

VENOUS LEG ULCERS: MODERN EVALUATION AND MANAGEMENT

Steven E. Zimmet, MD

Dermatologic Surgery, volume 25, 236-241, 1999

A Common but Neglected Problem

Epidemiological studies have found that the prevalence of leg ulceration in the adult population, either active or healed, is about 1-2%. Although a variety of etiologic factors can cause leg ulcers, the majority of leg ulcer patients have venous disease. While chronic venous insufficiency has received less attention than arterial insufficiency, it is estimated to be 10 times more common. Despite the prevalence of venous ulcers, they are often neglected or managed inadequately. Patients may walk around for months or even years with just a local dressing over an ulcer. Emphasis may be placed on which ointment, salve, antibiotic or enzyme should be used. The ulcers may be grafted only to recur.



Recognizing a Venous Ulcer

The classical presentation of a venous leg ulcer is an irregularly-shaped partial thickness wound with well-defined borders, surrounded by erythematous or hyperpigmented indurated skin (acute or chronic lipodermatosclerosis).

Typical appearing venous ulcer of the gaiter area

location, but are usually found on the distal medial aspect of the lower leg ("gaiter" area). A lateral venous ulcer may be associated with short saphenous insufficiency. Varicose veins are often present in the venous ulcer patient. Typically there are telangiectatic veins of the medial ankle, so-called corona phlebectatica, indicative of chronic venous insufficiency. Edema of the ankle area is common, although in some patients the skin is brown, thickened and the ankle circumference is actually narrowed.

A yellow-white exudate is commonly observed. Venous ulcers vary in size and

Other etiologies must be considered. Metabolic, neuropathic, neoplastic, vasculitic, infectious, hematologic and collagen vascular diseases should be considered. However, if arterial insufficiency is ruled out and the patient has normal pinprick sensation in the face of a typical appearing venous ulcer, then a venous etiology will be found in about 95% of cases.

The Calf Muscle Pump

The calf muscle pump of the leg is the primary mechanism the body has to return blood from the leg to the heart. The calf pump mechanism consists of the calf muscles, the deep venous compartment or pump chamber, a superficial compartment connecting the superficial veins to the deep veins via perforators, and an outflow tract (popliteal vein).

During systole (calf muscle contraction), blood in the pump chamber moves cephalad through the outflow tract. During diastole (calf muscle relaxation), blood fills the emptied pump chamber with flow from the superficial veins via perforators and from distal deep veins. Normal valvular function prevents reflux and permits one-way flow from superficial to deep and from distal to proximal.

Calf pump dysfunction may occur because of deep venous insufficiency (primary or post-thrombotic), deep venous obstruction, perforator insufficiency, superficial venous insufficiency, arteriovenous fistulas, neuromuscular dysfunction, or a combination of the above. The result of calf pump dysfunction is a failure to lower venous pressure in the distal veins of the leg; a condition referred to as ambulatory venous hypertension.

Macrocirculatory Misconceptions

As noted above, abnormalities of any of the components of the calf pump may contribute to calf pump dysfunction. Nonetheless, the main factor in calf pump failure is usually venous insufficiency. A common misconception is that a venous leg ulcer is pathognomonic of a post-thrombotic syndrome. It is true that a deep venous thrombosis may cause deep venous insufficiency and/or obstruction and lead to venous hypertension. However, it is not uncommon for venous leg ulcers to be due solely to superficial venous disease and/or perforator disease. The common final pathway to venous ulceration is venous hypertension, whether the overload comes from superficial, perforator, deep vein or combination disease.

Microcirculatory Abnormalities

It is unclear exactly how ambulatory venous hypertension causes ulceration, although recent research is shedding light on potential pathways. Chronic venous hypertension is associated with a number of microcirculatory abnormalities. These include extravasation of macromolecules (fibrinogen, albumin, a-macroglobulin and others) pericapillary fibrin cuff formation, abnormalities of fibrinolysis, leukocyte trapping and activation, lymphatic microangiopathy and abnormalities of the capillary network.

In attempting to explain the pathogenesis of venous ulceration, Browse and Burnand put forth the fibrin cuff theory. They suggest that pericapillary fibrin cuffs, typically but not exclusively found in patients with chronic venous insufficiency, act as an oxygen diffusion barrier. A number of publications have cast doubt on this premise. A more recent theory involves white cell rheology. With the reduction of capillary blood flow in venous hypertension, trains of white blood cells cause temporary plugging of capillaries.

Glycoproteins cause leukocytes to become attached to capillary endothelium. These white cells become activated, releasing free radicals, proteolytic enzymes, and cytokines. Perhaps this chronic inflammatory state, if severe enough, leads to tissue damage and ulceration. Another hypothesis posits that fibrinogen and other macromolecules, which leak into the dermis as a result of venous hypertension and endothelial injury, "trap" growth factors and matrix proteins and render them unavailable for the maintenance of tissue integrity and repair processes. It is interesting to note that venous ulcer wound fluid, as distinguished from other acute wound fluid, inhibits in-vitro proliferation of cells involved in wound healing such as fibroblasts, endothelial cells, and keratinocytes. Bollinger states that the main factor in venous ulceration is focal microvascular ischemia secondary to the reduction of nutritive skin capillaries seen in chronic venous insufficiency. Obviously these theories are not mutually exclusive. As the pathogenesis of venous ulceration is elucidated, it is likely that therapeutic advances will occur.

The History and Physical

Details relating to the ulcer such as the duration and past treatment of the ulcer, the presence and characteristics of exudate, and the presence of pain and factors that aggravate and alleviate the symptoms should be sought. A history of similar lesions and their course and management is useful. In addition, a history of thromboembolic events, varicose veins, past vein treatment, tobacco abuse, history of arterial disease, diabetes, arthritis, ankle joint immobility, inflammatory bowel disease, and collagen vascular disease should be obtained. The patient's occupation and social situation should be determined.

Physical examination should include a careful inspection and palpation of the legs, from the foot to the groin, for varicose veins. The suprapubic area should also be inspected for varicosities, which might represent collateral bypass of an old ileofemoral thrombosis.



Suprapubic varices in a patient with a remote ileofemoral thrombosis

Percussion of veins helps to trace the origin and extent of varices. Examine for signs of chronic venous insufficiency such as ankle flare, eczema, hyperpigmentation, induration and atrophie blanche. Ankle and calf diameters should be recorded for both legs. The characteristics of edema (pitting vs. non-pitting) should be noted.

The ulcer(s) size, base, appearance and location, in addition to the condition of the surrounding skin, should be described. The presence and characteristics of exudate and signs of true tissue infection are noted. Note that acute lipodermatosclerosis, characterized by an erythematous tender area of induration, is commonly mistaken for cellulitis.



Acute painful lipodermatosclerosis

It is an inflammatory condition due to venous insufficiency, which does not cause fever and is unresponsive to antibiotics.

Signs of arterial insufficiency (cool skin, loss of extremity hair, shiny and atrophic skin, pallor on leg elevation) should be noted. Arterial pulses should be palpated. If there is suspicion of arterial insufficiency, an ankle brachial index (ABI; systolic pressure at the ankle divided by that at the brachial artery; normal > 0.9) should be done. Note that the ABI is unreliable in

assessing arterial insufficiency in diabetes and other conditions where there may be arterial calcification. In such cases, metatarsal or toe pressures are more reliable. Ankle mobility and gait should be evaluated. Peripheral sensation should be checked.

Elucidate the Underlying Abnormal Hemodynamics

It is important to define the underlying abnormal hemodynamics of a venous ulcer patient because of the implications for treatment (see Individualize Treatment section below). In addition to a history and physical, a functional and anatomical test should be used to obtain a complete picture of the venous abnormality. Duplex ultrasound is a non-invasive approach that yields both anatomic and functional information about the venous system of the legs. Investigation of the greater saphenous vein, lesser saphenous vein, perforating veins, femoral vein, popliteal vein and deep veins of the calf should be done. Plethysmographic tests, such as photoplethysmography and air plethysmography, are functional tests that can be used to evaluate venous reflux, calf pump function and venous outflow. Utilizing tourniquets to occlude superficial veins, these plethysmographic tests can help assess the likelihood of hemodynamic improvement following treatment of superficial and perforator vein incompetence in a patient who also has deep vein disease. Invasive tests are generally not necessary.

Compression is the Cornerstone

All ambulant patients with uninfected venous ulceration require compression treatment. Such treatment should be sustained compression that produces a pressure gradient (highest at the ankle). Bandages (elastic and inelastic) and stockings have been used. Inelastic compression devices such as the CircAid (CircAid®, Circaid Medical Products, Inc., San Diego, CA) have also been used. Generally the adage is true that compression bandaging obtains a result and compression stockings maintain the result. In the decongestive phase, compression bandaging is best done with inelastic "short-stretch" bandages. Expertise in applying a short-stretch bandage is required. Short-stretch bandages may be left on for several days up to a week. Early in treatment, until exudate and edema diminish, it may be necessary to re-apply the bandages more frequently. In the face of concomitant arterial insufficiency, one must exercise considerable caution; it is

imperative that any compression exert a low resting pressure (inelastic compression). If arterial insufficiency is severe, compression of any type may be contraindicated.

Examples of short-stretch bandages are Unna's paste bandage and Comprilan® (Beiersdorf Medical, Charlotte, NC). Ace® bandages are inappropriate as a treatment of venous ulceration. Prescription compression stockings can be used in the maintenance phase of treatment. Generally calf length stockings are used with 30-40 mmHg or 40-50 mmHg. It is easier for some patients to apply a zippered stocking over a cotton liner (Jobst Ulcercare®; Jobst-A Beiersdorf Company, Charlotte, NC) or to superimpose two 20-30 mmHg stockings (yielding 40 mmHg). Consider intermittent pneumatic compression in patients who don't respond to standard compression measures and in patients who are not ambulatory.

Compression leads to increased venous flow, decreased pathological reflux while walking, and increased ejection volume with activation of the calf pump. Tissue pressure is increased which favors resorption of edema fluid. In order to achieve maximum benefit from compression the patient needs to ambulate.

Wound Care

Local wound care is a matter of clinical judgment. Debridement can be accomplished with surgical instruments, topical enzymatic agents and by autolytic debridement with occlusive dressings. Generally it is appropriate to choose the least invasive methods first. Normal saline can be used for wound cleansing. Wounds should be covered with a semipermeable dressing or nonadherent gauze. If there is a lot of exudate, choose a dressing which is highly absorptive, such as Allevyn (Smith & Nephew) or Cutinova-Foam (Biersdorf-Jobst). Remember that good compression is useful in reducing non-infectious exudate. Moisture-retentive dressings frequently cause a malodorous yellow discharge that many patients mistakenly think represents infection. A foam pad worn over the dressing and under the compression bandaging increases local compression and helps reduce local venous hypertension. Topical antibiotics are generally not used. In fact, contact dermatitis to topical antibiotics commonly develops in patients with chronic venous insufficiency. However, one study found venous ulcer patients treated with silver sulfadiazine cream plus compression healed significantly faster than a group treated with compression alone. In the face of an acute weeping dermatitis, consider advising leg elevation and the use of saline soaks followed by a mid-potency cortisone cream. If there is a concern about cortisone sensitization, consider a short course of oral corticosteroids. Petrolatum or other bland emollients can be used on surrounding dry skin. If true tissue infection is suspected, cultures should be taken and treatment begun with systemic antibiotics.

Individualize Treatment

If a patient has hemodynamically significant superficial venous disease, either isolated or in combination with perforator or deep vein disease, important hemodynamic

improvement will be obtained by treating the varicose veins and the long-term prognosis thereby greatly improved. Treatment may include surgery, sclerotherapy, or both. Classically, it is stated that the exception may be in the face of significant deep venous obstruction, where the superficial varices act as an important outflow tract. Removal of superficial veins, in this situation, was said to be contraindicated. However, a recent study found that less than 10% of patients with deep venous obstruction had a significant decrease in venous outflow fraction when superficial veins were occluded. These authors suggested that deep vein collaterals may be more important than superficial collaterals following significant deep vein obstruction.

The hemodynamic significance of perforators in chronic venous insufficiency remains controversial. Nonetheless, the recent development of subfascial endoscopic ligation has significantly improved the surgical treatment of incompetent medial calf perforators. Although early reports are enthusiastic, failure of ulcer healing or recurrence of ulceration after endoscopic perforator ligation has ranged from 2.5% to 22%. A potential limitation of this technique is the difficulty in accessing perimalleolar perforators. A recent study found that 50% of incompetent perforators within 10 cms of the sole of the foot, identified pre-operatively by duplex ultrasound, were missed at subfascial endoscopy.

Deep venous reconstruction should only be done as a last resort and probably only as part of an appropriately designed clinical study. The fundamental treatment of deep venous insufficiency is lifelong compression. However, sclerotherapy of periulcer varices and perforators can significantly improve local venous hemodynamics and speed ulcer healing. Also, recent studies have demonstrated that some incompetent deep veins normalize following treatment of incompetent superficial veins, presumably as a result of reducing load on the deep veins.

Ancillary Measures

Patients should be instructed to maintain a normal weight and to avoid smoking. Nutritional deficiencies should be corrected. Regular brisk walking, 3-4 times per day for at least 30 minutes per walk, should be strongly encouraged. Long periods of sitting and standing and hot baths should be avoided. It's helpful to have the patient periodically elevate their leg above heart level and to raise the foot of their bed with 6" blocks. Manual lymphatic drainage, performed by trained therapists, can reduce the edema of chronic venous insufficiency. Physical therapy can improve ankle joint mobility. Diuretics generally are not used. Pentoxifylline seems to reduce WBC trapping and may improve venous ulcer healing when used in conjunction with compression therapy.

If a patient doesn't respond to appropriate therapy, the physician should question the adequacy of compression and/or patient compliance. The diagnosis needs to be reconsidered. Is there a tissue infection that is impairing healing? One should consider obtaining a biopsy of the ulcer edge to rule out malignancy.

Conclusion

There is a significant social and economic burden caused by chronic venous insufficiency. Newer methods of investigation have led to an improvement in our understanding of the pathophysiology of venous disease. Compression should serve as the cornerstone of treatment in venous ulcers. However, superficial and/or perforator disease may be the underlying cause of venous ulceration in a significant percentage of patients. Treatment of these patients with surgery and/or sclerotherapy can greatly improve their prognosis. Thus, one must define the basic underlying abnormality of the venous system and any associated diseases to form a rational, individualized management plan for the patient with venous ulceration.

References

1. Callam MJ, Ruckley CV, Harper DR. et al. Chronic ulceration of the leg: Extent of the problem and provision of care. *Br Med J* 1985;290:1855-6.
2. Widmer LK. Peripheral venous disorders. Prevalence and sociomedical importance. Basel Study III. Bern: Hans Huber, 1978:43-50.
3. Baker SR, Stacey MC, Jopp-McKay AG, Hoskin SE, Thompson PJ. Epidemiology of chronic venous ulcers. *Br J Surg* 1991;78:864-7.
4. Scriven JM, Hartshorne T, Bell PRF, Naylor AR, London NJM. Single-visit venous ulcer assessment clinic: the first year. *Br J Surg* 1997;84:334-36.
5. O'Donnell TF Jr. Chronic venous insufficiency: an overview of epidemiology, classification, and anatomic considerations. *Seminars Vasc Surg* 1988;1(2):60-65.
6. Goldman MP, Fronek A. The Alexander House Group. Consensus Paper on Venous Leg Ulcer. *JDSO* 1992;18:592-602.
7. Bass A, Chayan D, et al. Lateral venous ulcer and short saphenous vein insufficiency. *J Vasc Surg* 1997;25:654-57.
8. Cornwall JV, Lewis JD. Leg ulcers revisited. *Br J Surg* 1983;70:681.
9. Burton CS. Successful leg ulcer management. Annual Meeting of the AAD, 1993.
10. Hanrahan LM, Araki CT, Rodriguez AA, et al. Distribution of valvular incompetence in patients with venous stasis ulceration. *J Vasc Surg* 1991;13:805-11.
11. Hoare MC, Nicolaidis AN, Miles CR et al. The role of primary varicose veins in venous ulceration. *Surgery* 1982;92:450-3.
12. Darke SG, Penfold C. Venous ulceration and saphenous ligation. *Eur J Vasc Surg* 1992;6:4-9.
13. Zimmet SE. Leg Ulcers. *J Am Acad Derm* 1992;27:487-88.
14. Falanga V, Eaglstein WH. The "trap" hypothesis of venous ulceration. *Lancet* 1993;341:1006-8.
15. Browse NL, Burnand KG. The cause of venous ulceration. *Lancet* 1982;ii:243-5.
16. Coleridge Smith PD, Thomas P, Scurr JH, et al. Causes of venous ulceration: a new hypothesis? *Br Med J* 1988;296:1726-7.

17. Stibe E, Cheatle TR, Coleridge Smith PD, et al. Liposclerotic skin: A diffusion block or perfusion problem? *Phlebology* 1990;5:231-6.
18. Cheatle TR, McMullin GM, Farrah et al. Skin damage in chronic venous insufficiency: Does an oxygen diffusion barrier really exist? *J R Soc Med* 1990;83:48-9.
19. Michel CC. Oxygen diffusion in oedematous tissue and through pericapillary fibrin cuffs. *Phlebology* 1990;5:223-30.
20. Claudy AL, Mirshahi M, Suria C, et al. Detection of undegraded fibrin and tumor necrosis factor- α in venous leg ulcers. *J Am Acad Derm* 1991;25:623-7.
21. Bucalo B, Eaglstein WH, Falanga V. The effect of chronic wound fluid on cell proliferation in vitro. *J Invest Dermatol* 1989;92:539.
22. Bollinger A. A rejected letter to the editors of *The Lancet* and the need for angiologists to prove their usefulness. *VASA* 1993;22:361-63.
23. Partsch H. Laboratory Evaluation of the Patient with Chronic Venous Insufficiency. In Goldman MP and Bergan JJ, editors: *Ambulatory Treatment of Venous Disease: An illustrative guide*. St. Louis, 1996, pp 13-22, Mosby.
24. Bishop JB, Phillips LG, et al. A prospective randomized evaluator-blinded trial of two potential wound healing agents for the treatment of venous stasis ulcers. *J Vasc Surg* 1992;16:251-7.
25. Labropoulos N, Voltea N, Leon M, et al. The role of venous outflow obstruction in patients with chronic venous insufficiency. *Arch Surg* 1997; 132:46-51.
26. Bergan J. Endoscopic Subfascial Perforator Vein Interruption. In Goldman MP and Bergan JJ, editors: *Ambulatory Treatment of Venous Disease: An illustrative guide*, St. Louis, 1996, pp 173-178, Mosby.
27. Pierik EGJM, van Urk H, Wittens CHA. Efficacy of subfascial endoscopy in eradicating perforating veins of the lower leg and its relation with venous ulcer healing. *J Vasc Surg* 1997;26:255-59.
28. Qeral LA, Francisco JC, et al. The role of sclerotherapy as an adjunct to Unna's boot for treating venous ulcers: A prospective study. *J Vasc Surg* 1990;11:572-5.
29. Walsh JC, Bergan JJ, et al. Femoral venous reflux abolished by greater saphenous stripping. *Ann Vasc Surg* 1994;8:566-70.
30. Dormandy JA. Pharmacologic Treatment of Venous Leg Ulcers. *J CV Pharm* 1995;25 (suppl):S61-65.