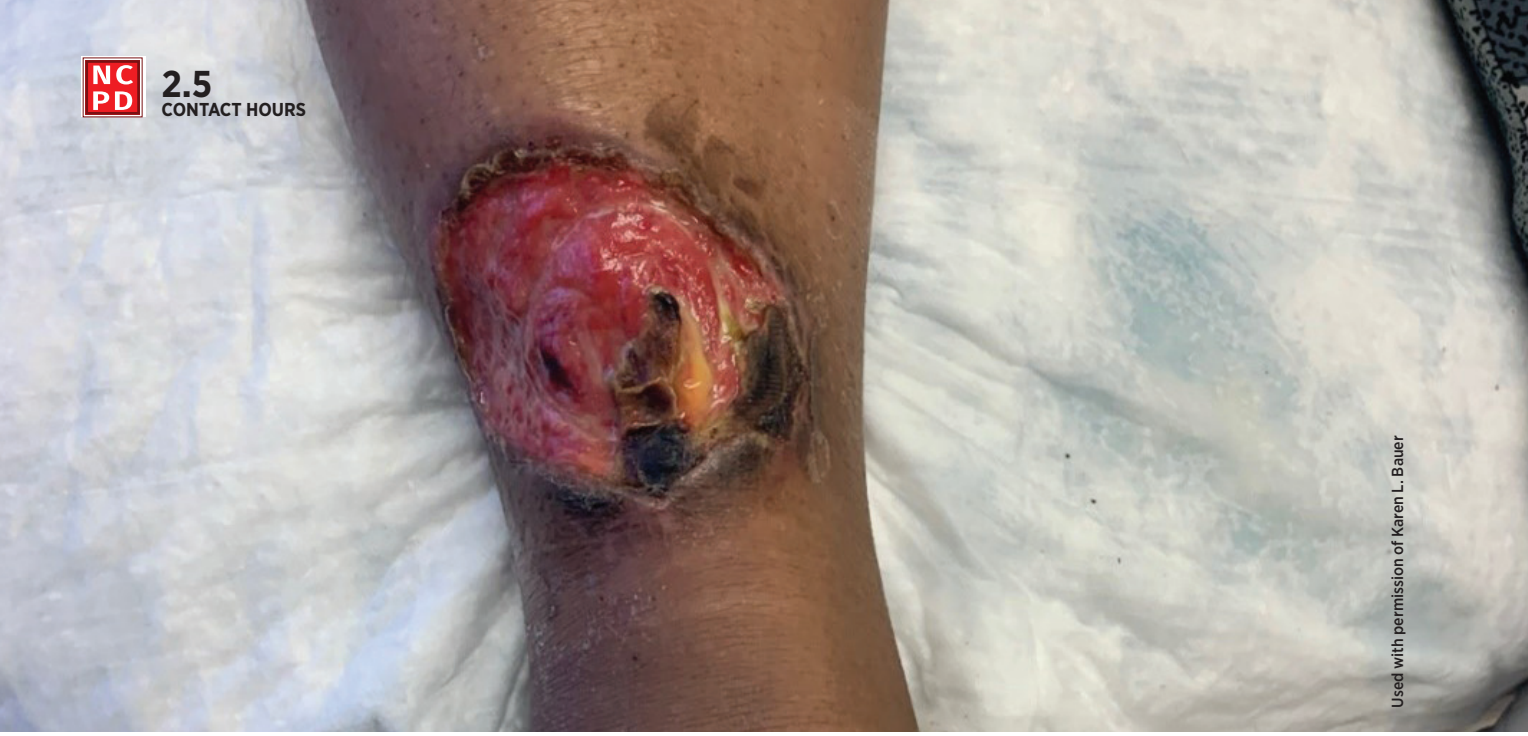
NCPD 2.5 CONTACT HOURS



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**ABSTRACT**

Venous and arterial insufficiency are two common etiologies of lower extremity ulceration that present with different risk factors, symptoms, and characteristics. Diagnostic and management principles are based on accurate assessment, which mandates knowledge of the underlying disease processes and the complex interplay of contributing factors. Early diagnosis, initiation of basic management principles, and referral are paramount to improving key patient- and systems-related outcomes. NPs, especially in the primary care setting, are uniquely positioned for early recognition of these diseases, which can have a significant impact on morbidity, mortality, and quality of life for patients with venous or arterial insufficiency ulcerations.

**Keywords:** arterial ulcer, chronic limb-threatening ischemia, chronic venous disease, chronic venous insufficiency, leg wound, lower extremity ulcer, peripheral artery disease, venous ulcer

# Lower extremity ulceration:

## Differentiating arterial from venous in presentation, diagnosis, and management

By Karen L. Bauer, DNP, APRN-CNP, CWS, FAAWC

Studies show that chronic ulcers of various etiologies have a pooled prevalence of 2.21 per 1,000 population globally. Chronic wounds pose a significant challenge to patients, families, and healthcare systems. Chronic wounds are defined as wounds that fail to improve in an organized and timely fashion. Usually, wounds will heal in four stages, each with its own typical timeframe: 1) hemostasis; 2) inflammation; 3) proliferation; and 4) remodeling.[1] If at any point this wound healing cascade is interrupted, subsequent stages are thwarted and the wound becomes chronic. Numerous factors contribute to slow or stalled wound healing, both intrinsic and extrinsic.[2] See *Table 1* for contributing factors.[3]

Lower extremity (LE) ulcers pose a significant health burden globally, with an estimated prevalence of 0.12% to 1.8% of the adult population, especially in those age 65 and older.[4] Venous and arterial insufficiency are two common causes of chronic LE wounds, each with distinct pathophysiology and clinical presentations. The majority of LE ulcers are venous in nature, with venous leg ulcers (VLUs) accounting for about 70% of all LE ulcers.[5] Conversely, arterial ulcers account for about 22% of LE ulcers.[5] LE

ulcers usually reflect a complicated interplay of differing etiologic and comorbid factors. It is important to understand the various causes and contributing elements to effectively treat these ulcers. Furthermore, differentiation of the underlying etiologies is necessary to formulate an accurate diagnostic and management plan.

## PATHOPHYSIOLOGY

Chronic venous disorders describe an expanse of structural and functional abnormalities of the venous system. The term chronic venous disease refers to several disorders that include chronic venous insufficiency, venous occlusive disease, a combination of both occlusion and insufficiency, and conditions such as arteriovenous malformations and other congenital problems. Chronic venous insufficiency is implicated in the majority of nonhealing VLUs; superficial venous reflux is identified in 20% to 30% of VLUs, and both superficial and deep reflux is identified in another 30%.[6] Venous ulcers can also develop in patients with a history of deep vein thrombosis (DVT), called post-thrombotic syndrome.[7]

The pathophysiology of VLUs reflects a complex and intricate interplay of both macro- and microscopic processes within the venous system, such as venous dilation, incompetent valves, venous reflux, and venous hypertension. This leads to a cyclical proinflammatory response, cell injury, increased cell permeability, glycocalyx alteration, leukocyte infiltration, and high dermal tension, all of which may contribute to VLU development.[7,8] Venous leg ulceration is the most extreme presentation of chronic venous disease; however, only a minority of patients with chronic venous disease develop a VLU. Although recent research has advanced understanding of the nature of chronic venous disease and venous ulcers, the above chronic inflammatory processes are not yet fully elucidated.[7]

Conversely, arterial ulcers are usually secondary to ischemia resulting from peripheral artery disease (PAD). Chronic limb-threatening ischemia (CLTI), or PAD accompanied by tissue loss (arterial ulcer) or ischemic rest pain, is considered end-stage PAD. Arterial ulcers occur due to narrowing or obstruction of arterial blood supply to the extremities, resulting in insufficient tissue oxygenation. Up to 1 in 10 patients with PAD has CLTI and 5% to 10% of patients with asymptomatic PAD or intermittent claudication progress to CLTI after 5 years.[9] CLTI is underrecognized, undertreated, and associated with high rates of major amputation and major adverse cardiovascular events.[10] Like chronic venous disease, PAD is a complex pathophysiologic phenomenon. It involves the build-up of atherosclerotic plaque within arteries and results in damage to the endothelial wall and a subsequent inflammatory reaction. In early PAD, the body compensates and attempts to maintain vessel patency, but eventually, the vessels narrow, sometimes to the point of full occlusion.

It is important to recognize the difference between acute limb ischemia, which is of sudden (less than 2 weeks) onset and typically involves thromboemboli from either a cardiac or large artery source or acute thrombosis on the background of already-present arterial occlusive disease (acute on chronic disease), and CLTI, which is a chronic process (more than 2 weeks).[11] The same pathophysiologic principles apply in other vascular beds, and studies have shown that 46% to 68% of patients with PAD also have polyvascular disease, further emphasizing the need for early recognition, diagnosis, and management to slow disease progression.[12] Conditions such as diabetic angiopathy, thromboembolism, Buerger disease, and vasospastic conditions such as Raynaud disease also have ischemic components which can cause arterial ulceration and exacerbate LE ulcers of other etiologies.

## RISK FACTORS

Early recognition of risk factors is a necessary precursor to the diagnosis and management of VLUs and arterial ulcers.

Several genetic, environmental, demographic, and intrinsic factors have been found to contribute to chronic venous disease and VLUs.[7] Risk factors for chronic venous disease are family history of venous disorders, female sex, older age, pregnancy, prolonged standing or sitting, certain genetic blood disorders such as sickle cell disease, major leg trauma, calf muscle pump dysfunction, hip or knee surgery, and obesity.[13] Risk factors for VLUs may include male sex, advanced age, history of DVT, diabetes mellitus (DM), hypertension, musculoskeletal disease, high body mass index, family history of ulceration, personal history of nonvenous ulceration, pregnancies, and deep vein incompetence.[13] Although studies elucidate numerous contributing factors in the development of a VLU, a thorough and standardized profile of VLU risk factors has not been clearly identified in the literature.[14]

PAD is often asymptomatic, and PAD risk factors such as DM, smoking, obesity, hypertension, hypercholesterolemia, chronic kidney disease (CKD), family history, and advanced age are underrecognized. Smoking is known to be a strong independent PAD risk factor, and CKD, particularly end-stage renal disease (ESRD), correlates not only to PAD but to major amputation, especially in the setting of DM.[15] Elevated total cholesterol and low-density lipoprotein cholesterol are known to be PAD risk factors and decreased high-density lipoprotein cholesterol levels also appear to correlate with increased mortality in PAD. Men have been reported to have a higher prevalence of PAD in high-income countries, but women tend to have a higher prevalence of PAD in low- and middle-income countries. PAD is more common among Black individuals than among Asian, Hispanic, and White individuals. The association between obesity and PAD has been suggested but is inconsistent.[15] Nontraditional PAD risk factors have also been suggested, such as food insecurity; lack of access to housing; lower income; lower educational levels; and lower social and familial support. Because of the risk of cardiovascular events and limb loss associated with PAD and CLTI, aggressive secondary prevention strategies are of paramount importance.[15]

## HISTORY, PHYSICAL EXAM, AND CLINICAL PRESENTATION

A full history and physical exam should be performed on patients presenting with LE ulceration. Key history elements in patients with a VLU include personal or familial history of all the following: DM, hypertension, CKD, DVT or pulmonary embolism, varicose veins, VLUs, genetic disorders, rheumatologic diseases, and connective tissue disorders. Personal history of pregnancy, ankle/LE injury or surgeries, decreased mobility, LE swelling, and nonhealing ulcers should be ascertained. Additionally, a work history involving prolonged standing or sitting is pertinent. Obesity can also contribute to reduced calf muscle pump function and increased abdominal pressure, and adipose tissue may lead to venous changes and subsequent VLU.[14] Hemosiderin staining, or hyperpigmented, ruddy skin coloration, is a classic sign of chronic venous disease. Signs and symptoms of chronic venous disease that may accompany VLUs include varicose veins; achy, tired legs; a feeling of fullness, burning, or tingling in the legs; leg pruritus; swelling of the legs; and dry, flaky, leathery skin on the legs.

**TABLE 1. Factors that contribute to slow wound healing[3]**

| | |
|---|---|
| Comorbidities | Diabetes<br>PAD/CLTI<br>Chronic venous insufficiency<br>CKD/ESRD<br>Malnutrition<br>Obesity<br>Infection involving other body systems<br>CAD/CHF<br>COPD |
| Medications | Steroids*<br>Anticoagulants**<br>Chemotherapeutic agents |
| Lifestyle | Smoking<br>Food scarcity/poor diet<br>Alcohol intake<br>Stress |
| Wound characteristics | Exudate (too much or too little)<br>Necrotic tissue<br>Biofilm/bioburden<br>Wound depth/exposed structure<br>Foreign body/debris<br>Osteomyelitis |
| Environmental/ Extrinsic | Sustained local pressure<br>Friction/shear |
| Other | Older age<br>Immunocompromised status |

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; CLTI, chronic limb-threatening ischemia; COPD, chronic obstructive pulmonary disease; PAD, peripheral artery disease; ESRD, end-stage renal disease.

*Helpful in some scenarios, such as pyoderma gangrenosum/vasculitis ulcers

**Beneficial in CLTI and certain cardiac conditions

A full cardiovascular history and physical exam should be performed in a patient presenting with an LE ulcer, especially in suspected ischemic tissue loss or arterial ulceration. It is important to elicit any history of DM, hypercholesterolemia, hypertension, CKD/ESRD, coronary or LE revascularization, myocardial infarction, stroke, aneurysm, vasculitis, or rheumatologic or genetic diseases. Especially because PAD is often asymptomatic until later stages, recognition of an arterial component in any LE ulcer is crucial.

Ischemic rest pain usually affects the forefoot and is often worse at night or when the patient is supine or elevating their legs. The patient may have thickened toenails, dry or shiny skin, pallor, numbness, and diminished or absent pulses in the feet. Arterial ulcers may present as dry or wet gangrene.

It should be noted that mechanisms in both venous leg ulceration and arterial ulceration may act in conjunction with other factors. Diabetic foot ulcers frequently develop concurrent to neuropathy, trauma, or arterial insufficiency. Up to 25% of lower leg ulcers have arteriovenous components, displaying the need to ensure a broad history and physical exam to avoid minimizing the contribution of ancillary factors.[2] See *Table 2* for description of VLU and arterial ulcer clinical presentations and *Figures 1* and *2* for pictorial representations of each.[16] (Additional images of arterial and venous ulceration, *Figures 3* through *8*, are published online as Supplemental Digital Content available at http://links.lww.com/NPR/A30.)

Tissue loss related to small vessel disease, such as in Buerger disease or diabetic angiopathy, usually occurs on the distal aspects of the toes and may be accompanied by pain induced by stress, cold, stimulants, friction, or activity and exacerbated by infection, inflammation, or systemic illness. Clinicians must differentiate these conditions and recognize that these patients often have good proximal blood flow manifested by palpable larger arteries such as the pedal arteries.[17]

## CLASSIFICATION

Both chronic venous disease and chronic arterial disease are classified to reflect the severity of the disease. Chronic venous disease has been classified using the Clinical manifestation, Etiology, Anatomic distribution, Pathophysiology (CEAP) system, which considers signs and symptoms, etiology, and pathophysiology.[18] Other classification systems include the Venous Clinical Severity Score (VCSS), the Venous Disability Score, and the Venous Segmental Disease Score (VSDS).[2] VLUs are the most severe manifestations of chronic venous disease, with skin and soft tissue damage propagated by valvular dysfunction, venous hypertension, and chronic inflammatory processes.[19]

Classification systems for arterial ulcers primarily center on PAD: the Rutherford Classification System; the Wound, Ischemia, and foot Infection (WIfI) Classification System; and the Global Limb Anatomic Staging System (GLASS) are the most common systems used in clinical practice.

**TABLE 2. Clinical characteristics of venous and arterial ulcers[16]**

| | Arterial | Venous |
|---|---|---|
| **Location** | Distal<br>Dorsal toes/foot<br>Malleolar | Gaiter area (ankle and midcalf)<br>Surrounding malleoli<br>Over varicose veins |
| **Exudate** | Dry: scant to none | Moderate to heavy drainage |
| **Tissue type** | Pale<br>Hypogranular<br>Necrotic/gangrene | Granulated |
| **Edges** | Discrete<br>"Punched out" | Jagged<br>Irregular |
| **Pain** | Very painful | Not usually painful |

## DIAGNOSIS

With proper synthesis of risk factor analysis, patient history, and physical exam, clinicians can determine an accurate diagnosis of the underlying disease and contributing factors to establish an appropriate management plan. Important in this process is the establishment of a differential diagnosis to guide diagnostic studies. See *Table 3* for differential diagnosis in LE ulcers.

The diagnosis of chronic venous disease is primarily clinical and based on the presence of edema, hemosiderin staining or hyperpigmentation, venous-related skin changes, clinical symptoms, and the location and characteristics of ulcerations. When a venous component to an LE ulcer is suspected, the main evaluation tool is venous duplex ultrasonography (VUS) for venous reflux. Although VUS is used to evaluate for DVT or superficial vein thrombus, venous reflux studies assess vein diameter, valvular function, and backflow or reflux in both deep and superficial veins. In general, reflux in a normal vein should last less than half a second. Venous reflux studies can also identify tributary veins and refluxing perforating veins or varicose veins.[20] If iliocaval (iliac vein or inferior vena cava) obstruction or compression, such as in conditions like May-Thurner syndrome, is suspected, computed tomography venogram (CTV) or magnetic resonance venogram (MRV) is needed. Iodinated contrast material is needed for CTV, so awareness of the patient's renal function is necessary. See *Figure 3* for an example of venous reflux imaging.

If atypical components to a VLU are suspected, such as in pyoderma gangrenosum or vasculitis, lab data should include a rheumatoid panel, C-reactive protein, and erythrocyte sedimentation rate. Tissue biopsy (histology) will elucidate malignancy or atypical

etiologies and should be performed if a VLU does not respond to standard therapy or if an atypical component is suspected. Cultures are not routinely indicated in the presence of a VLU.

PAD or CLTI are traditionally diagnosed by physical exam and noninvasive arterial doppler studies, including ankle-brachial indices (ABIs) or arterial duplex. However, advanced imaging modalities, such as computed tomography angiography (CTA), are important in the absence of femoral pulses to evaluate aorto-iliac disease and for operative planning.[2]

A normal ABI result (>1.0) in the absence of signs or symptoms is adequate to rule out significant PAD. In patients with noncompressible arteries, such as in DM, toe pressure and toe-brachial index can be measured, as digital arteries are usually spared from calcification. Toe-brachial index offers assessment of smaller digital arteries and is predictive of cardiovascular mortality in patients with PAD. It is measured with a small sphygmomanometer toe cuff and photoplethysmograph sensor, which are available in most vascular labs.[21] See *Figure 4* for an ABI report and readings.

To determine the level of occlusive disease, segmental pressures are obtained by measuring systolic pressures over multiple limb segments in the thigh, calf, ankle, and toe. The systolic pressure is compared by segment in the same limb and bilaterally on the same level. Normal differences between segments or legs are within 20 mm Hg. A larger difference in the pressures reflects the presence of arterial disease.[22] Segmental pressures are challenging and usually avoided in patients with stents and bypass grafts.

Newer technology has allowed for evaluation of micro-circulatory perfusion near ulcerated sites. Modalities such as hyperspectral imaging, thermography, near-infrared spectroscopy, and indocyanine green fluorescence angiography are being utilized to further assess tissue oxygenation and help in amputation planning.[23] See *Table 4* for delineation of diagnostic terms in PAD and chronic venous disease.

**FIGURE 1. Example of venous ulceration**

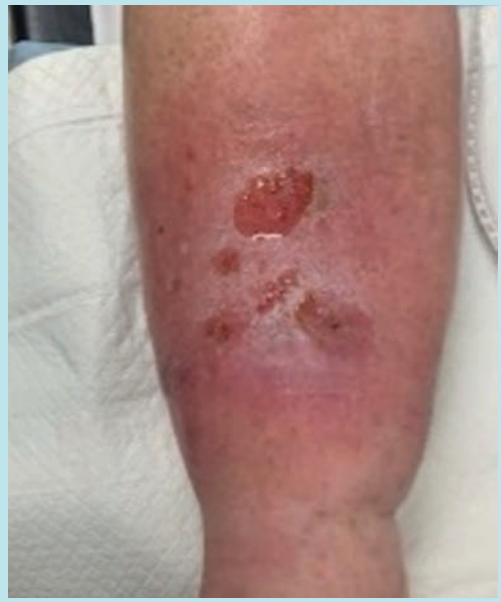

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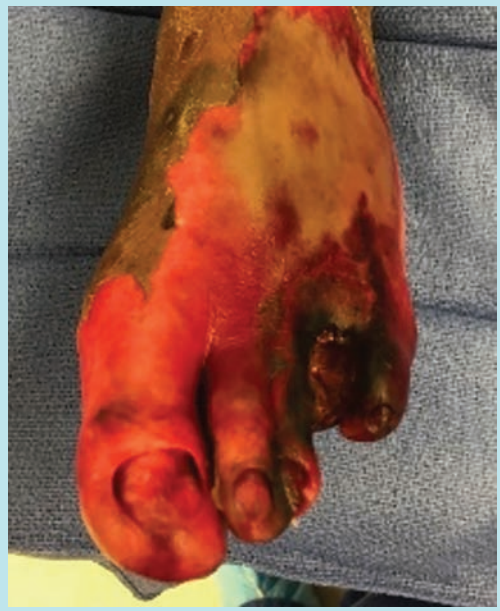
**FIGURE 2. Example of arterial ulceration**



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## MANAGEMENT

The technical complexity and medical challenges in LE ulcer cases require customized care and interdisciplinary collaboration. Early identification and investigation by primary care providers and other clinicians is crucial to appropriate management. Adequate treatment of chronic venous disease with compression and endovenous intervention is needed to minimize risk of venous leg ulceration. Treatment of patients with a VLU should employ measures to reduce edema using compression therapy. While medical grade compression stockings are adequate for

the early stages of chronic venous disease, multiple studies show that multilayer compression bandages are most beneficial in VLU healing.[15] Compression should reach 40 mm Hg at the ankle. Milder compression should be used in patients with concurrent PAD; compression bandage systems reaching 20 mm Hg are available for these patients. Long stretch or elastic bandages, such as ACE™ wraps, are inadequate in the setting of a VLU and can cause undue arterial compression in patients with PAD. Because of this, it is advantageous for any patient with significant venous skin changes or ulceration to be referred early to a wound care center or a vascular specialist. It is also imperative to assess the patient's arterial status prior to or concurrent with implementation of compression therapy. In the presence of palpable dorsalis pedis pulses and in the setting of a low PAD risk factor profile, it is acceptable to begin compression therapy. If risk factors or clinical signs of PAD are present, noninvasive arterial testing should be completed before employing compression therapy.

Even when adequate compression is applied, the patient must employ tactics such as leg elevation, calf muscle pump exercises, and avoidance of prolonged sitting or standing. In addition to compression, there are multiple advanced modalities such as cellular, acellular, and tissue-based products that can augment healing once host factors have been optimized. The primary goal in topical management of VLUs is exudate management, with an aim to keep the wound moist but not wet. The frequency of both dressing and compression modality changes are dictated by the amount of exudate, availability of supplies and trained personnel to apply, and social and other factors, but compression wraps are generally coupled with topical therapies and changed once to twice weekly. Compression bandage systems do require licensed and trained clinicians and should generally not be applied by patients or family members.

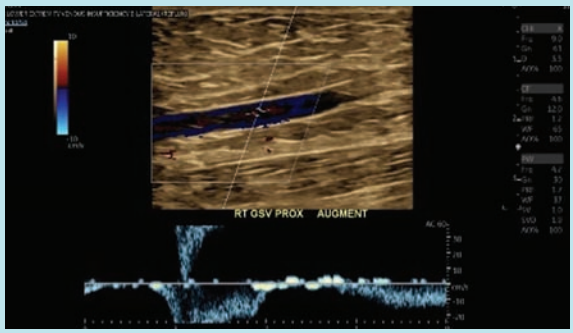
Although multicomponent compression therapy is the gold standard for venous leg ulceration, it is often not sufficient alone to achieve ulcer resolution. As supported by the Society for Vascular Surgery and American Venous Forum VLU clinical practice guidelines, management of a VLU requires a multifaceted approach and, based on the presence of venous reflux, procedural or surgical intervention may be necessary to promote ulcer closure and to help reduce recitivism.[13,18,24] It is well established that endovenous ablation of superficial venous incompetence in combination with compression improves leg ulcer healing.[15] Still, continued research is needed to further elucidate optimal modalities of endovenous ablation.[25] In the management of VLUs, it is also important to address iliocaval compression or obstruction when identified on venous imaging (that is, CTV). Additional modalities in the management of VLUs include venoactive medications such as pentoxifylline and micronized purified flavonoid fraction.[26] It is also crucial to include

**TABLE 3. Differential diagnosis in LE ulcers**

| |
|---|
| Autoimmune, rheumatologic, and connective tissue disorders: pyoderma gangrenosum, vasculitis, systemic lupus erythematosus skin manifestations, rheumatoid arthritis |
| Malignancy/neoplastic transformation |
| Pressure ulcer |
| Arterial/ischemic ulcer |
| Venous ulcer |
| Diabetic ulcer, necrobiosis lipoidica |
| Calciphylaxis |
| Dermatologic manifestation of blood dyscrasia: sickle cell disease, thalassemia, thrombocythemia, polycythemia, and others |
| Martorell ulcer (in uncontrolled hypertension) |
| Infection |
| Trauma |
| Small vessel diseases: Buerger disease, diabetic angiopathy |
| Warfarin-induced skin necrosis, heparin-induced necrosis |
| Injection drug use sites |

Abbreviation: LE, lower extremity.

**FIGURE 3. Venous reflux study image**

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weight loss and exercise in the treatment of chronic venous disease.[27]

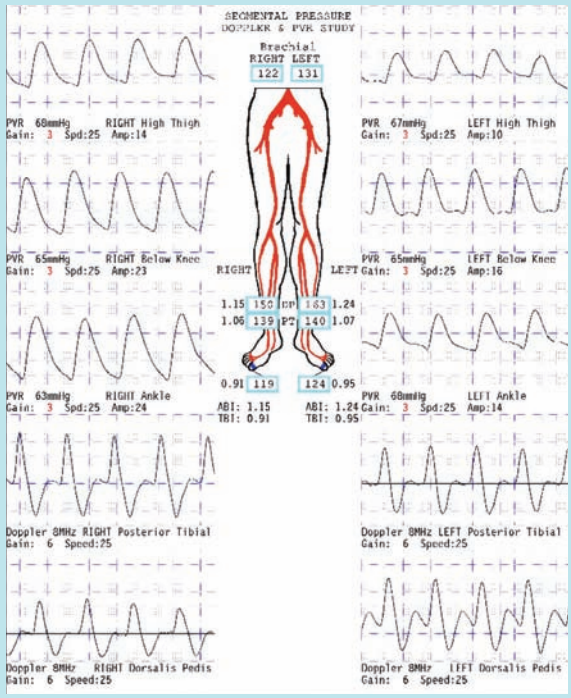
With appropriate wound care and compression therapy, VLUs may close within about 6-12 months, but because of limited use of and adherence to adequate compression as well as numerous clinician and patient factors, these ulcers may take far longer to completely resolve. Recurrence rates of VLUs are also high.[15,28] Thus, once the ulcer is closed, emphasis shifts to long-term disease management and prevention of recurrence. Preventive measures including continued compression therapy and venotonic medications could also reduce the risk of progression to chronic venous insufficiency and VLU in susceptible individuals.[7] Once the VLU has closed, insurance generally inhibits continued use of multicomponent compression systems and thus the patient can transition to compression stockings (at the highest level tolerated) or intermittent pneumatic compression pumps and should be educated about the risk of recurrence and need for lifelong therapy.

Arterial ulcers and CLTI are also a multimorbid phenomenon that mandate coordinated, multidisciplinary management to satisfy care standards and reduce limb loss, but there is a common misconception that limb diseases are not fatal. Despite the high clinical burden in PAD, there is a wide variance in management research-to-practice gaps. PAD is recognized as an independent risk factor for major adverse cardiovascular events and major adverse limb events but is not commonly identified as a disabling condition.[29] Still, team-based vascular limb salvage services aimed at addressing the complexity of CLTI are gaining popularity and are backed by expert consensus and research.[30] Such collaboration among vascular surgeons and other interventionalists (such as specialists in radiology and cardiology), podiatrists, advanced practice providers, wound care specialists, orthotists, endocrinology specialists, physical therapists, infectious disease specialists, and others is crucial in limb preservation efforts.

The management of patients with arterial ulcers has significantly changed with the advent of new endovascular approaches; increased attention to cardiovascular risk factors; innovations in the management of DM; and recognition of the complex interaction among infection, wound management, and ischemia. Revascularization to establish inline arterial flow is the standard of care in arterial ulceration; without direct blood flow, arterial ulcers cannot resolve, increasing the risk of serious complications. Management goals in CLTI are to optimize survival, resolve ulceration without infection, reduce pain, increase function, prevent amputation, and maximize quality of life. Cilostazol, a common medication used for patients with PAD and claudication, should be reserved for use in patients to improve walking distance and is not indicated in the setting of ischemic ulceration. Other medications, such as prostanoids, are not used unless revascularization fails or in the setting of noncandidacy for revascularization. When reviewing nonrevascularizable disease, it is important to help patients and their caregivers understand the significance of arterial ulceration as an indicator of end-stage disease.[31]

Five-year mortality for major limb amputation from PAD or DM ranges from 50% to 68%, which is

**FIGURE 4. Example of ABI results**




| ABI measurement | Interpretation |
|---|---|
| ≥1.3 | Abnormal calcification |
| 1.0-1.29 | Normal value |
| 0.9-0.99 | Borderline PAD |
| 0.7-0.89 | Mild PAD |
| 0.5-0.69 | Moderate PAD |
| <0.5 | Severe PAD with impending gangrene |

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Abbreviations: ABI, ankle-brachial index; PAD, peripheral artery disease.

**TABLE 4. Terminology**

| Arterial | | Venous | |
|---|---|---|---|
| **Lower extremity arterial disease** | Atherosclerotic disease and subsequent narrowing of the arteries supplying the legs. Often used interchangeably with peripheral artery disease. | **Lower extremity venous disease** | A broad term for a variety of venous disorders that impair blood flow back to the heart from the lower extremities. Often used interchangeably with chronic venous disease or chronic venous insufficiency. |
| **Peripheral artery disease** | Atherosclerotic disease and subsequent narrowing of the peripheral arteries. Often used interchangeably with lower extremity arterial disease, although peripheral artery disease also applies to the upper extremities and other arteries outside of the coronary artery blood supply. | **Chronic venous disease** | A broad term for a variety of venous disorders that impair blood flow back to the heart from the lower extremities. Often used interchangeably with lower extremity venous disease or chronic venous insufficiency. |
| **Chronic limb-threatening ischemia** | Represents the end stage of peripheral artery disease. Requires objectively documented atherosclerotic peripheral artery disease in association with ischemic rest pain or tissue loss (ulceration or gangrene). | **Chronic venous insufficiency** | A form of venous disease that occurs when veins in the legs are damaged. Can occur in deep, superficial, or perforating veins. Often used interchangeably with chronic venous disease and lower extremity venous disease. |
| **Acute limb ischemia** | Sudden (<2 weeks' duration) decrease in arterial perfusion of the limb, with a potential threat to the survival of the limb, requiring urgent evaluation and management. | **Venous leg ulcer** | Open skin lesion of the leg or foot that occurs in an area affected by venous hypertension. |

comparable to the 5-year mortality for many malignancies.[32] In the setting of CLTI, limb salvage efforts should involve all necessary specialties, and should incorporate advanced wound management modalities in addition to diligent vascular management.[32] Due to the exceptionally high mortality following major amputation, limb salvage programs play a crucial role not only in reducing amputations but also in decreasing mortality.

Once there is tissue loss related to PAD, the goal becomes to slow disease progression and prevent infection until and as revascularization is achieved.[33,34] Wound management principles focus on keeping gangrenous areas clean and dry; in the setting of CLTI, the usual concept of maintaining a moist wound healing environment is overpowered by the need for infection prevention.

Atherosclerotic risk reduction therapies are known to improve outcomes in patients with CLTI and include antiplatelet therapy, pharmacologic and nonpharmacologic management of hypertension, dyslipidemia, DM, and smoking cessation. Shared decision-making encompasses consideration of the cost and accessibility of therapies, need for caregiver involvement, and other lifestyle factors that are necessary when care plans are developed. Education must center on the patient's preferred learning method and level of understanding to promote understanding of and adherence to recommendations.

### Management of mixed arteriovenous ulcers

It is established that management of the venous component in mixed arteriovenous leg ulcers (AVLUs) is paramount for ulcer closure. Patients with an AVLU with an ABI between 0.5 and 0.8 may benefit from modified compression therapy (20-30 mm Hg), and patients with an AVLU and an ABI of less than 0.5 can be considered for modified or full compression therapy after successful revascularization, with close attention to patient tolerance, ulcer improvement, and preservation of graft patency.[35] Sclerotherapy in patients with an AVLU and documented varicose veins near the ulcer has also been shown to be effective in the treatment of AVLUs, even in cases where revascularization wasn't used.[36] In the case of AVLUs, an interdisciplinary team approach is needed, with evaluation by a vascular specialist being paramount.

## SOCIAL DETERMINANTS OF HEALTH

Recent studies have shown that hardships related to a patient's socioeconomic status, environment, and psychosocial stress level are associated with impaired wound healing and are also thought to be associated with increased pain response, decreased initial inflammatory responses, and increased infection risk. Factors such as food scarcity, which impedes proper nutrition, and access to and trust in medical care and dressing supplies also affect the clinical course of patients

with wounds. There is increasing investigation into the impact of social determinants of health on individual biology and heritability, which have been linked to variations in wound healing and wound infection rates.[37]

There is a paucity of research examining the correlation between race/ethnicity and VLUs. Researchers need to increase racial and ethnic diversity in large-scale studies to identify their association with development of VLUs.[38]

As PAD increases in prevalence and severity, increased clinician and community awareness of the condition is crucial.[33,34] Black and Hispanic patients in the US have higher rates of PAD-associated adverse events, but lower PAD-related mortality than non-Hispanic White patients. Black and Hispanic populations typically present with more severe disease, display more atypical symptoms, have disproportionally higher cardiovascular risk factor burden, are less likely to receive timely and appropriate care, and experience higher rates of adverse events. This emphasizes the need for improved awareness, risk factor modification, and patient-centered care for PAD in these communities.[39] Awareness that health literacy levels, access to trusted healthcare services, environmental factors, and food insecurity/lack of access to healthy food choices all impact the development and progression of PAD is needed to fully address the growing prevalence of PAD.

## NP PRACTICE IMPLICATIONS

LE ulcerations are complex and multifactorial. Early recognition and management of risk factors and underlying disease processes such as chronic venous disease and PAD are essential to slowing disease progression and preventing ulceration where possible. Prevention is key for NPs in the primary care setting and in other specialty fields. Lifestyle modifications such as smoking cessation, exercise, healthy diet, glycemic control, guideline-directed medical therapy, and weight loss are key points of intersection for the NP. Identification and distinction of chronic venous disease and PAD signs and symptoms should occur in the primary care setting; doing so offers a unique opportunity to positively affect patient- and system-related outcomes. Adherence to evidence-based, goal-directed medical therapy, especially in the management of PAD and chronic venous disease, is another opportunity for NPs in all settings to positively impact morbidity, mortality, and quality of life.

For the generalist or specialty NP, early recognition of PAD and chronic venous disease risk factors, symptoms, and clinical signs as discussed in this article is imperative and should be accompanied by early referral to a vascular specialist for early diagnosis and management.

Lastly, NPs are especially positioned as coordinators who can play an imperative role in streamlining patient understanding of and adherence to therapies and liaise with specialty care to ensure a systematic approach to the care of these complex patients. NP

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