Management of Venous Leg Ulcers and Venous Insufficiency

Here’s an update on this common condition.

BY WINDY COLE, DPM

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Following this article, an answer sheet and full set of instructions are provided (pg. 124).—Editor

Mllions of Americans are affected with painful, open, draining ulcers on their legs. These ulcers are commonly referred to as venous leg ulcers (VLUs). These ulcers are the cause of significant clinical and economic burden to the healthcare system and society as a whole. VLUs often take weeks or months of treatment in order to heal. Oftentimes, even under the best circumstances, these ulcers can be recalcitrant and recurring. It is not uncommon for physicians to see patients who have suffered for years with VLUs or have faced amputation of their limb. Many patients even consider amputation of the limb as an option to alleviate the pain. Pain is one of the most common complaints in patients with VLUs and it can be difficult to control. A study by Phillips in 1994 found that 65% of patients with VLUs related severe pain and 68% of patients stated that the ulcers caused negative emotional and psychological impact. Some of the reported feelings were that of fear, social isolation, anger, depression, anxiety and negative self-image.

The Problem

Venous leg ulcers are the end result of a condition known as chronic venous insufficiency. This malady is caused by an abnormality of the veins in the lower extremity. The lower extremity venous system is composed of both a superficial and deep system connected by an elaborate series of perforating veins. Under normal conditions, valves within these veins direct blood from the superficial into the deep system that in turn carries the blood back towards the heart. The flow in the deep system is directly impacted by the pumping action of the musculature in the legs during physical activity. A host of illnesses and...
disease states can directly affect the anatomic function of the venous system. Some examples include a history of deep vein thrombosis in patients who may have had damage caused to their valves in their veins. Women who have experienced pregnancy may experience functional and structural changes in the venous system due to increased hormone levels and damage caused by pressures put on the inferior vena cava by the enlarging fetus. There is also a hereditary predisposition in some individuals to develop valve dysfunction over time. Obesity and sedentary lifestyle can quicken this progression. In these instances, blood can then flow in a reverse fashion from the deep vein system to the superficial system. This reversal of flow leads to pooling of the blood and fluid in the legs. The patient may first experience swelling or edema in the lower extremities. Over time, hallmark trophic changes in the tissues occurs. These include hyper-pigmentation, venous stasis dermatitis, hemosiderin deposits, loss of hair, thickened nails, atrophy blanch, and lipodermatosclerosis. As a result of these changes, skin breakdown can occur, resulting in ulcerations. VLUs typically occur in the gaiter region of the lower leg.

The Pathophysiology

The venous system in the leg is composed of the long and short saphenous veins and their tributaries. These offshoots drain blood from the microcirculatory bed. The deep venous system consists of the main axial veins between muscle compartments and the venous sinuses with the calf muscles. The superficial and deep venous systems connect at the sapheno-popliteal and sapheno-femoral junctions, as well as communicating through the perforator veins (Figure 1). Perforator veins either connect directly to the main axial veins or link to the veins and venous sinuses within the muscles, thus draining indirectly into the main axial veins. The bicuspid valves in veins ensure that the venous return is unidirectional towards the heart. Valves in the perforator veins also serve to protect the superficial venous system from high compartmental pressures present in the deep veins during contraction of the calf muscle pump. The muscle pump assists in the return of blood against gravity. In a leg with normal venous return, the hydrostatic pressures within the superficial and deep venous systems are both approximately 80 mmHg when a person is upright at rest. However, during exercise such as walking or plantarflexion, calf muscle contraction increases pressure within the deep veins. This action closes the valves in the perforator veins and propels the blood in the deep veins towards the heart. Subsequent muscle relaxation causes pressures in the deep venous system to fall abruptly to a level lower than that in the perforator veins. This sudden pressure drop of between 0 and 10 mmHg ensures the valves in the superficial system open to refill the deep venous system. Proper functioning of this venous return is dependent on competent valves within the veins to prevent retrograde flow or reflux from the deep to the superficial system.

Dysfunction in venous return occurs through incompetent valves in the superficial, perforating or deep veins, outflow obstructions in the deep veins, and/or calf muscle pump failure because of immobility or disease of the lower limb. These conditions contribute to venous reflux resulting from valvular incompetency, leading to sustained increases in venous pressure in the superficial system. This venous hypertension is the hallmark of chronic venous insufficiency (CVI). Clinical manifestations of CVI can include:

- Telangiectasia or spider veins
- Varicose veins
- Dependent edema in the lower leg
- Atrophy blanche or smooth white scar tissue
- Hyperpigmentation caused by deposition of red blood cell pigments in the dermis
- Eczematous skin changes, such as dry, flaky skin
- Induration of the lower leg caused by fibrosis of subcutaneous fat

The superficial venous system is composed of the long and short saphenous veins.

The microcirculatory cascade form venous hypertension to ulceration of the leg has still not been fully described. Although the understanding of the pathogenesis of venous leg ulcers is incomplete, many hypotheses exist. Some of these theories include pericapillary fibrin cuff formation, presenting a barrier to oxygen diffusion. White cell plug in capillaries causing tissue hypoxia and fibrin cuffs trapping growth factors. The most current theory of ulcer pathogenesis is thought to be an inflammatory chain brought on by a chronic ischemia-reperfusion...
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An inflammatory cascade involving cytokines, oxygen-derived free radicals, and activated polymorphonuclear neutrophils promotes the deposition of capillary cuffs, trapping growth factors and cellular adhesion molecules. These matrix plugs attract and activate more white blood cells.

The repeated activation of this cascade eventually overwhelms the body’s compensatory capacity and the balance tips in the favor of tissue destruction. Although the observed causes of lower leg ulcers may, in many cases, seem to be mechanical (traumatic), healing cascades are arrested or counteracted by the ischemic-reperfusion cycle. Correction of the underlying venous hypertension is the crux of treatment for VLUs.

Compression Therapy

The therapeutic mainstay in the management of venous leg ulcers is graduated compression bandaging. Compression therapy is one of the most ancient treatments employed by man. Its role has been defined over centuries by a wealth of experience and scientific studies. The first documentations our ancient ancestors left behind were prehistoric cave paintings from the Neolithic period 500-2500 BC (Figure 2). Hippocrates used cloth compression dressings for the treatment of lower leg ulcers. He also held to the belief that this therapy helped to redirect blood flow back to the heart. In 1783, Dr. Benjamin Collins Brodie was the first to scientifically describe venous insufficiency. He devised the very first test for valvular incompetency called the Brodie-Trendelenburg percussion test. Dr. Paul Gerson Unna introduced his famed zinc paste boots in 1885 for the treatment of stasis dermatitis and leg ulcerations.

Compression therapy works by harnessing the powers of the laws of physics. The degree of compression produced by any bandage system is influenced by several complex factors. Of particular importance is the physical structure and elastomeric properties of the bandage itself. Secondly, the number of layers and the technique in which it is applied comes into play. The shape and size of the limb should also be considered. The skill and technique of the bandager plays a role as well. Lastly, the type and amount of physical activity that the patient participates in is crucial. LaPlace’s law

LaPlace’s law must therefore be considered when applying compression therapy. In its essence, this law accounts for sub-bandage pressure by determining the relationship between the pressure and tension of the bandage as well as the radius of the limb. Applied pressure is directly proportional to the tension in a bandage, but inversely proportional to the radius of the limb to which it is applied. With increased application tension, the bandage applied pressure will increase. As the number of bandage layers increases so does the bandage pressure. The circumference of the limb will then inversely affect bandage pressure. The practical consequence of LaPlace’s law is that with constant tension and increase of limb radius applied bandage pressures will decrease. Therefore, the natural pressure gradient of the leg will be maintained. Subsequently, it is not advised to apply increased tension to the compression bandage at the ankle as compared to the knee. To achieve true graduated compression, the bandage should be applied at a consistent tension and be able to keep its shape over time. The pressure exerted on the limb is also directly attributed to the number of layers applied. The more layers, the increased pressure.

There are two main forms of compression bandages, elastic and inelastic (Figure 3). Inelastic bandages, also known as short stretch bandages, only offer effective compression during movement. These types of bandages rely on muscle contraction to contribute to the volume changes in the leg. Short stretch bandages have minimal stretch and can only extend to 30 to 70 percent of their length. This attribute may allow for safer use in patients having venous ulcers with mildly decreased arterial flow. Inelastic bandages may not be the choice for patients with inadequate calf pumps or limited mobility. Examples of inelastic bandages, otherwise known as short-stretch, include Unna Boots, Coban, and Coloplast. The recommended method of application of inelastic bandages is a spiral wrapping technique from the base of the toes to two fingerbreadths under the patella.

Elastic bandages, as implied by their name, have high elasticity and can stretch up to several times their length. These products are therefore often referred to as long-stretch. Elastic bandages exert continuous pressures on the leg, allowing them to adjust to volume changes in the limb during both ambulation and relaxation. These compression bandages are therefore recommended in immobile patients or those having inadequate calf pumps. They are contra-indicated in patients with arterial insufficiency. Examples of elastic compression bandages include ACE, Setopress, and SurePress wraps.

Multilayer compression bandages are composed of a combination of in-
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Elastic and elastic bandages. Patients with poor calf pump function can benefit from the elastic components with the inelastic layers provide high working pressures with lower resting pressures. There are many multi-layer compression kits on the market. These products vary widely and it is always wise to review the product insert prior to application.

Intermittent pneumatic compression pumps may also be used to treat lymphedema, venous insufficiency, PVD, venous stasis ulcers, and ineffective muscle pumps. These garments typically act on a short cycle, utilizing overlapping compression chambers of adjustable pressure to pump the limb from distal to proximal. Contra-indications to this therapy include DVT/PE, inflammatory phlebitis, infection, decompensated cardiac failure, and severe PAD.\(^2\)

After venous ulcers have healed, it is imperative to transition patients into maintenance compression therapy to prevent recurrence. Physicians should prescribe some type of daily wear garment. Graduated compression stockings with slip-on adjustable devices are among the most common options recently gaining favor. Compression levels of 30 to 40 mmHg are recommended for the treatment of chronic venous insufficiency and venous ulcer prevention.

**Advanced Therapies**

Biologic matrices, both with and without living cells, provide clinicians with additional viable therapeutic options in the treatment of chronic wounds. These products are especially useful in the management of venous leg ulcers found in patients with PVD. These therapies are intended to facilitate the innate human repair mechanisms for tissues and skin. Cellular and tissue-based products (CTPs), formerly known as skin substitutes, are tissue-engineered, biologically active products designed to replace, either temporarily or permanently, the form and function of the skin. CTPs are used in the treatment of chronic ulcers in care to improve heal rates and decrease risks of infection.

Wound healing is a dynamic process involving interactions between cells, extracellular matrix (ECM) and growth factors that reconstitute tissue following injury. The extracellular matrix (ECM) plays an important role in tissue regeneration and provides a structural support for cells.\(^2\) Biologics contain reconstituted or natural collagen matrix that aims to mimic the structural and functional characteristics of native ECM. CTPs have emerged over the past 20 years as the most carefully studied and proven of the advanced wound management technologies. The ideal skin substitute is non-toxic, has little or no antigenicity. CTPS should be immunologically compatible. Processing of these products renders them safe to be used in human subjects without transmission of disease.

Most bio-engineered tissue can be divided into two major categories: Cellular and Acellular. Acellular products, such as cadaveric human dermis, have had all cellular components removed. They contain a matrix of hyaluronic acid, collagen and fibronectin.\(^2\) When placed in the wound bed, the three-dimensional matrix provides a temporary scaffold or support into which cells can migrate and proliferate. Cellular products contain living cells such as keratinocytes, fibroblasts, or mesenchymal stem cells within a matrix.\(^2\) These cells can be autologous, allogeneic, or from another species all together.

The thought is that by introduction of these cells into the wound it will provide the patient the components needed to help heal the wound. A multitude of biologically active CTPs have been developed. Their availability has expanded the options for the wound care physician when faced with managing complex wounds such as VLUs. Understanding the composition, advantages/disadvantages, and risk/benefit of each product, as well as the indications for each product’s use facilitates the selection of the appropriate CTP in patients with chronic wounds. Adjunctive therapies such as biologically active CTPs can speed healing time in VLUs in a clinically meaningful way and can result in overall lower treatment costs as well as reducing risks and complications in this patient population.

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**Conclusions**

Edema causes an alteration in the endothelium that begins a complex cascade of detrimental events. Neutrophils become activated and adhere to capillary walls, thus creating a reperfusion injury. These adhesion molecules release cytokines, oxygen free radicals, and proteolytic enzymes that are detrimental to the soft tissue structures. As hypoxia increases, so does inflammation and harmful matrix metalloproteinases, causing dermal tissue fibrosis and ulceration.\(^2\) With the use of compression therapy, blood flow accelerates, subsequently causing white blood cell detachment from the endothelium. As perfusion improves, the tissue environment stabilizes and tissue fibrosis and breakdown decreases.\(^2\) Compression therapy in and of itself can only do so much to help heal wounds that are already present. Additional research and advances in care are still needed to aid in healing of these chronic and often painful ulcers caused by long-standing PVD.

The need for clinical trials providing level one evidence is a must in this segment of medicine. One such study is the investigation of a Beta-Glucan topical cream. In essence, the cream contains the skeletal polysaccharide structure of a yeast cell envelope while the active cellular constituents are removed. The product is thought to act by increasing the activity of specific macrophages, resulting in enhanced physiologic wound debridements. As previously mentioned, VLUs are in a state of inflammatory response and this is possibly one method of reversing the chronicity of these wounds and altering impaired wound healing. Many more such investigations are necessary in order to improve patient outcomes across the continuum. While we have some answers as to the physiology of this far-reaching condition, we still look to understand the entire pathogenesis of venous dysfunction and VLU formation more thoroughly. PM

**References**

1. Ballard JL, Bergan JJ, editors. Chronic

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7 Ginekol Pol. Risk factors for the development of venous insufficiency of the lower limbs during pregnancy—part 1. Review Article 2012 Dec; 83(12):939–42.


14 Falanga V. The “trap” hypothesis of the venous ulceration. Lancet 1993; 341:1006–1008.


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CME EXAMINATION

SEE ANSWER SHEET ON PAGE 125.

1) Which is a true statement regarding venous leg ulcers?
   A) They affect millions of Americans.
   B) Frequently, loss of employment occurs in those patients afflicted.
   C) Pain is one of the frequent complaints in these patients.
   D) All of the above.

2) The venous system of the leg is composed of which of the following?
   A) A two-way flow system.
   B) A superficial and deep system connected by a series of perforating veins.
   C) Deep vein thrombosis aiding in blood flow to the extremities.
   D) A system that channels blood flow from the heart to the extremities.

3) What vein(s) compose the superficial venous system?
   A) The long saphenous vein.
   B) Popliteal vein.
   C) The short saphenous vein.
   D) Both A and C

4) Which of these statements about the function of bicuspid valves are true?
   A) They serve to protect the superficial venous system from high compartment pressures.
   B) They activate with contraction of the calf muscle pump.
   C) They assist in propelling the blood in the deep veins toward the heart.
   D) All of the above are true.

5) Dysfunction in venous return can be the result of all of the following EXCEPT:
   A) Incompetence in the valves of the veins.
   B) Correct mechanics of the venous system.

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CME EXAMINATION

C) Outflow obstructions in the deep vein system.
D) Calf muscle pump failure.

6) Clinical manifestations of chronic venous disease include which of these conditions:
A) Telangiectasia and/or spider veins.
B) Varicose veins and hyperpigmentation.
C) Dependent edema in the lower leg.
D) All of the above.

7) Venous hypertension is thought to cause microcirculatory dysfunction by:
A) Activating white blood cells.
B) Increasing oxygenation to the tissues.
C) Resulting in fibrin cuff formation posing a barrier to oxygen diffusion.
D) Delivering growth factors into the dermis.

8) What is the most defining property of compression bandages?
A) The product manufacturer location.
B) The structure and the elastomeric quality of the bandage itself.
C) The length of the bandage.
D) The color of the wrap.

9) What is the practical consequence of LaPlace’s law in the role of compression?
A) With increased application tension, the bandage applied pressure will decrease.
B) The number of layers and the technique in which it is applied is not important.
C) Applied pressure is directly proportional to the tension in a bandage, but inversely proportional to the radius of the limb to which it is applied.
D) As the number of bandage layers increases, the bandage pressure decreases.

10) All of the following are true of compression bandages except:
A) There are two main forms of compression bandages, elastic and inelastic.
B) Elastic bandages exert continuous pressures on the leg, allowing them to adjust to volume changes in the limb during both ambulation and relaxation.
C) Elastic bandages are not contraindicated in patients with arterial insufficiency.
D) Inelastic bandages, also known as short stretch bandages, only offer effective compression during movement.

SEE ANSWER SHEET ON PAGE 125.

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