CRITICAL REVIEW

Venous Leg Ulcers: A Review of Published Assessment and Treatment Algorithms

Stéphanie F. Bernatchez,[1,*] Jill Eysaman-Walker,[2] and Dot Weir[3]

[1]3M Medical Solutions Division, 3M Company, St. Paul, Minnesota, USA.
[2]Catholic Health Advanced Wound Healing Centers, Cheektowaga, New York, USA.
[3]Saratoga Hospital Center for Wound Healing and Hyperbaric Medicine, Saratoga Springs, New York, USA.

Stéphanie F. Bernatchez, PhD

Submitted for publication December 3, 2020. Accepted in revised form January 27, 2021.

*Correspondence: 3M Medical Solutions Division, 3M Company, 3M Center Bldg 270-4N-01, St. Paul, MN 55144-1000, USA
(e-mail: sfbernatchez@mmm.com)

Significance: Chronic venous disease (CVD) is prevalent in the aging population and leads to venous leg ulcers (VLUs). These wounds can last and recur for years, significantly impacting quality of life. A large body of literature exists on CVD and VLU diagnosis and treatment. Multiple algorithms, guidelines, and consensus documents have been published on this topic, highlighting the importance of this issue in clinical practice. However, these documents are not fully aligned with each other.

Recent Advances: The latest update of the internationally used classification system for CVD was recently published. Our review aims to summarize the existing information to provide an educational tool for clinicians new to this topic, and to highlight the commonalities between the published recommendations.

Critical issues: VLUs need to be treated with consideration for the extent of venous disease present in the patient. This requires a good understanding of the various components involved and the possible additional concomitant conditions by the first-line clinician who encounters the patient. A multidisciplinary team is necessary for a successful overall treatment plan, and this plan should be tailored to each patient's specific needs and lifestyle.

Future Directions: Compression is still the mainstay of treatment for CVD and VLUs. Compression is needed long term, but it does not suffice by itself to prevent recurrences without interventional correction. Venous intervention should be offered early to prevent or slow disease progression and reduce recurrence.

Keywords: venous leg ulcers, chronic venous disease, treatment algorithms, review, compression

SCOPE AND SIGNIFICANCE

This review on venous leg ulcers (VLUs) describes this condition and presents the various assessment and treatment algorithms that have been published over the years to provide guidance on how to manage it. A large body of literature exists on this topic and multiple organizations have published guidelines, consensus documents, and treatment recommendations. Our goal is to summarize the existing information and provide an up-to-date educational resource for practitioners new to this topic.

DOI: 10.1089/wound.2020.1381

TRANSLATIONAL RELEVANCE

This review focuses on summarizing the various algorithms and guidelines/consensus documents published on the management of VLU to provide education and clinical guidance to clinicians.

CLINICAL RELEVANCE

VLUs are the most common leg ulcers, with a prevalence of 1.69% in the elderly population.[1] Their economic burden in the United States has been estimated at $14.9 billion annually.[2] VLUs are linked to venous insufficiency, a slow-progressing chronic disease. They are chronic and recurrent by nature, with associated morbidity and reduced quality of life.[3] Cases are often complex because as patients advance in age, they are likely to have concomitant health conditions, which also negatively impact wound healing, such as diabetes and arterial disease. Therefore, multiple factors need to be considered for proper assessment and treatment.

BACKGROUND

VLUs are a manifestation of long-term chronic venous disease (CVD), also termed chronic venous insufficiency (CVI) when describing the more advanced stages of the disease.[4,5] This is defined as an abnormally functioning venous system caused by venous valvular incompetence. Venous outflow may or may not be obstructed, and the abnormal function may affect the superficial venous system, the deep venous system, or both.[6] The development of this condition is influenced by multiple factors, including genetics, female sex, pregnancies, age, prolonged standing, trauma, and obesity. Some of these factors can be mitigated through lifestyle (increasing exercise, controlling body weight, and avoiding smoking), but others are not modifiable and many individuals will inevitably develop CVD over time.[7] This condition is diagnosed based on history, clinical presentation, and diagnostic tests, with duplex ultrasound being the gold standard.[8] Understanding how this disease progresses and how it can be slowed or prevented is critical in managing it.

An assessment tool to precisely describe cases of CVD has been developed with two parts: a classification of CVD and a severity scoring system. The classification system describes the stages of chronic venous disease using the Clinical manifestations, the Etiologic factors, the Anatomic distribution of disease, and the underlying Pathophysiologic findings (CEAP). The severity scoring is achieved

Table 1. *Updated 2020 CEAP classification*

C (Clinical)		*E (Etiologic)*		*A (Anatomic)*		*P (Pathophysiologic)*	
C_0	No visible or palpable signs of venous disease	Ep	Primary (degenerative process of venous valve and/or wall)	As	Superficial veins	Pr	Reflux
C_1	Telangiectasia[a] or reticular veins[b]	Es	Secondary	Ad	Deep veins	Po	Obstruction
C_2	Varicose veins[c]	Esi	Secondary—intravenous (secondary cause of venous disease)	Ap	Perforator veins	Pr,o	Reflux and obstruction
C_{2r}	Recurrent varicose veins	Ese	Secondary—extravenous (no venous wall or valve damage)	An	No venous location identified	Pn	No venous pathophysiology identifiable
C_3	Edema	Ec	Congenital	Name any of 18 venous segments as locators for pathology[h]			
C_{4a}	Pigmentation or eczema	En	No cause identified				
C_{4b}	Lipodermatosclerosis[d] or atrophie blanche[e]						
C_{4c}	Corona phlebectatica[f]						
C_5	Healed venous ulcer						
C_6	Active venous ulcer						
C_{6r}	Recurrent active venous ulcer						
S	Symptomatic[g]						
A	Asymptomatic						

[a]Dilated intradermal venules <1 mm in size.
[b]Dilated, nonpalpable, subdermal veins 4 mm in size or less.
[c]Dilated, palpable subcutaneous veins generally larger than 4 mm.
[d]Induration caused by fibrosis of the subcutaneous fat.
[e]White scar tissue.
[f]Fan-shaped pattern of numerous small intradermal veins on the medial or lateral aspects of the ankle and foot.
[g]Ache, pain, tightness, skin irritation, heaviness, muscle cramps; other complaints attributable to venous dysfunction.
[h]Superficial veins: telangiectasias (Tel) or reticular veins (Ret); great saphenous vein above knee (GSVa); great saphenous vein below knee (GSVb); small saphenous vein (SSV); anterior accessory saphenous vein (AASV); nonsaphenous veins (NSV). Deep veins: inferior vena cava (IVC); common iliac vein (CIV); internal iliac vein (IIV); external iliac vein (EIV); pelvic veins (PELV); common femoral vein (CFV); deep femoral vein (DFV); femoral vein (FV); popliteal vein (POPV); crural (tibial) vein (TIBV); peroneal vein (PRV); anterior tibial vein (ATV); posterior tibial vein (PTV); muscular veins (MUSV); gastrocnemius vein (GAV); soleal vein (SOV). Perforator veins: thigh perforator vein (TPV); calf perforator vein (CPV).

The CEAP classification system describes the stages of chronic venous disease using the Clinical manifestations, the Etiologic factors, the Anatomic distribution of disease, and the underlying Pathophysiologic findings.

Adapted from Bergan *et al.*,[4] Porter and Moneta,[9] Eklof *et al.*,[10] and Lurie *et al.*[11]

by reporting the anatomic segments involved with either reflux or obstruction. This classification system was first published in 1995[9] following a consensus conference with international representation and endorsement by the joint councils of the Society for Vascular Surgery and the North American Chapter of the International Society for Cardiovascular Surgery. The scale has been updated over time and published as the Revised CEAP classification[10] and the 2020 update of the CEAP classification system and reporting standards.[11] Today, most published clinical articles on CVD use the CEAP classification system or at least some portion of it. Table 1 presents the CEAP classification system. Additional scoring systems intended to complement the CEAP were also proposed: a Venous Clinical Severity Score (0–3 grading scheme for nine attributes of CVD); a Venous Segmental Disease Score (based on venous segmental involvement with reflux or obstruction as determined by imaging), and a Venous Disability Score (to accommodate for differences between patients on what constitutes "usual activities").[12] The Venous Clinical Severity Score was revised in 2010 for better applicability.[13]

The progression in severity of CVD is variable and proceeds along different pathways in different patients. Examples have been investigated and have shown that the predominant pathology is venous reflux caused by dysfunctional venous valves.[7] This leads to a cycle of venous hypertension, inflammation, capillary damage, and edema. The venous hypertension seems central to the skin changes in CVD.[4] Skin changes result from the capillary leakage, and a chronic inflammation microenvironment develops that exacerbates tissue damage and delays healing. The pathophysiology of CVD has been reviewed in detail in the literature.[4,7,14–16]

The CEAP classification is not always used by clinicians treating VLUs in their wound care practice because by the time an ulcer is present, all patients fall under the C6 classification for the observable clinical manifestation; therefore, this tool does not provide much differentiation between ulcer patients from a clinical ulcer assessment perspective. The tool is useful, however, when visible clinical signs are present in patients, as its higher classifications (C_4 to C_6) correlate with patients at higher risk for developing leg ulcers and for ulcer recurrence.[14] Figure 1 illustrates examples of clinical signs at various levels of the CEAP classification.

In addition, the Etiologic, Anatomic, and Pathophysiologic components of the CEAP classification involve a more detailed diagnostic workup that

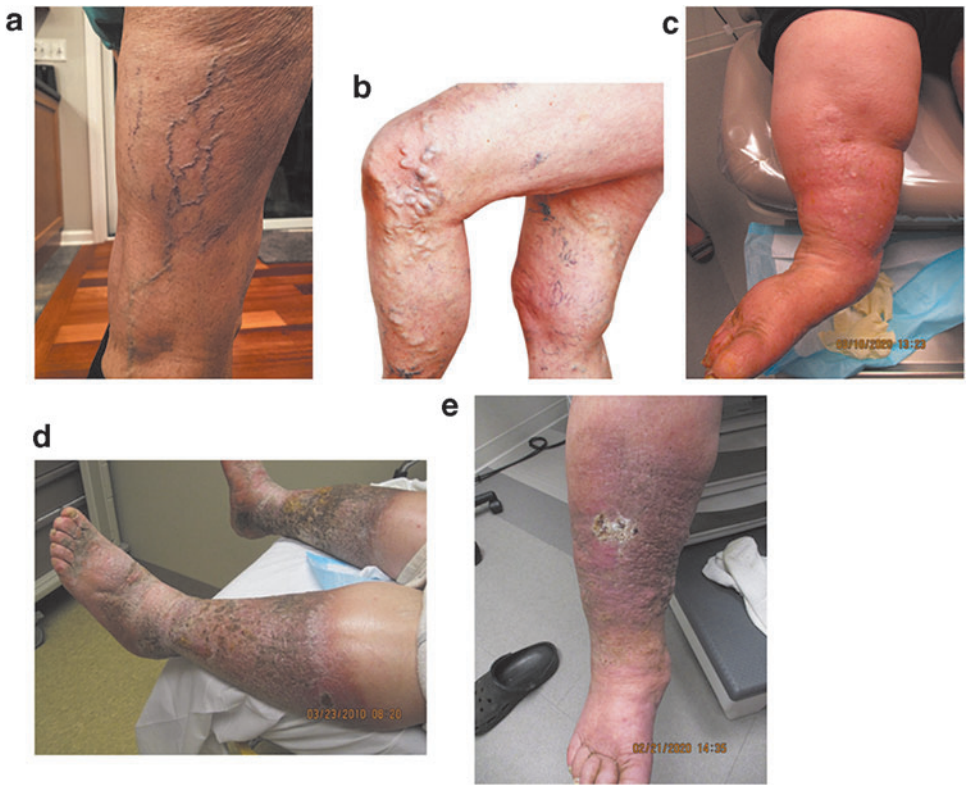

Figure 1. Examples of chronic venous disease. **(a)** Telangiectasias (C_1). **(b)** Varicose veins (C_2). **(c)** Edema (C_3). **(d)** Eczema (C_{4a}). **(e)** Lipodermatosclerosis (C_{4b}).

allows to characterize the venous disorder and possibly treat it before an ulcer develops. The duplex ultrasound examination can establish the anatomical patterns of the veins and abnormalities of venous blood flow in the limbs, with details on which saphenous junctions are incompetent and the extent of the reflux. This information has a significant impact on the type of treatment considered most appropriate.[8]

Conservative treatment primarily consists of compression therapy and supportive measures (physical therapy, manual lymphatic drainage, and the use of phlebotonics for symptom relief). Other approaches include sclerotherapy, surgical procedures, and endovenous thermal and chemical procedures.[15] These more invasive approaches are often reserved for patients who do not respond satisfactorily to conservative measures, although it has been suggested that earlier use of venous ablation should be considered in symptomatic patients.[14] Early treatment aimed at preventing venous hypertension, reflux, and inflammation could attenuate symptoms and reduce the risk of ulceration if performed early in the course of CVD.[4] The concept of surgical intervention remains valid once an ulcer is present: it is not sufficient to treat the ulcer because the cause of the problem also needs to be addressed.[17] Supporting this idea, a randomized controlled trial, including 500 patients demonstrated that surgery to correct superficial venous reflux combined with compression reduces ulcer recurrence compared with compression alone.[18]

Once a VLU is present (examples shown in Fig. 2), multiple assessment and treatment algorithms have been proposed to optimally manage the condition. An important factor to consider when managing these wounds is the possibility of concomitant arterial disease: a mixed etiology is estimated to affect up to 26% of patients with lower extremity ulcerations.[19] This article will review the literature on VLUs, specifically treatment algorithms, guidelines, and guidance documents, and provide an up-to-date educational resource for practitioners new to the field.

Figure 2. Examples of venous leg ulcers. **(a)** Venous ulcer surrounded by atrophie blanche (white scar tissue). **(b)** Venous ulcer surrounded by hemosiderosis. **(c)** Venous ulcer with hemosiderosis and stasis dermatitis. **(d)** Venous ulcer surrounded by hemosiderosis.

The literature search for venous insufficiency classifications and treatments was conducted in PubMed and Embase in June 2020. These databases have comprehensive global coverage of health, biology, nursing, and chemistry academic journals. The search strategy used the following keywords and terms: venous insufficiency, venous stasis, VLUs, stratification classification, algorithm, treatment, pathophysiology, and pathomechanism. Two hundred and fifty-nine articles were evaluated for applicability to the topic; 37 were selected as relevant to the topic and reviewed. Fourteen were included.

Articles found in the bibliographies of these 37 articles were also reviewed for possible inclusion (47 additional articles reviewed, 31 of which were included). Additional literature deemed generally relevant to cover the topic (but not related to an algorithm, a classification system, or a guideline/consensus document) and already available to the authors was also included (22 additional articles and 1 book chapter). In total, 106 articles and 1 book chapter were reviewed and 68 documents were cited.

DISCUSSION OF FINDINGS AND RELEVANT LITERATURE

An algorithm is a set of instructions designed to perform a specific task and is typically presented with various decision points in a stepwise fashion. Treatment algorithms allow to break down a complex decision-making process in a sequence of steps and provide guidance along the way. Over the years, various algorithms have been published regarding the diagnostic and/or management of VLUs (including those with mixed arterial component) and we are describing this literature in this study. In addition to articles describing algorithms, several guidance documents and consensus recommendations from government agencies or professional societies have been published on VLUs (some of them also include algorithms). We also review these documents below.

Among all the articles reviewed, a total of 26 articles were identified presenting either a classification system (discussed in the Background section), an algorithm related to the management of lower extremity wounds (including those describing the CEAP classification presented above), or a guideline/consensus. Seven articles provided exhaustive descriptions of classification systems, eleven articles proposed algorithms, and twelve were original guidelines, summarized guidelines, consensus documents, or articles discussing and/or summarizing guidelines or consensus documents. This distribution is presented in Table 2 (two of the guidelines and two consensus documents also offered algorithms, which is why these references are listed in more than one category in Table 2).

Table 2. *Distribution of the literature reviewed presenting either a classification system or an algorithm regarding the management of venous leg ulcers*

Classification Systems	*Algorithms*	*Guidelines*	*Consensus Documents*
Porter *et al.*[6]	Korstanje[20]	O'Donnell and Balk[21]	WUWHS[22]
Porter and Moneta[9]	McGuckin *et al.*[23]	Vowden and Vowden[24]	Harding *et al.*[25]
Rutherford *et al.*[12]	Thomas[26]	O'Donnell *et al.*[27]	Ratliff *et al.*[28]
Eklof *et al.*[10]	Vowden and Vowden[24]	Widener[29]	Harding[30]
Krishnan and Nicholls[31]	Eberhardt and Raffetto[14]	Wittens *et al.*[32]	Franks *et al.*[33]
Vasquez *et al.*[13]	Harding *et al.*[25]	Ito *et al.*[34]	
Lurie *et al.*[11]	Wittens *et al.*[32]	Tan *et al.*[35]	
	Hedayati *et al.*[19]		
	Ratliff *et al.*[28]		
	Alavi *et al.*[36]		
	Gould *et al.*[37]		

The large number of publications in this area focusing on instructions and guidance reflects the difficulty and complexity of treating lower leg ulcers. Experts generally agree that there are substantial variations in practice[33] and that compression is underutilized in spite of the fact that it is considered the gold standard therapy.[24,30,38,39]

Published algorithms for the clinical management of VLUs and CVI

Compression therapy is considered the cornerstone of standard care for VLUs,[3] but a small fraction of cases do not respond to it. The first algorithm encountered in our literature search results was published by Korstanje in 1995[20] and was proposed as a guideline for choosing the best therapeutic option for VLUs that are resistant to compression therapy (stated as <10% of cases by this author). The author stresses that surgical or medical management is only palliative (there is no true cure for venous insufficiency), therefore, all these options should still be done in conjunction with compression. Several options are possible: sclerotherapy, saphenous ligation, stripping of the long saphenous vein, skin grafts, subfascial ligation of deep venous perforators, and venous reconstruction. Simple procedures should always be performed before attempting more complicated ones and the algorithm may serve as a guideline for choosing the best suitable option.

Another algorithm was published later[23] in a study intended to validate the clinical efficacy and

the cost effectiveness of VLU guidelines in the United States and in the United Kingdom. This study demonstrated that implementation of a guideline for diagnosis and treatment of VLUs resulted in the improvement in diagnosis, decrease in healing time, and an increase in healing rates resulting in lower costs. The algorithm later proposed by Thomas in 2013[26] focuses on assessing for arterial disease before applying compression and states that roughly half of patients with clinical features of CVI have some degree of arterial impairment.

Vowden and Vowden also published in 2013[24] a "preferred management pathway" in which Ankle–Brachial Pressure Index (ABPI) is used to determine the level of compression (after venous diagnosis is confirmed), then venous duplex is used to define the need for surgery/ablation, and if the venous disease is correctable, surgery is implemented based on ulcer improvement, that is, done before healing if the ulcer is not improving, or deferred until the ulcer is healed if it is showing progress with compression alone.

In 2014, Eberhardt and Raffetto[14] offered a simplified overview for the diagnosis and treatment of CVI based on the pathophysiologic mechanism, to be applied when signs and symptoms of CVI are present (not necessarily waiting for an ulcer to develop). The approach is to use conservative management with compression therapy and proceed with testing if the response is not satisfactory or the disease keeps progressing. Noninvasive testing (duplex and/or air plethysmography will allow to determine if obstruction, reflux, or muscle pump dysfunction is present and guide further treatment.

A consensus document published in 2015[25] by a group of experts working to encourage wider adoption of compression therapy proposed an algorithm that assesses the wound etiology and defines "simple," versus "complex" VLUs versus mixed etiology ulcers, which then helps determine healing targets (simple VLUs are expected to heal within 12 weeks, complex VLUs are expected to heal within 18 weeks, and the time to healing for mixed ulcers depends on the underlying etiology, comorbidities, and lifestyle factors).

The publication by Wittens *et al*. in 2015,[32] similar to the one by Eberhardt and Raffetto[14] the previous year, offered an algorithm for the management of all stages of CVI (including preulceration): testing is used as soon as a patient is symptomatic to distinguish between superficial versus deep vein pathology. Then, the location and exact nature of the problem is determined to select the proper intervention. Another algorithm published in 2015 by Hedayati *et al*.[19] specifically addressed ulcers of mixed etiology; the article also discussed possible interventions to address arterial disease as well as venous reflux.

The Wound, Ostomy, and Continence Nurses (WOCN) Society appointed a task force (20 consensus panel experts and 21 content validation experts) to develop an algorithm for compression for primary prevention, treatment, and prevention of recurrent VLUs in patients with CVI, which was published in 2016.[28] This work involved a literature search from 2005 to 2015 to identify evidence-based clinical practice guidelines for prevention and management of VLU and CVI; eight guidelines met the inclusion criteria and were used to construct the algorithm. It also refers to a previous publication from the WOCN[40] regarding the Ankle–Brachial Index (ABI) values to assess vascular disease and make a determination on compression therapy, and to the CEAP classification[10] for prevention and treatment.

Alavi *et al.* published in 2016 a Continuing Medical Education (CME) document in two parts on the evaluation[36] and treatment[3] of VLUs and presented an algorithm for evaluation and initial management, which considers the possible presence of diabetes in addition to vascular disease, and complements the ABPI measurement with the toe pressure measurement. The reason for this is that ABPI may be unreliable in patients with arterial calcification and advanced atherosclerosis caused by diabetes, and a direct toe systolic pressure (or toe brachial index, TBI) is more reliable because the digital arteries are rarely heavily calcified.[36,41] The TBI was shown to be more reliable in patients with noncompressible arteries, medial artery calcinosis, and/or neuropathy.[42]

The 2020 Standards of Medical Care in Diabetes from the American Diabetes Association[43] recommends at least one additional test beyond ABPI in diabetic patients with a foot ulcer and peripheral arterial disease: skin perfusion pressure (≥40 mmHg), toe pressure (≥30 mmHg), or transcutaneous oxygen pressure ($TcPO_2$ ≥25 mmHg). In these patients, urgent vascular imaging and revascularization should be considered if ankle pressure is <50 mmHg, toe pressure <30 mmHg, or $TcPO_2$<25 mmHg.

Gould *et al.* published their algorithm in 2016[37] based on a combination of society guidelines, Cochrane reviews, and over 80 primary articles with high-level evidence for an integrated approach to treating patients with venous ulcers. This one includes a statement to consider venous ablation to prevent recurrence after ulcer healing and to reassess every 6 months.

Table 3. *Decision points in the published algorithms for the diagnostic and/or treatment of venous leg ulcers*

References	*Decision Points*
Korstanje[20]	Brakial to ankle Doppler pressure ratio (to rule out arterial disease and decide on compression)
	Light reflection rheography (or Photoplethysmography) (to measure venous blood flow in lower legs to evaluate venous valve function and venous muscle pump effectiveness)
	Doppler and/or Duplex scan (to determine/locate incompetent junction)
	Ascending phlebography or Duplex scan (to determine if there is obstruction)
	Descending phlebography or Duplex scan (to assess extent of reflux)
McGuckin *et al.*[23]	Clinical signs of venous disease?
	No: VLU guideline not applicable
	Yes: Continue algorithm below
	Clinical signs of arterial disease: obtain Doppler ABI
	Underlying conditions? Evaluate and manage
	Evidence of infection? Culture and treat
	Granulating wound bed?
	Yes: apply appropriate dressing;
	No: Is debridement necessary? Yes: select method; No: apply dressing
	Apply compression
	After healing, maintenance phase
Thomas[26]	Assess for venous disease: Duplex ultrasound
	Consider MRI, CT, or venogram
	Assess for arterial disease: ABI
	Consider exercise ABI, MRI, CT, arteriogram
	If venous disease, apply moist topical treatment and multilayer compression
	If improving, continue topical and compression
	If not healing, consider bioengineered skin or graft; consider venous surgery
Vowden and Vowden[24]	Establish diagnosis (venous or non venous)
	ABPI to define level of compression
	Venous duplex to define need for surgery/ablation
	Compression hosiery (long-term maintenance)
Eberhardt and Raffetto[14]	Signs and symptoms of CVI: compression therapy
	If unsatisfactory response or advanced clinical disease: Duplex and/or APG
	If obstruction: venography; consider venous stenting
	If reflux, superficial: consider ablation (or foam sclerotherapy or stripping)
	If reflux, deep: venography; consider valve reconstruction
	If reflux, perforator: consider ablation, foam sclerotherapy, or surgery
	If muscle pump dysfunction: consider exercise program
Harding *et al.*[25]	Assess wound
	Assess periwound skin
	Assess leg and foot for clinical signs of CVI
	Assess patient
	Assess family/caregivers (ability to participate in care)
	ABC model: Assessment and diagnosis; Best practice wound and skin management; Compression therapy for treatment and prevention of recurrence
	Simple VLU (ABPI 0.8–1.3, area $<100\,cm^2$, present <6 months): compression
	Complex VLU (ABPI 0.8–1.3, area $\geq 100\,cm^2$, present ≥6 months, additional factors): Refer to VLU specialist, investigate further (*e.g.*, duplex scans)
	Mixed etiology ulcer (ABPI <0.8 or >1.3, symptoms of arterial disease, diabetes, rheumatoid arthritis, uncontrolled cardiac failure): Refer to appropriate specialist, investigate further (*e.g.*, duplex scans)
	ABPI >1.3: arterial calcification may be present
	ABPI >1.0–1.3: Probably no PAD
	ABPI 0.81–1.00: No significant or mild peripheral arterial occlusive disease
	ABPI 0.51–0.80: Moderate peripheral arterial occlusive disease
	ABPI <0.5: Severe PAD, "critical ischemia"
Wittens *et al.*[32]	History and Clinical assessment (VCSS, CEAP)
	Duplex of superficial and deep venous systems
	If superficial vein pathology with saphenous incompetence: thermal ablation, nonthermal ablation, conservative
	If superficial vein pathology with tributary incompetence: sclerotherapy, foam sclerotherapy, phlebectomy, conservative
	If deep vein pathology with deep venous obstruction: conservative, stenting, endophlebectomy, AV fistula
	If deep vein pathology with deep venous incompetence: conservative, valvuloplasty, valve/vein transposition, neovalve
	If vascular malformations: multidisciplinary approach

(*continued*)

Table 3. (*Continued*)

References	*Decision Points*
Hedayati *et al.*[19]	Mixed arterial venous ulcer
	If ABI >0.5, start compression and aggressive wound care
	Treat underlying superficial venous reflux
	If ABI <0.7: arterial revascularization with continued wound care and compression
	If ABI >0.7: continue wound care and compression; if not healing, consider revascularization if good operative candidate
	ABI <0.9 indicates PAD
	ABI <0.5 typically indicates severe arterial insufficiency
Ratliff *et al.*[28]	Health history
	Physical assessment
	ABI to exclude significant arterial disease
	Differential diagnosis to determine severity of CVI (use CEAP)
	Proceed to appropriate CEAP pathway
	CEAP 1–2: Determine need for compression based on symptoms
	CEAP 3–4: Refer to ABI (ABI ≥0.8 and ≤1.3: proceed to compression; ABI 0.5 to 0.8: consider use of light compression based on patient tolerance; ABI <0.5 or >1.3: do not use compression)
	CEAP 5: Refer to ABI (ABI ≥0.8 and ≤1.3: proceed to compression; ABI 0.5 to 0.8: consider use of light compression based on patient tolerance; ABI <0.5 or >1.3: do not use compression); consider use of pentoxifylline to enhance microcirculation and prevent recurrence
	CEAP 6: Wound care (topical dressing to manage exudate; emollients on intact skin to prevent dermatitis or topical steroids to treat dermatitis/eczema); Refer to ABI (ABI ≥0.8 and ≤1.3: proceed to compression; ABI 0.5 to 0.8: consider use of light compression based on patient tolerance; ABI <0.5 or >1.3: do not use compression); if no healing, consider referral and further testing for interventional therapies if indicated
Alavi *et al.*[36]	LE ulcer: no diabetes, no vascular disease suspected: biopsy
	LE ulcer with diabetes: clinical history, physical exam with LE pulses, monofilament test, ABPI, and toe pressure
	ABPI >0.8, toe pressure >80 mmHg, TBI >0.6: no relevant arterial disease
	ABPI >0.5, toe pressure >50 mmHg, TBI >0.4: some arterial disease (modify compression)
	ABPI >0.4, toe pressure >30 mmHg, TBI >0.2: arterial disease predominates
	ABPI <0.4, toe pressure <30 mmHg, TBI <0.2: high risk for limb ischemia
	LE ulcer with vascular disease suspected: clinical history, physical exam with pulses, ABPI and toe pressure, venous duplex
	Venous ulcer: local wound care, compression therapy
	Mixed arterial venous ulcer: local wound care, modified compression therapy
	Arterial ulcer: local wound care, no compression therapy
Gould *et al.*[37]	History/Physical consistent with venous disease
	Assess for arterial disease: if ABI <0.9 then vascular surgery assessment before multilayer compression (modified for ABI 0.5–0.8 or impaired mobility), debridement, dressing for exudate management
	If ulcer closing ≥40% in 4 weeks: continue compression; debride if indicated; modify dressings for reduced exudate
	If ulcer has abnormal appearance: biopsy
	If ulcer >10 cm^2, present >12 months, recurrent: Consider skin substitute or skin graft, refer for venous duplex
	When ulcer healed, life-long compression stockings, skin care; consider venous ablation to prevent recurrence
	Reassess every 6 months

ABI, Ankle–Brachial Index; ABPI, Ankle–Brachial Pressure Index; APG, air plethysmography; AV, arteriovenous; CT, computed tomography; CVI, chronic venous insufficiency; LE, lower extremity; MRI, magnetic resonance imaging; PAD, peripheral arterial disease; TBI, toe–brachial pressure index; VCSS, Venous Clinical Severity Score; VLU, venous leg ulcer.

Finally, the last algorithm identified in our search came from a 2016 publication[34] that translated in English the guidelines for the management of lower leg ulcers/varicose veins published in 2011 in the Japanese Journal of Dermatology by the Japanese Dermatological Association. The evidence reviewed covered the period of January 1980 to December 2008, and the objective was to "properly guide the diagnosis and treatment of lower leg ulcers/varicose veins by systematically presenting evidence-based recommendations that support clinical decisions," with dermatologists in mind since patients often consult first with this specialty. This algorithm includes varicose vein considerations in addition to lower leg ulcers; it proposes compression therapy as the most important element but also shows the selection of surgery and sclerotherapy options. Table 3 offers a summary listing the decision points proposed in the various algorithms found in the literature.

Guideline documents and consensus recommendations

In addition to the publications offering algorithms for the management of VLUs and CVI, guidelines and consensus documents have been published by numerous organizations. These documents sometimes also contain algorithms, which is why a few references listed below overlap with the previous section. Of interest is also a consensus document on terminology and definitions used to discuss chronic venous disorders.[5]

O'Donnell and Balk[21] reviewed in 2011 14 existing guidelines published between 1995 and 2008 and concluded that there was consensus on strong recommendations for dressings and compression only. Interestingly, their survey demonstrated that guidelines for VLU care are infrequently used in the United States (20%), but used by a majority of single-payer systems in Canada and Europe (82%). Several studies have demonstrated that after the institution of a VLU guideline in a given clinical setting, there were improvements in healing and recurrence rates, and reduced resource use and costs, supporting adoption of VLU guidelines.[23,44,45]

In 2014, O'Donnell *et al.*[27] went on to publish a very comprehensive guideline with best practices and recommendations on the management of VLUs, the clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. Its objective is to focus on complete management of VLUs at all levels of care and quality of supporting evidence to guide specific recommendations, to achieve the best outcomes for the most reasonable cost. These guidelines were summarized by Widener[29] for recommendations on wound evaluation, wound therapy, compression, and operative or endovascular management. A "recommendation" is provided when the benefit clearly outweighs the risks; otherwise, a "best practice guideline" is provided when care is needed but no clear evidence is available.

The European Society for Vascular Surgery has also published clinical practice guidelines in 2015[32] and included 67 recommendations and a flow chart for the management of CVD (included in Table 2). Another consensus document was published in 2015 by Wounds International.[25] This one presents the ABC model to simplify VLU management (Assessment and diagnosis; Best practice wound and skin management; Compression therapy) and offers a checklist for the clinician.

In 2016, an expert working committee assembled by the European Wound Management Association and Wounds Australia identified eight guidelines related to VLUs published from 2010 to 2015 and issued clinical practice statements to enhance the patient journey.[33] They found considerable variation between the published guidelines in the development process and the strength of recommendations but noted some common key points: comprehensive assessment by trained clinicians, including measure of ABPI before commencement of compression therapy (but no consensus on minimum ABPI value required); use of inelastic compression for VLUs and compression hosiery for healed ulcers.

An article by Andriessen *et al*. reviewed multiple guidelines on compression.[46] This review included 20 guidelines, clinical pathways, and consensus articles on compression therapy for VLUs and CVD, which agreed on three absolute contraindications (arterial occlusive disease, heart failure, and ABPI <0.5). However, definitions used were not consistent and there were conflicting recommendations, leading to the conclusion that evidence-based guidance is needed to inform clinicians on risk factors, adverse effects, complications, and contraindications.

Finally, the latest article we identified on this topic was a review of multiple VLU clinical practice guidelines using a structured assessment tool to assess their quality.[35] The tool used was the Appraisal of Guidelines for Research and Evaluation II (AGREE II) and the authors found that only 4 of the 14 eligible guidelines identified were considered of adequate quality for clinical use, indicating a need to consolidate efforts to reduce the heterogeneity seen in currently published guidelines. Some of these guidelines were posted on websites that were no longer accessible at the time of writing this article and could not be incorporated in this study.

Diagnostic methods

The various diagnostic tools involved in the workup for the assessment of chronic venous disease have been described in detail in literature reviews on this topic and it is beyond our scope in this study to describe all the test methods.[14,31,32,36,47,48] The general principle is that the venous and arterial systems have to be assessed to confirm the diagnosis and choose the appropriate treatment. In addition, if persistent edema is present, the lymphatic system will work to reabsorb the accumulating fluid and may become damaged over time from the chronic inflammation that accompanies CVD.[49] Therefore, in such cases, an assessment of the patency of the lymphatic system may also be indicated.

Lymphedema classification is described in more detail in a recent book chapter by Magnan and Niezgoda.[50] Common signs and symptoms of lymphatics involvement are edema that extends above the knee and prior history (*e.g*., surgery, radiation, tumor, trauma). If imaging is desired for confirmation or to plan a surgical intervention, lymphoscintigraphy is currently the gold standard method. A specific diagnostic algorithm for chronic lower extremity swelling has been proposed by Gasparis *et al.*[51] to include lymphedema. The investigation of the venous system can be conducted using venous Doppler ultrasonography, color flow duplex ultrasonography, air plethysmography, or venography.[36]

The investigation of the arterial system involves a review of the micro- and macrocirculation. The microcirculation is assessed with transcutaneous oxygen pressure ($TcPO_2$), laser Doppler flowmetry, and transcutaneous carbon dioxide pressure ($TcPCO_2$) measurements and capillaroscopy; macrocirculation assessment includes the ABPI and toe pressure, Doppler arterial waveforms, duplex ultrasonography, angiography, and magnetic resonance imaging.

Treatments

Compression is recognized as the cornerstone treatment for VLUs[3] but is often underutilized for fear of complications if the patient has concomitant arterial disease.[52] Several articles describing algorithms and consensus documents provide compression guidance based on the measurement of the ABPI. However, these sources are not fully consistent with each other regarding the exact ABPI threshold values.[19,22,25,26,28,32,33,46] This is reflected in Fig. 3, which presents the ABPI interpretations published in these various references.

Other authors have argued that absolute values of the ankle pressure are more relevant than the ABPI because what matters is that the compression pressure does not exceed the local arterial perfusion pressure.[53] Illustrating this, a statement from a consensus document[33] suggests to apply "modified compression in patients with less severe arterial disease, *i.e.*, ABPI >0.5 or absolute ankle pressure >60 mmHg." The absolute value of the systolic ankle pressure is of higher practical relevance than the ABPI because it characterizes the perfusion pressure of the distal leg independently from the systemic blood pressure.[54] For example, an ABPI can be the result of an ankle pressure of 50 mmHg and a brachial pressure of 100 mmHg, but also of an ankle pressure of 90 mmHg and a brachial pressure of 180 mmHg. A compression pressure of 40 mmHg would be dangerous in the first example, but safe in the second case.[55]

In addition to the specific ABPI values guiding what level of compression to use, there is abundant literature describing the types of compression materials and the way in which compression is applied. It was originally believed that "graduated compression" (with highest pressure applied at the ankle and gradually reduced toward the knee as the circumference of the limb increases toward the calf)[56] was the proper method to apply compression based on Laplace's law, which defines pressures exerted on curved surfaces. However, Schuren and Mohr's work[57] using artificial legs and pressure

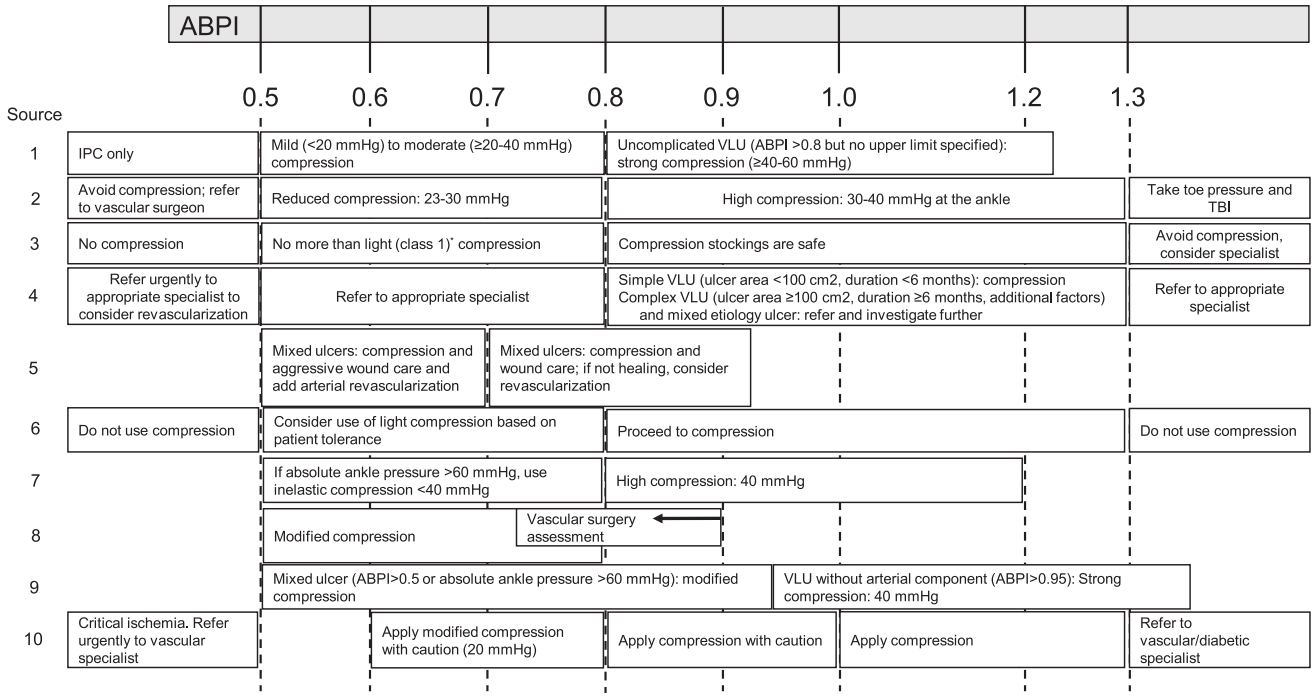

Figure 3. Compression recommendations based on ABPI, Ankle–Brachial Pressure Index. Sources: 1: WUWHS[22]; 2: Wound Ostomy and Continence Nurses Society Subcommittee[40]; 3: Thomas[26] (*Class 1 compression defined as 10–20 mmHg over the counter, 20–30 mmHg prescription, or 18–21 mmHg in Europe); 4: Harding *et al.*[25]; 5: Hedayati *et al.*[19]; 6: Ratliff *et al.*[28]; 7: Alavi *et al.*[3]; 8: Gould *et al.*[37]; 9: Franks *et al.*[33]; 10: Andriessen *et al.*[46]

transducers showed that using Laplace's law to calculate these values does not accurately predict sub-bandage pressures. None of the bandages they tested could provide dependable graduated compression. The widespread belief that correctly applied compression should provide 40 mmHg at the ankle and 17 mmHg below the knee in a graduated fashion is based solely on theoretical mathematical equations but is not supported by the results of experimental studies.

Schuren and Mohr[58] later demonstrated that the dynamics of effective compression therapy are explained by Pascal's Law: when a pressure is applied on a fluid (a muscle or muscle group) in a closed container (fascia muscularis and compression bandage), there is an equal increase at every other point in the container. Publications by others have later supported these concepts and debunked the dogmas and controversies in compression therapy.[56,59] It is now believed that progressive compression (where lower ankle than calf pressure is applied) may be used to improve venous pump function for the treatment of venous ulceration at least in mobile patients and that it is as effective as traditional graduated compression and well tolerated in the presence of peripheral arterial disease.[55,60,61]

Although there is a multitude of products available, compression bandages essentially come in two types: elastic and inelastic. Elastic bandages stretch and recoil back to their original length, exerting a sustained squeeze on the tissue. For this reason, they exert a high pressure during rest, but a low pressure during exercise because they stretch along with the expansion of the calf muscle. On the other hand, inelastic bandages form a rigid sleeve after application and exert a low resting pressure because they do not compress the leg any further once that rigid sleeve is formed. However, during exercise, the rigid sleeve provides resistance to the calf muscle expansion, creating a high working pressure.

Inelastic compression is more effective in reducing venous reflux and improving the venous pumping function, and it is better tolerated at rest.[62] Inelastic materials or short-stretch multicomponent bandages produce great differences between resting and working pressure and high pressure peaks. These bandages are comfortable at rest and more effective in improving venous hemodynamics in standing position and during muscle exercise compared with elastic bandages or compression stockings.[33]

There is overall evidence that healing outcomes are better with compression than without it, and that multicomponent systems are more effective than single component systems.[63,64] The agreed-upon absolute contraindications are arterial occlusive disease, heart failure, and an ABPI <0.5.[46] Adverse events from compression are very rare if compression is used correctly and contraindications are taken into consideration.[65] Compression, however, does not address the root cause and endovascular procedures are now available to improve long-term maintenance by slowing disease progression and reducing recurrences.[15,66] Venoactive drugs (phlebotonics), such as pentoxifylline, micronized purified flavonoid fraction, and sulodexide, are also available to improve venous tone/contractility and microcirculation, and to reduce edema and inflammation.[67,68]

FUTURE DIRECTIONS

Commonalities between algorithms

Drawing the commonalities between the algorithms, the general diagnostic and treatment approach for VLUs can be summarized as follows:

- Confirm venous etiology and evaluate ulcers in the context of the severity of the chronic disease.
- Assess for possible arterial component (mixed etiology) to see if compression needs to be modified (to milder compression) or avoided and if specialist referral is necessary. ABPI is typically used for this determination.
- Locate anatomically the site(s) of malfunction and consider operative treatment to address venous reflux or obstruction.
- Provide wound care and compression therapy using a multilayer system.

Some important additional considerations listed in the more recent publications include the use of the CEAP classification system to determine the severity of CVI, and the addition of the absolute ankle pressure to properly assess potential arterial disease to the ABPI information, as well as the toe pressure for diabetic patients.

Recommendations for practice

- Confirm arterial inflow: Confirm appropriate arterial inflow because if it is compromised, compression can be dangerous and deleterious. Follow compression product instructions (ABPI) and clinician judgment (pulse assessment; vascular surgery consultation if indicated for additional tests).
- Choose multilayer compression system: A short stretch system (inelastic) is the correct choice for very active patients or for those who have a more tenuous arterial supply.

A long stretch system (elastic) is better suited for more sedentary patients.

- Apply compression system: This should be performed by a health care professional trained for the application of the specific product used (competency-based training).
- Maintain a multidisciplinary approach: A team approach, including wound provider, vascular surgery, nursing, and physical therapy is ideal to tailor a treatment plan that is most effective for each individual patient.

TAKE-HOME MESSAGES

- Adopting a VLU guideline in a clinical setting leads to improvements in healing rate.
- Lower leg ulcers require proper diagnosis to select the appropriate treatment and a multidisciplinary team is needed when mixed etiologies are present.
- Compression is the mainstay of therapy for CVD and for venous ulcers; multilayer, inelastic systems are most effective.
- The literature reports three absolute contraindications to compression: the presence of arterial occlusive disease, heart failure, or an ABPI <0.5.[46] However, in clinical practice, patients with heart failure but a good ejection fraction can be treated with compression. Also, an ABPI can still be low after a stent has been placed to restore adequate blood flow. Therefore, individual patient assessment must prevail and this is why specific complex cases require clinical judgment and a comprehensive multidisciplinary approach to treatment.
- Compression alone does not solve the underlying disease and interventional correction may be necessary.

SUMMARY

Lower leg ulcers can be associated with various underlying pathologies (venous insufficiency, arterial disease, diabetes) or a combination thereof. Proper assessment and diagnosis are important to choose the appropriate course of treatment. When venous disease is suspected, Doppler and Duplex scanning should be used to evaluate the venous and arterial circulations and confirm diagnosis.

Compression is the mainstay of treatment for symptomatic CVD and for venous ulcers. It is underutilized because of a lack of clinician knowledge, unclear referral pathways, local unavailability of compression, and patient unwillingness to receive compression.[25,30] A fear of adverse events can be another reason for underutilization, but those are very rare if compression is used correctly and contraindications are taken into consideration.[65] Compression, however, is not a long-term solution by itself and the option of interventional correction should be offered early to prevent or slow disease progression and reduce recurrence.[66]

ACKNOWLEDGMENT AND FUNDING SOURCES

The authors would like to thank Mark Eells, Medical Information Manager from 3M Medical Solutions Division, for conducting the literature search. The preparation of this publication was funded by 3M.

AUTHOR DISCLOSURE AND GHOSTWRITING

S.F.B. is an employee of 3M. J.E.-W. and D.W. are consultants for 3M. All authors contributed to writing this article and no ghostwriters were used to write this article. This review did not involve a clinical study protocol nor study participants; the clinical images included in Figs. 1 and 2 were provided by D.W. and J.E.-W. with patients' permission.

ABOUT THE AUTHORS

Stéphanie F. Bernatchez, PhD, in Interdisciplinary Sciences (University of Geneva, Switzerland). She currently resides in Minnesota and works for 3M (Medical Solutions Division). Her work at 3M has included research and development in the area of advanced wound care using *in vitro* and *in vivo* assays, as well as clinical research work. **Jill Eysaman-Walker, DO, MS, CWS-P, ABWMS, FACCWS** (Lake Erie College of Osteopathic Medicine). She specializes in the diagnosis and treatment of chronic wounds, including venous, arterial, and diabetic ulcers. She also practices Hyperbaric Medicine in conjunction with wound care. She practices at Catholic Health Advanced Wound Healing Centers in Cheektowaga, NY. **Dot Weir, RN, CWON, CWS** (Valencia College and Chamberlain College of Nursing). Dot is an educator on all aspects of wound care and is the Co-Chair for the Symposium on Advanced Wound Care and on the faculty of the Wound Certification Prep Course. She is a wound care clinician at the Saratoga Hospital for Wound Healing and Hyperbaric Medicine in Saratoga Springs, NY.

REFERENCES

1. Margolis DJ, Bilker W, Santanna J, Baumgarten M. Venous leg ulcer: incidence and prevalence in the elderly. J Am Acad Dermatol 2002;46:381–386.
2. Rice JB, Desai U, Cummings AK, Birnbaum HG, Skornicki M, Parsons N. Burden of venous leg ulcers in the United States. J Med Econ 2014;17:347–356.
3. Alavi A, Sibbald RG, Phillips TJ, et al. What's new: management of venous leg ulcers: treating venous leg ulcers. J Am Acad Dermatol 2016;74:643–664; quiz 665–666.
4. Bergan JJ, Schmid-Schönbein GW, Coleridge Smith PD, Nicolaides AN, Boisseu MR, Eklof B. Mechanisms of disease—chronic venous disease. N Engl J Med 2006;355:488–498.
5. Eklof B, Perrin M, Delis KT, et al. Updated terminology of chronic venous disorders: the VEIN-TERM transatlantic interdisciplinary consensus document. J Vasc Surg 2009;49:498–501.
6. Porter JM, Rutherford RB, Clagett GP, et al. Reporting standards in venous disease. J Vasc Surg 1988;8:172–181.
7. Labropoulos N. How does chronic venous disease progress from the first symptoms to the advanced stages? A review. Adv Ther 2019;36(Suppl 1):13–19.
8. Coleridge-Smith P, Labropoulos N, Partsch H, Myers K, Nicolaides A, Cavezzi A. Duplex ultrasound investigation of the veins in chronic venous disease of the lower limbs—UIP consensus document. Part I. Basic principles. Eur J Vasc Endovasc Surg 2006;31:83–92.
9. Porter JM, Moneta GL. Reporting standards in venous disease: an update. International Consensus Committee on Chronic Venous Disease. J Vasc Surg 1995;21:635–645.
10. Eklof B, Rutherford RB, Bergan JJ, et al. Revision of the CEAP classification for chronic venous disorders: consensus statement. J Vasc Surg 2004;40:1248–1252.
11. Lurie F, Passman M, Meisner M, et al. The 2020 update of the CEAP classification system and reporting standards. J Vasc Surg Venous Lymphat Disord 2020;8:342–352.
12. Rutherford RB, Padberg FT, Jr., Comerota AJ, Kistner RL, Meissner MH, Moneta GL. Venous severity scoring: an adjunct to venous outcome assessment. J Vasc Surg 2000;31:1307–1312.
13. Vasquez MA, Rabe E, McLafferty RB, et al. Revision of the Venous Clinical Severity Score: venous outcomes consensus statement: special communication of the American Venous Forum Ad Hoc Outcomes Working Group. J Vasc Surg 2010;52:1387–1396.
14. Eberhardt RT, Raffetto JD. Chronic venous insufficiency. Circulation 2014;130:333–346.
15. Santler B, Goerge T. Chronic venous insufficiency—a review of pathophysiology, diagnosis, and treatment. J Dtsch Dermatol Ges 2017;15:538–556.
16. Raffetto JD. Pathophysiology of chronic venous disease and venous ulcers. Surg Clin North Am 2018;98:337–347.
17. Word R. Medical and surgical therapy for advanced chronic venous insufficiency. Surg Clin North Am 2010;90:1195–1214.
18. Barwell JR, Davies CE, Deacon J, et al. Comparison of surgery and compression with compression alone in chronic venous ulceration (ESCHAR study): randomised controlled trial. Lancet 2004;363:1854–1859.
19. Hedayati N, Carson JG, Chi YW, Link D. Management of mixed arterial venous lower extremity ulceration: a review. Vasc Med 2015;20:479–486.
20. Korstanje MJ. Venous stasis ulcers. Diagnostic and surgical considerations. Dermatol Surg 1995;21:635–640.
21. O'Donnell TF, Jr., Balk EM. The need for an Intersociety Consensus Guideline for venous ulcer. J Vasc Surg 2011;54(6 Suppl):83S–90S.
22. World Union of Wound Healing Societies (WUWHS). Principles of best practice: compression in venous leg ulcers. A consensus document. London: MEP Ltd., 2008:1–12.
23. McGuckin M, Waterman R, Brooks J, et al. Validation of venous leg ulcer guidelines in the United States and United Kingdom. Am J Surg 2002;183:132–137.
24. Vowden P, Vowden K. Are we fully implementing guidelines and working within a multidisciplinary team when managing venous leg ulceration? Wounds UK 2013;9(Suppl 2):17–20.
25. Harding K, Dowsett C, Fias L, et al. Simplifying venous leg ulcer management. Consensus recommendations. Wounds International, 2015. www.woundsinternational.com (last accessed October 14, 2020).
26. Thomas DR. Managing venous stasis disease and ulcers. Clin Geriatr Med 2013;29:415–424.
27. O'Donnell TF, Jr., Passman MA, Marston WA, et al. Management of venous leg ulcers: clinical practice guidelines of the Society for Vascular Surgery (R) and the American Venous Forum. J Vasc Surg 2014;60(2 Suppl):3S–59S.
28. Ratliff CR, Yates S, McNichol L, Gray M. Compression for primary prevention, treatment, and prevention of recurrence of venous leg ulcers: an evidence-and consensus-based algorithm for care across the continuum. J Wound Ostomy Continence Nurs 2016;43:347–364.
29. Widener JM. Venous leg ulcers: summary of new clinical practice guidelines published August 2014 in the Journal of Vascular Surgery. J Vasc Nurs 2015;33:60–67.
30. Harding K. Challenging passivity in venous leg ulcer care—the ABC model of management. Int Wound J 2016;13:1378–1384.
31. Krishnan S, Nicholls SC. Chronic venous insufficiency: clinical assessment and patient selection. Semin Intervent Radiol 2005;22:169–177.
32. Wittens C, Davies AH, Baekgaard N, et al. Editor's choice—management of chronic venous disease: clinical practice guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg 2015;49:678–737.
33. Franks PJ, Barker J, Collier M, et al. Management of patients with venous leg ulcer: challenges and current best practice. J Wound Care 2016;25(Suppl 6):1–67.
34. Ito T, Kukino R, Takahara M, et al. The wound/burn guidelines—5: guidelines for the management of lower leg ulcers/varicose veins. J Dermatol 2016;43:853–868.
35. Tan MKH, Luo R, Onida S, Maccatrozzo S, Davies AH. Venous leg ulcer clinical practice guidelines: what is AGREEd? Eur J Vasc Endovasc Surg 2019;57:121–129.
36. Alavi A, Sibbald RG, Phillips TJ, et al. What's new: management of venous leg ulcers: approach to venous leg ulcers. J Am Acad Dermatol 2016;74:627–640; quiz 641–642.
37. Gould LJ, Dosi G, Couch K, et al. Modalities to treat venous ulcers: compression, surgery, and bioengineered tissue. Plast Reconstr Surg 2016;138(3 Suppl):199S–208S.
38. Fife CE, Carter MJ, Walker D. Why is it so hard to do the right thing in wound care? Wound Repair Regen 2010;18:154–158.
39. Mooij MC, Huisman LC. Chronic leg ulcer: does a patient always get a correct diagnosis and adequate treatment? Phlebology 2016;31(1 Suppl):68–73.
40. Wound Ostomy and Continence Nurses Society Subcommittee. Ankle Brachial Index: quick reference guide for clinicians. J Wound Ostomy Continence Nurs 2012;39(2 Suppl):S21–S29.
41. Sibbald RG, Goodman L, Woo KY, et al. Special considerations in wound bed preparation 2011: an update. Adv Skin Wound Care 2011;24:415–436.
42. Wukich DK, Shen W, Raspovic KM, Suder NC, Baril DT, Avgerinos E. Noninvasive arterial testing in patients with diabetes: a guide for foot and ankle surgeons. Foot Ankle Int 2015;36:1391–1399.
43. American Diabetes Association. Standards of medical care in diabetes—2020. Diabetes Care 2020;43(Suppl 1):1–224.
44. Olson JM, Raugi GJ, Nguyen VQ, Yu O, Reiber GE. Guideline concordant venous ulcer care predicts healing in a tertiary care Veterans Affairs Medical Center. Wound Repair Regen 2009;17:666–670.

45. Nelzen O. Fifty percent reduction in venous ulcer prevalence is achievable – Swedish experience. J Vasc Surg 2010;52(5 Suppl):39S–44S.

46. Andriessen A, Apelqvist J, Mosti G, Partsch H, Gonska C, Abel M. Compression therapy for venous leg ulcers: risk factors for adverse events and complications, contraindications—a review of present guidelines. J Eur Acad Dermatol Venereol 2017;31:1562–1568.

47. Youn YJ, Lee J. Chronic venous insufficiency and varicose veins of the lower extremities. Korean J Intern Med 2019;34:269–283.

48. Wounds UK. Best practice statement: addressing complexities in the management of venous leg ulcers. Wounds UK, 2019. www.wounds-uk.com (last accessed October 14, 2020).

49. Olszewski WL. The "third" circulation in human limbs—tissue fluid, lymph and lymphatics. Phlebologie 2012;41:297–303.

50. Magnan VJ, Niezgoda JA. Wound Care Essentials, Practice Principles, 5th ed. Philadelphia, PA: Wolters Kluwer, 2020:435–466.

51. Gasparis AP, Kim PS, Dean SM, Khilnani NM, Labropoulos N. Diagnostic approach to lower limb edema. Phlebology 2020;35:650–655.

52. Bernatchez SF, Peterson L, Fife CE. Compression therapy: the key to unlocking VLU healing. Today's Wound Clinic 2017;11:20–22.

53. Partsch H, Mortimer P. Compression for leg wounds. Br J Dermatol 2015;173:359–369.

54. Mosti G, Iabichella ML, Partsch H. Compression therapy in mixed ulcers increases venous output and arterial perfusion. J Vasc Surg 2012;55:122–128.

55. Vowden P, Kerr A, Mosti G. Demystifying mild, moderate and high compression systems—when and how to introduce "lighter compression." Wounds International, 2020. www.woundsinternational.com (last accessed November 10, 2020).

56. Anderson I. New research in compression therapy principles. Wounds UK 2013;9(Suppl 2):21–23.

57. Schuren J, Mohr K. The efficacy of Laplaces's equation in calculating bandage pressure in venous leg ulcers. Wounds UK 2008;4:38–47.

58. Schuren J, Mohr K. Pascal's law and the dynamics of compression therapy: a study on healthy volunteers. Int Angiol 2010;29:431–435.

59. Flour M, Clark M, Partsch H, et al. Dogmas and controversies in compression therapy: report of an International Compression Club (ICC) meeting, Brussels, May 2011. Int Wound J 2013;10:516–526.

60. Shepherd J. Progressive compression versus graduated compression for the management of venous insufficiency. Br J Community Nurs 2016; 21:S13–S18.

61. Couzan S, Pouget JF, Le Hello C, Chapelle C, Laporte S, Mismetti P. High tolerance of progressive elastic compression in peripheral arterial disease. Vasa 2019;48:413–417.

62. Mosti G. Compression and venous surgery for venous leg ulcers. Clin Plast Surg 2012;39:269–280.

63. O'Meara S, Cullum N, Nelson EA, Dumville JC. Compression for venous leg ulcers (review). Cochrane Database Syst Rev 2012;11:1–196.

64. Mauck KF, Asi N, Elraiyah TA, et al. Comparative systematic review and meta-analysis of compression modalities for the promotion of venous ulcer healing and reducing ulcer recurrence. J Vasc Surg 2014;60(2 Suppl):71S.e1–e2–90S.e1–e2.

65. Rabe E, Partsch H, Morrison N, et al. Risks and contraindications of medical compression treatment—a critical reappraisal. An international consensus statement. Phlebology 2020;35:447–460.

66. Raju S, Lurie F, O'Donnell TF, Jr. Compression use in the era of endovenous interventions and wound care centers. J Vasc Surg Venous Lymphat Disord 2016;4:346–354.

67. Jull AB, Arroll B, Parag V, Waters J. Pentoxifylline for treating venous leg ulcers. Cochrane Database Syst Rev 2012;12:CD001733.

68. Mansilha A, Sousa J. Pathophysiological mechanisms of chronic venous disease and implications for venoactive drug therapy. Int J Mol Sci 2018; 19:1–21.

Abbreviations and Acronyms

ABI = Ankle–Brachial Index
ABPI = Ankle–Brachial Pressure Index
APG = air plethysmography
CEAP = classification system for chronic venous disease using Clinical manifestations, the Etiologic factors, the Anatomic distribution of disease, and the underlying Pathophysiologic findings
CT = computed tomography
CVD = chronic venous disease
CVI = chronic venous insufficiency
LE = lower extremity
MRI = magnetic resonance imaging
PAD = peripheral arterial disease
TBI = toe brachial index
$TcPO_2$ = transcutaneous oxygen pressure
VCSS = Venous Clinical Severity Score
VLU = venous leg ulcer
WOCN = Wound, Ostomy, and Continence Nurses