Etiology lower limb venous insufficiency:

In a normal venous anatomy, the venous system functions both as a reservoir in storing blood and in returning deoxygenated blood to the heart. This system depends upon a well-functioning series of valves and muscle pumps, most notably the calf muscle for the lower extremities. The veins are divided into superficial and deep veins connected by perforator veins[1]. A series of bicuspid valves are located throughout this system, ensuring the blood flows in the cephalad direction and preventing blood from returning to the feet while upright. The number of bicuspid valves increases as one moves from the trunk towards the distal leg which prevents an increase in pressure within the distal veins resulting from gravity.

Valvular incompetence creates impairment of blood flow and increased venous pressure (venous hypertension). This in turn puts increased pressure on the calf muscle pump. For those with peripheral venous insufficiency, some have likened the calf muscle to a pump (like a heart) with a natural stroke volume but with an increased preload due to blood backflow[2]. Further, in those with deep venous insufficiency, the calf muscles possess a reduced "stroke volume" due to the destruction and reduction of the volume of the deep veins of the calf. This results in an increased afterload of blood because of high outflow resistance created by venous obstruction and value insufficiency and; the increased preload from superficial and deep veins. Venous hypertension as mentioned above, leads to excessive accumulation of fluid (with swelling) and fibrinogen in the peripheral subcutaneous tissue ultimately resulting in ulceration[3]. The prognosis of venous ulcers is rather poor with delayed healing (in >50% of patients) and recurrent ulceration[4,5].

In the US, it is estimated that upwards of 25% of adults have varicose veins and 6% have more advanced chronic venous disease (CVD)[6]. There is a significant socioeconomic impact from this resulting a reduced quality of life and an increased financial burden on the system – approaching $3 billion annually[7].

Effect of an incompetent venous system on the lower extremity peripheral arterial system:

An incompetent venous system can create a vicious cycle of pathology on the lower extremity muscles (i.e. calf muscle pump) and the lower extremity arterial system. Since incompetent vein valves do not prevent retrograde flow of venous blood, pressure is built up in the venous system (including the superficial, perforator, and deep venous system). This "high pressure" (or lack of a negative pressure) in turn prevents arterial inflow[8]. A lack of oxygenated blood to the extremities and muscles results in muscle atrophy and pumping capability. This in turn creates a situation where the calf muscle pump is compromised creating the potential for venous ulceration[9]. Further, the deficiency of the calf muscle pump is significant to the severity of venous ulceration[9].

Resulting medical conditions based on above:

Chronic venous insufficiency describes a condition affecting the venous system of the lower extremities with the elements of this condition being hypertension, pain, edema, skin pigmentation changes (including varicose eczema), varicose veins, liposclerosis**,** and at the extremes venous ulceration and deep vein thrombosis (DVT)[7,8].

- Venous hypertension results from a combination of factors including valvular incompetence (superficial, perforator and deep) and impaired calf muscle function. Venous reflux results with no real reduction in the pressure within the venous system.
- Varicose veins result from a high pressure in the superficial system due to failure of valves in the communicating perforator system[10,11]. Blood seeps backward into the superficial system and along with high pressure transmission from the calf muscle pump produces venous dilation[7]. Over time these can become progressively more tortuous and enlarged. They may also create occurrences of superficial thrombophlebitis – a condition where blood clots in the veins resulting in pain.
- Skin pigmentation changes can develop in the perimalleolar (or gaiter area - just above the ankle) and is a typical sign of venous disease. This brown discoloration occurs when blood cells leak out of the blood vessels and into the surrounding tissues. Hemoglobin from the red blood cells is broken down into a compound called hemosiderin (a yellowish-brown granular intracellular pigment that is formed during disturbances of iron metabolism – hence the brownish or rust color). Further varicose eczema can occur with the skin becoming red, wet and scaly in appearance.
- Pain results from prolonged standing and can interfere with daily activities
- Edema (or swelling) also occurs in the region just above the ankle and can ascend up the leg over time
- Liposclerosis or a hardening of the underlying subcutaneous tissue directly under the skin. In this condition (typically accompanying varicose veins) the skin becomes woody in its feel and loses all is suppleness.
- DVT is a dysfunction of the valves of the deep venous system resulting from venous blood sitting idle and thrombosing. In its most severe form, DVT can result in pulmonary embolism, a potentially life-threatening complication, caused by a detached clot that travels to the lungs and embolizes.

How the Flowaid device works in treating lower limb chronic venous insufficiency and how it is different than Intermittent Pneumatic Compression (IPCs):

The Flowaid FA-100 device is an external, portable sequential contraction compression device (SCCD) that has a similar mode of action to intermittent external pneumatic compression devices (IPC) but with a different mechanism of action. Both produce an increase in venous and arterial blood flow. IPCs however cause a deformation of arteries and veins and increases the shear stress within each system causing movement of blood[12,13]. As well, since IPCs provide an external mechanism of action, there is not strengthening of the musculature as; no physiologic changes occur[14]. The Flowaid FA-100 functions via a circular circuit of electrodes placed on the muscles of the calf creating a sequence of contractions and; causing increased circulation. Specifically, these electrical impulses initiate a series of peristaltic wave contractions and activate the musculature. Activating the musculature of the calf muscle results in the following: an increase in the metabolic demand of the musculature[15], an increase in both venous and arterial flow, development of muscle mass (through use), and the stimulation of angiogenesis[16,17]. The Flowaid FA-100 electrodes/patches (of which there are 4) are applied above (2) and below (2) the calf muscle. These electrodes are then attached to a mobile phone size “generator” (which can be attached to a belt) and should be worn up twice daily for up to 2 hours each time. Unlike IPDs, the Flowaid device allows for complete mobility while being treated.

The Flowaid's mode and mechanism of action is different from other SCCDs in the following ways:

- It is an electrical circuit, which provides a series of muscle contractions forming a peristaltic wave along the longitudinal axis from distal to proximal. Other electrical impulse products provide for different modes and mechanisms such as indirect stimulation of the muscle via the common peroneal nerve (the Geko device)[18]. While the Geko device has demonstrated a positive effect on microcirculation via muscle contraction (due to stimulation of the peroneal nerve), its studies have focused on healthy subjects[18,19,20]. Geko has stated as one of its limitations that patients with circulatory disorders would likely not respond in a similar fashion (as healthy subjects would)[18]. A number of conditions that result in and/or are caused by venous and arterial insufficiencies (immobility, diabetes, varicose veins) result in peroneal neuropathy, which in turn would likely render treatment with the Geko device suboptimal[21,22,23]. In contrast, the Flowaid FA100's compressions are performed on **multiple sites** (in patients with venous and arterial disease), while the distal compressions are held. Therefore all the blood that is moved caudal (towards the head) will remain in that direction even when the valves are damaged. As well, it can be used in patients with peroneal neuropathies;
- It is portable and can be worn while a patient is mobile;
- It works on both the venous and arterial systems;
- It works on both healthy and diseased tissues.

Demonstration of the clinical benefits of the Flowaid F-100:

Clinical benefit	**Proof source:**
Pain reduction from peripheral arterial disease	Rosenblum J, Gimmelreich D, Greenberg, N. Sequential contraction compression has a positive effect on patients with peripheral arterial disease
Improved walking distance prior to claudication	Rosenblum J, Gimmelreich D, Greenberg, N. Sequential contraction compression has a positive effect on patients with peripheral arterial disease. Journal Novel Physiother 2016, 6:3 Open Access.
Improved venous blood flow	Shashar D, Heldinberg E, Miller MS, Tamir J. Acute effect of the Flowaid FA-100 muscle pump activation (MPA) device on popliteal venous blood flow
Improved arterial blood flow	Rosenblum J. The effectiveness of Flowaid FA-100 muscle pump activation system (MPA) at increasing microcirculation velocity in PAD patients. Rosenblum J. The effectiveness of Flowaid FA-100 muscle pump activation system (MPA) at forefoot temperature changes in PAD patients.

Summary statement:

The Flowaid FA-100's mechanism of action via an electronic circuit, provides for the following clinical benefits: improvement of both venous and arterial blood flow; development of muscle mass and strengthening of the musculature and, pumping action of the calf muscle; and stimulation of angiogenesis. These in turn can improve upon outward symptoms such as pain, walking distance, edema, varicose veins, liposclerosis, and skin pigmentation. Additionally since the Flowaid is a "portable" device, it can be worn while a patient is mobile.

Complete list of presentations and posters:

Paper/presentation	Findings
Shashar D, Heldinberg E, Miller MS, Tamir J. Acute effect of the Flowaid FA-100 muscle pump activation (MPA) device on popliteal venous blood flow.	Increase in popliteal venous blood flow velocity in healthy patients (n=13)
Tamir J. A novel portable muscle pump activator system (MPA) Flowaid FA-100 to enhance venous return and stimulate arterial blood flow in the extremities, a preliminary study.	Increase in venous (n=5) and arterial (n=10) lower extremity blood flow in patient with venous and arterial insufficiency. Decrease in edema and pain.
Rosenblum J. The effectiveness of Flowaid FA-100 muscle pump activation (MPA) at forefoot temperature changes in PAD patients.	Increase in foot temperatures in patients with a primary diagnosis of PAD (n=10)
Rosenblum J. The effectiveness of Flowaid FA-100 muscle pump activation (MPA) for pain reduction.	Significant pain reduction in patients with PAD (n=14)
Rosenblum J. The effectiveness of Flowaid FA-100 muscle pump activation system (MPA) at increasing microcirculation velocity in PAD patients.	Increase in microcirculatory flow velocity using Laser Doppler assessment in patients with PAD (n=5)
Rosenblum J, Gimmelreich D, Greenberg, N. Sequential contraction compression has a positive effect on patients with peripheral arterial disease. Journal Novel Physiother 2016, 6:3 Open Access.	Significant increase in walking distance and significant reduction in pain in patients with PAD (n=18)
Rosenblum J, Greenberg N, Weiss S. The effect of contraction compression device on a hypoesthetic diabetic foot: A case report. Medical Reports & Case Studies. Accepted for publication 6/16/16.	Flowaid FA-100 used to hyperperfuse the foot in a diabetic man, obese, and 74 years of age. This in turn helped to repair a choked off nerve.

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