Emerging Treatment Options for Venous Ulceration in Today’s Wound Care Practice

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Abstract: Lower-extremity ulcers represent the largest group of ulcers presenting to an outpatient wound care clinic and, of those, ulcers due to venous insufficiency and venous hypertension make up the largest subgroup of these ulcers. Interventions for chronic venous ulcers have evolved to painless, minimally invasive, office-based procedures performed under local anesthesia. Recent advances in the endovascular management of lower-extremity superficial venous insufficiency have the potential to significantly enhance initial and long-term management of these patients, as minimally invasive procedures provide faster recoveries and fewer procedural risks. Early intervention for venous insufficiency has been shown to significantly decrease long-term ulcer recurrence rates, and may increase healing of venous ulcers as well. Purpose. The purpose of this review and algorithm is to enhance understanding of venous ulceration and its underlying causes. Venous anatomy and pathophysiology will be reviewed. The etiology of chronic venous ulceration will be examined. Current practice guidelines and clinical outcomes will be reviewed. The newest treatment options, including minimally invasive therapy will be described. The current literature will be reviewed. A new algorithm for treatment that integrates the endovascular treatment of venous insufficiency into the current standard care for venous leg ulceration will be proposed. Method. A literature review was performed to review all current treatments for venous ulceration. Treatments that have Level I evidence (with a grade of recommendation of A or B) to support their use for venous leg ulceration were selected for incorporation into a new treatment algorithm. The level-of-evidence and strength-of-recommendation scheme used in the algorithm is based upon the system used by the Wound Healing Society in its chronic wounds clinical practice guidelines. Conclusion. It is intended that this new algorithm and approach to treatment will improve the immediate care of venous leg ulcer patients, reduce recurrence rates, increase patient satisfaction, and potentially expedite initial wound healing in the outpatient wound clinic setting.

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Venous Ulcers of the Legs — Treatable and Preventable

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There is great opportunity to fundamentally improve treatment results in venous leg ulceration. Leg ulcers are one of the largest single groups of ulcers treated in wound care centers in the United States, making up as much as 80% of leg ulcer series. Presently accepted statistics indicate that venous ulcers require an average of 24 weeks to heal; approximately 15% never heal; and recurrence is found once or multiple times in 15%–71% of cases. In reported populations of venous ulcers, 15%–71% are found to be recurrent lesions. The cost of treatment for venous ulcers in the United States is estimated to be $1–$5 billion annually.

In a venous ulcer, the extremity must have reflux in the superficial or deep veins or in sites of obstruction in the venous outflow sufficient to be a cause of ulceration in the observed site. These findings require an objective imaging test, usually a non-invasive venous duplex scan. There are “pure” venous ulcers, in which the only identifiable cause for ulceration is found in the venous system; and “mixed” venous ulcers, in which other factors exist that are capable of creating a leg ulcer in addition to the venous abnormality. Examples of such other causes include arterial insufficiency, lymphatic insufficiency, obesity, rheumatologic autoimmune disorders, and a long list of other unusual disorders.

TREATMENT OPTIONS HAVE ADVANCED

An attitude that venous ulcers are not curable and are destined to recur in the majority of instances developed when the diagnosis of a venous cause for an ulcer was based on soft clinical impressions without objective substantiation. Further, treatment was directed at simple closure of the skin wound without correction of the underlying venous abnormality. The cogent reasons for these attitudes have been changing during the past three decades with the advent of improved diagnosis using objective ultrasound imaging and the introduction of minimally invasive treatment techniques and highly focused interventions.

The key to these advances in managing venous ulcers has been the emergence of accurate, affordable, noninvasive ultrasound diagnosis of lower-extremity veins. Leg vein imaging by ultrasound emerged as the dominant diagnostic test in the 1980s and was refined for another decade into the present venous duplex ultrasound examination that is available worldwide. In 1994, a new classification of chronic venous disease was developed and subsequently refined. This has become the dominant international standard. The CEAP (clinical, etiologic, anatomic, and pathophysiologic) classification covers the four key aspects of the chronic venous condition.

Since then, published studies have become better standardized to report these critical aspects of the clinical cases, allowing for correlation of clinical states with anatomic distribution of sites of reflux and obstruction, segment by segment throughout the lower-extremity venous tree. It is now possible to safely and affordably observe the reflux and obstructive changes in the veins that underlie the appearance of venous ulcers.

At the same time, minimally invasive outpatient techniques have emerged to correct underlying venous defects and provide protection against recurrence once an ulcer is healed. Armed with accurate anatomic data for sites of reflux and obstruction, the surgeon or treating interventionalist can focus treatment on these critical sites. Thermal ablation has further improved minimally invasive treatments of the saphenous and perforator veins. Off-label use of liquid and foam sclerotherapy allows for more precise delivery to sites in the perforator and saphenous veins, in addition to conventional use in the peripheral varices.

CAUSES AND CLINICO-PATHOLOGIC COURSES OF ULCER FORMATION

The two important causes of venous ulceration are primary degenerative disease and post-thrombotic disease. One-half to two-thirds of venous ulcers are due to slowly progressive primary reflux disease that begins as varicose veins.

Over decades, a pure venous reflux problem with asymptomatic varicose veins progresses to a stage of variable discomfort, often with swelling, followed by a more advanced stage in which skin changes emerge and lead to ulceration. The skin changes often begin with brownish pigmentation, which pro-
gresses into dermal and subcutaneous thickening and scarring, and later results in tissue breakdown with ulcer formation. The risk of this conversion increases as patients reach 60–70 years. The other one-third to one-half of venous ulcers develop after deep vein thrombosis (DVT) and are prone to advance more rapidly to the ulcer stage in periods from 6 months to several years after the DVT event. These cases also have brownish discoloration of the skin — the so-called post-phlebitic appearance of pigmented, thickened, swollen legs. The clinical appearance of ulcers from primary venous reflux disease and post-thrombotic deep vein changes are similar enough that diagnosis of the ulcer’s cause requires an imaging examination by duplex scan in every case.

OPPORTUNITIES FOR DECREASING THE OCCURRENCE OF ULCERATION
The concept of life-long development of primary venous insufficiency leading to the late appearance of venous ulceration is important. This knowledge allows the primary physician to observe the status of the patient over a longitudinal time span and refer the patient for definitive diagnostic studies as the early varicose veins progress from aching pain and leg heaviness, to swelling, to skin changes.

Along this path, a definitive venous scan should be done, along with arterial evaluation with ankle/brachial ratios, to establish the validity of using compression wraps when the patient reaches later stages of the process. Ideally, the patient would be treated for axial superficial reflux when symptoms warrant treatment or when skin changes develop, before the first ulcer appears. When the disease has progressed to the first ulcer, immediate referral to the wound care or venous specialist is warranted to check the venous and arterial circulations, and to institute effective removal of axial venous reflux in the subcutaneous and perforator veins. This should be done at the same time that conventional pressure therapy is used to heal the ulcer. Failure to correct the axial reflux results in markedly higher ulcer recurrence rates7–9 and should be avoided. Combined obstructed and reflux disease due to scarring of the deep veins are likely in post-thrombotic ulceration. Often, there is superficial vein reflux due to associated primary disease. Managing these cases involves using effective compression with support stockings or garments and selective anticoagulation to prevent recurrent thromboses. Superficial reflux should be eliminated when the deep veins are found adequate to maintain venous return — a determination that can be evaluated by plethysmographic and volume outflow studies in the vascular laboratory.

SPECIFIC STEPS TO EFFECTIVE MANAGEMENT OF VENOUS ULCERATION
In the author’s practice, the prescription for effective treatment of venous leg ulcers and prevention of the first or the recurrent ulcer has several key elements:

1. Early, accurate diagnosis of the venous defect and stratification into pure and mixed venous ulcers is crucial. The earlier this determination can be made, the better for the long-term outlook. Delay in diagnosis may result in chronic scarring of the distal leg tissues, creating an extremity in which the distal tissues are too fibrotic to sustain a healthy state.
2. Early application of compression should be performed to correct swelling and progressive scarring and to initiate the healing process by improving the venous microcirculation.
3. Aggressive correction of axial reflux in the superficial and perforator veins of the affected leg should be performed. The use of the newer minimally invasive techniques of thermal ablation and selective sclerotherapy facilitates patient acceptance and outpatient ambulatory treatment.
4. Surveillance of the leg for new recurrent or progressive venous disease should be ongoing for the indefinite future. This can be done by the venous specialist or the informed primary physician.
5. The medical profession should change its attitude fundamentally to view chronic venous disease as a chronic degenerative malady that can be managed effectively to minimize the occurrence of both initial and recurrent ulcers. The primary physician needs to be engaged in the care of this disease entity.
6. Specialist attitudes must change to view venous leg ulcers as diagnosable and treatable, with recognized patterns of reflux and obstruction that can be successfully managed to minimize occurrence and recurrence of lower leg ulcers in the majority of cases.
7. Leg ulcer patients should be referred to wound care centers or venous specialists for definitive diagnosis and treatment early — ie, before the tissues of the lower leg become irreversibly scarred from prolonged swelling and venous hypertension.

References
Review and Benefits of Non-Invasive Diagnostic Ultrasound and Thermal Ablation

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Treatment of chronic venous leg ulcers has long centered on graduated compression therapy. Although this therapy is a major component of wound healing, it fails to prevent recurrences. Poor long-term adherence and suboptimal results with compression alone, even in the most adherent patients, has driven the search for a better option.¹

State-of-the-art surgical treatment for all forms of venous disease — from spider veins to venous ulceration — increasingly depends on an accurate anatomic and physiologic assessment of both the superficial and deep venous systems of the lower extremities. This can be accomplished with a comprehensive venous duplex scan of the lower extremity venous system. When performed correctly by an experienced vascular technician, this highly sensitive and specific noninvasive test is extremely accurate for diagnosing venous disease of the lower extremities.

PATIENT ASSESSMENT

Patients with CEAP Classification V or VI disease (advanced grades of venous insufficiency) often have both superficial as well as deep system venous pathology.² In general, the most advanced venous hypertension is associated with patients who have dual system involvement, concomitant venous thrombosis, or perforator incompetence. It is the venous hypertension that causes the subsequent chronic inflammation and eventual ulceration.

A recent clinical trial has clearly showed underlying reflux to be associated with the skin changes of chronic venous insufficiency.³ Results such as these have driven treatment toward intervention for the underlying reflux. Successful treatment of the reflux of the venous system leads to decrease in the venous pressure of the leg, commonly described as the ambulatory venous pressure. A decrease in the ambulatory venous pressure is associated with local improvement in the microcirculation of the skin and subcutaneous tissues, decreased pain, and decreased edema in patients with chronic venous disease.⁴⁻⁶

THE VENOUS DUPLEX SCAN

A comprehensive venous duplex scan of the lower extremities should be performed for all patients with advanced venous disease, including patients with venous ulceration. The information gained from the evaluation is necessary to direct specific surgical treatment.

The evaluation is a complete mapping of the deep and superficial venous systems, from the inguinal ligament to the foot. There are three systems of veins in the lower extremities: deep, superficial, and perforating. The anatomy and physiology of each of the three venous systems is completely evaluated. The great saphenous, small saphenous, intersaphenous, accessory saphenous, and all incompetent perforating veins are sized and the diameters are recorded. The absence and/or closure of a great saphenous vein or small saphenous vein from a previous surgical procedure is noted. Areas of acute or chronic thrombosis, scarring or thickening, tortuosity, and reflux (incompetence) are marked. If incompetent perforating veins are found, their location and size are noted on the worksheet. The location and vein of origin of all varicose clusters are noted as well. The deep venous system is evaluated for thrombosis, scarring, and reflux. When performed by an experienced technician, a detailed map of the venous system is obtained with all relevant pathology marked. See Figure 1 for an example of a complete duplex scan from a vascular lab.

The study must include an evaluation of the area in and around the ulcer bed, as frequently incompetent perforating veins are adjacent to or underneath the ulcer bed. This requires that all compression wraps or Unna boots and local/topical ulcer dressings be removed at the time of the scan. It is these authors’ practice to routinely perform duplex evaluations on ulcer patients the same day, just before a patient’s second visit to the wound care center. This results in uninterrupted wound care and provides the wound care center physician with the venous pathology early in the treatment course, allowing for early referral to a vein specialist.

The test is performed with the patient is both supine and standing positions. B-mode ultrasound imaging, color
flow imaging, and Doppler spectral waveform analysis are used to evaluate the venous system. The reverse Trendelenberg or standing position is an absolute requirement for accurate diagnosis of reflux and incompetence of the superficial and perforating systems.

The tests should be performed by a registered vascular technologist (RVT) who has had additional specialty training in venous disease or who currently works with a vascular interventionalist who regularly treats venous disease. It is best to establish a relationship with a venous specialist and the vascular lab to provide patients with optimal care.

Duplex scan findings can sometimes be quite surprising, given the patient’s history of previous surgeries or previous venous problems. Nothing should be presumed about the current venous pathology when evaluating a patient. For example, patients who have a history of great saphenous vein (GSV) stripping have not always had their GSVs stripped.

Venous disease is progressive, just like arterial disease. Pathology found and treated earlier in life does not guarantee long-term absence of further venous pathology. In fact, recurrent ulceration frequently is accompanied by new venous pathology, such as the development of new varicosities, new locations of reflux, or new incompetent perforating veins.

Based on the authors’ extensive experience, all patients with a venous ulceration should be evaluated with a comprehensive duplex scan upon initial presentation, yearly thereafter, and upon any ulcer recurrence in the future. All correctable venous pathology should be treated immediately.

MINIMALLY INVASIVE TREATMENT FOR VENOUS REFLUX

Minimally invasive procedures to treat valvular reflux disease have changed treatment approaches to patients with venous ulceration. Surgical treatment of reflux disease is now performed by almost all vein specialists under local anesthesia in an office setting. Treatment is directed at ablating, sclerosing, or closing incompetent veins in the superficial or perforator systems responsible for the venous hypertension that delays ulcer healing.

Because these procedures are easy to perform, they can be offered early in the treatment course of patients with ulceration. The most common treatments are sclerosing, thermal ablation via laser or radiofrequency energy, and local surgical excision. (Radiofrequency thermal ablation is the only one of these FDA-approved specifically for treatment of incompetent perforator veins; laser ablation is an off-label use.) These procedures are performed under ultrasound guidance with tumescent and topical anesthesia used for analgesia.

Expertise in the use of ultrasound and interpretation of duplex images is essential for completion of these procedures. Once mastered, these procedures provide patients with minimally invasive, painless, incisionless, office-based treatment for venous reflux disease.

Endovenous ablation has revolutionized the care of patients with valvular reflux disease and venous ulceration, and is becoming the standard of care. There is almost no role for vein stripping procedures in modern venous practice. The goal of treatment is to eliminate all sources of venous hypertension caused by valvular reflux in the superficial and perforator systems in the effected leg. Endovenous ablation is used routinely to treat incompetence of the GSV, small saphenous vein (SSV), accessory saphenous vein (ASV), and perforating veins (PV). Once the diagnosis is made, surgical treatment is outlined for each patient and these procedures are routinely performed as early as possible during the course of treatment.

The procedures do not interfere with the care of the ulcer bed; in these authors’ opinions, they should be performed prior to ulcer healing, even if this requires treatment of an incompetent perforating vein under or adjacent to an open ulceration. Ablations of PVs can be safely performed through an open ulceration without worry of infection or bacteremia.

IN-OFFICE TECHNIQUE

Patients are given topical anesthesia in the form of 2% lidocaine cream and valium 5 mg before the procedure. Lidocaine cream is placed on the area of the leg to be
treated 1 hour before the procedure. The procedure is started with the placement of the patient in reverse Trendelenberg position on a Midmark or similar table.

Ultrasound imaging then is performed to identify the location of the vein or veins to be ablated. Ultrasound imaging can be performed by the physician doing the procedure, but most commonly is performed by a technician. The leg then is prepped with povidone-iodine. Additional lidocaine or ethyl chloride spray then is used on the skin at the entry point chosen for the start of the procedure.

With the patient in a reverse Trendelenberg position, an ultrasound-guided venapuncture with a micropuncture needle is performed on the vein to be ablated. A wire is placed into the vein, followed by a sheath. A catheter or laser fiber then is placed through the sheath and the tip of the catheter is placed 2 cm distal to the saphenofemoral junction, which is identified with ultrasound imaging.

Tumescent anesthesia then is delivered around the vein being ablated under ultrasound guidance to provide additional analgesia and to compress the vein around the treatment catheter. The tumescent anesthesia used is a mixture of 500 cc saline with 60 cc of 1:100,000 epinephrine and 5 cc of sodium bicarbonate solution. The patient then is placed into a reverse Trendelenberg position, and the vein then is treated with laser or radiofrequency energy.

Upon completion of the procedure, ultrasound and duplex imaging are performed to confirm closure of the vein and to ensure that a deep venous thrombosis had not occurred at the saphenofemoral junction. Multiple veins can be ablated in a single session if necessary, including PVs. The entire procedure takes 30 minutes for a GSV, 20 minutes for a SSV, and 10 minutes for each perforator vein.

Post-procedure, topical silver dressings are applied to the ulcer bed, and either elastic or inelastic compression is reapplied as dictated by the wound care team. Alternately, the patients can go immediately to the wound care center for application of an appropriate compression dressing.

There are no incisions to heal; there is no post-procedure pain. Skin puncture sites usually close within 48 hours. The patient should continue the same level of activity as outlined by the wound care center. A follow-up ultrasound is required in 48–72 hours to ensure adequate closure of the vein and absence of a deep venous thrombosis.

Routine follow-up is required at the wound care center until complete healing of the ulcer has occurred. An ultrasound is routinely performed at 6 months to evaluate the venous system. Ulcer healing may be expedited by performing these procedures early in the treatment course, but the literature seems to suggest that the major advantage of these surgical procedures is the prevention of ulcer recurrence.12–14

**EARLY INTERVENTION IS KEY**

Goals for intervention for venous disease are to improve symptoms of chronic venous insufficiency, expedite wound healing, and prevent recurrent ulceration. Multiple studies clearly show the benefit of early intervention for superficial and perforator venous reflux in patients with venous leg ulcers.15–18 The treatment approach has evolved to the current practice of early treatment of superficial venous reflux disease in patients with venous ulceration. Not only does it enhance wound closure, but it helps prevent recurrence. Cosmetic results are excellent; patient satisfaction is high. With today’s treatment strategy, reducing the number of patients with chronic venous leg ulcers is a realistic goal.

**References**

CLINICAL PRESENTATION AND DIFFERENTIAL DIAGNOSIS

The clinical presentation of venous leg ulceration can be recurrent or long-standing. A history of previous deep vein thrombosis (DVT) may or may not be present. Patient-reported symptoms include dull pain, heaviness, tiredness, restlessness, a feeling of tightness in the skin, and mild to moderate edema. Symptoms often improve with elevation of the legs, unless concomitant arterial disease is also present.

Physical findings include edema, hyper- or hypopigmentation, lipodermatosclerosis, weeping of the skin, and ulceration. The venous leg ulcer is irregularly shaped but with well-defined borders and located in the supramalleolar area (“gaiter” distribution), although they can be medial, lateral, or posterior. The ulcer bed is often exudative, and bacterial and fungal overgrowth on the wound and surrounding skin surface is common.

The specific characteristics of the ulcer should be defined. An uncomplicated venous leg ulcer should not have an eschar or exposed bone or tendon. Upon physical examination, evidence of telangiectasias, superficial vein distention, and visible and palpable varicosities. A palpable thrill or a bruit over a varicosity suggests the presence of an underlying arteriovenous fistula.

Color duplex ultrasound scanning utilizing an appropriate protocol visualizing the superficial and deep venous system with selective scanning of perforating veins should be performed to 1) confirm the presence of deep or superficial venous valvular incompetence and 2) identify incompetent perforators especially in the area adjacent to or beneath the ulcerations. In some cases, other venous diagnostic studies (air plethysmography, CT or MRI, contrast venography, or intravascular ultrasound) may be warranted.

It must be remembered that superficial and deep venous insufficiency leading to venous hypertension and ulceration can co-exist with other conditions that can produce ulceration or affect healing, including peripheral arterial disease (estimated to occur in 10%–25% of patients). At minimum, an examination of peripheral pulses and an ankle-brachial index (ABI) should be performed. Any abnormality should prompt further arterial assessment by segmental pressure measurement and pulse volume recording. ABI <1.0 suggests some degree of underlying arterial
disease. Guidelines for compression with an abnormal ABI are provided below.

An atypical ulcer presentation or evidence of a contributory concomitant etiology on patient history should prompt additional diagnostic studies. Additionally, any lower-extremity ulcer presumed to be of venous etiology that fails to make sufficient progress toward healing in the first 4–6 weeks of therapy should prompt further directed evaluation to determine if another primary or contributing etiology is present.

Table 2 lists the differential diagnosis of lower-extremity ulcers excluding diabetic foot ulcers. A full discussion of the evaluation of each of these disorders is beyond the scope of this article, but recent reviews have outlined diagnostic approaches including physical assessment, ulcer biopsy, and ancillary studies when vasculitis or vasculopathic etiologies are suspected.10,11

EXPECTED HEALING OUTCOMES

Reported healing rates of venous leg ulcers treated with compression therapy alone vary greatly; 49% of the venous ulcers treated with compression therapy alone in the control arm of a randomized clinical trial for a bioengineered skin substitute healed in 24 weeks.12

Negative predictors for venous leg ulcer healing have been identified in a large retrospective analysis and include ulcer size ≥ 10 cm², duration ≥ 12 months, history of venous ligation or venous stripping, history of hip or knee replacement surgery, ABI of < 0.80, and the presence of fibrin on more than 50% of the wound surface for 24-week healing.13,14 Data also suggest that a venous leg ulcer that fails to decrease in size by 30% of its initial size over the first 4 weeks of treatment has a 68% probability of failing to heal within 24 weeks.15

TREATMENT OPTIONS

Treatment options fall broadly under three categories: compression, local wound care, and advanced technologies. A detailed discussion of each of the interventions that may be of benefit in the treatment of venous leg ulcers is beyond the scope of this article. However, the following have been demonstrated to be of benefit in the effective treatment of venous leg ulcers:

1. compression,
2. debridement,
3. management of microbial burden,
4. moist ulcer care,
5. bioengineered skin substitutes and skin grafting, and
6. systemic agents.

Compression therapy is the core intervention in venous leg ulcer treatment. Compression bandaging systems can be either short-stretch (typically multilayer or the traditional Unna’s boot), producing high working pressures and best utilized in ambulatory patients; or long-stretch (typically single layer or highly elastic), producing higher resting pressure and best utilized in non-ambulatory patients. Although there is substantial evidence for the effectiveness of compression over no compression, within the categories of short-stretch and long-stretch, there is little evidence supporting one intervention over another.16 Compression typically should provide 30–40 mm Hg at the ankle, although compression pressure should be reduced in the setting of peripheral arterial disease (ABI < 0.8–0.7, use reduced compression pressure; < 0.7, compression relatively contraindicated).

In a recent review of the impact of debridement on venous leg ulcer healing,17 ulcer surface area reduction was greater in visits after debridement. Attention should be paid to removal of all necrotic tissue, densely adherent slough and exudate, and reshaping of the ulcer margins, eliminating epibole or margination of ulcer edge keratinocytes. Local ulcer care should

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**Table 1. Levels of Evidence and Grades of Recommendation**

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Strength of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I: meta-analysis of multiple randomized clinical trials (RCTs) or at least two RCTs supporting the intervention of the guideline</td>
<td>Level A: strongly recommended/likely to be of benefit</td>
</tr>
<tr>
<td>Level II: less than Level I, but at least one RCT and at least significant clinical series or expert opinion papers with literature reviews supporting the intervention</td>
<td>Level B: recommended</td>
</tr>
<tr>
<td>Level III: suggestive data of proof of principle, but lacking sufficient evidence such as meta-analysis, RCT, or multiple clinical series</td>
<td>Level C: recommended but not essential</td>
</tr>
<tr>
<td>Level IV: suggestive data such as case series, expert opinion papers without literature reviews supplying the intervention or experience with the intervention in different settings</td>
<td>Level D: NOT recommended</td>
</tr>
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**Table 2. Differential Diagnosis of Lower-Extremity Ulcers**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous leg ulcer</td>
<td>Venous leg ulcer</td>
</tr>
<tr>
<td>Ischemic ulcer</td>
<td>Arterial insufficiency</td>
</tr>
<tr>
<td>Bacterial, viral, fungal, protozoan</td>
<td>Cutaneous infections</td>
</tr>
<tr>
<td>Squamous cell, basal cell carcinoma</td>
<td>Malignancy (primary)</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma, T-cell lymphoma, metastatic</td>
<td>Malignancy (secondary)</td>
</tr>
<tr>
<td>Myeloma, Waldenstrom’s macroglobulinemia</td>
<td>Malignancy (manifestation of distant malignancy)</td>
</tr>
<tr>
<td>Marjolin’s ulcer</td>
<td>Malignancy (acquired)</td>
</tr>
<tr>
<td>Connective tissue disease, systemic lupus erythematosus, rheumatoid arthritis, large and small vessel vasculitis, inflammatory bowel disease</td>
<td>Inflammatory</td>
</tr>
<tr>
<td>Sickle cell, hypercoagulable states</td>
<td>Hematologic</td>
</tr>
<tr>
<td>Cyroglobulinemia, cryofibrinogenemia</td>
<td>Cyroglobulinemia</td>
</tr>
<tr>
<td>Atrophe blanche</td>
<td>Other</td>
</tr>
</tbody>
</table>

*excluding diabetic foot ulcers**
Algorithm for Venous Leg Ulcer Management Including Management of Underlying Venous Disease

Assess for venous disease:
1. Venous duplex ultrasound of superficial and deep venous systems, directed perforator evaluation
2. Other tests as indicated (air plethysmography, CT, MRI, venous angiogram)

Venous Disease Confirmed

Assess for arterial disease:
1. Pulse examination
2. Ankle-brachial pressure index (ABI)
3. Toe pressure, skin perfusion pressure (SPP), transcutaneous PO2 if indicated

Abnormal

Refer for further assessment and treatment of arterial disease
(return to algorithm as indicated)

Rule out or treat associated etiologies
1. Malignancy
2. Inflammatory disease
3. Infectious disease
4. Nonhealing ulcers of unknown etiology

Refer for immediate treatment of venous insufficiency
1. Active/mobile patient use multi-layer (elastic long-stretch, inelastic short-stretch) compression bandage or stockings
2. Immobile/fixed ankle patient use multi-layer elastic long-stretch compression bandage

Debridement to resolve epibole, any wound bed necrosis or adherent slough or exudate

Optimize ulcer bed:
1. Moisture balance, exudate management
2. Protection of surrounding skin
3. Microbial balance
4. Address associated inflammatory, vasculitic, microthrombotic processes

Consider systemic agents

Negative prognostic indicators present:
1. VLU: ulcer size ≥ 10cm²
2. Ulcer duration ≥ 12 months
3. Presence of PAD
4. Greater than 50% of ulcer consisting of fibrous connective tissue

Consider application of bioengineered skin substitute, skin grafting

Monitoring response to therapy for ulcer healing
≥30% closure in 4 weeks?

Refer for treatment of venous insufficiency:
1. For prevention of recurrence
2. For ulcer healing

Refer for treatment of venous insufficiency

UO: 1. Treatment of venous insufficiency:
   Saphenous reflux (± deep system reflux) ± endovenous ablation ± phlebectomy
   Perforator incompetence ± percutaneous ablation of perforators
   Deep system reflux alone...consider valve transplant
2. Systemic agents with Level 1 Grade A/B evidence include pentoxifylline and diosmin-hesperidin (flavonoid)

Patient with lower extremity ulcer and edema ± lipodermatosclerosis

Figure 2. Algorithm.
emerging treatment options for venous ulceration in today’s wound care practice

maintain an appropriately moist ulcer base while removing excess exudate from the ulcer and protecting the surrounding skin from maceration. The product chosen also should reduce pain during application and at removal. There is no evidence that clearly favors one topical ulcer care product over another, provided these conditions are met. Since venous leg ulcers are frequently colonized with multiple bacterial species and fungal organisms, careful cleansing at each dressing change and the use of a short course of a topical antimicrobial wound dressing also may be beneficial.18 When there is clinical evidence of cellulitis, systemic antibiotic therapy should be administered.

Facilitation of re-epithelialization once edema and exudate control have been achieved and microbial balance obtained may be achieved by the application of a bioengineered skin substitute19 or by split-thickness skin grafting. These interventions may be of greatest value relative to cost in the ulcer presenting with the negative prognostic indicators previously described present at the time of initial evaluation, or when a positive predictor healing rate is not observed during the first 4–6 weeks of appropriate compression therapy and local wound care.

Finally, two systemic agents, pentoxifylline20 and diosmin-hesperidin, a micronized purified flavonoid fraction,21 have been shown in randomized controlled clinical trials to accelerate ulcer healing and should be considered as adjunctive therapy, particularly in the patient identified as having a high risk for initial ulcer healing failure or ulcer recurrence.

INTEGRATING VENOUS DISEASE MANAGEMENT FOR TREATMENT, PREVENTION

Recent reviews of multiple RCTs discussed elsewhere in this supplement have demonstrated the value of endovascular treatment of the underlying venous pathophysiology in both reducing ulcer recurrence rates and possibly accelerating ulcer healing rates in circumstances where subulcer perforator ablation can be achieved. These advances in the management of superficial venous insufficiency, when applied in concert with optimal local treatment of the venous leg ulcer, can change the paradigm for both resolution of recalcitrant ulcers and reduction in recurrence rates.

The recently published Multi-society Consensus Quality Improvement Guidelines for the Treatment of Lower-extremity Superficial Venous Insufficiency with Endovenous Thermal Ablation from the Society of Interventional Radiology, Cardiovascular Interventional Radiological Society of Europe, American College of Phlebology, and Canadian Interventional Radiology Association22 and the American Venous Forum’s Handbook of Venous Disorders23 have been integrated into a traditional algorithm for the outpatient management of venous leg ulceration (see Figure 2).

Direct treatment of venous insufficiency has been integrated into the algorithm in three circumstances: 1) during the initial management of the ulcer presenting with one or more risk factors for poor healing and demonstrated treatable venous disease on duplex ultrasonography; 2) in the ulcer that has failed to respond to appropriate therapy with or without identifiable negative predictors; and 3) after resolution of the ulcer to reduce the rate of ulcer recurrence.

References

Venous Ulcers

TREAT THE SOURCE, NOT JUST THE SYMPTOM

Surgical treatment of chronic venous insufficiency results in:

- Faster ulcer healing\textsuperscript{1,2,3}
- Lower ulcer recurrence\textsuperscript{1,2,3}

The **Closure\textsuperscript{TM}** procedure

A minimally invasive alternative to surgery

For additional information visit www.vnus.com

References:


INDICATIONS: The VNUS Closure procedures treat leg veins in the superficial and perforating systems that have venous reflux, the underlying cause of varicose veins and venous ulcers. Individual results may vary based on each patient's condition.

CONTRAINDICATIONS: Patients with thrombus in the vein segment to be treated.

Caution: No data exists regarding the use of this catheter in patients with documented peripheral arterial disease (PAD). The same care should be taken in the treatment of patients with significant PAD as would be taken with a traditional vein ligation and stripping procedure.

POTENTIAL COMPLICATIONS: Potential complications include, but are not limited to, the following: vessel perforation, thrombosis, pulmonary embolism, phlebitis, infection, adjacent nerve injury, arteriovenous fistula, skin burn, and hematoma or discoloration.