The Evaluation of Lower-Extremity Ulcers

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ABSTRACT

Lower-limb ulceration is prevalent in Western countries. There are many different types of ulcers with several causes. The most prevalent are those due to vascular disease, of which venous is the most common, accounting for over two-thirds of all types of ulcers. There are also many other causes for ulceration such as malignancy, infections, and skin, drug-induced, and autoimmune diseases. The ulcers have different characteristics, which may be differentiated by the history and clinical examination of the patients. However, objective documentation for the ulcer etiology is necessary prior to instigating treatment. The methods for diagnosing the causes for the ulcers include plethysmography, ultrasound, angiography, computer tomography, magnetic resonance imaging, and skin biopsy. All these tests should be used in conjunction with the clinical presentation of the patient. They should be performed in a cost-effective manner to avoid delays in diagnosis and reduce costs and usage of resources.

KEYWORDS: Lower-limb ulcers, clinical examination, diagnostic tests

Objectives: Upon completion of this article, the reader will be able to list the characteristics of the lower-limb ulcers, their differential diagnosis, and all the available tests used on their diagnosis and management.
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PREVALENCE AND IMPACT OF ULCERATION

Lower-extremity ulceration is a debilitating phenomenon not only affecting the patient directly but having a great impact on the economy since a significant amount of recourses are spent every year to treat, prevent, or decelerate the progression of the disease. The prevalence of lower-extremity ulceration is 0.18 to 2%, and in patients over 65 years of age, it is up to 5%.

In the United States, for chronic venous disease only at least 4.6 million work days are lost and over $1 billion is being spent per year.[1,2] Adding all other causes for ulceration, this increases the overall burden in our society significantly. Research related to causes and treatment of ulceration is prompted by the recurrent nature of the disease, the ineffectiveness of treatments, and the high cost related to health care. It is important to understand the pathophysiology and clinical characteristics of the different types of ulcers and to recognize the risk factors, diagnostic tools, and treatment modalities.

TYPES OF ULCERS

There are many different types of lower-limb ulceration. These include venous, arterial, neurotrophic, lymphatic, malignant, infectious, medication induced,

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Table 1 Differential Diagnosis of Common Leg Ulcers

Type	History	Usual Location	Pain	Bleeding with Manipulation	Lesion Characteristics	Surrounding Inflammation	Associated Findings
Ischemic/ arterial	Smoking, intermittent claudications	Distal, on dorsum of foot or toes, over bony prominences	Severe, particularly at night; relieved by dependency	Little or none	Irregular edge; poor granulation tissue, dry necrotic base; round or punched-out with sharp demarcation	Absent	Trophic changes of chronic ischemia, pale, hair loss, atrophic skin, cool feet; absence of pulses, prolonged capillary refill (>4–5 s); ABI <0.5; dependent rubor, elevation pallor
Venous	Varicose veins, DVT, trauma, surgery, multiple pregnancies; aching/swelling worse at end of day, relieved with elevation	Lower third of leg (gaiter area); between malleolus and lower calf, majority at medial malleolus	Mild; relieved by elevation	Venous ooze	Shallow, irregular/shaggy shape; granulating base; flat or steep elevation margins; fibrinous material at ulcer bed with moderate to heavy exudate	Present	Lipodermatofibrosis/ lipodermatosclerosis, pigmentation, edema, atrophie blanche; telangiectasia; normal capillary refill time (<3 s), normal ABI
Neurotrophic	Numbness, paresthesias, burning, loss sensation in foot, DM	Under calluses or pressure points (e.g., plantar aspect of first or fifth metatarsophalangeal joint)	None	May be brisk	Punched-out, with deep sinus, variable depth partial thickness to severe involving tendon, fascia, joint capsule, or bone	Present	Demonstrable neuropathy, may be associated with underlying osteomyelitis
Vasculitis	History of primary or secondary connective tissue disease	Pretibial and dorsum of foot but not always geographically limited	Extremely painful	Hemorrhagic vesicle	Multiple, punched-out, inflamed indurated base (pathergy phenomenon)	Present, surrounding skin shows reticulated vascular pattern	Fat necrosis/chronic panniculitis on pathology
Hypertensive (local infarct)	Normal pulses	Lateral malleoli	Severe	—	Black necrosis	Present	Also called Martorell's ulcer; seen in patients with prolonged/ suboptimal controlled hypertension
Pyoderma Gangrenosum	Unknown pathogenesis	Develops in sites of previous trauma, around scars, donor sites used for grafting	Severe	Little or none	Ulceration with purulent base; well-defined, bluish, undermined borders; surrounding erythema; deep necrotic ulcer	Noninfective ulcer, surrounding inflammation	Seen with inflammatory bowel disease, immunodeficient states, myeloma, leukemia, Behcet's syndrome

ABI, ankle-brachial pressure index; DM, diabetes mellitus; DVT, deep vein thrombosis.

and inflammatory. The characteristics of the categories of ulcers are seen in Table 1.

Venous

Most leg ulcers are caused by venous disease alone (72%).[3] According to a Swedish population of 270,800, ulcers of venous origin comprised 54% of the total lower-extremity ulcers (Fig. 1). The median duration of ulcer was significantly longer for venous ulcers versus nonvenous ulcers; a ration of 13.4 versus 2.5 years ($P < 0.001$).[4] A recent study has shown that 95% of venous ulcers were predominately confined in the gaiter area above the medial malleolus, 3.2% in the calf, and 1.8 in the dorsum of the foot.[3]

The main mechanisms behind venous ulcers are reflux, venous outflow obstruction, or the combination of the two.[5] Reflux is the most common reason, whereas obstruction is rare. Reflux and obstruction have the highest odds for skin damage.[6] Malfunction in the foot and calf muscle pumps by itself could cause ulceration, but it is most prevalent in patients with venous disease.[5] All the causes listed above result in an increased ambulatory venous pressure, which is transmitted to the capillaries of the subcutaneous tissues and the skin.[7] This eventually leads though a cascade of inflammatory events into skin damage and ulcer development.[8,9]

Arterial

Ulcers secondary to arterial disease are the second most common, ranging from 10 to 30% of lower-extremity ulcers.[10–12] Typically, these lesions are painful and affect the toes and/or pressure points, such as the heel, malleoli, or anterior shin (Fig. 2).[10] Many arterial pathologies can lead to arterial ulcers, but the one unifying cause is arterial obstruction. Peripheral arterial disease (PAD) is a major contributor, affecting 8 to 12 million Americans with significant associated morbidity and mortality.[13] Atherosclerotic obstruction usually occurs in the iliac, femoropopliteal, and the distal branches (peroneal and tibial arteries). In some cases, only small-sized arterial branches are affected, leading to limited infarctions of skin and subcutaneous tissue.[11] Patients with PAD have heightened endothelial and platelet activation secondary to a proinflammatory/prothrombotic state, among other complex processes. Some risk factors for PAD include smoking, diabetes mellitus, elevated low-density lipoprotein, hypertension, elevated fibrinogen, and advanced age.[14,15] Consequently, lower-extremity ulceration in these patients could be caused by more than one etiology. Thrombotic events due to emboli from the heart, aneurysms, plaques, and hypercoagulable states may also be responsible for developing ischemic ulcers.[16]

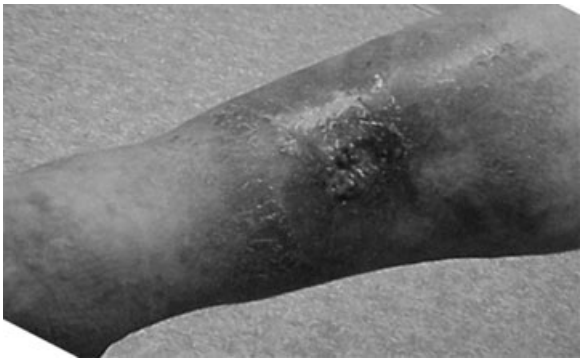

Figure 1 Venous ulcer in the medial calf of the right lower extremity. The patient had chronic venous disease of over 15 years in duration. Prolonged reflux was found in the great saphenous vein and in many thigh and calf tributaries. Multiple perforator veins were dilated and incompetent in the calf.

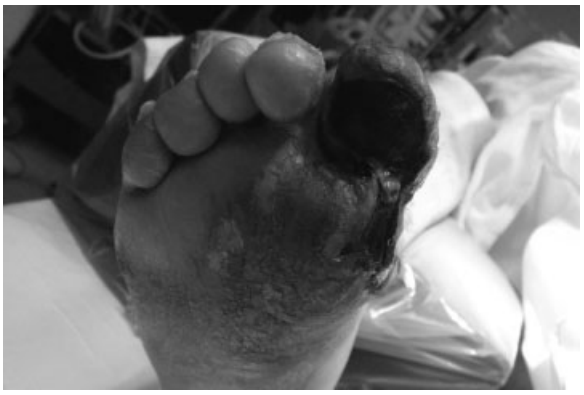

Figure 2 Tissue loss with gangrenous and ulcerative changes in the big toe of the right lower extremity. The patient had multilevel arterial disease involving the pelvic thigh and calf arteries.

Neuropathic

The next most common ulcers are neuropathic in origin, and comprise 15 to 25% of leg ulcers.[10,11] Typically these are patients with diabetes that is poorly controlled and/or long-standing. About 60 to 70% of diabetics have only neuropathy, 15 to 20% have PAD only, and 15 to 20% have a mixture of both. The neuropathy that these patients suffer is threefold: motor, sensory, and autonomic. Motor neuropathy causes atrophy of the muscles of the foot and leg with clawing of the toes and pronouncement of the metatarsal heads, sensory neuropathy results in lost sensation with repetitive trauma to the feet, and autonomic neuropathy alters skin turgor, promoting acceleration of ulcer formation.[17,18] These neuropathic features, coupled with the propensity for diabetics to heal poorly due to decreased synthesis of collagen, abnormal synthesis of extracellular matrix proteins, and decreased fibroblast proliferation, create the perfect milieu for a nonhealing ulcer. Furthermore, these

Table 2 Infectious Causes of Limb Ulcers

Disease	Pathogens
Erysipelas (bullosa)	*Streptococcus pyogenes*
Fasciitis necroticans	*Streptococcus hemolyticus*
Ulcerating pyoderma	*Staphylococcus aureus*
Gas gangrene	Clostridium
Ecthyma gangrenosum	Pseudomonas
Septic embolism	Meningococcus and others
Anthrax	*Bacillus anthracis*
Diphtheria	*Corynebacterium diphtheriae*
Osteomyelitis	Several microorganisms
Herpes, CMV, lues maligna	HSV, CMV, *Treponema pallidum*
Tularemia	*Francisella tularensis*
Tropical ulcer	Bacteroides, *Borrelia vincentii*, and other bacteria
Maduromycosis (eumycetoma/mycetoma)	*Nocardia brasiliensis*, *Exophiala jeanselmei*
Chromoblastomycosis; coccidiomycosis; sporotrichosis; granuloma trichophyticum	Several bacteria; *Coccidioides immitis* or *Coccidioides posadasii*; *Sporothrix schenckii*; Dermatophytes of the genera Trichophyton and Microsporum
Histoplasmosis	*Histoplasma capsulatum*
Bacillary angiomatosis	*Bartonella henselae* or *Bartonella quintana*
Ulcerating cutaneous tuberculosis	Mycobacterium tuberculosis
Amoebiasis	*Entamoeba histolytica*, Acanthamoeba
Leishmaniasis	*Leishmania donovani* complex, *Leishmania mexicana* complex, *Leishmaniatropica*; *Leishmaniamajor*; *Leishmaniaaethiopica*
Leprosy	*Mycobacterium leprae* and *Mycobacterium lepromatosis*

CMV, cytomegalovirus; HSV, herpes simplex virus.

patients are susceptible to wound infections, secondary to elevated glucose levels and/or impaired granulocytic function and chemotaxis.[11]

Other rarer conditions that may cause neuropathic ulcers include alcoholism, leprosy, tabes dorsalis, spina bifida, paraplegia, poliomyelitis, multiple sclerosis, and syringomyelia.[11,18]

Lymphatic

There is little information in the literature about the prevalence of ulceration in patients with lymphedema. Unlike patients with arterial and venous disease, only a few patients with lymphedema develop ulceration. In a large study of patients with chronic leg ulceration where the etiology was determined, only 17 of the 689 limbs (2.5%) had lymphatic etiology.[3] Another 11 patients (1.6%) had mixed lymphatic and venous disease. However, no other information was given in that study for the characteristics of the ulcer or the patients with the lymphatic disease.

Infectious

Multiple studies site ulceration in the lower extremity due to infectious causes. These include mostly a variety of bacteria, but also viruses, parasites, and fungi. There is no large experience with the infectious causes as they have been reported as a small series or case reports. A list of the different pathogens is displayed in Table 2.[11] The mechanisms by which the infectious ulcers are caused are dependent on the pathogens.

Mixed Etiology

In several studies it has been shown that many ulcers have more than one etiology.[3,4,19,20] In a study of 689 limbs, 100 (14.5%) had developed ulceration from mixed arteriovenous etiology and 11 limbs (1.6%) from mixed lymphedema and venous disease.[3] Ulcers from arteriovenous etiology may develop anywhere on the calf or foot, and healing requires correction of arterial insufficiency. Though the dominant disease process must be treated first, in arteriovenous ulcers it is imperative to determine first the degree of arterial insufficiency by the ankle-brachial pressure index (ABI).[20] Besides arteriovenous etiology, patients with rheumatoid arthritis have been described to have limb ulcers, and half of the cases had concomitant arterial or venous disease. Revascularization or vein surgery on these patients proved to improve healing of limb ulcers.[3,19]

OTHERS CAUSES

Recently it has been shown that super-obese patients may get venous ulcers without having venous disease

Table 3 Other Causes of Limb Ulcers

Causes	
Physical or chemical injury	Pressure (decubitus), pressure by shoes, plaster of Paris, orthopedic appliances, compression bandages, trauma, burn wounds, freezing, electricity, intra-articular injection of yttrium-90, chemical (corrosive agents), sclerotherapy, artificial (automutilation)
Malignancy	Sarcoma, lymphoma, SCC, BCC, metastatic cancer, Kaposi's and pseudo-Kaposi's sarcoma, cutaneous T-cell and B-cell lymphoma, Hodgkin's disease
Drug-induced	Steroid ulcus (intralesional injection), vaccination ulcer (BCG), halogens, ergotamine, methotrexate, hydroxyurea, paravasal injection of cytostatic and other drugs, granulocyte colony-stimulating factor
Ulcerating skin diseases	Pseudoepitheliomatous hyperplasia, epithelioma, *Pyoderma gangrenosum*, pemphigoid, panniculitis, periarteritis nodosa, erythema induratum, Behcet's disease, cutaneous discoid and systemic lupus erythematosus, scleroderma, lichen planus, keratosis actinica, contact dermatitis, fat necrosis or pancreatic fat necrosis
Autoimmune	Dermatitis, lupus, rheumatoid arthritis, vessel: small-vessel leukocytoclastic vasculitis, microscopic polyangiitis, Wegener's granulomatosis, allergic granulomatosis (Churg–Strauss), Henoch–Schonlein purpura, essential cryoglobulinemic vasculitis, erythema induratum Bazin, livedo reticularis, livedo vasculitis and Sneddon syndrome, polyarteritis nodosa, Kawasaki disease
Metabolic	Diabetes mellitus, necrobiosis lipoidica, porphyria cutanea tarda, gout, calciphylaxis, calcinosis cutis, homocysteinuria, prolidase deficiency, hyperoxaluria
Hematologic disorders	Sickle cell anemia, thalassemia, hereditary spherocytosis, glucose-6-phosphate dehydrogenase deficiency, essential thrombocythemia, thrombotic thrombocytopenic purpura, granulocytopenia, polycythemia, leukemia, Waldenstrom's disease, multiple myeloma, cryofibrinogenemia, purpura, hyperglobulinemia, cold agglutinins
Clotting disorders	Factor V Leiden, lupus anticoagulant, antiphospholipid syndrome, disturbed fibrinolysis, factor XIII deficiency, antithrombin III deficiency, protein C or S deficiency, Marcoumar necrosis, large hematoma, purpura fulminans, diffuse intravasal coagulation

detected.[21] These ulcers are probably caused by the functional obstruction of the venous and lymphatic flow, the need for the patients to sleep with head elevation, and the lack of mobility and exercise. As obesity is becoming a very common problem, it is likely that these types of ulcers may increase. Another less common cause of limb ulceration is sickle cell disease. In a recent study, the prevalence rates ranged from 8 to 10% of patients with sickle cell disease aged 10 to 50 years.[22,23] It is thought that vessel obstruction by sickle cells, increased venous and capillary pressure, secondary bacterial infection, and decreased oxygen-carrying capacity of the blood all contribute to the development of the ulcer. The medial malleoli are the most common site of leg ulceration in sickle cell disease and in other chronic hemolytic anemias, suggesting perhaps that stasis may play a role in leg ulceration associated with chronic hemolytic anemia.[22]

Pyoderma gangrenosum, a noninfective ulcer, is another cause of less common limb ulceration. It may be associated with inflammatory bowel disease, inflammatory arthropathies, or myeloproliferative disorders.[18] Half of these ulcers are associated with chronic disease and the other half are idiopathic. Lesions on the lower limbs start as painful pustules with rapid development of necrosis and ulceration. Fully established ulcers are single or multiple with well-defined, raised, purple, serpiginous and undermined borders.[22]

Studies report that 9 to 10% of patients with rheumatoid arthritis and ~25% of patients with Felty syndrome have leg ulcers. The etiologies of these ulcers are frequently multifactorial.[22] Other rare causes on limb ulcers are included in Table 3.

CLINICAL EXAMINATION

History

To determine the cause of any lower-extremity ulcer, a complete physical exam in imperative to accurately assess the patient's condition. Any comorbid conditions that may contribute to the development of the ulcers, such as diabetes mellitus, autoimmune disease, peripheral vascular disease, atherosclerosis, inflammatory bowel disease, and connective tissue disease, must be investigated. Any history of deep vein thrombosis, recent surgery, prolonged bed rest, pregnancy, multiple spontaneous abortions or genetic causes (i.e., factor V Leiden, antithrombin mutation, protein S deficiency, protein C deficiency, prothrombin G20210A mutation) may suggest a prothrombotic state and the presence of venous disease. Patients with venous ulcers

on physical examination describe a sensation of heaviness when they stand, which is relieved when legs are elevated.

History of heavy smoking and drinking can contribute to vascular disease and eventually leg ulceration. Inquires about patient social and occupational situation must be made—for example, patients who stand during work for majority of the day can exacerbate preexisting disease. An understanding of the patient's history of venous and arterial signs and symptoms and consideration of body shape (especially the morbidly obese and extremely tall) influence the treatment regimen for many leg ulcers.[24]

Neurotrophic ulcers from diabetes present with numbness, paresthesias, burning, or loss of sensation in the feet. Poor diabetic control not only causes neuropathies but increases risks of leg infections and impairs wound healing. Seldom, isolated cases of rare ulcers have shown that medications can contribute to the development of leg ulcers, such as hydroxyurea, which makes it imperative to ask patients about medications they are on.[11] Previous history of ulcers with recurrent behavior can give insight in the management of leg ulcers.

Skin Assessment

The skin assessment in some cases identifies the underlying pathology. Venous disease may present with some brawny skin, hemosiderin staining, lipodermatosclerosis, reticular or varicose veins, atrophic blanche (patchy areas of ischemia), telangiectasia, and stasis eczema. When evaluating leg ulcers, even though we are tempted to focus only on the ulcer, it is important to evaluate the surrounding tissue. In venous ulcers, the surrounding skin may be erythematous with scaling, irregular shaggy borders, pruritus, crusting, moderate to heavy drainage, and presence of fibrinous material at ulcer bed with good granulating tissue.[18]

On the other hand, patients with arterial disease have trophic changes of chronic ischemia; the skin is pale and often hairless, cool, shiny with thickened nail and changes of foot structure. Arterial ulcers have irregular edges with poor granulation tissue, often deeper, with dry necrotic base and round or punched-out appearance with sharp demarcation. These ulcers may involve structures such as muscle, tendon, and bone in the base. The absence of venous or arterial signs and symptoms raises the possibility of less common causes of ulceration. Sun-damaged skin, Bowen disease, or a history of previous skin cancer treatment is an alert to a malignant lesion. Neurotrophic ulcers, most likely from diabetes, present with punched-out lesions with deep sinus, variable-depth partial thickness to severe, involving tendon, fascia, joint capsule, or bone.

Limb Assessment

A complete clinical examination of the lower extremities should include palpation of pulses and a search for signs of venous hypertension. These signs include prominent veins in the lower extremity, varicose veins, and pigmentation of the skin over the lower leg. Mobility should also be assessed because patients with reduced mobility may develop ulcers in the gaiter area because of venous hypertension resulting from inadequate functioning of the calf muscle pump.[10] Limb assessment includes ankle and calf circumferences of both legs identifying the presence and severity of edema. Leg shape, especially venous changes, can also assist in diagnosis. Some legs will need to be reshaped with compression routines over time to ensure preventive stockings fit after healing.

The very thin leg with an ankle circumference less than 18 cm must be padded out to at least 20 cm before the application of any compression to prevent skin necrosis due to pressure injury.[24] Leg range of motion at ankle/knee/hip should also be assessed to distinguish between pain from inflammation and pain from arterial insufficiency.[18]

Ulcer Assessment

The location of leg ulcers is a key component of any physical exam. Venous leg ulcers usually occur in the gaiter region of the lower leg, most often medially, and are superficial with poorly defined margins. The base of the wound is usually red granulation tissue with moderate to high levels of exudate. Exudate levels vary depending on ulcer size, the presence of leg edema, compression regimens in current use, and the presence or absence of infection. Some obese patients will present with coexisting lymphedema adding to the edema and exudate problems.

Arterial ulcers can occur anywhere on the lower leg and may appear in the gaiter region. Many arterial/ischemic ulcers occur over a bony prominence and have a history of pressure related to the cause. They have sloughy, devitalized tissue in the wound base and low levels of wound exudate. In patients with ulcers on the sole of the foot, the sole should be examined for signs of ascending infection, including proximal tenderness and appearance of pus on proximal compression of the sole. Surrounding calluses are typical of neuropathic ulcerations, and sinus track formation should be explored by probing the wounds.[18]

Neuropathic ulcers occur on the sole of the feet under the metatarsal heads, in the area with the most postural pressure exerted. They are more prevalent in diabetic patients. In diabetics, the ABI number is seldom elevated because these patients' arteries are resistant to compression from the underlying Monckerberg's medial sclerosis.[10]

The degree of discomfort or pain can give clues to the underlying condition. Arterial ulcers are particularly painful at night, can become severe, and are relieved by dependency and made worse by elevation, even to a horizontal position in bed. Venous ulcers are mildly painful, relieved with elevation, and often get relief from a gentle massaging of the surrounding skin.

Any suspicious ulcer should be biopsied to exclude malignancy. Ulcers with a violaceous (purple) border, inflammation, and extreme pain may be related to a vasculitis problem or underlying connective tissue disorder. They often present with a rapid increase in size, severe pain, and necrotic tissue in the wound base. Lesions that present as blisters such as bullous pemphigoid are related to an autoimmune condition and are sometimes "diagnosed" and managed unsuccessfully as a vascular problem.

NONINVASIVE DIAGNOSIS

Clinical examination of the lower extremities must be combined with noninvasive or invasive assessment of the circulation to solidify the clinical impression. Also, diagnostic tests should be performed according to indications based on history and physical examination (Fig. 3).

ABI

ABI testing is very important for the diagnosis of an ischemic ulcer. Ankle blood pressure determination using a cuff sphygmomanometer and a handheld Doppler should ideally be measured after 10 minutes' rest with the cuff placed proximal to the malleoli. The maximum cuff pressure at which the pulse can be heard with the probe is recorded and divided by the systolic blood pressure measured at the brachial artery. ABI values below 0.9 have been widely accepted as evidence of peripheral arterial occlusive disease.[10] ABI can be an inaccurate or invalid because the arteries may be hard to compress due to calcification usually seen in patients with diabetes. In such occasions, a toe pressure is measured as it is most often spared from calcification. ABI testing can be performed before and after exercise to

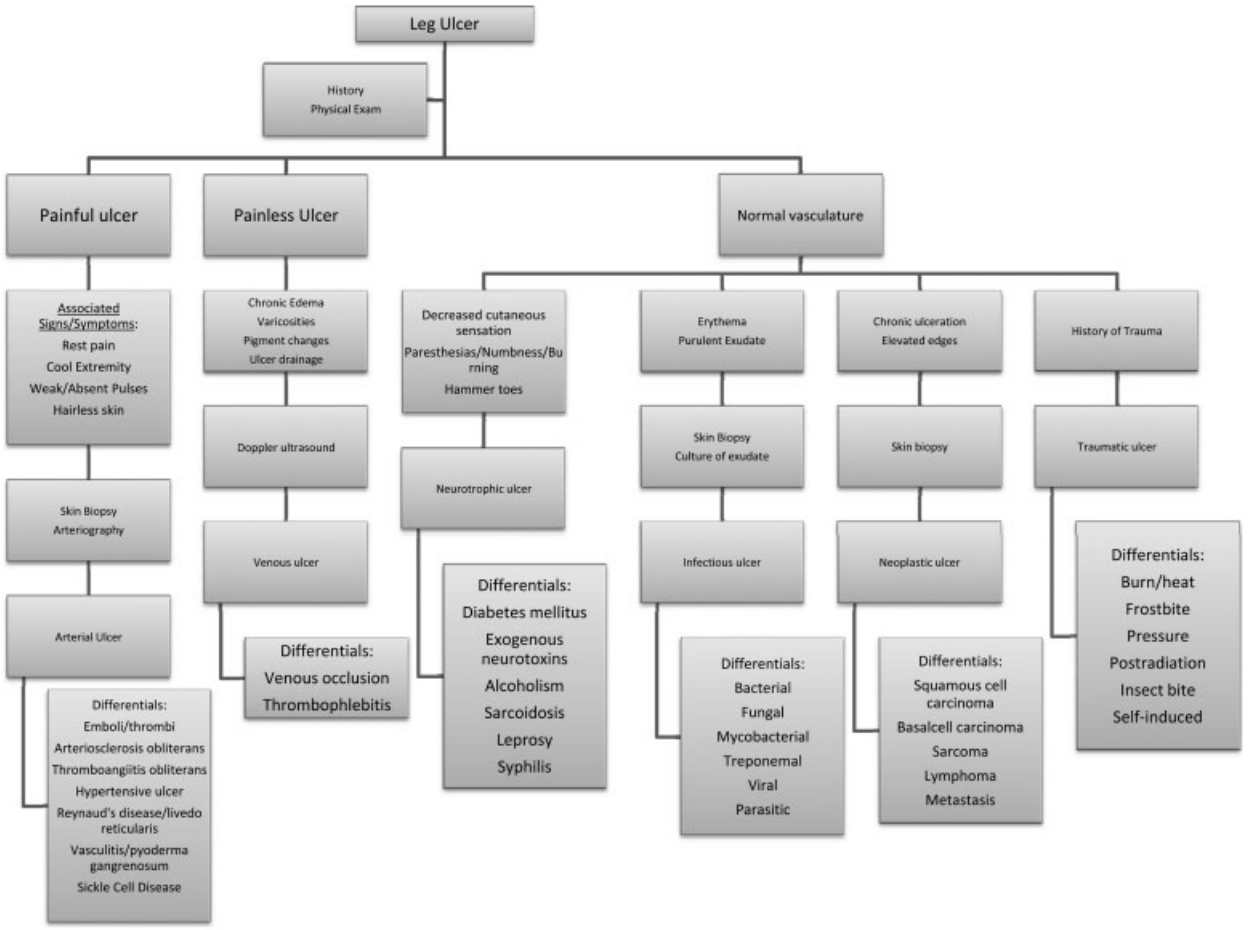

Figure 3 Differential diagnosis for lower-limb ulceration.

uncover mild peripheral arterial atherosclerosis that presented with normal values at rest.[10]

Duplex Ultrasound

Duplex ultrasound is an inexpensive, quick, and noninvasive method that enables vascular specialists to detect the distribution and extent of vascular disease. It is regarded as the test of choice for diagnosis of venous reflux, thrombosis, arterial obstruction, and aneurysms.[25,26] It differentiates between stenosis and occlusion and provides information for the plaque content and surface characteristics to aid and also guide treatment. It also helps to identify acute chronic and recurrent thrombosis as well as to demonstrate collateral pathways and the flow dynamics. It is also an excellent tool for differential diagnosis as tumors, cysts, hematoma, and other pathologies may be detected during the vascular examination. Furthermore, it is used for studying the effect of treatment, progression of disease, or developments of new pathology.

Plethysmography

There are several types of plethysmography, such as air, photo, and strain gauge. It is used to detect and quantify arterial and venous disease.[27,28] Depending on the device used, pressure and flow measurements, waveform patterns, volume changes, amount of reflux, degree of venous obstruction, and the efficiency of the calf muscle pump can be estimated. All these are important as the severity of the disease can be demonstrated to determine their impact on ulceration. There are good tests to measure the effect of treatment and disease progression.

Computer Tomography

Computed tomography angiography (CTA) is an accurate modality to assess presence and extent of PAD in patients. CTA is increasingly attractive due to rapid technical developments. Shorter acquisition times, thinner slices, higher spatial resolution, and improvement of multidetector computed tomographic (CT) scanners enable scanning of the whole vascular tree in a limited period with a decreasing amount of contrast.[29] Computer tomographic venography (CTV) is also accurate to determine proximal venous obstruction but unable to determine reflux with the exception of recognizing varicose veins by using 3-D volume-rendering techniques.[30] CT is also a great modality to detect aneurysms and is an excellent tool for differential diagnosis.

Magnetic Resonance Imaging

Magnetic resonance arteriography (MRA) is a noninvasive method to visualize the peripheral vasculature, to detect hemodynamically significant stenosis, and to distinguish focal from long segment occlusive disease.[31] In patients with arterial occlusive disease, MRA is used to confirm the diagnosis. MRA has the ability to define the pattern of the disease and help in planning for arterial access sites (retrograde or anterograde). More specifically, MRA has proven useful in detecting occult runoff channels, which can be used for distal bypass.[32] Ulcerations should be bright on T2-weighted imaging, with peripheral enhancement of the ulcer base.[17]

Magnetic resonance venography has a great accuracy in detecting proximal vein obstruction and may differentiate acute from chronic thrombosis.[33] MRI/MRV is unable to demonstrate venous reflux but it provides great differential diagnosis.

Phlebography

Phlebography identifies the location and extent of blood clots and enables the condition of the deep leg veins to be assessed. It is especially useful when there is a strong suspicion of deep vein thrombosis, after noninvasive tests have failed to identify the disease. Phlebography can also be used to evaluate congenital vein problems and assess the function of the deep vein valves. Ultrasound, however, has replaced phlebography in most cases. Phlebography is a great method to demonstrate the extension of obstruction and all the collateral pathways. It can guide treatment and at the same time assess its effect. It is not used often, because it is painful, expensive, and time-consuming, exposes the patient to a fairly high dose of radiation, and can cause phlebitis, tissue damage, and the formation of deep vein thrombosis in a healthy leg. It is reserved for evaluating limbs that may need deep vein reconstruction or to open proximal vein obstruction.[34,35]

Arteriography

Contrast arteriography is the gold standard for evaluation of arterial disease. It demonstrates the arterial tree in its entirety, to readily delineate the site of arterial stenosis and occlusion. It is indicated for select patients, most likely the ones who will undergo revascularization to reestablish perfusion.[36] In addition to providing valuable anatomic information, pressure measurements across arterial stenoses can be obtained to gauge the hemodynamic severity of a lesion. More importantly, interventions can be done using balloons, stents, and other devices. In patients with vascular malformations, selective catheterization can be performed to obliterate the feeding vessels. Other than being expensive, it has complications such as hematoma, pseudoaneurysm, arteriovenous fistula formation, embolization, dissection, and renal failure.

Intravascular Ultrasound

Intravascular ultrasound (IVUS) is not only used to determine both plaque volume within the wall of the artery and/or the degree of stenosis but to discriminate between normal and diseased components. Small lesions (e.g., intimal flaps or tears) are well visualized because of their high fibrous tissue content and the contrasting echoic properties of surrounding blood. Intramural thrombus appears as echogenic homogenous mass with varying image attenuation beyond the location. IVUS can also differentiate noncalcified vessels versus calcified because the latter appear as a bright image with dense acoustic shadowing because the ultrasound energy is reflected by calcified plaque. It is also used to identify proximal venous obstruction. It allows precise estimation of the stenosis and the diameter of the lumen so the correct balloons and stents are used in the best possible position.[34,37]

SKIN BIOPSY

Skin biopsies are being performed in patients with ulcers of undetermined cause or when suspect malignancy. Patients with chronic stasis ulcers can develop malignant transformation of the ulcers. Though a rare phenomenon, the most common type of cancer described is squamous cell carcinoma as opposed to basal cell carcinoma (BCC). The ulcers may often be painless, appear hypertrophic or hemorrhagic with irregular borders, and exhibit a low progressive growth. The malignant transformation is difficult to diagnose because of the absence of a clear clinical picture of malignancy. The malignant ulcers can be present from up to 18 years. It is the second most common form of skin cancer and often arises on sun-exposed areas of middle-aged and elderly individuals of light complexion.[22] BCC is the most common type of skin cancer, typically arising on areas of chronic sun exposure, especially the head and neck. Any wound that is suspected of a malignant process must be biopsied, especially if refractory to treatment for at least 3 months, and tissue sample must be taken from the wound bed and the edge including surrounding skin.

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