic foot ulcers. The beneficial mechanisms of hyperbaric oxygen therapy are reported to include an antimicrobial effect and increased oxygenation at the ulcer tissue bed via stimulation of angiogenesis [8, 31]. Table 32.5 summarizes trials comparing hyperbaric oxygen therapy to standard wound care for healing diabetic foot ulcers. A 2010 study by Londahl compared patients with chronic diabetic foot ulcers receiving either hyperbaric oxygen therapy ($n=47$) or hyperbaric air therapy ($n=41$). At 1-year follow-up, 53 % of the HBO patients remained healed versus 28 % of the hyperbaric air patients. In an accompanying editorial, Boulton suggests that, "this study puts HBO on firmer ground for diabetic patients with chronic foot ulcers who do not respond to standard therapy and in whom vascular reconstruction is not possible" [31].

Surgical Management

One key to understanding the surgical management of diabetic foot ulcers and infections is that they often extend deeper into the foot than apparent from the skin surface. A deep space abscess is frequently present when the wound looks fairly innocuous externally. Figure 32.5 shows the effects of a deep space infection. The goal of surgical intervention is to evacuate any abscess, remove necrotic tissue, and minimize the risk of further infection and tissue damage. Fisher has proposed a stepwise surgical approach to management of diabetic foot infections [32]. This strategy is depicted in Fig. 32.6. First, an initial skin incision must be made that will allow access to and drainage of all infected tissues while taking into account future surgical plans like eventual wound closure. These incisions are directed by an understanding of the three major plantar spaces: the medial, central, and lateral spaces. Next the wound is investigated in order to locate all possible abscess collections, foreign bodies, necrotic tissues, tracts, and fistulas. Debridement then removes all nonviable tissues. Wound lavage and copious irrigation help reduce the bacterial burden in the wound. The choice of irrigation fluid, normal saline versus antibiotic solution, is likely less important than the volume of irrigation and is left to operator's choice. Final closure of the wound may be attempted once infection is under control and adequate viable soft tissues are present. Closure most often occurs after serial debridement, local wound care, and negative pressure wound therapy to prepare the wound bed.

Revascularization

The indications for revascularization in diabetics are no different as compared to nondiabetic patient population. These indications include the usual incapacitating claudication, rest

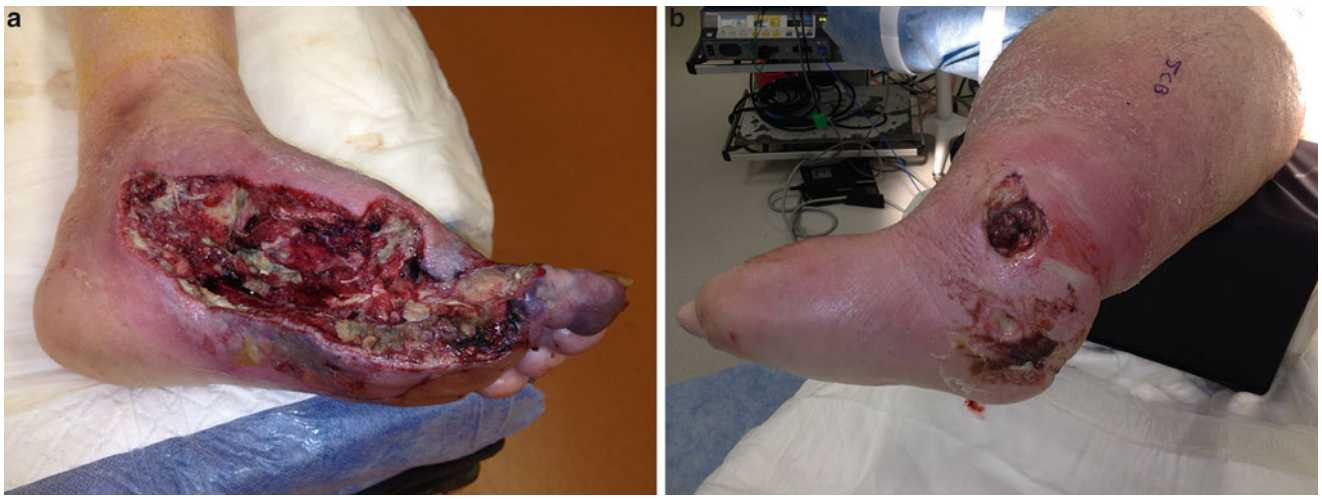

Fig. 32.5 Examples of diabetic foot infection. (**a**) Diabetic foot with extensive deep space infection after initial debridement. (**b**) Severe diabetic foot infection and ulceration in patient with Charcot foot

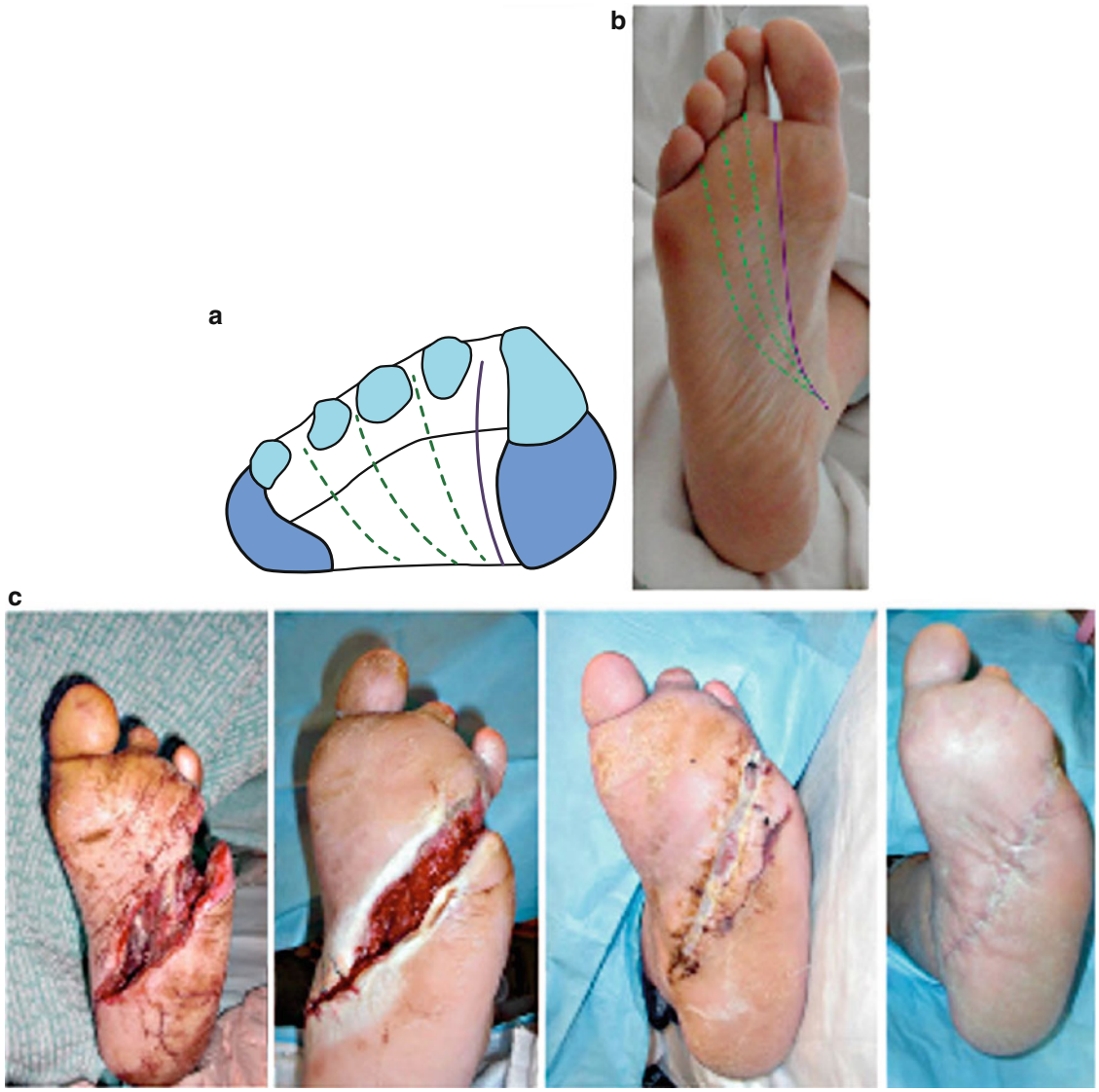

Fig. 32.6 Surgical incisions for diabetic foot infections. From Fisher TK, Scimea CL, Bharara M, Mills JL Sr, Armstrong DG. A step-wise approach for the surgical management of diabetic foot infections. J Vasc Surg. 2010 Sep;52(3 Suppl):72S–75S. Reprinted with permission from Elsevier

pain, and tissue loss such as ulcers or gangrene. After physical exam and noninvasive physiological testing, the severity of arterial ischemia should be determined. In some cases appropriately selected diabetic foot ulcers may heal without revascularization and this is guided by the physiologic testing. If the decision is made to revascularize the diabetic limb in order to heal an ischemic ulcer, the goal of therapy is to restore pulsatile blood flow to the foot.

The classic distribution of arterial occlusive disease in diabetics involves the tibial vessels. Therefore, diabetic limb salvage often involves infragenicular, or distal, revascularization. Ipsilateral greater saphenous vein is the conduit of choice for surgical distal revascularization. When vein is used for distal bypasses in diabetics, comparable patency and limb salvage rates can be obtained as for those performed in nondiabetics [11]. Of note, these results are comparable despite more bypasses performed for limb salvage in the diabetic group.

Diabetic patients often present with extensive tissue loss in the foot. The relative value of endovascular versus open surgical revascularization for diabetic limb salvage must be considered when choosing a revascularization strategy. Endovascular therapy for critical limb ischemia leads to high restenosis rates attributable to risk factors of age, diabetes, and chronic renal failure [34]. In 2010, Abularrage assessed the influence of diabetes on long-term outcomes of percutaneous transluminal angioplasty, with or without stenting in patients with peripheral vascular disease. He concluded that diabetes is an independent predictor of decreased long-term primary patency after PTA/stent [33].

We have presented data that indicate surgical bypass provides faster and more complete healing with wounds greater than 2-cm diameter when compared to endovascular revascularization [34]. Bypasses ($n=142$) and endovascular procedures ($n=148$) were performed for limb salvage in a cohort of patients that had 58 % diabetics. Of those presenting with larger wounds, 76 % healed completely after bypass compared with only 41 % after endovascular therapy. This difference only reached statistical significance in the group with initial wounds greater than 2-cm diameter. Median time to healing was also 34 days faster in the surgical group compared to the endovascular group. While the study has selection bias and a variety of endovascular techniques making firm conclusions difficult, we prefer bypass as the first choice for patients with tissue loss and long-segment tibial artery occlusive disease. Endovascular therapy is offered for limb salvage in critical limb ischemia patient that is deemed too high risk for surgery.

Surgical Bypass Options

Ipsilateral greater saphenous vein is the conduit of choice for distal bypass to tibial arteries. However, despite the use of duplex ultrasound vein mapping, 30 % of patients that need distal revascularization do not have adequate saphenous vein. That percentage increases to 50 for patients needing reoperation for limb salvage. Alternative conduits include arm vein, lesser saphenous vein, composite veins, and polytetrafluoroethylene (PTFE) with or without adjunctive techniques. The results of these alternative conduits are not equivalent to saphenous vein bypass [35–38].

Historically, tibial artery bypasses using PTFE anastomosed directly to the artery have dismal results. One-year patency rates between 20 and 50 % with 3-year patency rates of 12–40 % have been reported [39, 40]. Failure of the bypass is secondary to the technical difficulties of anastomosing the noncompliant prosthetic graft to a small diseased often calcified artery and aggressive myointimal hyperplasia that forms at the toe and heel of the graft [41].

Adjunctive procedures have been devised to increase patency of the prosthetic tibial bypasses. These maneuvers have included the Miller cuff and the Taylor "patch." The goal of these adjuncts was to optimize anastomotic surface area, provide a biological buffer, and possibly provide a mechanical buffer by increasing compliance at the anastomosis by placing a segment of vein between the prosthetic graft and the recipient tibial artery. These adjuncts improved prosthetic graft patency, but were technically challenging. Our group popularized the distal vein patch (DVP) technique [42, 43]. In this technique a segment of suitable vein is attached to the recipient artery as a simple Linton vein patch. The PTFE graft is then anastomosed to the vein patch to complete the bypass. In an early series, the DVP bypass resulted in 62 % primary patency rate and 79 % limb salvage at 4-year follow-up. The addition of a distal arteriovenous fistula to the DVP (the patchula) resulted in 62 % patency and 57 % limb salvage at 24 months in a patient cohort otherwise being considered for primary amputation [44].

The "angiosome" concept divides the body into three-dimensional vascular territories supplied by specific source arteries [45]. The foot has six angiosomes arising from the posterior tibial artery (three), anterior tibial artery (one), and peroneal arteries (two). A full description of the arteries and their related angiosomes is provided by Attinger [46]. Direct revascularization involves the artery supplying the angiosome in which the wound is located. Indirect revascularization involves an artery that does not directly perfuse the ischemic angiosome. A study by our group demonstrated a significant advantage in wound healing when direct revascularization was performed (91 %) compared to indirect revascularization (62 %). Similar conclusions were found when a study looked at direct versus indirect endovascular revascularization [47]. When there is a choice of target vessels for revascularization, one should consider the artery that will directly perfuse the angiosome feeding the wound in question.

The Limb Salvage Team

It is well established that limb salvage teams can reduce the rate of major amputations in diabetic foot ulcer patients. Kim et al. states that the major amputation rate is reduced by more than 50 % when diabetic foot patients are treated by a team approach [48]. Driver et al. cite several studies that show as much as a 78 % reduction in major amputations after implementing a multidisciplinary team for diabetic foot patients [49]. They site another study of a podiatry and vascular surgery team that produced 83 % limb salvage rates at 5 years. Through economic modeling and studies, Driver shows that multidisciplinary limb salvage care following established guidelines is cost effective and even cost saving compared to usual fragmented care. Sumpio et al. found that establishing an identifiable limb salvage "center" can increase patient referrals for participating physicians [50].

The multidisciplinary limb salvage team optimally includes vascular surgeons, podiatrists, interventionalists, infectious disease specialists, plastic and reconstructive surgeons, diabetologists, physical therapists, and orthotists. Kim et al. discuss the role of the podiatrist in prevention and treatment of diabetic foot ulcers [48]. Kim nicely describes the importance of podiatrists as "biomechanical surgeons" as they "rebalance and reconstruct the biomechanically unstable or mal-positioned foot." Rogers et al. detail the "irreducible minimum" of a diabetic podiatrist and vascular surgeon for a "toe and flow" program to prevent, diagnose, and treat diabetic foot patients and their complications [51].

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