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The Efficacy of a New Stimulation Technology to Increase Venous Flow and Prevent Venous Stasis☆

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Abstract *Objectives:* Electrical stimulation of calf muscles has been shown to be effective in prevention of DVT. The aim was to determine: (a) dependence of venous blood velocity and ejected volume on the rates of stimulated calf contractions: (b) clinical factors affecting efficacy in healthy individuals.
Methods: The maximum intensity stimulus tolerated was applied to calfs of 24 volunteers. In popliteal veins, Peak Systolic Velocities (PSV), ejected volume per individual stimulus (Stroke Volume SV) and ejected Total Volume Flow per minute (TVF) of expelled blood were determined using ultrasound. Stimulation rates from 2 to 120 Beats Per Minute (bpm) were applied.
Results: Mean baseline popliteal PSV was 10 cm/s. For stimulation rates between 2 and 8 bpm, the PSV was 10 times higher and reached 96—105 cm/s. Stroke volume (SV) per individual stimulus decreased in a similar fashion. With increasing rates of stimulation the TVF increased by a factor of 12 times (from 20 ml/min to 240 ml/min).
Conclusion: Electrical stimulation is an effective method of activating the calf muscle pump. Enhancements of popliteal blood velocity and volume flow are key factors in the prevention of venous stasis and DVT. Further studies are justified to determine the stimulation rates in those with a compromised venous system.
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Introduction

Electrical stimulation has been used in the past to effectively activate the natural calf muscle pump. It significantly reduced the incidence of perioperative and postoperative deep venous thrombosis (DVT).[1–7] At that time, because of the pain associated with the stimulation its practical use was limited to anesthetized patients. Recently, an

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electro-stimulator for calf muscles, the VEINOPLUS® (Ad Rem Technology, Paris, France) has been reported to improve quality of life.[8,9]

The aim of this pilot study was to determine the effect of VEINOPLUS® on: (a) popliteal vein blood velocity and (b) blood volume ejected from calf at broader rates of stimulation in a group of normal healthy volunteers. But also to determine the effect of age, gender, calf circumference, maximum stimulation intensity tolerated and popliteal vein diameter on (a) and (b).

Material and Methods

Stimulators

The VEINOPLUS® stimulator is a CE-certified and FDA-cleared, portable, battery (9V) powered device. It produces bursts of square-wave stimuli of 50 ms duration with adjustable voltage of 0–5 V_{RMS}, which result in safe, comfortable, painless calf muscle contractions. The maximum stimulation energy per phase delivered by the device is in the range of 3–24 micro-Coulombs (μC), which is 30% below international standard safety limits (AAMI/ANSI; NS4:1986/(R) 2002) and 250 times less than that used in the 1970s for the prevention of DVT.[4] The rates of calf contractions produced by the device quoted above[10,11] ranged from 60 to 100 per minute.

For the purpose of this study 12 rate-modified VEINO-PLUS devices delivering rates from 2 to 120 bpm in 12 discrete steps were used.

Participants and procedure

Twenty-four normal volunteers (12 females, 12 males) 8 from each of three age groups (18–30, 31–50, 51–61) were recruited to the study via information documents approved by the ethics committee for public display on 2 general hospital notice boards and a General Practitioner's waiting room. The potential volunteers were then screened during a telephone interview to confirm their suitability. The exclusions were small in number as the public notice was extremely detailed but over subscription to a particular age group namely the younger age group led to the some of these individuals being excluded. Clinical examination and duplex scanning were initially performed to ensure a normal venous system. Participants with superficial or deep venous disease, previous varicose vein surgery, congestive heart failure, patients with pacemaker, lower limb arterial disease (ABPI < 0.9) or active clinically suspected infection were excluded. Study protocols and informed consent were approved by the Regional Ethics Committee and the Medical Devices Committee. All participants gave written informed consent. After applying the pre-gelled stimulating electrodes (VeinoPack 5x13 by Ad Rem Technology, Paris France) to the posterior aspect of the calf (Fig. 1) each participant was placed in a semi-recumbent position and allowed to rest for 15 min. This was to ensure baseline equilibrium thereby reflecting more accurately the volunteer's true unaffected baseline venous flow. The intensity of the stimulus was gradually increased until the highest intensity comfortably tolerated by each
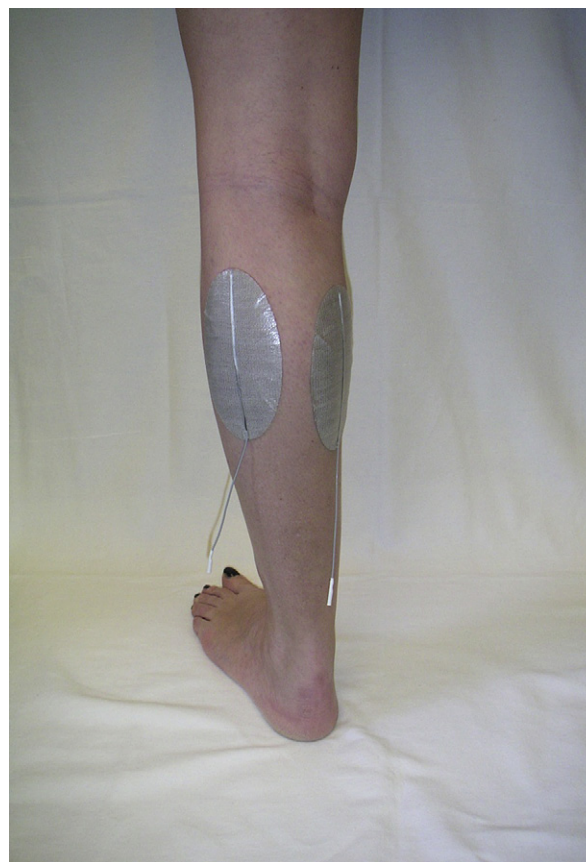

Figure 1 Position of VEINOPLUS® electrode pads to the posterior aspect of the calf.

participant was established. This particular intensity was then used for the rest of the examination. Different rates of stimulation were then applied ranging from 2 to 120 per minute in 12 steps (2, 3, 4, 5, 6, 8, 12, 15, 20, 30, 60, 120 bpm). Blood velocity in popliteal vein and volume flows were measured at rest before any stimulus was applied and during stimulation as described below. Only one leg per volunteer was tested. The side examined was determined randomly.

Ultrasound measurements

The popliteal vein was imaged in a longitudinal section using the IU22 ultrasonic scanner (Philips Medical, Seattle, WA) and a broad bandwidth L9-5 linear array transducer. Measurements were taken at popliteal fossa, just proximal to the confluence of the gastrocnemius veins. The Doppler sample gate was positioned across the entire vein diameter. Subsequently, peak systolic velocity (PSV) (cm/sec), diameter of the vein at the point of sampling and the duration of the Doppler spectral waveform produced by the calf muscle contraction were measured. The equipment's software was then able to calculate the cross-sectional area of the vein, the time averaged mean velocity (TAMV) and volume flow in ml/min (Fig. 2). These measurements were repeated using 12 different rates of stimulation as outlined above. Knowing that resting venous blood flow in a subject can change over
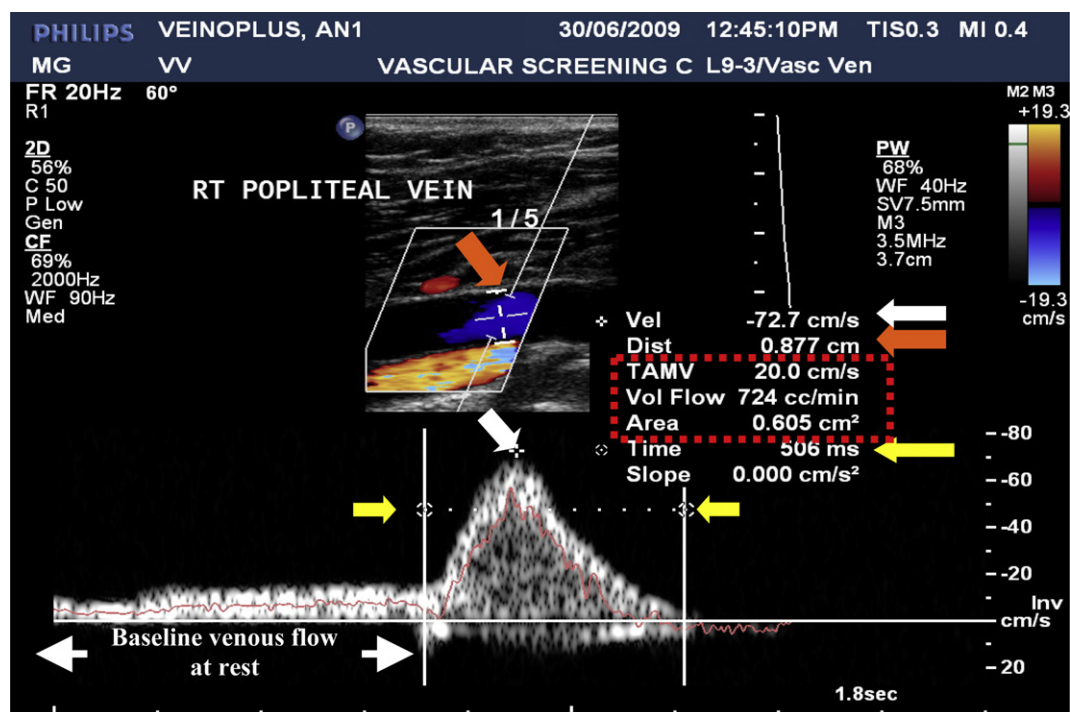
Figure 2 Typical Doppler waveform from one calf muscle stimulation. The orange coloured arrows highlight the popliteal vein diameter measured at the exact point where the sample volume "straddles" the whole vein. From these measurements the software then calculates the time averaged mean velocity (TAMV) and cross-sectional area to produce the volume flow, outlined by the red box. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

time[10] and patterns of flow will change according to breathing and the cardiac cycle[11] strict protocols were observed with the ultrasound measurements being repeated 3 times and the mean value taken. An interval of 3–5 min was allowed between different rates of stimulation to ensure return to baseline flow.

The volume expelled during a single stimulus and the volume expelled per minute as a result of the muscle contractions were calculated from the following equations:

$$\text{Volume expelled during single stimulus (ml)} =$$
$$(\text{Volume Flow (ml/min)}/60) \times \text{Ejection Time (sec)}$$

$$\text{Volume Expelled per minute (ml/min)} =$$
$$\text{Volume expelled during stimulus (ml)}$$
$$\times \text{ Number of stimuli/minute.}$$

Statistical analysis

The Kolmogorov–Smirnov test was used to test for normal distribution of the data. Age, calf circumference and popliteal vein diameter measurements were normally distributed; ultrasonic measurements were not. PSV, ejected volume per stimulus and ejected volume per minute were plotted against the stimulation rate. Kruskal–Wallis test was used for significance. Subsequently, PSV, ejected volume per stimulus and ejected volume per minute of subgroups of gender, calf circumference stimulus intensity tolerated, popliteal cross-sectional area and age were

compared. Subgroups were based on median values of clinical features. Finally, logistic regression analysis was performed (a) with PSV and (b) volume ejected per minute as dependent variables with value above or below the median and clinical parameters as covariates. Because of nonlinear relationship of the odds ratio of covariates of calf circumference, stimulus intensity and vein area were converted into classes according to the median. Age was subgrouped as less than or more than 50 (lower 2 tertiles vs. upper tertile) because the odds ratio decreases markedly at this cut-off point. The statistical package SPSS for windows (version 18), Chicago, Illinois was used throughout. $P < 0.05$ was considered to be significant.

Reproducibility study

In 24 measurements repeated twice the intra-class correlation co-efficient and 95% CI for PSV and ejected volume per minute was = 0.952 (0.897–0.979) and 0.83 (0.606–0.926) respectively.

Results

The effect of the stimulation rate on PSV is shown in Fig. 3. Before stimulation was applied, during quiet breathing, mean popliteal PSV was 10 cm/s. For stimuli between 2 and 8 per minute PSV was 10 times higher at levels of 96–105 cm/s. As the stimuli increased further to the maximum of 120 per minute the peak velocity decreased rapidly to approximately 35 cm/s. Ejected volume per
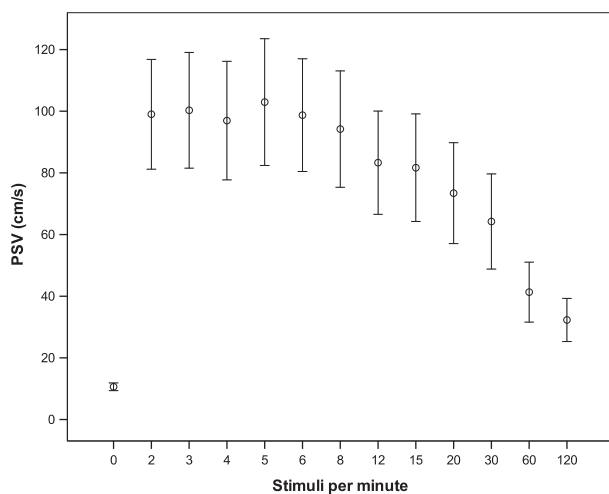
Figure 3 Peak systolic velocity (PSV) (mean and 95% CI) at different rates of stimulation. 0 indicated quiet breathing without any calf stimulation. Kruskal–Wallis test: $P < 0.001$.

individual stimulus decreased in a similar fashion (Fig. 4). There was a 19 fold higher ejected volume seen at 2 stimuli per minute compared to 120 stimuli per minute. However, with increasing rates of stimulation the ejected volume per minute increased 12 times from 20 ml/min to 240 ml/min (Fig. 5).

Male gender, increased calf circumference, high stimulus intensity, large popliteal cross-sectional area and increased age were associated with a higher PSV across all rates of stimulation (Table 1). However, only male gender, increased calf circumference, and a large popliteal cross-sectional area were associated with higher values of ejected volume per minute.

In a logistic regression analysis, only male gender, stimulus intensity, popliteal vein cross-sectional area and age greater than 50 were independently associated with PSV (Table 2). Using the same covariates only male gender, calf circumference and popliteal vein cross-sectional area
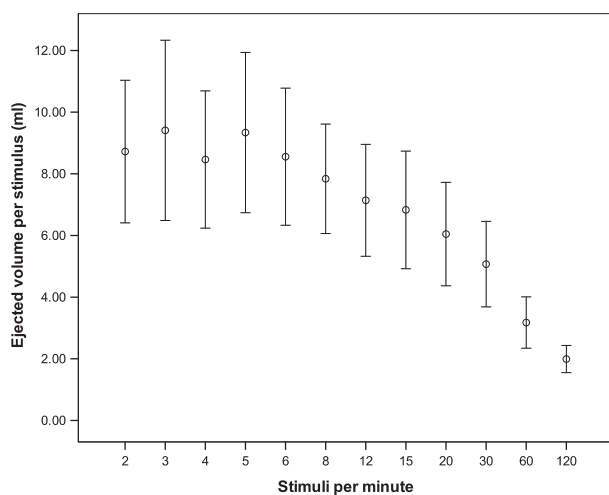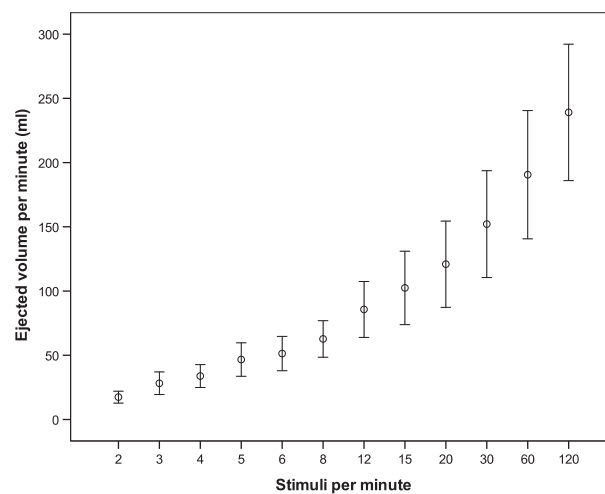

Figure 5 Ejected volume per minute (mean and 95% CI) at different rates of stimulation. Kruskal–Wallis test: $P < 0.001$.

were independently associated with ejected volume per minute (Table 3).

Discussion

In this study on normal volunteers, we evaluated a calf muscle stimulator when using the maximum stimulus intensity that would produce a visible contraction of the calf muscles and can be tolerated comfortably by each individual. We demonstrated that this stimulus is effective in increasing both: peak velocity (PSV) and the total volume of flow in popliteal veins. It was noted that different rates of stimulation have a different effect on PSV and on volume flow. Low stimulation rates (from 2 to 8/min) are associated

Figure 4 Ejected volume per stimulus (mean and 95% CI) at different rates of stimulation. Kruskal–Wallis test: $P < 0.001$.

Table 1 Median and (interquartile range) of peak systolic velocity (PSV) and median ejected volume per minute and (interquartile range) in subgroups of clinical features. Subgroups are created using median values. *P* value using Kruskal–Wallis test.

Feature	PSV(cm/s)	P	Ejected volume /min (ml)	P
Gender				
Female	50 (31; 84)		43 (23; 102)	
Male	88 (41; 137)	<0.001	100 (49; 194)	<0.001
Calf circumference (cm)				
<37	53 (32; 94)		48 (25; 104)	
≥37	82 (44; 126)	<0.001	102 (46; 194)	<0.001
Stimulus intensity				
<19	58 (35; 97)		67 (30; 140)	
≥19	75 (38; 126)	<0.044	65 (31; 142)	0.86
Popliteal vein cross-Sectional area (cm^2)				
<0.628	54 (32; 95)		45 (23; 104)	
≥0.628	81 (41; 124)	0.005	95 (45; 185)	<0.001
Age				
<39	65 (39; 134)		75 (33; 152)	
≥39	59 (36; 93)	0.012	60 (28; 121)	0.152

Table 2 Logistic regression with peak systolic velocity (PSV) < 70 or ≥ 70 cm/s (median) as the dependent variable and clinical features as covariates.

Feature	OR	95% CI	P
Gender (M/F)	2.01	1.21–3.35	0.007
Calf circumference ($<37/\geq37$)	1.75	0.99–3.10	0.053
Stimulus intensity ($<19/\geq19$)	3.06	1.77–5.29	<0.001
Popliteal vein cross-Sectional area ($<0.628/\geq0.628$)	2.12	1.19–6.55	0.010
Age ($<50/\geq50$)	3.54	1.92–6.55	<0.001

with high PSV and low total volume expelled per minute (TVF). In contrast, high stimulation rates are associated with lower PSV and higher TVF. This is probably due to the fact that at high stimulation rates; the interval between muscle contractions is too short to allow for venous refilling. The observation that PSV does not decrease until the rate of stimulation is greater than 8 per minute indicates that at least 7.5 s are required for the leg veins to refill in the semi-recumbent position. Higher rates of stimulation with shorter intervals between stimuli produce lower PSV but at the same time, substantially increase the TVF ejected from the calf per minute because of the higher number of muscle contractions. At the minimal rate of 2 contractions per minute the highest velocities were observed, yet during a period of 30 s between contractions, the blood stagnates. At the maximal rate of 120 contractions per minute the PSV was rather low, but the results showed a high total TVF ejected from the calf. In essence, the VEINOPLUS® Technology can provide either high velocities or high volumes. Therefore perhaps an optimal stimulus for DVT prevention might feature a rotation of different stimulation rates over a period of several minutes. This type of stimulation should provide a simultaneous combination of high velocities and high volumes of blood expelled.

It is not difficult to understand why men and individuals with bigger calfs and greater vein diameters have a higher PSV and higher volume flows. Perhaps future studies should normalise (adjust) velocity and volume measurements to calf circumference and popliteal vein cross-sectional area. Larger numbers are required to confirm the findings of the logistic regression analysis.

Based on the results of this study, this technology seems to have a number of potential applications not only for the prevention of DVT, for which more clinical studies should be encouraged. Reduction of edema, presumably by reducing

Table 3 Logistic regression with volume ejected per minute < 66 or ≥ 66 ml (median) as the dependent variable and clinical features as covariates.

Feature	OR	95% CI	P
Gender (M/F)	3.32	2.01–5.50	< 0.001
Calf circumference ($<37/\geq37$)	1.88	1.07–3.30	0.028
Stimulus intensity ($<19/\geq19$)	1.24	0.72–2.11	0.437
Popliteal vein cross-Sectional area ($<0.628/\geq0.628$)	2.04	1.15–3.60	0.014
Age ($<50/\geq50$)	1.66	0.91–3.03	0.100

venous pressure has already been demonstrated[8,9] and actions on the calf muscle pump could also improve venous hemodynamics in patients with chronic venous disease but this needs to be explored in more depth.

It must be remembered that this study has been conducted in a normal population and only in one position (semi-recumbent), so the results can hardly be extrapolated to patients with chronic venous disease or individuals in different life situations. We did not investigate the contribution of reactive hyperemia to the increased ejected volume at high rates of stimulation. Future studies to include popliteal artery flow measurements at different stimulation rates and in different positions are also needed. Such studies may involve the anaesthetized patient and there maybe concerns over the effect of diathermy on its application. However the VEINOPLUS electrode pads placed on the skin and connected to the device have a maximum current density below 0.1 mA/cm2 operating approximately 1000× less than quoted Standards. As it is a battery-powered it assures absolute isolation of the stimulating circuit from the ground and from the power lines of electrosurgical devices.

If efficacy of such a device in preventing DVT can be shown, the small size, its portability and most importantly simplicity of use may make this device an important therapeutic tool. Such assets could prove very useful in trying to improve the application and compliance[12–14] rates amongst a "patient" population thereby optimising thrombo-prophylaxis. Low application and compliance rates are often contributing factors to the reduced effectiveness of mechanical methods of prophylaxis.

In reference to one of the elements involved in Virchow's triad,[15] namely venous stasis, the VEINOPLUS® stimulation is an effective way of activating the calf muscle pump. The enhancements of popliteal blood velocity and volume flow, as shown by this study, are key factors in preventing venous stasis and such technology seems likely to become an additional method for prevention of venous thrombo-embolism.

Further studies are justified in order to determine the rates and configurations of stimulation, which would be applicable in the presence or absence of clinical factors and venous reflux, all of which influence calf pump output.

Funding

Conflict of Interest

No benefits in any form have been received or will be received from any commercial party relating to this article.

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