Active Dynamic Compression: A New Look at VLU and Lymphedema Treatment

Koya's Flexframe® technology changes the landscape of lower extremity edema management.

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Introduction

The lower extremity venous system is composed of both a superficial and deep system connected by an elaborate series of perforating veins.[1,2] Under normal conditions, valves within these veins direct blood from the superficial into the deep system, which 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. Deep vein thrombosis, for example, damages the valves in the veins of the deep and superficial systems. Pregnancy increases the risk of chronic venous insufficiency and venous leg ulcers (VLUs); functional and structural changes occur in the venous system secondary to elevated hormone levels and damage caused by elevated pressure on the inferior vena cava by the enlarging fetus.[4] In addition, there is a hereditary predisposition toward valvular dysfunction eventually leading to the development of VLU. Obesity and a sedentary lifestyle can also contribute to the development of venous insufficiency.

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The common etiology of venous insufficiency is the reversal of blood flow from the deep to the superficial venous system.[1,2,3] This reversal of flow leads to pooling of the blood and fluid in the legs. The patient may experience swelling or edema in the lower extremities as a first sign of disease. Over time, hallmark trophic changes in the tissues appear: hyper-pigmentation, venous stasis dermatitis, hemosiderin deposits, loss of hair, thickened nails, atrophy blanche and lipodermatosclerosis.

Lymphatic vessels also play a key role in removing the protein-rich fluid from the tissues and rapidly dilate to several times their normal diameter early in the inflammatory phase to increase overall lymphatic flow rates. Increased tissue edema leads to lymphatic stasis creating a proinflammatory state in the tissues. Normal functioning lymphatic mechanisms and venous drainage are required for the body to remove inflammatory mediators from the subcutaneous tissues.[4-6] Venous insufficiency at the microvascular level results in lymphatic overload, causing subcutaneous fluid build-up in the tissues and an accumulation of pro-inflammatory substances.[4-6] Patients may suffer from aching or heavy legs, difficulty ambulating, hard and tight skin, wart-like growths on the skin, and fluid leakage. If left untreated, fibrosis of the endothelium will lead to skin necrosis and breakdown.

Additionally, persistent inflammatory states can perpetuate chronic pain. Tissue injury and inflammation lead to the local release of substances including glutamate, serotonin, bradykinin, Substance P, nerve growth factor (NGF), and norepinephrine (NE).[4] These substances are transmitted to the central nervous system by primary afferent nociceptors, resulting in lower nociceptor activation thresholds in the periphery, contributing to chronic pain.[4] Therefore, uncontrolled swelling and associated

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New Concepts and Studies

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dermal lymphatic stasis may also play a part in the initiation of chronic pain states.

As a result of these pathologic processes taking place in the venous and lymphatic systems, skin breakdown can occur, resulting in wounds referred to as VLUs. Millions of Americans are afflicted with painful, open, draining VLUs on their lower extremities. VLUs cause significant clinical and economic burden to the healthcare system and society.[2,3] It is not uncommon for clinicians to see patients who have suffered for years with chronic non-healing ulcers. VLUs typically occur in the medial gaiter region of the lower leg. This corresponds to the position of the perforating veins connecting the superficial and deep systems.

A more recent theory of ulcer pathogenesis suggests that increased inflammation brought on by a cycle of chronic ischemia-reperfusion leads to skin breakdown.

Several competing theories aim to describe the progression from chronic venous hypertension to skin breakdown and ulceration. A popular hypothesis is that hypertension in the venous system leads to the development of a pericapillary fibrin cuff that forms a barrier to oxygen diffusion. The skin and subcutaneous tissue become hypoxic and subsequently ulcerate.[7,8] The final common pathway for all the theories is tissue ischemia: another theory suggest that white cells plug the capillaries causing tissue hypoxia.[8]

A more recent theory of ulcer pathogenesis suggests that increased inflammation brought on by a cycle of chronic ischemia-reperfusion leads to skin breakdown.[9] Neutrophils, activated by repeated ischemia-reperfusion release oxygen-derived free radicals (ROS). The ROS stimulates the formation of capillary cuffs that impair oxygenation and trap more neutrophils, creating a vicious cycle of inflammation. The repeated activation of this cascade eventually overwhelms the body's compensatory capacity and the balance tips in the favor of tissue destruction.[10] In many cases, the immediate cause of the ulceration is a traumatic event; however, healing is disrupted by one or a combination of factors described above.[9] Controlling the underlying venous hypertension and reversing lymphatic dysfunction via compression therapy is the crux of treatment for VLUs.

Figure 1: The Koya Medical Dayspring active dynamic compression garment with breathable mesh, adjustable fasteners, and Flexframe.

Traditional Compression Therapy

Compression therapy harnesses the basic principles of physics to reduce lower extremity edema. LaPlace's law describes the relationship between the application tension and sub-bandage pressure: The greater the tension applied with the bandage, the greater the sub-bandage pressure. In addition, sub-bandage pressure is inversely proportional to the radius of the limb. A bandage applied to a thin leg will result in greater pressure. Finally, the greater the number of layers, the higher the pressure.[11] The practical consequence of LaPlace's law is that a wrap placed with constant tension to a limb that increases in size from ankle to knee will result in graduated compression: greatest compression at the ankle, decreasing as the wrap covers the more proximal limb.[12]

Multilayer compression bandages contain both inelastic and elastic wraps. This combination allows for use across all patients with VLUs and lymphedema. The elastic component benefits ambulatory patients with poor calf pump function, while the inelastic portions provide higher sub-bandage pressure, benefiting all patients. 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.

Treatment guidelines and manufacturers strongly recommend obtaining an objective measure of the patient's vascular status, such as ankle brachial index, prior to the application of compression. Peripheral arterial disease is a contra-indication to compression therapy.[13]

After successful treatment, patients are transitioned to maintenance compression garments to reduce the risk of lower extremity edema and ulcer recurrence.[14] Prevention guidelines endorse the use of graduated compression stockings worn daily along with routine elevation of the extremities.[15] The suggested compression levels of 30 to 40 mmHg are recommended for the treatment of chronic venous insufficiency and venous ulcer prevention.[15]

Unfortunately, the use of traditional compression garments in this patient population can be a challenge due to difficulty with donning the devices. Increased age, limited range of motion, decreased dexterity, poor eyesight, and decreased strength and agility are common reasons

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patients have difficulty adhering to compression garment use. Innovative alternatives to 'old school' knee high compression stockings are sorely needed.

Active Dynamic Compression

In early 2021, the U.S. Food and Drug Administration (FDA) granted 510(k) clearance for the first lower extremity active dynamic compression treatment, the Dayspring from Koya Medical (Oakland, CA). The Dayspring device is comprised of an active compression system designed for movement and mobility while promoting lymphatic function, improving venous flow, and reducing wound healing time in the lower extremities. The system includes a low-profile active garment made of soft, breathable mesh, using Koya's proprietary Flexframe® technology (Figure 1); a rechargeable, hand-held controller that can be worn on a lanyard; and a mobile app that allows users or their clinicians to program custom treatment options. The patented innovative non-pneumatic Flexframes® in the low-profile garment contract and relax to reduce edema, maintain limb volume, and minimize interferences with daily living.


Figure 2: Dayspring patient fully mobile while wearing the device.

The Dayspring device is comprised of an active compression system designed for movement and mobility while promoting lymphatic function, improving venous flow, and reducing wound healing time in the lower extremities.

The wearable device has a smart calibrated, active gradient pressure, full-leg compression garment (Figure 2). The device is segmental and programmable, and applies controlled sequential pressure from the distal to proximal-end of the limb in a cyclic manner. These patterns are like advanced pneumatic compression devices, which are known to produce safe, well-regulated compression. Unlike similar pneumatic devices, the Dayspring allows the patient to be completely ambulatory and mobile during treatment.

There are many tangible advantages to the Dayspring active compression device. First off, the Flexframes® are designed to enable gentle stretching of skin and stimulating the lymphatic capillaries underneath; encouraging and permitting entry and transport of fluid, like the light stimulation performed during manual lymph drainage (MLD). Secondly, external compression applied by the device is an effective treatment option in managing ongoing chronic edema. Additionally, muscle contractions during walking and exercises stimulate lymph flow through direct action on the lymphatic and venous vessels. Dayspring makes it possible for lymph and venous flow to be optimized through daily activities and routines during treatment.

A non-randomized, open-label study testing the safety and effectiveness of the Dayspring device over a 12-week period was published in 2022.[16] The primary end points of the investigation were reduction in swelling and improvement in patient quality of life (QOL). Twenty-four subjects were enrolled in the trial.[16] The majority of subjects were female[17] with secondary lymphedema.[16] Eighteen subjects completed the study. The Dayspring device produced statistically significant improvements in QOL, functioning, and lower leg edema volumes.[16]

After three months of use, subjects had improvement in overall QOL compared with the baseline ($p < 0.05$).[16] Limb volume improved (up to 50% reduction in edema) with an average reduction in affected limb edema of 39.4%.[16] This study demonstrated that use of the Dayspring device was a useful and effective therapy for lower extremity edema management. Future studies should incorporate randomization, larger sample sizes, and greater durations of observation to affirm the positive findings of this study.

Conclusion

Edema causes an alteration in endothelium that begins a complex cascade of detrimental events. Neutrophils become activated and adhere to capillary walls, thus creating ischemia-reperfusion injury and releasing free oxygen species.[9] The resulting inflammation damages the vasculature and soft tissues.[9] As hypoxia ensues, inflammation worsens, and harmful matrix metalloproteinases cause dermal tissue fibrosis and eventual ulceration.[9] Compression therapy facilitates the removal of lower extremity edema. White blood cells detach from the endothelium and inflammation lessens.[14]

As perfusion improves, the tissue environment stabilizes and tissue fibrosis decreases. New devices are entering into the space that have the potential to improve patient outcomes. Innovations in compression therapy such as the Dayspring device may prove useful in this at-risk patient population, with benefits including fewer amputations and medical transfers, lower wound recidivism, and higher treatment completion rates. **PM**

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