Review Article

New Indian Journal of Surgery
Volume 14 Number 2/April - June 2023
DOI: https://dx.doi.org/10.21088/nijs.0976.4747.14223.6

Venous Leg Ulcer: A Review

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How to cite this article:
Jacob Antony Chakiath, Ravi Kumar Chittoria/Venous Leg Ulcer: A Review/New Indian J Surg. 2023;14(2): 81–93.

Abstract

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. 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; Varicose Vein.

INTRODUCTION

Venous leg ulcers (VLU) 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.[1-5] 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]

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Received on 09-02-2023 **Accepted on** 06-03-2023

Aetiology

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

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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 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]

Classification

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]

C (Clinical)		E (Etiologic)		A (Anatomic)		P (Pathophysiologic)	
Co	No visible or palpable signs of venous disease	Ep	Primary (degenerative processof venous valve and/or wall)	As	Superficial veins	Pr	Reflux
CI	Telangiectasiaa or reticular veinsb	Es	Secondary	Ad	Deep veins	Po	Obstruction
C2	Varicose veinsc	Esi	Secondary—intravenous (secondarycause of venous disease)	Ap	Perforator veins	Pr,o	Ref lux and obstruction
C2r	Recurrent varicose veins	Ese	Secondary—extravenous (no venouswall or valve damage)	An	No venous location identified	Pn	No venous pathophysiology identifiable
C3	Edema	Ec	Congenital	Name any of 18 venous segments as locators for pathologyh			
C4a	Pigmentation or eczema	En	No cause identified				
C4b	Lipodermatosclerosisd or atrophieblanchee						
C4c	Corona phlebectaticaf						
C5	Healed venous ulcer						
C6	Active venous ulcer						
C6r	Recurrent active venous ulcer						
S	Symptomaticg						
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 4mm.
[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.
hSuperficial veins: telangiectasias (Tel) or reticular veins Met); great saphenous vein above knee IGSVa); great saphenous vein below knee IGSVb); small saphenous vein (SSW; anterior accessory saphenous vein (AASV); nonsaphenous veins (NSW. Deep

veins: inferior vena cava (IVC); common iliac vein ICIV); 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 (MUSA 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.
Adanind from Rnrnan et al[4] Pnrtar and Mnnnta[9] Fklnf et al[10] and I win et al[11]

Pathophysiology

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. 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 (C4 to C6) correlate with patients at higher risk for developing leg ulcers and for ulcer recurrence.

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

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 adressed.[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, 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. The literature search for venous insufficiency classifications and treatments was conducted in PubMed and Embase in June 2020. These data bases have comprehensive global coverage of health, biology, nursing, and chemistry academic journals.

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.

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. 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 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, 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.[21,22] 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 andthe 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. [24,25]

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 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. Non-invasive 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 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. WOCN40recommends 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 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 non-compressible 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 (>/-40mmHg), toe pressure (>/-30mmHg), or transcutaneous oxygen pressure (TcPO2 >/-25mmHg). In these patients, urgent vascular imaging and revascularization should be considered if ankle pressure is <50mmHg, toe pressure <30mmHg, TcPo2<25mmHg.

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.

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 2)

References	Decision Points
Korstanje[20]	Brakial to ankle Doppler pressure ratio Ito 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 Ito determine if there is obstruction)
	Descending phlebography or Duplex scan (to assess extent of reflex)
Mc Guckin et al.[23]	Clinical signs of venous disease?
	No: VIII guideline not applicable
	Yes: Continue algorithm below
	Clinical signs of arterial disease: obtain Doppler AB!
	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 MAI, CT, or venograrn
	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
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 goad 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 MI (MI zo.e and 51.3: proceed to compression; MI 0.5 to 0.8: consider use of light compression based on patient tolerance; MI <0.5 or >1.3: do not use compression)
	CEAP 5: Refer to ABI (MI z0.0 and 51.3: proceed to compression; ABI 0.5 to 0.8: consider use of light compression based on patient tolerance; ABI<0.5 or >13: 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 (ABIz0.8 and 51.3: proceed to compression; ABI 0.5 to 0.8: consider use of light compression based on patient tolerance; MI <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

Gould et al.	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
	History/Physical consistent with venous disease
	Assess for arterial disease: if ABI<0.9 then vascular surgery assessment before multilayer compression (modified for MI 0.5-0.8 or impaired mobility), debridement, dressing for exudate management
	If ulcer dosing >40% in 4 weeks: continue compression; debride if indicated; modify dressings for reduced exudate
	If ulcer has abnormal appearance: biopsy
	If ulcer^3 10cm^2, present >12 months, recurrent: Consider skin substitute or skin graft, refer for venous duplex
	When ulcer healed, lifelong compression stockings, skin care; consider venous ablation to prevent recurrence
	Reassess every 6 months

Guideline documents and consensus recommendations

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 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.

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 flow metry, and transcutaneous carbon dioxide pressure ($TcPCO^2$) measurements and capillaros copy; micro circulation 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] 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 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 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 (fasciamuscularis 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 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]

Chronic venous ulcers remain a significant health and economic burden and the treatment remains frustrating for both the surgeon and patient. Venous stasis followed by peri-vascular inflammation and ulceration follow a vicious cycle. Treatment includes surgical correction of the cause of venous hypertension, compressive dressings, wound care, limb elevation, etc. Once the cause of venous hypertension is treated, wound bed preparation followed by soft tissue cover will produce rapid wound healing. However, if surrounding inflammation persists, attempted soft tissue cover may fail. LLLT has been found to accelerate wound healing, tissue repair and regeneration. The biostimulatory properties of LLLT make it an effective tool in the management of chronic non healing ulcers including venous ulcers. The photo biological effects of LLLT depend on power, wavelength and duration of application. Most guidelines suggest that the energy density per treatment session should be within the range of 0.1 - 12.0 J/cm^2 and the wave length between 600nm-950nm. After the application of LLLT in and around the wound, it stimulates cytochrome c oxidase at the cellular level and converts it into an electronically excited status. This alters its redox status and stimulates the electron transfer in the respiratory chain of the cell, increasing ATP production and cell membrane permeability and cell signaling. This results in accelerated wound healing. It has been quoted that a part of the electronically excited status energy is converted into heat, causing a localized and transient heating in photoreceptors that accelerates wound healing. The commonly used LLLT lasers include Gallium Arsenide (Ga-As), Gallium Aluminum Arsenide (Ga-Al-As), Krypton, Helium Neon (He-Ne). LLLT appears to be an effective adjuvant therapeutic modality in promoting the healing of venous ulcer. (fig. 1)[69]

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

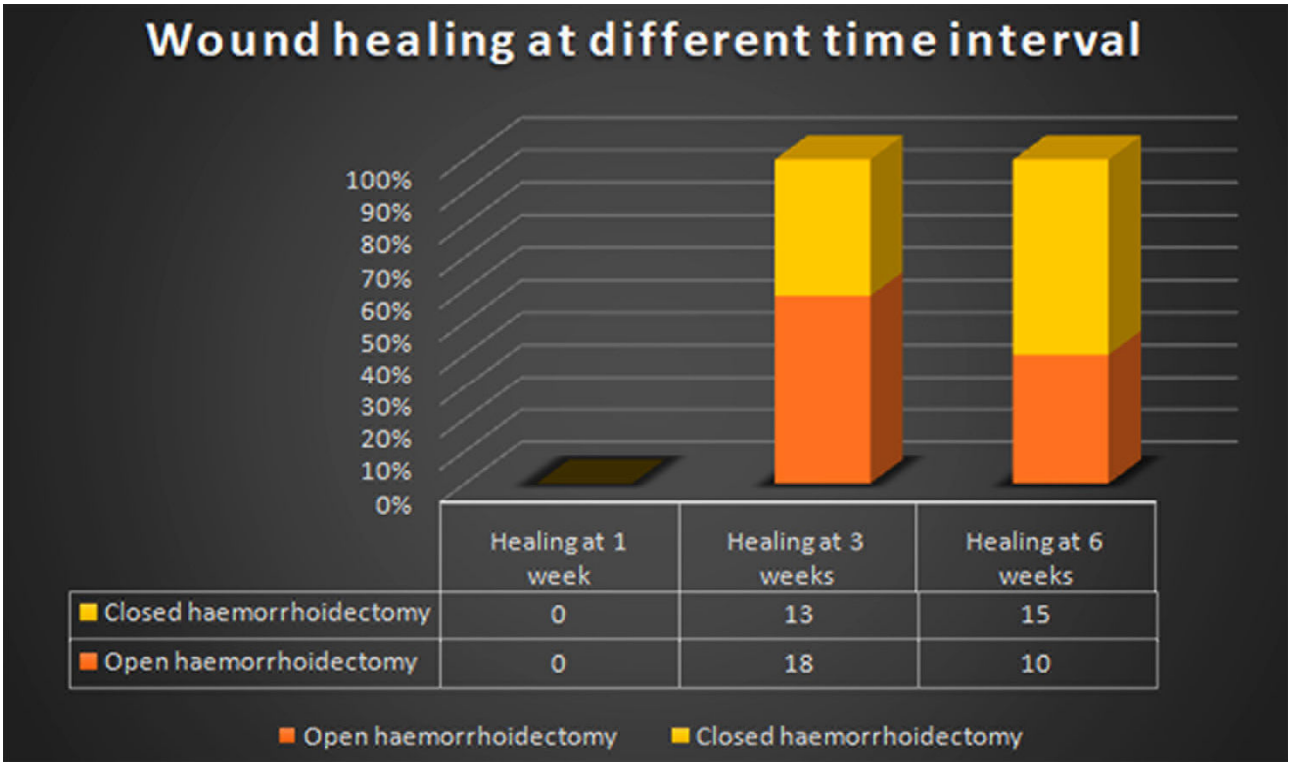


Fig 1. Photograph of Chronic venous ulcer right leg (IA), Machine to deliver Galium Arsenide lser (IB), wound being exposed to LLl. (Fig IC), wound after 2 weeks of LLLT.

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.

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]

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. 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.

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