A pilot study of venous flow augmentation using a novel mechanical graded intermittent sequential compression device for venous insufficiency

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ABSTRACT

Background: Guidelines as well as multiple RTCs support the use of intermittent pneumatic compression (IPC) for the treatment of venous leg ulcers when conservative measures fail. Unfortunately, the clinical usefulness of IPC is significantly limited by the physical limitations of pneumatic motors, which leads to bulky devices with slow inflation cycles, uncomfortable sleeves, lack of patient mobility, and ultimately poor patient compliance with therapy. A novel mechanical device for lower leg graded intermittent sequential compression was designed to address these limitations of IPC therapy for venous leg ulcer treatment by providing rapid compression cycles in a truly wearable device that offers the additional benefit of monitoring compression dose and patient compliance. The wearable intermittent compression (WIC) device was hypothesized to provide improved augmentation of venous flow compared with both baseline and standard IPC therapy.

Methods: Ten patients with Clinical, Etiologic, Anatomic and Pathophysiologic class 3 to 6 venous insufficiency were recruited under institutional review board approval. The primary end point for the study was augmentation of venous blood flow as measured by peak venous velocity. Patients underwent measurement of peak venous velocity in centimeters per second at the popliteal and femoral veins for the following conditions: (1) baseline, (2) WIC device on a low setting, and (3) WIC device on a high setting. In five patients, an additional measurement of peak venous velocity in centimeters per second at the popliteal and femoral veins was completed while wearing a commercially available IPC device.

Results: Both low and high settings of the WIC device resulted in higher average peak venous velocities when compared with both baseline and the IPC device ($P < .05$). No patients reported discomfort with either the WIC device or the IPC device during therapy.

Conclusions: The WIC device significantly increases the augmentation of venous flow as measured by peak venous velocity in both the popliteal and femoral veins in patients with Clinical, Etiologic, Anatomic and Pathophysiologic class 3 to 6 venous insufficiency. In addition, the WIC device was found to be easy to use and comfortable during therapy. Future studies are planned to determine if the WIC improvements in venous flow augmentation and patient compliance will lead to higher rates of venous ulcer healing. (J Vasc Surg: Venous and Lym Dis 2019;7:217-21.)

Keywords: Venous insufficiency; Intermittent pneumatic compression; Venous ulcer; Wearable compression; Mobile compression

Chronic venous hypertension increases the permeability of leg capillaries, resulting in tissue accumulation of fluid, proteins, and blood cells. Venous hypertension may also be associated with an increased inflammatory response, changes in the structure of the microvasculature, and decreased skin and tissue oxygenation. Overall, these effects increase the risk of leg ulceration and delayed healing. Chronic venous disease of the lower extremity is graded by the Clinical, Etiologic, Anatomic and Pathophysiologic (CEAP) 3 to 6 classification. Graded intermittent pneumatic compression (IPC) has been show in numerous studies to provide benefit across CEAP classifications of venous disease from varicose veins,[1] to edema,[2] and ultimately to active venous ulcers.[3]

The treatment of venous leg ulcers consists of compression therapy based on a mechanical concept of applying pressure to the limb to counteract venous hypertension. Initial treatment focuses on sustained pressure with different types of bandages, bandage systems, and ready-to-use garments. When this conservative therapy fails (typically a 6-month trial), clinicians can move on to more intensive therapeutic options. Percutaneous

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venous ablation has gained widespread adoption when a target vessel exists. IPC is also part of the venous leg ulcer (VLU) treatment algorithm after 6 months of failed conservative therapy. Specifically, guidelines from the Society for Vascular Surgery recommend IPC therapy when other compression options are not available, cannot be used, or have failed to aid in venous leg ulcer healing after prolonged compression therapy.[4]

Graded IPC was first proposed as an effective therapy for venous ulcers in 1981.[5] The intermittent nature of pulsatile external compression produces beneficial physiologic changes, which include hematologic, hemodynamic, and endothelial effects, which should promote healing of VLUs.[6]

IPC using different pressure parameters has been studied in randomized trials comparing IPC with no compression.[7] A Cochrane meta-analysis of IPC trials, including 387 participants, offered the following conclusion:

> IPC may increase healing compared with no compression. It is unclear whether it can be used instead of compression bandages. There is some limited evidence that IPC may improve healing when added to compression bandages. Rapid IPC was better than slow IPC in one trial.[7]

Rapid IPC refers to a pressure cycle that attempts to reduplicate the native calf muscle pump that contributes to venous blood flow. For example, about 90% of venous return from the legs is through the action of the muscle pumps and the calf muscle pump is the most important muscle pump in the leg, active during walking and ankle movement.[1,3]

The rapid IPC trial reviewed by the Cochrane meta-analysis randomized 104 patients with venous ulcer to either fast IPC (inflated over 0.5 second, compression for 6 seconds, and deflation over 12 seconds) or slow IPC (inflation over 60 seconds, compression for 30 seconds, and deflation over 90 seconds).[8] Ulcer healing was improved in the fast IPC group (45/52 [86%]) compared with the slow group (32/52 [61%]). The mean healing rate per day was more than twice as fast in the fast IPC group: 0.09 in the slow IPC group vs 0.04 in the fast group, resulting in complete healing in the fast IPC group at a median of 59 days vs 100 days in the slow IPC group.[8] Multiple hemodynamic studies have shown that rapid IPC leads to higher peak venous velocities at the level of the femoral veins,[9,10] including patients with post-thrombotic venous disease.[11]

Both device comfort and patient compliance have been identified as barriers to the effectiveness of IPC therapy. Harding et al[12] found that a portable adaptive IPC device used for both sustained and intermittent compression was equally effective as a convention four-layer bandage system in venous ulcer healing. The portable IPC device was found to be better accepted by patient with a higher quality of life score.[12]

ARTICLE HIGHLIGHTS

- **Type of Research:** Prospective, nonrandomized pilot study
- **Key Findings:** A wearable graded intermittent compression system improved venous flow augmentation over baseline and standard intermittent pneumatic compression in a study of 10 patients with Clinical, Etiologic, Anatomic and Pathophysiologic class 3 to 6 venous insufficiency.
- **Take Home Message:** The study suggests the wearable graded intermittent compression device is safe, comfortable, and physiologically effective with the potential to improve patient compliance with compression therapy and thereby improve care of patients with Clinical, Etiologic, Anatomic and Pathophysiologic class 3 to 6 venous disease.

A novel mechanical device for lower leg graded intermittent sequential compression (Cirvo, Radial Medical Inc, Mountain View, Calif) was specifically designed to address the limitations of IPC for VLU treatment (Fig 1). The use of wearable intermittent compression (WIC) as an alternative to IPC allows the delivery of rapid compression cycles. The device is portable and lightweight, which has the potential to improve compliance by allowing the patient to remain mobile during therapy. Finally, the device can monitor compliance and pressure cycles so that the physician can monitor treatment and make adjustments as necessary.

The WIC device was hypothesized to provide improved augmentation of venous flow compared with both baseline and standard IPC therapy.

METHODS

The experimental protocol and informed consent were approved by an institutional review board and all subjects gave informed consent. Ten patients with CEAP a 3 to 6 classification of chronic venous disease of the lower extremity were recruited. Exclusion criteria for the study are listed in Table I. The patient demographics are listed in Table II.

All vascular studies were performed by a single experienced registered vascular technologist (R.V.T.) under the supervision of a physician with Registered Physician Vascular Interpretation credentials. A single portable duplex venous ultrasound (Fujifilm Sonosite, Bothell, Wash) was used for the all vascular studies. After completing informed consent, patients underwent deep vein thrombosis (DVT) screening. Patients who passed the DVT screen went on to have measurement of peak venous velocity in centimeters per second at the popliteal and femoral veins for the following conditions: (1) baseline, (2) novel mechanical device on a low setting, and (3) novel mechanical device on a high

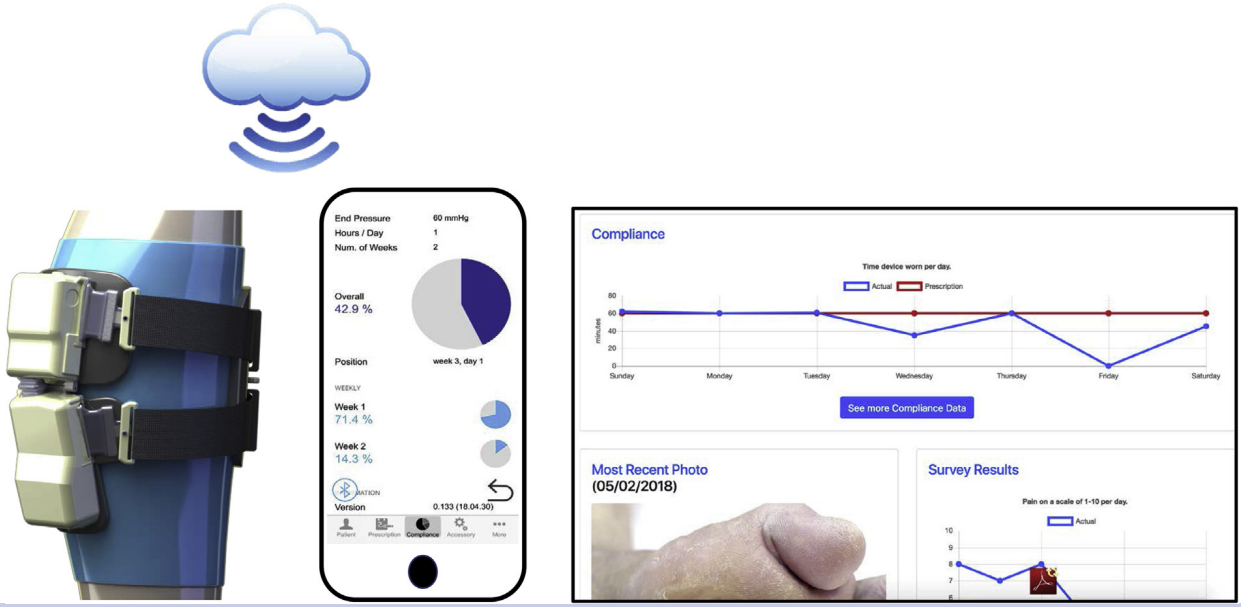

Fig 1. Left, The wearable intermittent compression (WIC) device is a wearable graded intermittent sequential compression system. **Right,** The mechanical mechanism enables the system to capture data on compression dose and patient compliance to engage patients and enable therapeutic decisions by physicians.

setting. In five patients, an additional measurement of peak venous velocity in centimeters per second at the popliteal and femoral veins was completed while wearing a commercially available portable IPC device. A minimum of three peak venous velocities were taken for each condition in the reverse Trendelenburg position.

The novel mechanical device (Cirvo, Radial Medical Inc) was programmed to deliver rapid intermittent compression. The device has a resting pressure of 5 mm Hg. Rapid compression occurs over 2 seconds and is held for 3 seconds. Compression is then released to baseline allowing 25 seconds of venous refill time. The device was additionally programmed to have two pressure settings (low and high). The device measures the exact pressure at the interface between the device and the calf and the device compresses to the pressure set for each cycle. The low setting was programmed to reach maximum pressure of 38 mm Hg with an allowable range of 30 to 45 mm Hg and the high setting was set to reach a maximum pressure of 52 mm Hg with an allowable range of 45 to 60 mm Hg. The commercially available IPC device (ActiTouch, Tactile Medical, Minneapolis, Minn) has a single IPC setting that was used for the study. In this setting, the system has a baseline graded compression of 40 mm Hg at the foot down to 20 mm Hg at the upper calf. The cycle time for intermittent compression of the device is approximately 75 seconds, during which the pressures increase to 50 mm Hg at the foot and 40 mm Hg at the upper calf. All patients were asked if they experienced any discomfort during therapy for the WIC device at both low and high settings and the IPC device in standard setting.

The primary end point for the study was augmentation of venous blood flow as measured by peak venous velocity. This was chosen as a short-term surrogate outcome for improved ulcer healing based on prior literature that shows rapid IPC cycles lead to higher peak venous velocities and rapid IPC cycles lead to improved VLU healing rates.[8-11] The study was powered for the primary end point at 80% to determine if blood flow could be augmented from 15 to 30 cm/s with a pretest predicted standard deviation of 8. The secondary end point was discomfort while undergoing IPC and WIC therapy. Statistics were performed using Excel (Microsoft, Redmond, Wash). A two-sided paired *t*-test was used to compare mean peak venous velocities. A *P* value of less than .05 was considered significant.

Table I. Exclusion criteria

History of acute DVT within the past 3 months
History of PAD unless the ABI is >0.9
History of pulmonary edema
History of decompensated CHF
Diabetes mellitus (type 1 or 2) requiring medication
Open Surgery or major trauma to the legs within the last 6 months
History of lower limb malignancy, primary or secondary
Acute infection of the leg of interest
Lower extremity gangrene
Acute symptomatic lower extremity thrombophlebitis
Pregnant or breastfeeding

ABI, Ankle-brachial index; *CHF,* congestive heart failure; *DVT,* deep vein thrombosis; *PAD,* peripheral artery disease.

Table II. Patient demographics

Demographic	Average (range)
Age	56 (33-78)
Weight, lbs	170 (103-277)
Body mass index, kg/m^2	26.6 (19.3-40.9)
Height, inches	66.1 (61-69)
Female sex	63%

RESULTS

Ten patients were successfully enrolled. Duplex venous ultrasound screening found a chronic DVT in one patient who was excluded from the therapeutic portion of the study. Nine patients underwent measurement of peak venous velocity at baseline and with the novel device in both low and high settings. Five patients underwent an additional measurement of peak venous velocities while wearing a portable IPC device.

Both settings of the WIC device resulted in higher average peak venous velocities when compared independently with baseline and the IPC device at both the popliteal vein and the femoral vein. A *P* value of less than .05 was found in all comparisons of WIC low and high peak venous velocities vs baseline and IPC peak venous velocities. The WIC low and high setting average velocities and standard deviation at the popliteal veins were 56.6 ± 7.9 and 58.3 ± 11.4, respectively. The baseline and IPC device velocities and standard deviation were 11.1 ± 5.2 and 12.9 ± 4.3, respectively. Fig 2 shows the average popliteal venous velocities for baseline, IPC, WIC low setting, and WIC high setting with 95% confidence intervals. The WIC low and high setting average velocities and standard deviation at the femoral veins were 45.5 ± 11.8 and 47.1 ± 10.3, respectively. The baseline and IPC device velocities and standard deviation were 13.5 ± 2.1 and 15.3 ± 7.8, respectively. Fig 3 shows the average femoral venous velocities for baseline, IPC, WIC low setting, and WIC high setting with 95% confidence intervals.

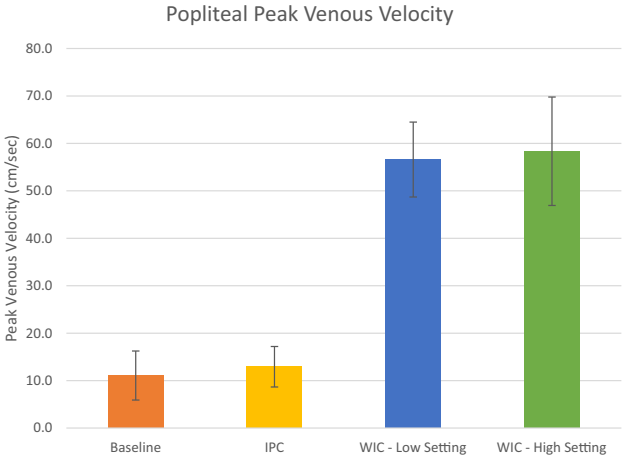

Fig 2. Popliteal peak venous velocity for baseline, intermittent pneumatic compression (*IPC*), wearable intermittent compression (*WIC*) low setting, and WIC high setting with 95% confidence intervals. $P < .05$ in all comparisons of WIC low and high peak venous velocities vs baseline and IPC peak venous velocities. IPC was not significantly higher than baseline ($P = .9$).

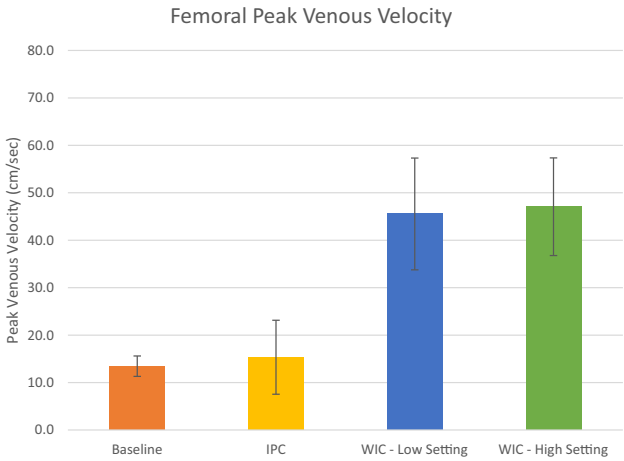

Fig 3. Femoral peak venous velocity for baseline, intermittent pneumatic compression (*IPC*), wearable intermittent compression (*WIC*) low setting, and WIC high setting with 95% confidence intervals. $P < .05$ for all comparisons of WIC low and high peak venous velocities vs baseline and IPC peak venous velocities. IPC was not significantly higher than baseline ($P = .7$).

The IPC device showed a trend toward higher peak venous velocity, but did not produce a significantly higher velocity at either the popliteal vein (11.1 ± 5.2 vs 12.9 ± 4.3; $P = .9$) or femoral vein (13.5 ± 2.1 and 15.3 ± 7.8; $P = .7$).

No patients reported discomfort during therapy with the novel device in either the low or the high setting. No patients reported discomfort during therapy with the IPC device.

DISCUSSION

Graded intermittent leg compression therapy has a role in the management of VLUs. The literature on IPC to date suggest benefit from rapid compression cycles that mimic the action of the calf muscle pump. However, owing to the high power demands, pneumatic devices cannot easily duplicate this pattern. The use of an alternative mechanical system enables compression that is delivered in a similar circumferential pattern as IPC, but with significantly faster cycle times. The system architecture is flexible so that software can be used to modulate all aspects of compression including maximum pressure, time to maximum pressure, hold time, release time, refill pressure, and refill time.

Beyond the power and flexibility of the compression cycles, portability is an important factor for patient adoption and compliance. Portability has been shown to

improve quality of life in VLU patients using portable IPC devices vs ones with a separate pump and tubing, even though the portable IPC device in the study had to be plugged in to a power outlet during active cycling. Overall, pneumatic pumps are ill-suited to miniaturization and, therefore, typically have to compromise on pressures and cycle times to enable portability. New mechanical technology enables lightweight portable compression with long battery lives.

Compliance with IPC therapy is problematic for multiple reasons. Discomfort is often cited by patients as a reason for not using IPC. Pneumatic bladders are airtight and thus nonbreathable. Mechanical compression can offer more flexibility in material choices, including breathable fabrics and less overall contact surface area with the lower leg. Finally, mechanical systems are more amenable to smart sensor data that can monitor patient compliance in real time. Mobile and cloud integration will allow such digital engagement. Patients and caregivers could choose to have goals of therapy set and be reminded by SMS or notification if they had forgotten to use their device in a timely manner.

CONCLUSIONS

A novel mechanical device for lower leg graded intermittent sequential compression addresses significant limitations of portable IPC therapy for VLU treatment by providing rapid compression cycles in a truly wearable device that offers the additional benefit of monitoring compression dose and patient compliance. The device significantly increases the augmentation of venous flow compared with baseline and IPC therapy as measured by peak venous velocity in both the popliteal and femoral veins in patients with CEAP class 3 to 6 venous insufficiency. In addition, the WIC device was found to be comfortable during therapy. Future studies are planned to determine if the WIC improvements in venous flow augmentation and patient compliance will lead to higher rates of venous ulcer healing.

AUTHOR CONTRIBUTIONS

Conception and design: JW, EJ, AS, RS, TF
Analysis and interpretation: JW, AS, RS, BJ, TF
Data collection: JW, BJ, EJ
Writing the article: JW
Critical revision of the article: JW, EJ, BJ, AS, RS, TF
Final approval of the article: JW, EJ, BJ, AS, RS, TF
Statistical analysis: JW
Obtained funding: EJ
Overall responsibility: JW

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