Annals of Internal Medicine®

In the Clinic®

Venous Leg Ulcers

Prevention

Diagnosis

Treatment

Practice Improvement

Venous leg ulcers are a major health problem, in part due to their high prevalence, often long healing time and high recurrence rate, high cost of care, and effect on quality of life (1). These ulcers are caused by chronic venous insufficiency, which may be overlooked by health care providers. Clinicians may also not recognize the various presenting manifestations and, as a result, the impact of the problem may be underestimated. In the United States, 10%–35% of adults have some degree of chronic venous insufficiency and estimates suggest a worldwide prevalence of 60% (2). The annual burden to U.S. payers (i.e., Medicare and private insurance) is $14.9 billion (1). The individual-patient cost over a lifetime may exceed $400 000 (3).

The CME quiz is available at www.annals.org/intheclinic.aspx. Complete the quiz to earn up to 1.5 CME credits.

Physician Writers
Alejandra Vivas, MD
Hadar Lev-Tov, MD, MAS
Robert S. Kirsner, MD, PhD

doi:10.7326/AITC201608020

CME Objective: To review current evidence for prevention, diagnosis, treatment, and practice improvement of venous leg ulcers.

Funding Source: American College of Physicians.

Disclosures: Drs. Vivas and Lev-Tov, ACP Contributing Authors, have nothing to disclose. Dr. Kirsner, ACP Contributing Author, reports personal fees from Organogenesis and 3M, outside the submitted work. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M16-0831.

With the assistance of additional physician writers, the editors of ***Annals of Internal Medicine*** develop **In the Clinic** using **MKSAP** and other resources of the American College of Physicians.

In the Clinic does not necessarily represent official ACP clinical policy. For ACP clinical guidelines, please go to https://www.acponline.org/clinical_information/guidelines/.

ACP American College of Physicians®
Leading Internal Medicine, Improving Lives

1. Rice JB, Desai U, Cummings AK, Birnbaum HG, Skornicki M, Parsons N. Burden of venous leg ulcers in the United States. J Med Econ. 2014; 17:347-56. [PMID: 24625244]
2. Rabe E, Guex JJ, Puskas A, Scuderi A, Fernandez Quesada F; VCP Coordinators. Epidemiology of chronic venous disorders in geographically diverse populations: results from the Vein Consult Program. Int Angiol. 2012;31:105-15. [PMID: 22466974]
3. Khan MN, Davies CG. Advances in the management of leg ulcers–the potential role of growth factors. Int Wound J. 2006;3:113-20. [PMID: 17007341]
4. Callam MJ, Ruckley CV, Harper DR, Dale JJ. Chronic ulceration of the leg: extent of the problem and provision of care. Br Med J (Clin Res Ed). 1985;290:1855-6. [PMID: 3924283]
5. Ruckley CV. Socioeconomic impact of chronic venous insufficiency and leg ulcers. Angiology. 1997;48:67-9. [PMID: 8995346]
6. Yim E, Richmond NA, Baquerizo K, Van Driessche F, Slade HB, Pieper B, et al. The effect of ankle range of motion on venous ulcer healing rates. Wound Repair Regen. 2014;22:492-6. [PMID: 25041619]
7. Browse NL, Burnand KG. The cause of venous ulceration. Lancet. 1982;320: 243-5. [PMID: 6124673]

Venous leg ulcers (VLU) are more common with increasing age. However, over one fifth of affected persons develop VLU by 40 years of age and 13% do so before 30 years of age. This may have a substantial effect on work productivity (4, 5), as patients with VLU take nearly 50% more sick days than persons without (1). Proper diagnosis and adequate management are vital to promote faster healing and prevent recurrence.

Prevention

Why do patients with chronic venous insufficiency develop VLU?

Chronic venous insuffiency (CVI) is the most common cause of lower leg ulcers, accounting for nearly 80% of all leg ulcers. Patients with VLU have venous hypertension—abnormally sustained elevation of the venous pressure on ambulation (normal venous pressure decreases with walking)—which results from vein valve reflux, such outflow issues as venous obstruction, or both (**Figure 1**). Venous outflow may also be impaired as a result of poor function of the calf muscle pump, which impairs the venous system's ability to overcome gravitational forces as part of venous blood return to the heart. Legs with venous ulcers have significantly less calf muscle pump function than those with healed ulcers or no history of ulceration. Limitation of ankle movement seems to be an important contributor to calf muscle pump failure and a risk factor for ulceration (6).

Although venous hypertension results in ulceration, the exact mechanism remains unclear. Several hypotheses have been proposed, such as abnormalities of the fibrinolytic system, pericapillary fibrin cuff deposition causing decreased oxygen diffusion to tissues, trapping of growth factors by extravasated macromolecules around vessels and in the dermis limiting their function, and leukocyte margination and activation with subsequent local release of inflammatory mediators (7–9). Consequent microcirculatory changes lead to venous hypertensive microangiopathy (enlarged permeable capillaries, abnormally increased skin flux, edema, altered microlymphatic circulation, decreased PO_2 and increased carbon dioxide) that ultimately, likely in concert, results in ulceration (10).

What are the risk factors for VLU?

Several risk factors have been identified (see the **Box**). These include age older than 55 years; presence of venous reflux in deep veins; severe lipodermatosclerosis (LDS); and history of superficial or deep venous thrombosis, pulmonary embolism, or ulcer. Skeletal or joint disease in the lower extremities, higher body mass index, physical inactivity, family history of CVI, and parental history of ankle ulcers have also been identified as risk factors (11, 12). For women, the number of pregnancies is an additional risk factor (13). Whether race and sex are factors is controversial and seems not to be significant (12).

Are there measures that can prevent VLU or their recurrence?

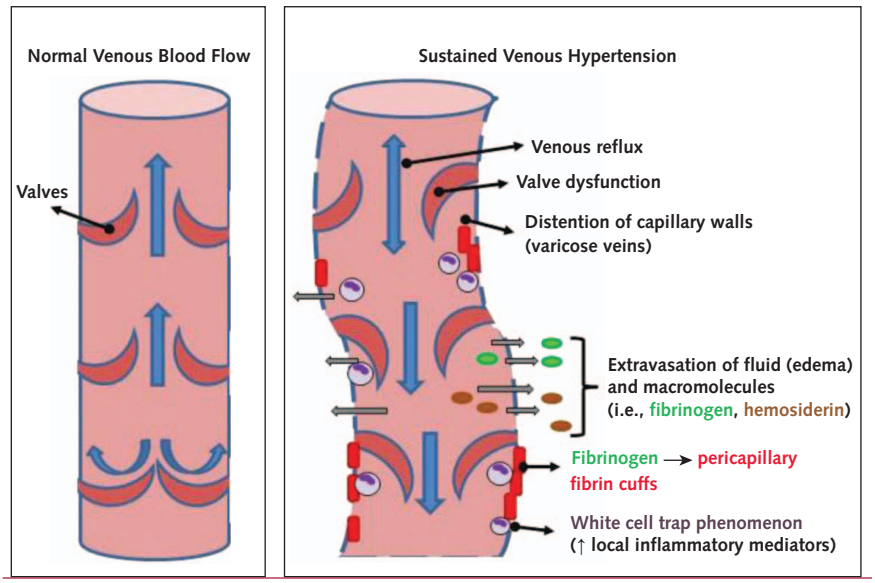
Prospective data on primary prevention of VLU are lacking. However, best practices suggest that prevention begin with aggressive management of reversible risk factors. Control of relevant comorbid conditions (e.g., congestive heart failure,

Risk Factors for VLU

- Age older than 55 years
- Family history of CVI
- Higher body mass index
- History of pulmonary embolism
- History of superficial/deep venous thrombosis
- Lower extremities skeletal or joint disease
- Number of pregnancies
- Parental history of ankle ulcers
- Physical inactivity
- Ulcer history
- Severe lipodermatosclerosis
- Venous reflux in deep veins

CVI = chronic venous insufficiency; VLU = venous leg ulcer.

Figure 1. **Effects of sustained venous ambulatory pressure.**



diabetes mellitus, and peripheral vascular disease), healthy diet, appropriate exercise, weight control, and management of a hypercoagulable state are sensible approaches. Some data are available on secondary prevention and recurrence prevention. These data suggest that compression stockings that achieve a pressure of at least 20–30 mm Hg can reduce VLU recurrence (14, 15). Notably, compliance decreases as the strength of compression increases. Because treatment compliance may significantly affect the overall success of VLU prevention efforts, patients should use the highest level of compression they can tolerate. Finally, venous ablation is a surgical option to reduce recurrence (16).

A trial in the United Kingdom (12) randomly assigned 500 patients to receive compression therapy combined with surgical intervention to eliminate venous reflux or compression therapy alone. At 4-year-follow up, healing was no different in the 2 groups but 56% of the patients in the compression-only group had ulcer recurrence compared with only 31% in the compression plus surgery group (P < 0.01). Interestingly, in a subgroup analysis based on the severity of reflux, results suggested that the effect of surgical intervention on ulcer recurrence is increasingly attenuated with more complex underlying venous disease (16).

Prevention... CVI is the leading cause of VLU and involves venous hypertension in the setting of calf muscle pump dysfunction. Prevention involves management of CVI, LDS, obesity, hypercoagulable states, skeletal and joint disease of the lower extremities, and other comorbid risk factors. Compression stockings can be used for primary and secondary prevention, and venous intervention can be used for secondary prevention.

CLINICAL BOTTOM LINE

8. Falanga V. Venous ulceration. J Dermatol Surg Oncol. 1993;19:764-71. [PMID: 8349918]
9. Thomas PR, Nash GB, Dormandy JA. White cell accumulation in dependent legs of patients with venous hypertension: a possible mechanism for trophic changes in the skin. Br Med J (Clin Res Ed). 1988;296:1693-5. [PMID: 3135881]
10. Incandela L, Belcaro G, Cesarone MR, De Sanctis MT, Griffin M. Changes in microcirculation in venous ulcers with Essaven gel–a pilot, crossover, placebo-controlled, randomized study. Angiology. 2001;52 Suppl 3: S23-7. [PMID: 11775645]
11. Vlajinac H, Marinkovic J, Maksimovic M, Radak D. Factors related to venous ulceration: a cross-sectional study. Angiology. 2014;65:824-30. [PMID: 24165114]
12. Abbade LP, Lastória S, Rollo Hde A. Venous ulcer: clinical characteristics and risk factors. Int J Dermatol. 2011;50:405-11. [PMID: 21413949]
13. Bérard A, Abenhaim L, Platt R, Kahn SR, Steinmetz O. Risk factors for the first-time development of venous ulcers of the lower limbs: the influence of heredity and physical activity. Angiology. 2002;53:647-57. [PMID: 12463617]
14. Vandongen YK SM. Graduated compression elastic stockings reduce lipodermatosclerosis and ulcer recurrence. Phlebology. 2000;15:33-7.
15. Nelson EA, Harper DR, Prescott RJ, Gibson B, Brown D, Ruckley CV. Prevention of recurrence of venous ulceration: randomized controlled trial of class 2 and class 3 elastic compression. J Vasc Surg. 2006;44:803-8. [PMID: 17012004]
16. Gohel MS, Barwell JR, Taylor M, Chant T, Foy C, Earnshaw JJ, et al. Long term results of compression therapy alone versus compression plus surgery in chronic venous ulceration (ESCHAR): randomised controlled trial. BMJ. 2007;335:83. [PMID: 17545185]

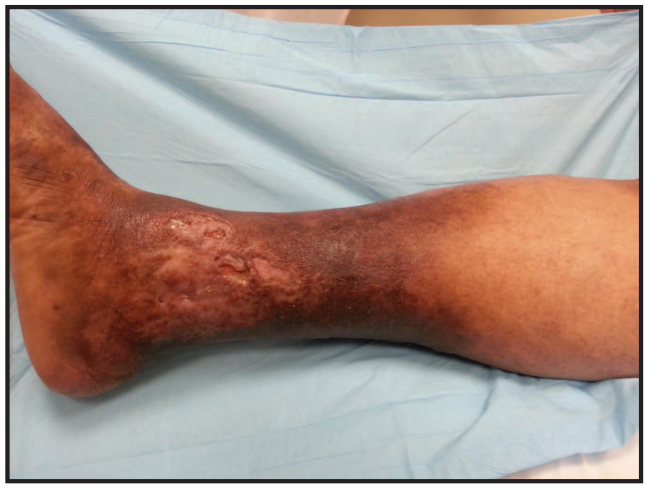
Diagnosis

What symptoms and physical findings are suggestive of CVI?

Patients with CVI commonly report swelling and aching of the legs that is often worse at the end of the day and may be exacerbated by gravitational dependency and improved by leg elevation. A history of ulcer recurrence, particularly at the same location, is characteristic. Commonly associated findings include dependent edema, telangiectasias, varicose veins (ranging from a submalleolar venous flare to various degrees of vessel dilatation), a reddish-brown pigmentation and purpura due to extravasation of erythrocytes through the dilated capillary walls, and subsequent hemosiderin deposition (**Figure 2**). Eczematous changes with redness, scaling, and pruritus, often referred to as "venous dermatitis", are also commonly present. There is evidence that this type of dermatitis is caused by venous hypertension and chronic edema, but it can also be aggravated by contact sensitization (more common because of the disrupted epidermal barrier) to applied topical products (17, 18). Atrophie blanche, which are smooth, ivory–white, stellate atrophic plaques of sclerosis speckled with telangiectases (**Figure 3**), is a common clinical sign in patients with CVI, particularly when it occurs in the lower leg and ankle.

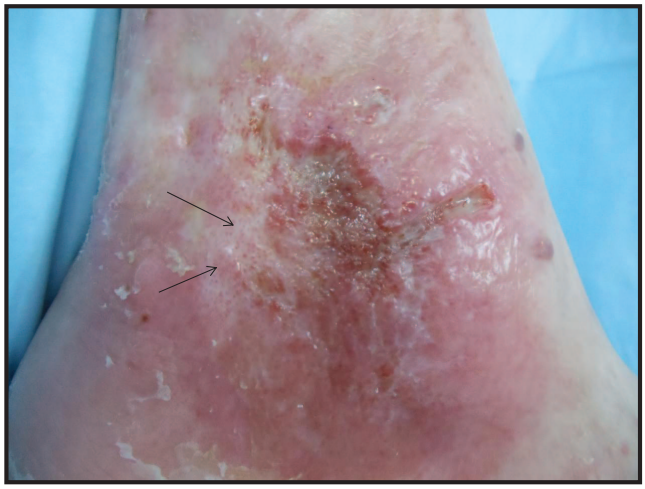
Long-standing venous disease leads to chronic LDS, which is induration and fibrosis of the dermis and subcutaneous tissues that is usually restricted to the medial lower leg and sharply demarcated from proximal normal skin. This indurated area, in contrast with proximal calf edema, resembles an inverted bottle (**Figure 2**). LDS suggests greater impairment of the fibrinolytic system and is highly associated with CVI (8, 19) and delayed healing (20). The acute phase of LDS, which sometimes precedes the chronic form, presents as an extremely painful, red, poorly demarcated, indurated plaque that most commonly appears over the medial malleolus. Recognition of the acute phase is important—it is often misdiagnosed as cellulitis,

Figure 2. **Pigmentary changes and lipodermatosclerosis with the "inverted bottle" shape.**



17. Sippel K, Mayer D, Ballmer B, Dragieva G, Läuchli S, French LE, et al. Evidence that venous hypertension causes stasis dermatitis. Phlebology. 2011;26:361-5. [PMID: 21646304]
18. Thomas Hess C. Venous dermatitis checklist. Advances Skin Wound Care. 2011;24:96. [PMID: 21242739]
19. Kirsner RS, Pardes JB, Eaglstein WH, Falanga V. The clinical spectrum of lipodermatosclerosis. J Am Acad Dermatol. 1993;28:623-7. [PMID: 8463465]
20. Moffatt CJ, Doherty DC, Smithdale R, Franks PJ. Clinical predictors of leg ulcer healing. Br J Dermatol. 2010;162:51-8. [PMID: 19785616]

Figure 3. **Atrophie blanch are porcelain-white stellate scars surrounding a venous leg ulcer.**

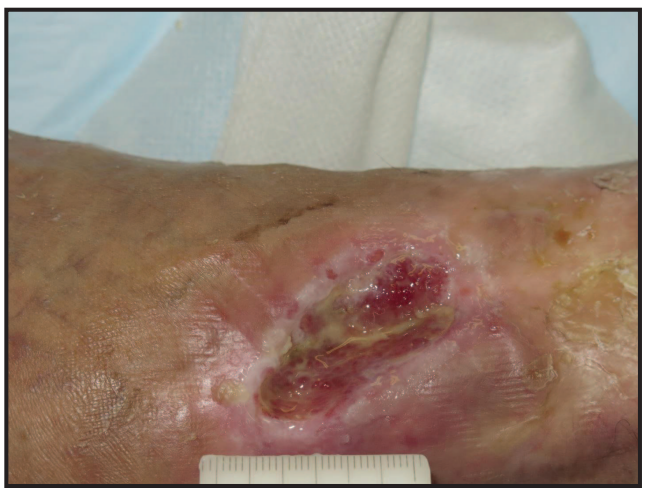


phlebitis, inflammatory morphea, or erythema nodosum and often results in pain and noncompliance with compression stockings in patients with VLU.

What symptoms and physical findings suggest that VLU are due to CVI?

The presence of CVI and its associated conditions strongly suggest venous disease as the culprit in a newly presenting ulcer or a nonhealing ulcer. Specifically, VLU may be painful, and a dull, aching or burning pain is often reported. Three quarters of patients report pain that adversely affects quality of life (21, 22). Ulcers are characteristically located over the medial lower third of the legs. Patients usually have one ulcer, with irregular, flat, or only slightly raised borders. The ulcer bed tends to be shallow with granulation tissue or fibrinous material (**Figure 4**). The wound surface rarely, if ever, shows necrosis, exposed tendons, or bone; the presence of these signs should lead the provider to

Figure 4. **Venous leg ulcer with granulating base and fibrinous material.**



21. Ebbeskog B, Ekman SL. Elderly persons' experiences of living with venous leg ulcer: living in a dialectal relationship between freedom and imprisonment. Scand J Caring Sci. 2001;15:235-43. [PMID: 11564231]
22. Wissing U, Ek AC, Unosson M. Life situation and function in elderly people with and without leg ulcers. Scand J Caring Sci. 2002;16:59-65. [PMID: 11985750]

consider another cause. As described, the presence of venous dermatitis, LDS, or atrophie blanche around the ankle may indicate a venous cause of a lower extremity ulcer. Assessment of patients with VLU should also include testing for neuropathy, which is often unrecognized. Severity of CVI correlates with decreased range of ankle motion and is associated with peripheral neuropathy with prolonged distal motor latency, reduced vibration threshold, diminished temperature perception, altered gait, and higher scores on neuropathy-specific scales (23–26). The pain of VLU is neuropathic in origin in some patients (27).

What other conditions should be considered during evaluation of a patient with possible VLU?

The causes of VLU are often multifactorial. It is important to develop a working differential diagnosis when first encountering a patient with VLU. The 4 most common causes of lower extremity ulcers are CVI, arterial insufficiency, diabetic neuropathy, and prolonged pressure (**Table 1**). Less common causes of leg and foot ulcers include trauma, inflammatory or metabolic conditions, cancer, and infections. When caring for a patient with lower extremity ulcers, the provider should identify the underlying cause to determine management and prognosis.

What is the role of laboratory testing?

No single laboratory test is diagnostic of VLU. A laboratory evaluation may be indicated based on the patient's own history, known comorbidities, and family history. Patients with a history of recurrent ulceration or thrombosis should be evaluated for hypercoagulable states (28).

What is the role of noninvasive tests, such as ankle–brachial index and duplex ultrasonography?

In most patients, VLU may be diagnosed on the basis of history and clinical examination findings. Although clinical and vascular findings of CVI support VLU diagnosis, the presence of venous insufficiency does not exclude other causes—up to 25% of patients have ulcers with mixed etiologies. Noninvasive methods for anatomical and functional evaluation of the venous and arterial systems should be performed and augmented by wound biopsy if necessary to establish an accurate diagnosis (29, 30).

The ankle–brachial index (ABI) is a simple, noninvasive screening method for detecting peripheral artery disease (PAD). The systolic blood pressure is obtained by placing a cuff around the calf and inflating it to occlude the pedal arteries. When the sounds of pedal pulses are heard with Doppler ultrasonography after deflation of the cuff, the ankle systolic pressure is obtained. Ankle systolic pressure is divided by the brachial systolic pressure to determine the ABI (normal range, 0.9–1.29) (31). Values less than 0.9 identify patients with PAD with a specificity of 83.3%–99.0% (32). False-normal results frequently occur in patients who are elderly or have diabetes mellitus (due to poorly compressible arteries from vascular calcification or stiffness); in these patients, transcutaneous oxygen measurement may be a preferred strategy for evaluating arterial flow. Further, in patients with lower extremity pain but normal ABI measurements at rest, treadmill exercise test and postexercise measurement of ABI may be considered to confirm or exclude PAD. The ankle pressure and ABI will decrease after exercise in

23. Yim E, Vivas A, Maderal A, Kirsner RS. Neuropathy and ankle mobility abnormalities in patients with chronic venous disease. JAMA Dermatol. 2014;150:385-9. [PMID: 24196260]
24. Newland MR, Patel AR, Prieto L, Boulton AJ, Pacheco M, Kirsner RS. Neuropathy and gait disturbances in patients with venous disease: a pilot study [Letter]. Arch Dermatol. 2009;145: 485-6. [PMID: 19380677]
25. Reinhardt F, Wetzel T, Vetten S, Radespiel-Tröger M, Hilz MJ, Heuss D, et al. Peripheral neuropathy in chronic venous insufficiency. Muscle Nerve. 2000;23: 883-7. [PMID: 10842263]
26. Shami SK, Shields DA, Farrah J, Scurr JH, Coleridge Smith PD. Peripheral nerve function in chronic venous insufficiency. Eur J Vasc Surg. 1993;7:195-200. [PMID: 8462710]
27. Miteva M, Romanelli P, Kirsner RS. Lipodermatosclerosis. Dermatol Ther. 2010;23:375-88. [PMID: 20666825]
28. Wiszniewski A, Bykowska K, Bilski R, Jaskowiak W, Proniewski J. Prevalence rate for inherited thrombophilia in patients with chronic and recurrent venous leg ulceration. Wound Repair Regen. 2011;19:552-8. [PMID: 22092793]
29. Scriven JM, Hartshorne T, Bell PR, Naylor AR, London NJ. Single-visit venous ulcer assessment clinic: the first year. Br J Surg. 1997;84:334-6. [PMID: 9117300]
30. McGuckin M, Stineman M, Goin J, Williams S. Draft guideline: diagnosis and treatment of venous leg ulcers. Ostomy Wound Manage. 1996;42:48, 50-2, 54 passim. [PMID: 8826138]
31. Lilly SM, Jacobs DR Jr, Kronmal R, Bluemke DA, Criqui M, Lima J, et al. Arterial compliance across the spectrum of ankle-brachial index: the Multiethnic Study of Atherosclerosis. Atherosclerosis. 2014;233: 691-6. [PMID: 24583417]
32. Dachun X, Jue L, Liling Z, et al. Sensitivity and specificity of the ankle–brachial index to diagnose peripheral artery disease: a structured review. Vasc Med. 2010; 15:361-9 [PMID: 20926495]

Table 1. **Clinical Aspects of Common Lower Extremity Ulcers**

Wound Type	*General Aspects*	*Pathophysiology*	*Clinical Presentation*
Venous leg ulcer	Most common type of leg ulcer. Increased incidence in elderly	Sustained venous hypertension due to chronic venous insufficiency (calf muscle pump failure, incompetent valves, venous reflux)	Typically over medial malleolus. Shallow, exudative, with granulating base and fibrin slough. Varicose veins and edema common. Peripheral neuropathy may be present. Associated complications include venous dermatitis and LDS
Neuropathic ulcer	Most common type of foot ulcer; most commonly due to DM. Peripheral neuropathy (sensorimotor) is the most important independent risk factor	Peripheral neuropathy. Frequently concomitant PAD. Associated foot deformities with uneven distribution of foot pressures. Repetitive, unnoticed mechanical trauma and abnormal gait	Usually on plantar surface over bony prominences. Deep, often exposed bone, undermined edges, surrounded by callus. Osteomyelitis common. Dry, cracked skin
Pressure ulcer	In patients with limited mobility. More commonly seen in elderly. Risk factors include bowel incontinence, dependence in dressing and grooming, malnutrition	Sustained high pressure and shear forces. Increased frictional forces. Loss of elastin in aged skin. Excess skin moisture (sweat, urine, feces, wound drainage)	Located over bony prominences (sacrum, coccyx, heels, and hips). Area of erythema, erosion, or ulceration. Necrosis is common
Arterial ulcer	Progressive atherosclerosis most common cause. Exacerbated by smoking, poorly controlled hypertension, and DM	Tissue ischemia	Commonly located on anterior leg, distal dorsal foot, and toes. Dry, fibrous base, poor granulation tissue, eschar and exposed tendons are common. Nonpalpable or diminished distal pulses. Cold extremities. Decreased ABI. Gangrene

ABI = ankle–brachial index; DM = diabetes mellitus; LDS = lipodermatosclerosis; PAD = peripheral arterial disease.

patients with claudication due to PAD. Detecting PAD is important because concomitant arterial disease occurs in approximately 20% of patients with VLU (33). Compression therapy, the mainstay of therapy for VLU, could lead to worsening of an arterial ulcer and potentially result in gangrene (30). In addition, low ABI may indicate the presence of or increased risk for atherosclerosis in other vascular beds (34, 35). Patients with abnormal ABI should be evaluated for coronary and carotid disease, and preventive measures should be put in place.

Guidelines (36) recommend that all patients with suspected VLU have color duplex ultrasonography for accurate diagnosis and to provide prognostic information. However, because VLU can be diagnosed in most patients on the basis of clinical history and examination, imaging may not be necessary (for the strict purpose of diagnosis) in a patient with typical VLU and no other suspected causes. Color duplex ultrasonography, which is the gold standard for evaluating venous disease, is accurate in diagnosing venous reflux and provides anatomical and functional information (37). Such information may be useful in assessing the extent and depth of venous disease as a prognostic factor, in patients with VLU who have an inadequate treatment response, and in patients with a leg ulcer of unclear cause. Other more complex examinations, such as photo and air plethysmography, allow the clinician to assess whole-limb venous hemodynamics at rest and after exercise and are adjuncts to duplex scanning. Computed tomography examination may detect proximal outflow obstruction in rare cases and is often re-

33. Callam MJ, Harper DR, Dale JJ, Ruckley CV. Arterial disease in chronic leg ulceration: an underestimated hazard? Lothian and Forth Valley leg ulcer study. Br Med J (Clin Res Ed). 1987;294:929-31. [PMID: 3107659]
34. Li J, Luo Y, Xu Y, Yang J, Zheng L, Hasimu B, et al. Risk factors of peripheral arterial disease and relationship between low ankle - brachial index and mortality from all-cause and cardiovascular disease in Chinese patients with type 2 diabetes. Circ J. 2007;71:377-81. [PMID: 17322639]
35. Shammas NW. Epidemiology, classification, and modifiable risk factors of peripheral arterial disease. Vasc Health Risk Manag. 2007;3:229-34. [PMID: 17580733]
36. O'Donnell TF Jr, Passman MA, Marston WA, Ennis WJ, Dalsing M, Kistner RL, et al; Society for Vascular Surgery. Management of venous leg ulcers: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg. 2014;60:3S-59S. [PMID: 24974070]

served for VLU patients with intractable edema associated with pain despite adequate compression. Invasive venography is usually reserved for investigation before surgical venous intervention.

What is the role of routine testing for infection?

Testing for infection with the swab culture technique in the absence of local signs of infection is not warranted given the high likelihood of positivity due to bacterial colonization. Wound infection is suggested by signs and symptoms, such as erythema and increased temperature of surrounding skin, increased pain, drainage from baseline, and fever. Infrequently, if an atypical infection is suspected, tissue obtained from a wound biopsy can be sent for microscopic examination and culture.

A 2014 Cochrane systematic review examined the use of antimicrobial therapy for treatment of VLU. The reviewers found no evidence to support the use of systemic antibiotic therapy to achieve wound healing. Of the myriad topical antibacterial preparations studied, there was evidence from 4 randomized, controlled trials (RCTs) to support use of cadexomer iodine to achieve wound healing compared with standard care alone after 4–12 weeks of treatment (relative risk [favors healing], 2.17 [95% CI, 1.30–3.60]). This suggests that antibiotic therapy should not be based on culture results but initiated only in clinically infected ulcers (38).

When should clinicians consider obtaining a biopsy or referring the patient to a surgical or nonsurgical specialist for diagnosis?

Patients with atypical-appearing ulcers or those that have not healed after 4 weeks of active treatment should be considered for biopsy and patient referral to a specialist to rule out other causes of VLU, especially cancer.

Diagnosis... The diagnosis of VLU is typically based on clinical history and physical examination and is suggested by the presence of CVI and a single, painful ulcer with irregular, flat borders and granulating or fibrinous bed on the medial lower third of the legs. Color duplex ultrasonography best characterizes venous disease and is suggested for all patients with suspected VLU. Arterial vascular evaluation, starting with measuring ABI, is suggested to exclude concurrent PAD. If VLU do not improve within 4 weeks of active therapy, a referral to a specialist or biopsy should be considered.

CLINICAL BOTTOM LINE

Treatment

What is the overall approach to treatment of VLU?

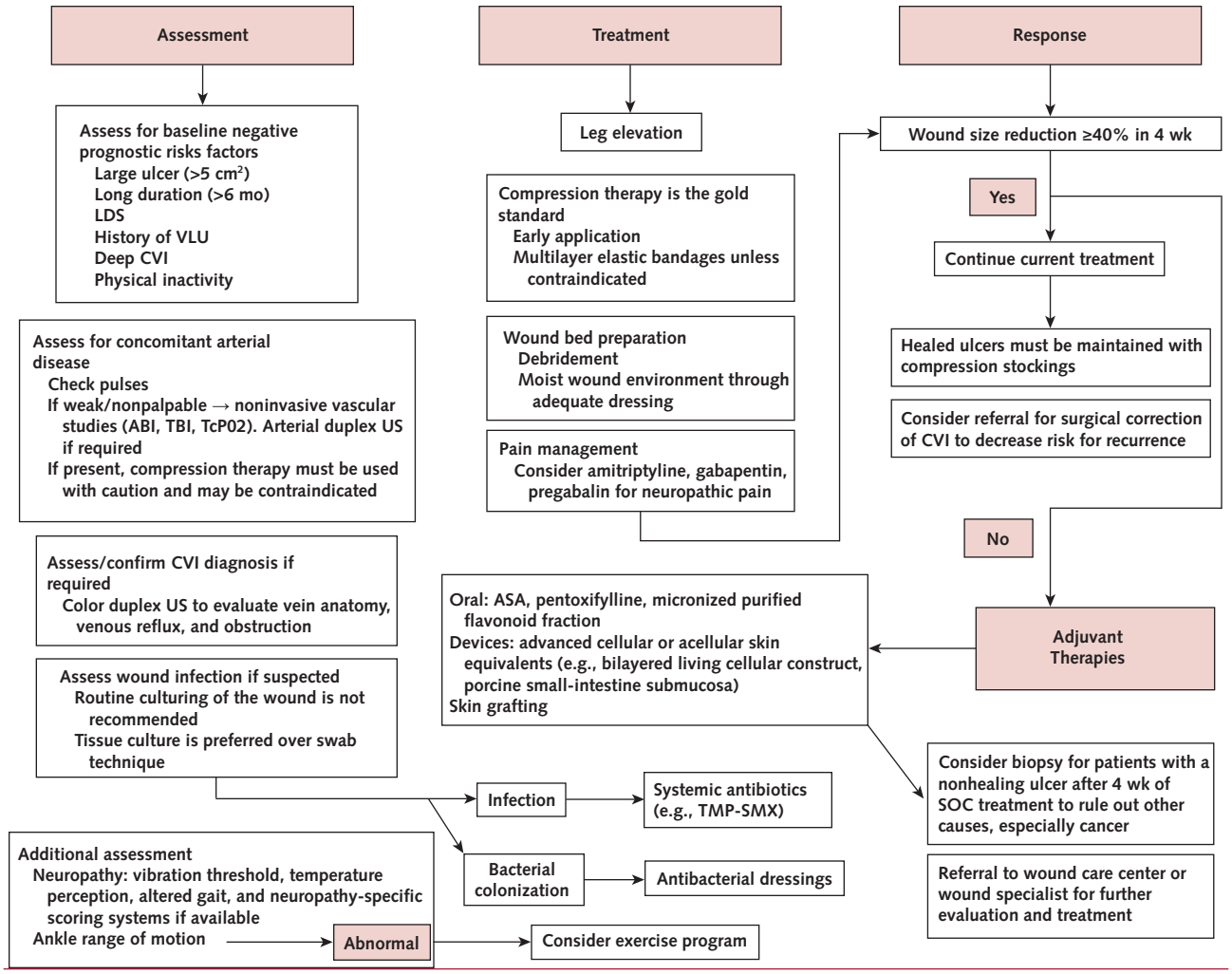
The goals of treating patients with VLU include reduction of edema and pain, ulcer healing, and prevention of recurrence (**Figure 5**). Achieving these goals requires a systematic approach with frequent assessments of treatment response and rapid escalation of treatment in unresponsive cases. The simplest method to reverse the effects of venous hypertension is bed rest with leg elevation. Elevation of the legs above the heart level for 30 minutes, 3 to 4 times daily, as well as leg elevation at night, allows swelling to subside and improves venous microcirculation (39). However, most patients find it difficult to follow this recommendation.

What is the role of compression therapy?

As adherence with sustained leg elevation is often impractical and difficult to achieve, graduated

37. Khilnani NM, Min RJ. Imaging of venous insufficiency. Semin Intervent Radiol. 2005;22:178-84. [PMID: 21326691]
38. O'Meara S, Al-Kurdi D, Ologun Y, Ovington LG, Martyn-St James M, Richardson R. Antibiotics and antiseptics for venous leg ulcers. Cochrane Database Syst Rev. 2014:CD003557. [PMID: 24408354]
39. Abu-Own A, Scurr JH, Coleridge Smith PD. Effect of leg elevation on the skin microcirculation in chronic venous insufficiency. J Vasc Surg. 1994;20:705-10. [PMID: 7966805]

Figure 5. **Algorithm for the care of a patient with a venous leg ulcer.**



ABI = ankle–brachial index; ASA = acetylsalicylic acid; CVI = chronic venous insufficiency; LDS = lipodermatosclerosis; SOC = standard of care; TBI = toe–brachial index; $TcPO_2$: transcutaneous oxygen tension; TMP-SMX = trimethoprim-sulfamethoxazole; US = ultrasonography; VLU = venous leg ulcer.

compression remains the cornerstone of therapy for patients with VLU. Application of external pressure to the calf muscle increases the interstitial hydrostatic pressure, which improves venous return and reduces venous hypertension and edema. Patients who adhere to compression therapy have improved ulcer healing rates; continuing compression therapy after ulcer healing prevents VLU recurrence. International recommendations on the optimal subbandage pressure for treating VLU patients lack consistency. An external pressure of 35 to 40 mm Hg at the ankle is appropriate to prevent capillary exudation and is generally considered to be the acceptable range of external compression (40).

There are 2 types of compression bandages: inelastic and elastic. The prototype of the rigid, inelastic bandage is the traditional Unna boot, a moist zinc oxide–impregnated paste bandage that hardens and becomes inelastic (41, 42). Inelastic bandages have the following disadvantages: They do not accommodate changes in the leg due to initial edema reduction, resulting in rapid loss of subbandage pres-

40. Fletcher A, Cullum N, Sheldon TA. A systematic review of compression treatment for venous leg ulcers. BMJ. 1997;315:576-80. [PMID: 9302954]

sures; they provide pressure only during muscle contraction (ambulation); and they have limited absorptive capacity for highly exudative wounds, requiring frequent reapplication. Moreover, a comparative clinical study found the Unna boot to be significantly less effective in achieving healing than elastic methods (43). Unna boots may be helpful in active patients with early, small, dry ulcers or with venous dermatitis, given the soothing effect of zinc oxide on the skin.

Elastic bandages are more commonly used because they seem to have superior efficacy and can accommodate leg changes, provide sustained pressure during rest and walking, have absorptive capacity, and require less frequent changes (about once a week). Multiple elastic layers are regarded as the gold standard and have the strongest evidence supporting increased healing rates and decreased recurrence rates compared with single layers (43, 44). Several multilayer bandage systems have been developed. Compression therapy, especially with elastic bandages, should be used cautiously in patients with congestive heart failure because lower limb compression can increase the preload volume and exacerbate heart failure. Compression therapy must also be used with caution in patients with arterial insufficiency and not used in patients with more severe arterial insufficiency because compression may cause limb ischemia, especially when the patient is recumbent and arterial flow is no longer aided by gravity.

Compression hosiery has traditionally been used to prevent recurrence of a healed ulcer, but a 2-layer compression hosiery system is becoming a viable alternative for treatment of VLU. Compared with 4-layer bandaging, this system was found to be as effective at healing VLU in 1 trial and superior in another trial (45, 46). However, compression hosiery has a higher risk for noncompliance because they are difficult to remove and can be easily soiled. Compression hosiery may also result in less-frequent patient follow-up and limit the clinician's ability to intervene in patients who do not improve or whose symptoms worsen. Therefore, compression bandages remain the standard of care for patients with VLU.

A recent open-label trial (43) tested the effects of 5 compression interventions in treatment of VLU. One hundred seventeen patients with VLU were randomly assigned to receive compression with an intermittent pneumatic system, 2-layer hosiery, 4-layer bandages, 2-layer short-stretch bandages, or Unna boots. After 2 months of treatment, healing rates were no different in the intermittent pneumatic system, 2-layer hosiery, and 4-layer bandage groups (57%, 57%, and 59%, respectively), and all 3 were significantly better than the 2-layer short-stretch bandages and the Unna boots (17% and 20%, respectively). Similar trends between the 5 groups were also found in specific wound measures of area, perimeter, and overall prognostic score.

How long should clinicians prescribe compression therapy?

Compression therapy should continue until the ulcer heals. After healing, patients should wear graded compression stockings or other removable compression devices indefinitely to prevent ulcer recurrence. Assuming proper measurement and fitting of stockings, specific instructions on how to put on compression stockings may enhance adherence. Arthritic, obese, or elderly patients often have difficulty donning the stockings and assistive devices may be helpful. Repeated use and washing reduces elasticity; thus, they should be replaced at least every 6 months.

What is the role of medication?

Aspirin, whose anti-inflammatory action may have beneficial effects in venous ulcers, has been

41. Margolis DJ, Cohen JH. Management of chronic venous leg ulcers: a literature-guided approach. Clin Dermatol. 1994;12:19-26. [PMID: 8180941]
42. Dickey JW Jr. Stasis ulcers: the role of compliance in healing. South Med J. 1991;84:557-61. [PMID: 2035072]
43. Dolibog P, Franek A, Taradaj J, Dolibog P, Blaszczak E, Polak A, et al. A comparative clinical study on five types of compression therapy in patients with venous leg ulcers. Int J Med Sci. 2014;11:34-43. [PMID: 24396284]
44. O'Meara S, Cullum N, Nelson EA, Dumville JC. Compression for venous leg ulcers. Cochrane Database of Systematic Reviews: Wiley-Blackwell; 2012.
45. Amsler F, Willenberg T, Blättler W. In search of optimal compression therapy for venous leg ulcers: a meta-analysis of studies comparing diverse [corrected] bandages with specifically designed stockings. J Vasc Surg. 2009;50:668-74. [PMID: 19595551]
46. Ashby RL, Gabe R, Ali S, Adderley U, Bland JM, Cullum NA, et al. Clinical and cost-effectiveness of compression hosiery versus compression bandages in treatment of venous leg ulcers (Venous leg Ulcer Study IV, VenUS IV): a randomised controlled trial. Lancet. 2014;383:871-9. [PMID: 24315520] controlled trial. Lancet. 2014;383.

shown to improve healing when given 300 mg daily in combination with compression compared with placebo. Similarly, a recent RCT found evidence of a 46% reduction in healing time at the same dose compared with compression alone (47).

A 2012, an RCT in Spain (47) randomly assigned 51 patients with VLU to receive standard care or standard care plus 300 mg of aspirin daily. Although ulcer healing rate in both groups was similar, the intervention group healed faster (12 weeks vs. 22 weeks in the control group). About 30% of patients in both groups had ulcer recurrence. However, patients in the intervention group had prolonged time to recurrence (39 days vs. 16 days in the control group), although the clinical significance of recurrence within 2.5 weeks compared with slightly more than a month could be questioned. Of note, the study was well-designed and featured a long follow-up period (more than 2 years); however, 1 weakness was the disproportionate number of patients with long-standing ulcers in the control group (more than 1 year), which is a known negative prognostic factor.

Pentoxifylline, a methylxanthine derivative, has been well-studied for treating VLU. An updated systematic review performed by the Cochrane Collaboration on the use of pentoxifylline to treat VLU analyzed 12 trials involving 864 patients and concluded that pentoxifylline (800 mg 3 times daily) is an effective adjuvant to compression bandages. Further, a dose of 400 mg pentoxifylline 3 times a day in conjunction with compression therapy significantly decreased both time to complete wound healing and ulcer size after 3 months (48). Stanozolol, a synthetic anabolic steroid with fibrinolytic properties, is a schedule III controlled substance that reduces pain and the inflammation and induration of LDS but does not speed healing. Oxandrolone, another anabolic steroid, has been studied less but may be similarly useful. Horse chestnut seed extract, with its active ingredient, aescin, has been studied extensively and is available without prescription. It is similar to compression stockings in its ability to reduce ankle circumference, edema, and associated symptoms (pain, heaviness, pruritus, and swelling); however, it has not been shown to improve healing. Finally, in light of emerging evidence of a neuropathic origin of pain in some patients with VLU, such medications as amitriptyline, gabapentin, and pregabalin should be considered.

What is the role of growth factors?

Double-blind, RCTs have demonstrated that topical and perilesional injection of granulocyte macrophage colony-stimulating factor (GM-CSF) significantly increases healing rates of chronic leg ulcers compared with control (49). It promotes wound healing through many mechanisms that affect one or all of the wound-healing phases (i.e., homeostasis, inflammation, proliferation, and maturation) and increases vascularization. Although GM-CSF is U.S. Food and Drug Administration (FDA)–approved for treating neutropenia, it is not approved for wound healing: Phase 3 trials were stopped because of significant bone pain associated with the perilesional injections.

What is the role of physical therapy or exercise?

Pilot studies have suggested that physical therapy or exercise programs targeting improvement of range of ankle movement and calf muscle pump function might be a useful adjunctive therapy for enhancing ulcer healing. However, existing evidence regarding these approaches has been conflicting and well-designed RCTs are lacking. A recently published underpowered study demonstrated a 24% effect size in healing of VLU with self-managed exercise intervention and

47. del Río Solá ML, Antonio J, Fajardo G, Vaquero Puerta C. Influence of aspirin therapy in the ulcer associated with chronic venous insufficiency. Ann Vasc Surg. 2012;26:620-9. [PMID: 22437068]
48. Jull AB, Arroll B, Parag V, Waters J. Pentoxifylline for treating venous leg ulcers. Cochrane Database of Systematic Reviews: Wiley-Blackwell; 2012.
49. Jaschke E, Zabernigg A, Gattringer C. Recombinant human granulocyte-macrophage colony-stimulating factor applied locally in low doses enhances healing and prevents recurrence of chronic venous ulcers. Int J Dermatol. 1999;38: 380-6. [PMID: 10369552]
50. O'Brien J, Finlayson K, Kerr G, Edwards H. Evaluating the effectiveness of a self-management exercise intervention on wound healing, functional ability and health-related quality of life outcomes in adults with venous leg ulcers: a randomised controlled trial. Int Wound J. 2016. [PMID: 26817648] nd J. 2016.
51. Meagher H, Ryan D, Clarke-Moloney M, O'Laighin G, Grace PA. An experimental study of prescribed walking in the management of venous leg ulcers. J Wound Care. 2012;21:421-2, 424-6, 428 passim. [PMID: 22990394]
52. Tew GA, Michaels J, Crank H, Middleton G, Gumber A, Klonizakis M. Supervised exercise training as an adjunctive therapy for venous leg ulcers: study protocol for a randomised controlled trial. Trials. 2015;16:443. [PMID: 26445318]
53. Alavi A, Sibbald RG, Phillips TJ, Miller OF, Margolis DJ, Marston W, et al. What's new: Management of venous leg ulcers: Approach to venous leg ulcers. J Am Acad Dermatol. 2016;74: 627-40. [PMID: 26979354]
54. Dimitrijevich SD, Paranjape S, Wilson JR, Gracy RW, Mills JG. Effect of hyperbaric oxygen on human skin cells in culture and in human dermal and skin equivalents. Wound Repair Regen. 1999;7:53-64. [PMID: 10231506]

showed that better adherence to the regimen was associated with superior results (50). Another study reported an association between an increased number of steps taken daily and decreased time to VLU healing (51). An RCT that involves 80 adults with VLU that compares compression therapy with compression therapy combined with 12 weeks of supervised exercise program is under way (52).

What is the role of hyperbaric oxygen therapy?

The use of hyperbaric oxygen therapy (HBOT) in treatment of chronic ulcers continues to be controversial. Briefly, HBOT involves administering 100% oxygen at 2–2.5 atmosphere absolute for 60- to 120-minute periods for approximately 15–30 sessions. It is considered an adjunct to standard wound care, and its goal is to increase the partial pressure of oxygen at the wound. Although tissue hypoxia is a driving force in healing acute wounds, the role of HBOT in the pathogenesis and treatment of chronic VLU is unclear and may be related to the fibrin cuff theory. Fibrin cuffs formed around precapillary vessels may result in wound hypoxia (53), and therefore it is hypothesized that increased oxygen could benefit the healing process. There is in vitro evidence to support a general role for HBOT in promoting wound healing (54, 55), yet clinical evidence relating this therapy specifically for treatment of VLU is extremely limited and thus not routinely used. Evidence is limited to a single small RCT (n = 16) that demonstrated a mild benefit of HBOT, 2.5 atmosphere absolute, applied 5 times a week for 6 weeks in reducing the wound area (35.7% reduction in the HBOT group at 6 weeks compared with 2.7% in the control group; $P < 0.001$) (56).

What is the role of surgical debridement or skin grafting?

Debridement involves removal of nonviable tissue to achieve an appropriate wound bed with granulation tissue. Surgical debridement involves the use of a sharp surgical instrument (e.g., curette or scalpel) to achieve this goal. Of note, enzymatic debridement (typically using collagenase cream) and biological debridement with larvae are additional options and may be useful in certain cases. Debridement remains the standard care despite a lack of controlled data on whether it has a clinically significant effect on healing. It is believed that adequate wound bed preparation is essential for removing unresponsive wound bed and wound edge cells, decreasing the bacterial burden, and promoting healthy granulation tissue (57).

Skin grafting has been used for large or slow-healing venous ulcers. In addition to enhancing healing, graft placement may rapidly decrease pain. Skin grafts also seem to result in improved functional status (58), better health-related quality of life, and self-esteem (59). Grafts work by a combination of graft "take" and provision of a pharmacologic stimulus to healing in the form of growth factors and cytokines, which result in edge healing (also known as the "edge effect"). Pinch grafts, split-thickness skin grafts, and micro-skin grafts have been successful in treating patients with VLU (60) but have not been subjected to well-done RCTs.

Skin equivalents, both cellular and acellular constructs, have been studied and used for refractory VLU. The bilayered living cellular construct (BLCC) (Apligraf, Organogenesis) is approved by the FDA to treat VLU. BLCC is an immunologically inert allogeneic cultured bilayer of human skin origin containing both epidermal and dermal compo-

55. Kairuz E, Upton Z, Dawson RA, Malda J. Hyperbaric oxygen stimulates epidermal reconstruction in human skin equivalents. Wound Repair Regen. 2007;15:266-74. [PMID: 17352760]
56. Hammarlund C, Sundberg T. Hyperbaric oxygen reduced size of chronic leg ulcers: a randomized double-blind study. Plast Reconstr Surg. 1994;93:829-33; discussion 834. [PMID: 8134442]
57. Falanga V, Saap LJ, Ozonoff A. Wound bed score and its correlation with healing of chronic wounds. Dermatol Ther. 2006;19:383-90. [PMID: 17199681]
58. Salomé GM, Ferreira LM. Impact of skin grafting of venous leg ulcers on functional status and pain. World J Surg. 2013;37:1438-45. [PMID: 23463396]
59. Salomé GM, Blanes L, Ferreira LM. The impact of skin grafting on the quality of life and self-esteem of patients with venous leg ulcers. World J Surg. 2013;38(1):233-40. [PMID: 24065417]
60. Jankunas V, Bagdonas R, Samsanavicius D, Rimdeika R. An Analysis of the Effectiveness of Skin Grafting to Treat Chronic Venous Leg Ulcers. Wounds. 2007;19:128-37. [PMID: 26110308]
61. Falanga VJ. Tissue engineering in wound repair. Adv Skin Wound Care. 2000;13:15-9. [PMID: 11074998]
62. Falanga V, Sabolinski M. A bilayered living skin construct (APLIGRAF) accelerates complete closure of hard-to-heal venous ulcers. Wound Repair Regen. 1999;7:201-7. [PMID: 10781211]
63. Brem H, Balledux J, Sukkarieh T, Carson P, Falanga V. Healing of venous ulcers of long duration with a bilayered living skin substitute: results from a general surgery and dermatology department. Dermatol Surg. 2001;27:915-9. [PMID: 11737123]
64. Mostow EN, Haraway GD, Dalsing M, Hodde JP, King D; OASIS Venus Ulcer Study Group. Effectiveness of an extracellular matrix graft (OASIS Wound Matrix) in the treatment of chronic leg ulcers: a randomized clinical trial. J Vasc Surg. 2005;41:837-43. [PMID: 15886669]

nents. When combined with standard-of care compression therapy, studies have shown that BLCC is significantly more effective in achieving complete wound closure ($P < 0.01$), 3 times more effective than compression alone at 8 weeks ($P = 0.008$), and 2 times more effective by 6 months ($P = 0.002$) (61, 62). Skin equivalents are particularly effective in long-standing VLU (more than 1 year in duration) that have been resistant to conventional treatment (63).

A biomaterial derived from porcine small intestine submucosa (Oasis, Smith & Nephew) also improves healing compared with compression therapy alone (64). However, when compared with BLCC in treatment of VLU in a comparative effectiveness evaluation, BLCC was superior, increasing the probability of healing by 29% (65). Another potentially useful, well-tolerated, and safe advanced wound care matrix is a poly-N-acetyl glucosamine membrane (Talymed, Marine Polymer Technologies), which was significantly more effective than standard of care alone when applied every other week to VLU (66). Amniotic membrane transplantation has been tried for years on chronic wounds and is considered safe; it reduced wound size and pain intensity (67) while promoting a good take of skin grafts (68). A recent RCT found amniotic membrane to reduce ulcer size and ulcer-related pain; however, it has not been shown to improve complete healing (69).

What is the role of venous surgery in treatment and prevention?

The role of superficial venous surgery for healing patients with VLU is controversial. Surgical correction of superficial venous reflux in addition to compression bandaging does not improve ulcer healing but reduces recurrence and results in more ulcer-free time (16, 70), especially for medial or recurrent ulcers. Multiple deep venous valve repairs have been associated with an increased number of healing ulcers in patients with primary deep venous incompetence (71); however, a recent Cochrane database systematic review found no evidence for benefit or harm of valvuloplasty in the treatment of these patients. Venous ligation by open surgery has significant potential morbidity (such as risks associated with general anesthesia, pain, bleeding, wound infection, deep venous thrombosis, and creation of another potentially nonhealing wound). Subfascial endoscopic perforator surgery is less invasive and safer and may be associated with improved healing as well as decreased recurrence (72) for certain VLU, although well-done studies are lacking. Minimally invasive procedures, such as endovenous thermal ablation with laser, radiofrequency, or steam; ultrasound-guided foam sclerotherapy; and cyanoacrylate embolization are also effective in obliterating incompetent superficial and perforating veins to treat CVI and decrease VLU recurrence.

When should clinicians consider referring the patient to a surgical or nonsurgical specialist for treatment?

Depending on wound size and duration, between 30% and 75% of patients with VLU heal by 6 months of treatment (40). Prognostic factors consistently associated with nonhealing are larger wound area (>5 cm^2) and long duration (>6 months) (73). Other proposed indicators of slow healing include LDS and ulcer history (40), elevated body mass index (>33 kg/m), physical inactivity (daily walking <200 m), depth of the ulcer (>2 cm) (74), prolonged venous filling time, deep venous insufficiency, and atypical location of the ulcer on the posterior

65. Marston WA, Sabolinski ML, Parsons NB, Kirsner RS. Comparative effectiveness of a bilayered living cellular construct and a porcine collagen wound dressing in the treatment of venous leg ulcers. Wound Repair Regen. 2014;22:334-40. [PMID: 24628712]
66. Kelechi TJ, Mueller M, Hankin CS, Bronstone A, Samies J, Bonham PA. A randomized, investigator-blinded, controlled pilot study to evaluate the safety and efficacy of a poly-N-acetyl glucosamine-derived membrane material in patients with venous leg ulcers. J Am Acad Dermatol. 2012;66:e209-15. [PMID: 21620515]
67. Alsina-Gibert M, Pedregosa-Fauste S. Amniotic membrane transplantation in the treatment of chronic lower limb ulcers. Actas Dermosifiliogr (English Edition). 2012;103:608-13. [PMID: 22578292]
68. Ward DJ, Bennett JP, Burgos H, Fabre J. The healing of chronic venous leg ulcers with prepared human amnion. Br J Plast Surg. 1989;42:463-7. [PMID: 2670029]
69. Serena TE, Carter MJ, Le LT, Sabo MJ, DiMarco DT; EpiFix VLU Study Group. A multicenter, randomized, controlled clinical trial evaluating the use of dehydrated human amnion/chorion membrane allografts and multilayer compression therapy vs. multilayer compression therapy alone in the treatment of venous leg ulcers. Wound Repair Regen. 2014;22:688-93. [PMID: 25224019]
70. Howard DP, Howard A, Kothari A, Wales L, Guest M, Davies AH. The role of superficial venous surgery in the management of venous ulcers: a systematic review. Eur J Vasc Endovasc Surg. 2008;36:458-65. [PMID: 18675558]
71. Lane RJ, Cuzzilla ML, McMahon CG. Intermediate to long-term results of repairing incompetent multiple deep venous valves using external valvular stenting. ANZ J Surg. 2003;73:267-74. [PMID: 12752280]

calf (75). On the other hand, a small ulcer surface, shorter duration, decreased calf circumference >3 cm, and emergence of new skin islets during the first 50 days of treatment have been suggested as favorable prognostic factors for ulcer healing (74). Wound Healing Society guidelines affirm that wounds that fail to decrease in size during the first month of treatment are unlikely to heal and would benefit most from adjuvant advanced therapies and referral to a wound specialist. Because there are no Accreditation Council for Graduate Medical Education–accredited fellowships that specifically focus on wound management, expertise in wound healing may be found in a variety of specialties, including vascular medicine and surgery, podiatry, and dermatology.

How should clinicians educate patients?

The mainstay of prevention of VLU is compression therapy, although adherence to therapy is often poor and this directly affects recurrence rates (76).

Although one study found that an educational intervention helped reduce recurrence, it did not improve adherence to compression therapy. Educational interventions, such as providing materials to patients on the pathophysiology, management, and prevention of VLU, may be helpful. Data suggest that video-based educational intervention improves patients' knowledge of their disease better than pamphlets (77). Patient support groups may be an avenue for providing education on self-management. A recent Cochrane review identified only 2 studies that tested educational interventions for VLU healing and prevention of recurrence (78). Interestingly, neither study found significant differences between the educational intervention groups and the control groups in long-term healing rates, recurrence rates, or compliance with compression therapy. The reviewers concluded that robust evidence on the efficacy of educational interventions for VLU management and prevention is lacking.

Treatment... The goals of treatment for patients with VLU include reducing edema, improving pain and LDS, ulcer healing, and preventing recurrence. Maintanence of a moist wound bed, regular sharp debridement, control of infection, and compression with elastic multilayer bandages are considered standards of care. Patients with VLU who do not improve within 4 weeks may benefit from referral to a wound expert and adjuvant therapies, such as aspirin, pentoxifylline, and cell-based or matrix-based grafting. Surgical interventions to correct venous disease may be considered, but the best data suggest that these treatments prevent recurrence as opposed to improving healing. Once healed, VLU are best prevented by indefinite use of compression stockings and vascular intervention.

CLINICAL BOTTOM LINE

Practice Improvement

What do professional organizations recommend regarding management of VLU?

Several treatment guidelines for management of VLU have been published and updated recently.

In the United States, the Wound Healing Society (79) as well as the Society for Vascular Surgery together with the American Venous Forum (36) have both published evidence-based management guidelines.

72. Tenbrook JA Jr, Iafrati MD, O'donnell TF Jr, Wolf MP, Hoffman SN, Pauker SG, et al. Systematic review of outcomes after surgical management of venous disease incorporating subfascial endoscopic perforator surgery. J Vasc Surg. 2004;39:583-9. [PMID: 14981453]
73. Margolis DJ, Berlin JA, Strom BL. Which venous leg ulcers will heal with limb compression bandages? Am J Med. 2000; 109:15-9. [PMID: 10936473]
74. Milic DJ, Zivic SS, Bogdanovic DC, Karanovic ND, Golubovic ZV. Risk factors related to the failure of venous leg ulcers to heal with compression treatment. J Vasc Surg. 2009;49: 1242-7. [PMID: 19233601]
75. Szewczyk MT, Jawien A, Migdalski A, Piotrowicz R, Grzela T, Brazis P. Predicting time to healing by anatomical assessment of venous pathology. Med Sci Monit. 2009;15:CR74-81. [PMID: 19179971]
76. Moffatt C, Kommala D, Dourdin N, Choe Y. Venous leg ulcers: patient concordance with compression therapy and its impact on healing and prevention of recurrence. Int Wound J. 2009;6: 386-93. [PMID: 19912396]
77. Baquerizo Nole KL, Yim E, Van Driessche F, Lamel SA, Richmond NA, Braun LR, et al. Educational interventions in venous leg ulcer patients [Letter]. Wound Repair Regen. 2015;23:137-40. [PMID: 25487073]
78. Weller CD, Buchbinder R, Johnston RV. Interventions for helping people adhere to compression treatments for venous leg ulceration. Cochrane Database Syst Rev. 2016; 3:CD008378. [PMID: 26932818]
79. Tang JC, Marston WA, Kirsner RS. Wound Healing Society (WHS) venous ulcer treatment guidelines: what's new in five years? Wound Repair Regen. 2012;20: 619-37. [PMID: 22805581] doi:10.1111/j.1524-475X.2012.00815.x

In the Clinic

Tool Kit

Venous Leg Ulcers

Patient Information

http://my.clevelandclinic.org/services/heart/disorders/arterial-disease/lower-extremity-ulcers
Information from the Cleveland Clinic on venous leg ulcers as well as other lower extremity ulcers and venous disease overview.

https://www.nlm.nih.gov/medlineplus/ency/patientinstructions/000744.htm
Medline Plus health information for patients about venous leg ulcers.

www.veinforum.org/patients/what-is-vein-disease/what-is-chronic-venous-disease.html
www.veinforum.org/patients/what-is-vein-disease/what-is-compression-therapy.html
Information from the American Venous Forum on chronic venous disease and compression therapy.

Clinical Guidelines

www.gacguidelines.ca/site/GAC_Guidelines/assets/pdf/LEGU05-6_Venous_Leg_Ulcer_Summary.pdf
Recommendations for preventing venous leg ulcers from the Guidelines Advisory Committee.

www.awma.com.au/publications/2011_awma_vlug.pdf
Australia and New Zealand clinical practice guideline on the prevention and management of venous leg ulcers.

www.sign.ac.uk/pdf/sign120.pdf
Management of chronic venous leg ulcers guidelines by the Scottish Intercollegiate Guideline Network.

www.jvascsurg.org/article/S0741-5214(14)00851-9/pdf
Clinical practice guidelines for management of chronic venous leg ulcers from the Society for Vascular Surgery and the American Venous Forum.

http://onlinelibrary.wiley.com/doi/10.1111/j.1524-475X.2006.00174.x/epdf
Guidelines for treatment of venous ulcers from the Wound Healing Society.

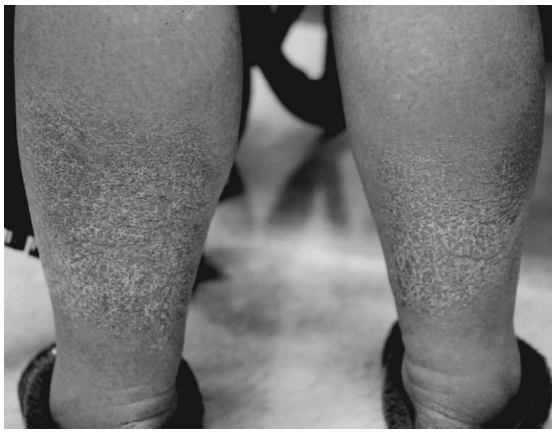
WHAT YOU SHOULD KNOW ABOUT VENOUS LEG ULCERS

In the Clinic
Annals of Internal Medicine

What Are Venous Leg Ulcers?

Venous leg ulcers (VLU) are sores or wounds that develop on the skin of the leg. These sores can take a long time to heal and sometimes come back after treatment. VLU happens because of poor blood flow in the veins of the legs. You are at higher risk for VLU if you:

- Are over 55 years old
- Have problems with blood flow in the legs
- Have a family history of blood flow problems
- Have a history of blood clots
- Have bone or joint disease, such as arthritis, in your leg or ankle
- Are a person with obesity
- Sit or stand for long periods
- Have had multiple pregnancies



What Are the Warning Signs?

- A painful sore on the lower leg or ankle
- Swelling and aching in the leg
- Discolored skin on the leg

How Are They Diagnosed?

- Your doctor will ask you questions about your medical history and closely examine the leg.
- Your doctor may take a picture of your veins called an ultrasound. Sometimes other tests are needed, such as a CT scan, which takes more pictures of your veins and gives additional information to your doctor.
- You may need a blood test. In some cases, your doctor may take a small sample of the skin from your leg for testing.

How Are They Treated?

- Your wound will be cleaned and bandaged to prevent infection and help it heal.
- Compression devices must be worn. These devices may be in the form of multiple tight bandages or a soft cast worn on your lower legs to help with blood flow and decrease swelling.
- Your doctor may tell you to raise your feet above your heart as often as possible. You can do this by lying down or sitting with your feet raised on a pillow or chair.
- Your doctor may prescribe medicines to help your sores heal.
- Over-the-counter medicines can be taken to help manage pain.
- If your VLU keeps coming back, you may need other treatments.

How Can They Be Prevented?

Doctors are not yet sure if VLU can be prevented. However, there are things you can do to lower your risk and prevent VLU from coming back:

- Keep health conditions, such as heart failure, diabetes, or peripheral artery disease (PAD), under control.
- Avoid sitting or standing for long periods.
- Eat a healthy diet and exercise regularly.
- Try to maintain a healthy weight.
- Wear compression stockings.
- Surgery to stop VLU from coming back may be an option for some people. Ask your doctor if it is right for you.

Questions for My Doctor

- What caused my VLU?
- What should I do if my VLU keeps coming back?
- Will I need surgery?
- Will I need more testing?
- Should I clean my sores with special soap?
- How often should I change my bandages?
- How should I dress my sores after I shower?
- Do I have to wear compression stockings all day and night?
- How can I reduce my risk for getting VLU again?

For More Information

ACP[SM]
American College of Physicians
Leading Internal Medicine, Improving Lives

American Academy of Family Physicians
www.aafp.org/afp/2010/0415/p1003.html

Medline Plus
www.nlm.nih.gov/medlineplus/ency/patientinstructions/000744.htm

Patient Information