Ann Phlebology 2025;23(2):67-77
https://doi.org/10.37923/phle.2025.23.2.67
pISSN 1598-6756, eISSN 2765-5628

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Review Article

# Practical Management of Venous Leg Ulcers: Guideline-Based Diagnosis, Compression, and Venous Intervention

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**ARTICLE INFO**
**Received** Dec 11, 2025
**Revised** Dec 24, 2025
**Accepted** Dec 24, 2025

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**Key Words**
Venous stasis ulcers
Chronic venous insufficiency
Compression bandages
Compression stockings
Endovascular procedures

Venous leg ulcers (VLUs) represent the most advanced manifestation of chronic venous disease and arise from sustained ambulatory venous hypertension due to superficial reflux, deep venous obstruction, or both. Accurate etiologic assessment is essential, with duplex ultrasound serving as the primary tool to identify axial reflux, perforator incompetence, and signs of proximal outflow obstruction in accordance with contemporary ESVS and SVS/AVF guidelines. Compression therapy remains the foundation of treatment, with inelastic or adjustable compression systems providing the most effective pressure reduction and edema control. Optimal wound care—including moisture-balancing dressings, debridement, and judicious use of antimicrobials—supports timely epithelialization. Adjunctive pharmacologic agents such as micronized purified flavonoid fraction, pentoxifylline, and sulodexide may further enhance healing. Early correction of superficial reflux accelerates healing and reduces recurrence, as demonstrated in the Early Venous Reflux Ablation trial. Iliac venous obstruction should be considered in nonhealing or recurrent ulcers, with IVUS-guided stenting appropriate when significant stenosis is confirmed. Integrating guideline-directed venous intervention, optimized compression, and structured wound care is central to improving long-term outcomes in VLU management.

## Introduction

Chronic venous disease (CVD) encompasses a broad clinical spectrum driven by sustained venous hypertension, ranging from telangiectasia to advanced skin changes and ulceration. The CEAP classification system describes CVD across Clinical, Etiologic, Anatomic, and Pathophysiologic dimensions and remains the standard framework for staging disease severity and guiding treatment selection [1]. Clinically significant CVD is generally considered to include CEAP classes C2–C6, while chronic venous insufficiency (CVI) refers to the more advanced stages (C3–C6), characterized by edema, lipodermatosclerosis, and ulceration [2].

Active venous leg ulcer (VLU), corresponding to CEAP class C6, represents the most severe clinical manifestation of chronic venous hypertension. Persistent superficial reflux, deep venous obstruction, or a combination of both contribute to microcirculatory injury, inflammation, and impaired tissue repair, ultimately resulting in ulcer formation and delayed healing [1,3,4]. Although the global prevalence of VLUs ranges from 0.06% to 2%, the burden is disproportionately high in older adults, with incidence peaking between 60 and 80 years of age [4,5]. VLUs account for a major proportion of chronic lower-extremity wounds and are associated with prolonged treatment duration, high recurrence rates, and substantial healthcare costs [1,6]. Recurrence rates frequently exceed 45–70%, particularly in patients with persistent venous reflux, inadequate compression, or underlying post-thrombotic

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disease [7].

The clinical impact of VLUs extends far beyond wound morbidity. Chronic pain, limited ambulation, sleep disturbance, social withdrawal, and depression significantly diminish quality of life [6]. The economic burden is similarly substantial, driven largely by repeated clinical visits, long-term dressing use, and delayed wound closure.

Given their chronicity and high recurrence rate, VLUs require a structured, etiologic, and guideline-based management strategy. Both the European Society for Vascular Surgery (ESVS) and the Society for Vascular Surgery/American Venous Forum (SVS/AVF) emphasize accurate CEAP classification, duplex ultrasound mapping of reflux and obstruction, optimization of compression therapy, and timely correction of superficial or deep venous pathology [1,3]. This review focuses on the practical management of venous stasis ulcers, integrating evidence-based recommendations with real-world strategies to support clinical decision-making and improve healing outcomes.

## Pathophysiology and Hemodynamics

The fundamental hemodynamic driver of venous ulceration is sustained ambulatory venous hypertension (AVH), resulting from superficial or deep venous reflux, venous outflow obstruction, or impaired calf muscle pump function. Venous reflux, the most common cause of AVH, develops from valvular incompetence in the superficial, deep, or perforating veins and leads to retrograde flow with progressive elevation of distal venous pressure [8].

Proximal venous obstruction, often occurring after deep vein thrombosis, also contributes to venous hypertension. Thrombus–vein wall interaction induces inflammation, mural fibrosis, and valve destruction, leaving residual stenosis or occlusion and frequently resulting in secondary deep venous reflux [8]. These mechanisms form the basis of post-thrombotic syndrome (PTS), which is associated with more severe clinical presentation and higher recurrence risk [1].

Physiologically, activation of the calf muscle pump normally reduces standing venous pressures from 80–90 mmHg to approximately 20–30 mmHg. In CVD, this reduction is inadequate, and persistently elevated ambulatory venous pressure correlates strongly with ulcer development and clinical severity [1].

At the microcirculatory level, chronic venous hypertension produces a cascade of inflammatory and structural changes that directly impair healing. Leukocyte trapping and release of inflammatory mediators (IL-1β, TNF-α) promote endothelial injury, while matrix metalloproteinase (MMP) overactivity degrades extracellular matrix and growth factors essential for repair. Increased intracapillary pressure widens endothelial gaps, allowing leakage of fibrinogen and erythrocytes. Breakdown of extravasated red blood cells generates hemosiderin, which deposits in the dermis and contributes to the characteristic brown hyperpigmentation of chronic venous disease. In parallel, pericapillary fibrin cuffs create a diffusion barrier that exacerbates tissue hypoxia. These combined mechanisms establish a chronically inflamed, proteolytic environment that prevents normal granulation and re-epithelialization, ultimately resulting in venous ulceration [8].

## Diagnostic Evaluation and Imaging Strategies

Accurate diagnostic evaluation is essential for determining the anatomic and hemodynamic causes of venous leg ulcers and for selecting appropriate interventions. Assessment begins with history taking and physical examination—evaluating edema, varicosities, skin changes, and ulcer characteristics—followed by classification using the CEAP system and the revised Venous Clinical Severity Score (r-VCSS) to document disease severity and treatment response [1-3].

Clinical assessment remains the first and indispensable step in the diagnosis of VLUs. Typical VLUs are shallow, irregularly shaped ulcers with gently sloping edges, most commonly located in the gaiter area—particularly around the medial malleolus (Fig. 1). The ulcer base often appears granulating or fibrinous, with moderate to heavy exudate, while surrounding skin frequently demonstrates signs of chronic venous hypertension, including edema, hyperpigmentation, lipodermatosclerosis, atrophie blanche, and venous eczema. Pain is usually mild to moderate and often improves with limb elevation.

Differentiation from other lower-extremity ulcers is essential, as management strategies differ substantially. Arterial ulcers are typically deeper, well-demarcated, and painful, with a punched-out appearance and minimal exudate. They commonly occur over pressure points such as the toes, heel, or lateral malleolus and are associated with cool skin, diminished pulses, and delayed capillary refill. Neuropathic ulcers, most frequently seen in diabetes, are usually painless, occur at plantar pressure points, and are surrounded by callus. Inflammatory or vasculitic ulcers often present with purpura, necrosis, or rapidly progressive tissue loss and may be accompanied by systemic symptoms.

Because clinical features alone may be insufficient in patients with mixed-etiology ulcers, visual inspection should be integrated with vascular assessment, including pulse ex-

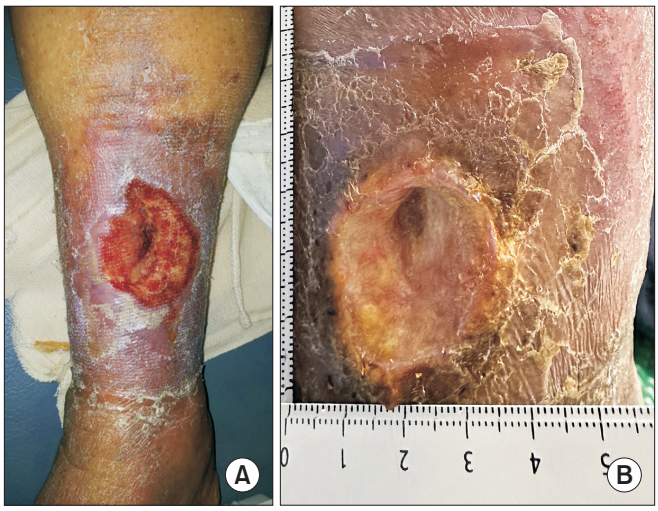



**Fig. 1.** Typical clinical appearance of venous leg ulcers. (A) Active venous leg ulcer located in the gaiter region of the lower leg, characterized by a shallow, irregularly shaped ulcer with a granulating wound bed and moderate exudate. The surrounding skin demonstrates features of chronic venous disease, including hyperpigmentation, edema, and venous eczema, consistent with sustained ambulatory venous hypertension. (B) Chronic venous leg ulcer with a fibrinous ulcer base and poorly defined margins, surrounded by marked lipodermatosclerosis, scaling, and induration of the peri-ulcer skin. A measurement scale is shown for size reference. The constellation of skin changes reflects long-standing venous hypertension and chronic inflammation.

amination and measurement of the ankle–brachial pressure index (ABPI), before compression therapy is initiated. ABPI assessment is essential to exclude significant arterial disease, which may delay healing and directly influence the safety and intensity of compression [9]. Once arterial insufficiency has been reasonably excluded, targeted imaging can be used to define the underlying venous hemodynamic mechanism.

Duplex ultrasound (DUS) is the primary imaging modality for evaluating venous anatomy, patency, reflux, and post-thrombotic changes [1-3]. Examinations should be performed in the standing or reverse Trendelenburg position to maximize venous distension and physiologic reflux [1,3]. Reflux is defined as >0.5 seconds of retrograde flow in superficial truncal, tibial, and perforating veins, and >1 second in deep axial veins (common femoral, femoral, popliteal) [2]. Although no minimum diameter is required for truncal vein reflux, the SVS/AVF guidelines define pathologic perforators as outward flow >500 ms with a diameter ≥3.5 mm beneath a healed or active ulcer (CEAP C5–C6) [3]. DUS mapping provides essential information on axial versus segmental reflux patterns, junctional incompetence, perforator location, and sequelae of prior thrombosis—all of which guide treatment planning.

When proximal venous outflow obstruction is suspected based on clinical presentation or duplex findings, cross-sectional imaging provides a valuable non-invasive intermediate step before proceeding to invasive evaluation. CT venography (CTV) allows assessment of the inferior vena cava and iliac venous system, identifying extrinsic compression, post-thrombotic changes, venous occlusion, and collateral formation. CTV is particularly useful for evaluating anatomic variants, pelvic masses, or skeletal compression syndromes and for excluding alternative causes of lower-extremity edema.

However, CTV may underestimate the functional significance of venous stenosis and has limited sensitivity for intraluminal webs or subtle post-thrombotic lesions. For this reason, intravascular ultrasound (IVUS) remains the reference standard for definitive diagnosis and procedural planning when clinically significant iliac or caval obstruction is suspected or when endovascular intervention is contemplated. IVUS has become the preferred modality for evaluating iliac and femoral venous obstruction, offering superior detection of intraluminal webs, mural fibrosis, and subtle stenoses not visible on venography or computed tomography venography or magnetic resonance venography [1,2]. IVUS also guides stent selection and deployment, though it remains an invasive test that requires traversal of the lesion with a guidewire [1]. Traditional contrast venography is now used primarily in conjunction with IVUS or when endovascular intervention is planned.

In practice, a structured diagnostic approach—integrating clinical classification (CEAP, r-VCSS), ABPI measurement, comprehensive duplex ultrasound mapping, and selective use of IVUS for suspected outflow obstruction—provides a reliable framework for characterizing venous reflux and obstruction. This etiologic assessment is essential for guiding individualized, evidence-based management of venous leg ulcers.

To illustrate how diagnostic evaluation informs subsequent management decisions, Fig. 2 presents an integrated diagnostic and therapeutic framework for venous leg ulcers. Initial assessment combines clinical examination and ulcer morphology with ABPI measurement to exclude clinically significant arterial disease. Duplex ultrasound serves as the primary imaging modality for evaluating superficial and deep venous pathology, while cross-sectional imaging and IVUS are selectively employed when proximal venous outflow obstruction is suspected. Management is centered on sustained compression therapy, optimized wound care, and timely correction of venous pathology, with treatment individualized according to anatomy, comorbidities, and healing response.

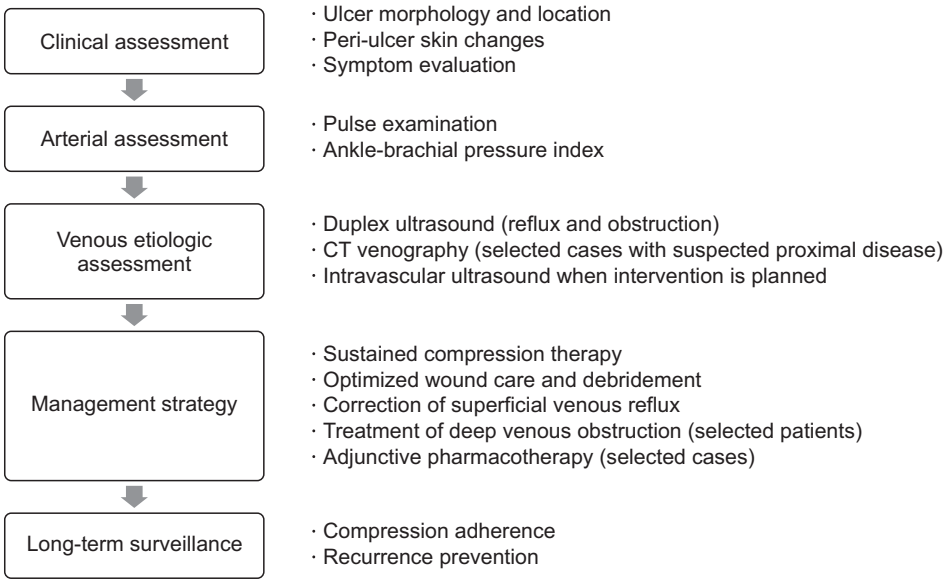



**Fig. 2.** Integrated diagnostic and management framework for venous leg ulcers. Simplified schematic illustrating the core elements of venous leg ulcer evaluation and treatment. Management integrates clinical assessment, exclusion of significant arterial disease, venous etiologic imaging, sustained compression therapy, wound-directed care, and selective venous intervention, emphasizing individualized, guideline-based decision-making.

# Management of Venous Leg Ulcers

## 1. Compression Therapy

Compression therapy remains the cornerstone of venous leg ulcer (VLU) management, as it restores venous return, reduces edema, and lowers ambulatory venous pressure. By narrowing the vein lumen and improving valvular coaptation, compression decreases venous reflux and limits the inflammatory extravasation of fluid and cytokines that contribute to ulcer chronicity and delayed healing [1,10].

A wide range of compression modalities is available, including elastic compression stockings (ECS), superimposed ECS kits, inelastic bandages, adjustable compression garments, multilayer systems, the Unna boot, and intermittent pneumatic compression. Inelastic systems, which generate high working pressure during ambulation, are particularly effective for active VLU healing. Both traditional inelastic bandages and adjustable compression garments achieve substantial reductions in venous hypertension, and a target ankle pressure of approximately 40 mmHg is generally recommended in patients with active ulceration [10]. Adjustable garments may improve adherence in patients who struggle with the technical demands of bandaging. Multilayer bandaging systems, which combine padding, inelastic components, and cohesive outer layers, have become the preferred choice in many clinical settings. Their ability to maintain therapeutic pressure over time and compensate for fluctuations in limb shape contributes to superior clinical performance compared with single-layer elastic wraps, especially in patients with significant edema or larger ulcers.

The Unna boot, a zinc oxide–impregnated gauze dressing, also functions as an inelastic compression device and is often beneficial in ambulatory patients with shallow ulcers and moderate edema [11]. After cleansing the wound and applying a primary non-adherent dressing, the medicated gauze is applied from the base of the toes to just below the knee with gentle overlap, molded to the contour of the leg, and then covered with a protective outer wrap to reinforce compression. This semirigid construct provides consistent working compression during ambulation and offers a moist environment that supports epithelialization and granulation. However, the Unna boot is less suitable in the presence of heavy exudate, limited mobility, or fluctuating limb volume, situations in which adjustable compression systems may offer greater practicality. Although evidence does not demonstrate clear superiority of the Unna boot over other compression modalities, it remains a relevant and widely used option in clinical practice, particularly in settings where inelastic compression and ease of application are prioritized.

Intermittent pneumatic compression (IPC) has a role when standard compression cannot be tolerated or when additional edema control is required, although its effectiveness is generally inferior to properly applied inelastic systems [10]. Compression therapy must be applied cautiously in patients with severe peripheral arterial disease; contraindications include

an ankle pressure below 60 mmHg, toe pressure below 30 mmHg, or an ankle–brachial index under 0.6. Severe heart failure, risk of skin necrosis, or allergy to compression materials also warrant careful consideration.

Although compression is highly effective, adherence may be limited by discomfort, heat, skin irritation, or difficulty donning garments. These challenges are particularly pronounced in elderly or obese individuals and those with restricted mobility. In such patients, adjustable compression garments or caregiver-assisted application can significantly improve real-world effectiveness. Newer technologies, including app-based tools for compression assessment and patient education, are currently under development to address adherence barriers and improve long-term outcomes [1]. A concise comparison of practical compression choices based on guideline-supported evidence is summarized in Table 1.

## 2. Pharmacological Therapy

Pharmacotherapy plays an adjunctive role in the management of CVD and VLUs, complementing compression therapy by targeting microvascular inflammation, capillary permeability, and venous tone. Venoactive drugs (VADs) may support ulcer healing and symptom control and are frequently used in combination with compression or procedural intervention.

Micronized purified flavonoid fraction (MPFF) enhances venous tone by prolonging noradrenergic activity and reducing leukocyte activation and capillary hyperpermeability [12]. Clinical studies demonstrate improvements in leg discomfort, edema, and ankle circumference, supporting its use as a symptomatic adjunct in patients with CVD. Pentoxifylline, a methylxanthine derivative with hemorheologic and anti-inflammatory properties, has been evaluated as an adjunct to compression therapy in venous leg ulcer management. Randomized trials and systematic reviews have demonstrated improved healing rates when pentoxifylline is used in combination with adequate compression, particularly in patients with delayed healing. Although earlier evidence was summarized in a 2012 Cochrane review, subsequent narrative reviews and guideline documents continue to support its selective use as an adjunctive therapy [5,13,14]. Recent large-scale studies from Asia have further suggested potential benefit, although heterogeneity in study design and outcome reporting limits direct comparison across trials [15].

Sulodexide, a mixture of glycosaminoglycans with antithrombotic and anti-inflammatory effects, has gained renewed interest in VLU management. A 2020 meta-analysis of 13 studies demonstrated significant improvements in symptoms such as pain, cramps, heaviness, and lower-limb swelling, suggesting a potential role as a supportive agent in selected patients [16].

Although VADs are not substitutes for adequate compression or correction of venous reflux or obstruction, they may serve as useful adjuncts to optimize symptom relief and promote healing in appropriately selected patients.

**Table 1. Practical selection of compression therapy for venous leg ulcers (evidence- and guideline-based)**

| Clinical situation | Preferred compression modality | Typical pressure target | Rationale |
|---|---|---|---|
| Active venous leg ulcer (most patients) | Inelastic bandages or multilayer compression system | ~40 mmHg at ankle | Highest working pressure, greater reduction of venous hypertension, improved healing rates vs. elastic wraps [1,11]. |
| Large ulcers or marked edema | Multilayer compression system (2- or 4-layer) | ~40 mmHg | Superior pressure maintenance and improved healing vs. single-layer systems (Cochrane evidence) [11]. |
| Shallow ulcer, moderate edema, ambulatory patient | Unna boot (zinc oxide inelastic dressing) | 20–30 mmHg (approx.) | Provides semirigid inelastic compression and moist environment; widely used though not clearly superior to other methods [1,11]. |
| Difficulty donning bandages (elderly, obese, limited mobility) | Adjustable compression garments | 30–40 mmHg | High stiffness, easier application, comparable healing outcomes; improves adherence [11]. |
| Small, early ulcers with minimal edema | Superimposed elastic compression stockings (ECS kit) | Up to 40 mmHg | Effective for smaller ulcers; greater comfort and long-term acceptability [11]. |
| Standard compression not tolerated or inadequate | Intermittent pneumatic compression (IPC) | Device-dependent | Useful as adjunct or alternative; less effective than inelastic systems [11]. |
| Mixed arterial disease (ABPI 0.5–0.8) | Modified/light compression | Typically 20–30 mmHg; close monitoring recommended | Compression still beneficial but high pressures avoided; guided by ABPI [1]. |
| ABPI <0.5, toe pressure <30 mmHg, severe ischemia | Contraindicated | - | Significant risk of ischemic injury; compression should not be applied [1]. |

ABPI: ankle–brachial pressure index, ECS: elastic compression stockings, IPC: intermittent pneumatic compression, VLU: venous leg ulcer.

Current clinical practice guidelines from the ESVS and the SVS/AVF do not recommend pharmacologic agents as standalone therapy for venous leg ulcers. However, both guideline documents acknowledge that selected venoactive or hemorheologic agents, such as micronized purified flavonoid fraction or pentoxifylline, may be considered as adjuncts to compression therapy and etiologic correction in patients with active ulcers, particularly when healing is delayed or symptoms persist despite optimal standard care [1,5].

## Local Wound Care and Ulcer-Directed Treatment

Optimal wound care promotes a moist, clean environment that supports epithelialization and prevents infection, forming a fundamental component of VLU management. Controlled moisture and reduced bioburden enhance keratinocyte migration, angiogenesis, and granulation, facilitating tissue repair [14,17]. Within this framework, ulcer-directed therapy centers on preparing a healthy wound bed, regulating exudate, and limiting microbial load to allow uninterrupted epithelial growth [14,17].

Debridement is essential for optimizing the wound bed. Removal of slough and biofilm improves oxygen diffusion, reduces inflammatory mediators, and enhances responsiveness to compression therapy [18]. Several modalities are available and selected based on ulcer characteristics. Autolytic debridement, achieved with moisture-retentive dressings such as hydrocolloids or hydrogels, promotes endogenous enzymatic breakdown of nonviable tissue and is useful for low-exudate ulcers. Enzymatic agents offer a selective alternative when sharp techniques are contraindicated. Sharp or surgical debridement provides immediate clearance of devitalized tissue and is often combined with other modalities when rapid wound-bed preparation is required [18].

Dressing selection aims to maintain balanced moisture while protecting peri-wound skin. Hydrocolloids support autolysis in low- to moderate-exudate ulcers, while foam dressings are preferred for moderate to heavy exudate because of their absorptive capacity [14,17]. Alginates are particularly suitable for highly exudative wounds, forming a gel that assists with fluid control and minor bleeding [14,17]. When bacterial burden or biofilm is suspected, short-term antimi-

**Table 2. Summary of common wound dressings for venous leg ulcers and their clinical use**

| Dressing type | Mechanism/key features | Best indications | Limitations/considerations |
|---|---|---|---|
| Hydrocolloids[14,17] | Moisture-retentive; promote autolytic debridement; occlusive or semi-occlusive | Low- to moderate-exudate ulcers; to support autolytic debridement | Not suitable for heavy exudate or infected wounds; may cause periwound maceration |
| Hydrogels [14,17] | High water content; soften necrotic tissue; promote autolysis | Dry or minimally exudative wounds; sloughy wounds requiring moisture | Require secondary dressing; risk of maceration if overused |
| Foam dressings [14] | High absorptive capacity; protect peri-wound skin; maintain moist environment | Moderate to heavy exudate; general-purpose VLU dressing | May dry out minimally exudative wounds; typically costlier |
| Alginate dressings [14,17] | Derived from seaweed; form gel upon contact with exudate; hemostatic properties | Highly exudative wounds; ulcers with minor bleeding | Require adequate exudate to gel properly; need secondary dressing |
| Hydrofiber dressings [14,17] | Similar to alginates but greater vertical wicking; reduce peri-wound maceration | Moderate to high exudate; deeper cavities | Not ideal for dry wounds; secondary dressing required |
| Film dressings [14,17] | Thin polyurethane; maintain moist environment; protect from shear/friction | Superficial, minimally exudative ulcers; to secure secondary dressing | Not appropriate for exudative wounds; may cause maceration |
| Antimicrobial dressings (silver, iodine, PHMB) [19] | Reduce surface bioburden and biofilm; short-term cytotoxic effect on bacteria | Suspected increased bioburden or early infection; short-term use | Routine use discouraged; ineffective for systemic infection; avoid prolonged application |
| Honey-based dressings [14,19] | Antimicrobial and anti-inflammatory activity; maintain moist environment | Mild to moderate exudate; wounds with concern for colonization | Sticky; may be uncomfortable; mixed evidence for superiority |
| Charcoal/Activated carbon [14] | Absorbs odor and moisture | Malodorous ulcers; heavy colonization | No direct effect on healing; adjunctive use only |
| Collagen or collagen/ORC dressings [14,17] | Bind excess proteases (MMPs) and support ECM regeneration | Chronic, nonhealing ulcers with suspected proteolytic burden | Higher cost; may require insurance approval |

ECM: extracellular matrix, MMP: matrix metalloproteinase, ORC: oxidized regenerated cellulose, PHMB: polyhexamethylene biguanide, VLU: venous leg ulcer.


https://doi.org/10.37923/phle.2025.23.2.67

crobial dressings containing silver or iodine may be used; however, routine antimicrobial use is discouraged, as most VLUs are colonized rather than infected [19]. A concise summary of commonly used wound dressings and their optimal indications is provided in Table 2.

Infection control emphasizes debridement and moisture management rather than antibiotics. Systemic antibiotics are reserved for clear clinical infection—such as cellulitis, osteomyelitis, or systemic signs—while topical antibiotics are generally avoided because of risks of resistance and sensitization [19]. For locally increased bioburden, antimicrobial dressings combined with mechanical biofilm disruption are preferred.

When ulcers fail to progress despite optimal compression and wound care, advanced adjunctive therapies may be considered. Platelet-rich plasma provides concentrated growth factors that stimulate granulation and epithelialization [20]. Negative-pressure wound therapy decreases edema, enhances perfusion, and manages heavy exudate, making it appropriate for large, deep, or refractory ulcers [17]. Bioengineered skin substitutes, including cellular and acellular matrices, offer temporary coverage and structural support for chronic nonhealing wounds and may be appropriate in selected patients unresponsive to standard therapy [21].

Effective VLU care often requires coordinated multidisciplinary involvement. Collaboration among vascular specialists, wound-care nurses, dermatologists, podiatrists, and nutrition or rehabilitation teams supports consistent debridement, individualized dressing selection, and long-term edema control. Such multidisciplinary models have been associated with improved healing and lower recurrence rates, reflecting the chronic and multifactorial nature of venous ulcer disease [22].

## Procedural Management of Superficial and Deep Venous Disease

In the context of venous leg ulcers, the primary objective of endovenous intervention is not simply truncal vein closure, but reduction of ambulatory venous hypertension to promote ulcer healing and prevent recurrence. Outcomes of interest therefore differ from those reported in general varicose vein populations and include time to ulcer healing, durability of healing, recurrence rates, and the interaction with deep venous pathology and compression adherence. Randomized and observational studies in patients with active venous leg ulcers have demonstrated that early correction of superficial venous reflux accelerates ulcer healing and reduces recurrence when combined with effective compression therapy. The Early Venous Reflux Ablation (EVRA) trial established that early endovenous ablation shortens time to healing compared with deferred intervention, highlighting the importance of timely reflux correction in this population [7]. Importantly, the benefit of superficial intervention is greatest when deep venous obstruction has been excluded or adequately treated and when post-procedural compression is maintained. Endovenous interventions can be broadly categorized into thermal ablation modalities—including endovenous laser ablation (EVLA) and radiofrequency ablation (RFA)—and non-thermal techniques such as mechanochemical ablation (MOCA) and cyanoacrylate closure (CAC).

EVLA relies on high-wavelength laser energy absorbed by the venous wall, producing controlled thermal injury and vein closure. Endovenous thermal ablation techniques reliably achieve high truncal vein closure rates in contemporary practice [23]. Radiofrequency ablation, typically performed using segmental thermal technology delivering uniform heating at 120°C, has demonstrated occlusion rates and postoperative pain scores comparable to EVLA [24]. Although deep venous thrombotic events have been reported following endovenous thermal ablation, the overall incidence remains low at approximately 1.7% [1,2].

Among non-thermal approaches, cyanoacrylate closure occludes incompetent superficial veins through polymerization-induced inflammation and fibrosis. Randomized studies have demonstrated noninferiority of CAC compared with RFA, with similar long-term outcomes to endovenous thermal ablation techniques [25,26]. Mechanochemical ablation combines mechanical intimal disruption with simultaneous chemical ablation. Reported three-year occlusion rates of 86.5% are somewhat lower than those of EVLA, suggesting that durability may vary among non-thermal systems [27].

The role of treating incompetent perforator veins remains debated. Ultrasound-guided foam sclerotherapy (UGFS) is the most commonly used modality, whereas subfascial endoscopic perforator surgery (SEPS) is now largely historical. According to the ESVS guidelines, perforator therapy is not recommended for patients with varicose veins without skin changes (Class III, Level C), but may be considered in patients with advanced disease (CEAP C4b–C6) who have isolated or residual perforator incompetence (Class IIb, Level C), or in those with active VLUs associated with superficial and perforator incompetence close to the ulcer (Class IIb, Level C) [1]. SVS–AVF guidelines also recommend restricting perforator intervention to cases with persistent or recurrent symptoms clearly attributable to perforator incompetence [2].

Post-thrombotic syndrome (PTS) reflects chronic venous hypertension resulting from deep venous obstruction after DVT. Treatment of asymptomatic chronic deep vein obstruction is not recommended; however, intervention may be

considered in symptomatic patients with CEAP C3–C6 disease when obstruction is hemodynamically significant. For patients with iliac vein outflow obstruction and severe symptoms, endovascular stenting is considered first-line therapy (Class IIa, Level B) [1]. The precise timing of intervention remains variable among studies, but early restoration of outflow in appropriately selected patients may support ulcer healing and reduce recurrence.

Several considerations are particularly relevant when applying endovenous interventions in patients with venous leg ulcers. Severe edema, active infection, or fragile peri-ulcer skin may complicate access, tumescent anesthesia, or post-procedural compression. Failure to recognize coexisting deep venous obstruction or post-thrombotic disease may result in incomplete symptom relief or delayed healing despite technically successful superficial ablation. In addition, nonadherence to compression therapy after intervention remains a major determinant of ulcer recurrence and may limit the long-term benefit of endovenous treatment.

Overall, current guidelines emphasize the importance of early identification and correction of superficial venous incompetence in venous leg ulcer management. Timely treatment of axial reflux accelerates ulcer healing and reduces recurrence, establishing minimally invasive endovenous techniques as the preferred first-line approach when anatomically feasible, in conjunction with compression and wound-directed therapy.

Nevertheless, optimal management requires an individualized strategy, and conventional surgical intervention retains an important role in selected patients in whom endovenous approaches are unsuitable or have failed. Surgical treatment may be advantageous in the presence of complex venous anatomy, extensive or aneurysmal varicosities not amenable to catheter-based techniques, or when endovenous access is limited by severe tortuosity, thrombosis, or prior intervention. High ligation and stripping of the great or small saphenous vein may be considered when endovenous ablation is contraindicated or unavailable, particularly in cases of large-diameter veins with marked aneurysmal degeneration or superficial thrombophlebitis extending to the junction. In patients with recurrent varicose veins after prior endovenous therapy, open surgical revision may provide definitive correction when neovascularization or junctional pathology is present.

Subfascial endoscopic perforator surgery, although largely supplanted by endovenous treatment, may still be considered in highly selected patients with advanced disease (CEAP C5–C6) and multiple incompetent perforators, particularly when less invasive options have failed or are not feasible. Surgical debridement and skin grafting also remain relevant adjuncts in selected patients with large, chronic, or refractory ulcers once venous hypertension has been adequately controlled.

## Prognosis, Recurrence, and Future Perspectives

VLUs remain prone to delayed healing and recurrence despite advances in compression therapy and endovenous interventions. Persistent ambulatory venous hypertension, inadequate correction of reflux or obstruction, and suboptimal adherence to compression contribute to ongoing risk. Understanding predictors of healing, implementing recurrence-prevention strategies, and integrating emerging therapies are central to improving long-term outcomes.

## Healing Rates and Predictors

VLU healing is influenced by both ulcer-related and patient-related factors. Ulcer size and duration are among the strongest predictors of delayed healing, with larger and longstanding ulcers demonstrating slower epithelialization. Clinical assessment tools such as the r-VCSS allow objective monitoring of treatment response, but ulcer area reduction remains the most direct indicator of progress.

Compliance with compression therapy is a critical determinant of healing, as consistent pressure reduces edema, inflammation, and venous hypertension. Conversely, deep venous pathology—particularly PTS—is associated with impaired healing due to persistent obstruction or reflux. Restoration of iliac outflow or correction of deep venous reflux may improve healing rates in selected patients [1].

## Strategies for Recurrence Prevention

Preventing venous leg ulcer recurrence requires long-term control of venous hypertension through sustained compression and timely correction of venous reflux. After ulcer healing, graduated elastic compression stockings remain the most effective strategy for recurrence prevention, with below-knee stockings delivering 30–40 mmHg generally recommended due to proven reductions in venous hypertension and recurrence risk [28]. Although higher pressures may offer additional benefit in patients with severe edema or post-thrombotic syndrome, adherence is ultimately the strongest determinant of recurrence. Studies have consistently shown that daily use of a well-tolerated stocking prevents recurrence more effectively than intermittent use of a high-pressure garment [29]. Below-knee stockings are preferred in clinical practice be-


https://doi.org/10.37923/phle.2025.23.2.67

cause they provide equivalent hemodynamic benefit with improved comfort, stability, and ease of application, all of which contribute to better adherence [28,29].

IPC may provide additional benefit for patients who cannot tolerate elastic stockings, those with significant edema or lymphatic dysfunction, or nonambulatory individuals with poor calf pump function. Although IPC is less effective than elastic compression alone, its use in combination with stockings may enhance venous pressure reduction in more advanced cases [10].

Timely correction of superficial venous reflux also plays a central role in recurrence prevention. The Early Venous Reflux Ablation trial demonstrated that early endovenous ablation accelerates healing and significantly reduces early recurrence by rapidly lowering ambulatory venous pressure [7]. In patients with post-thrombotic syndrome or iliac venous outflow obstruction, persistent deep venous hypertension markedly increases recurrence risk. When symptoms are significant and obstruction is hemodynamically relevant, endovascular stenting of the iliac veins can restore outflow and may contribute to improved long-term ulcer control, although optimal timing continues to evolve [1].

## Future Therapies: Regenerative and Digital Innovations

Emerging therapies aim to enhance healing through biological or technological pathways.

Stem cell therapies, including mesenchymal stem cells (MSCs) and adipose-derived stem cells (ADSCs), may promote angiogenesis, modulate inflammation, and support extracellular matrix regeneration. Early studies report encouraging healing responses, though standardized administration methods and dosing protocols are still under development [30].

Bioengineered skin substitutes, including cellular constructs (e.g., Apligraf) and acellular dermal matrices, provide structural support and deliver growth factors that promote tissue regeneration. Randomized trials have shown improved healing rates when used alongside compression in refractory ulcers, making them a valuable adjunct in selected patients [21].

Artificial intelligence-based wound monitoring is rapidly evolving. Smartphone imaging combined with convolutional neural network (CNN) algorithms can automatically assess wound area, tissue composition, and healing trajectory [31]. Telemedicine platforms allow remote monitoring of compression use and wound progression, improving adherence and enabling earlier intervention when healing stalls [31].

## Role of Clinical Registries

Clinical registries remain essential for understanding real-world outcomes in chronic venous disease. Programs such as Vascular Quality Initiative and VASCUNET international venous registry collect longitudinal, population-level data that complement randomized trials by capturing diverse patient presentations, operator experience, and procedural settings. Registries facilitate international benchmarking, quality improvement, and detection of rare events, and they support evidence-based updates to clinical guidelines and health policy.

## Conclusion

Venous leg ulcers remain a major clinical challenge, driven by chronic venous hypertension arising from superficial, perforator, and deep venous pathology. Effective management hinges on accurate etiologic assessment and timely intervention. Evidence consistently shows that early treatment of superficial reflux, together with sustained compression therapy, accelerates healing and is central to preventing recurrence. Optimal outcomes also require meticulous wound-bed preparation, infection control, and sustained patient engagement.

Despite progress, significant gaps persist, including inconsistent adherence to guideline-based care, limited access to vascular expertise, and difficulty maintaining long-term surveillance in patients with complex deep venous disease or recurrent ulcers. Emerging regenerative therapies, biologic dressings, and AI-assisted monitoring hold promise but require further validation and cost-effectiveness evaluation. Real-world data and registry-driven research will continue to shape best practices and refine prognostic assessment.

Ultimately, venous leg ulcer care demands a coordinated, multidisciplinary strategy that integrates precise diagnosis, targeted venous intervention, durable compression, and structured follow-up. Prioritizing early intervention and adherence support remains essential for reducing recurrence and diminishing the long-term burden of venous ulcer disease.

## Conflicts of Interest

The authors declare no conflicts of interest.

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