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Optimum Intermittent Pneumatic Compression Stimulus for Lower-limb Venous Emptying

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Objective: *intermittent pneumatic compression (IPC) of the foot (IPC_{foot}), calf (IPC_{calf}) or both ($IPC_{foot+calf}$) augments calf inflow, and improves the walking ability and peripheral haemodynamics of claudicants (IPC_{foot}, $IPC_{foot+calf}$), largely due to venous outflow enhancement. This cohort study, using direct pressure measurements in healthy limbs, determines the optimal combination of frequency (2–4 impulses/minute), applied pressure (60–140 mmHg), mode (IPC_{foot}–IPC_{calf}–$IPC_{foot+calf}$) and delay time of calf-to-foot impulse (0 s–0.5 s–1 s) that enables IPC to generate an almost complete and sustained decrease in venous pressure.*
Results: *(a) IPC_{foot} at 120 and 80 mmHg generated lower venous pressure than that with 100 and 60 mmHg ($p=0.036$) respectively, for 2–4 impulses/minute; venous pressure differences between applied pressures of 140 and 120 mmHg or between 80 and 100 mmHg were insignificant. (b) Venous pressure with IPC_{calf} at 80 mmHg was lower than that with 60 mmHg ($p=0.036$) (2–4 cycles/minute); differences in venous pressure between applied pressures of 140 and 100 mmHg or between 120 and 80 mmHg were insignificant. (c) At applied pressures 60–140 mmHg, $IPC_{foot+calf}$ with one-second delay generated lower venous pressure than that with half-second delay ($p=0.036$), the latter being more efficient than zero delay; increasing applied pressures produced lower venous pressure, but differences were small.*
Venous pressure decreased with increasing IPC frequency (from 2 to 3–4/minute), at applied pressures 60–140 mmHg.
Conclusions: *$IPC_{foot+calf}$ at applied 120–140 mmHg, a frequency of 3–4 impulses/minute and one-second delay, provided the optimum intermittent pneumatic stimulus.*

Key Words: Optimum pneumatic compression; venous pressure.

Introduction

The effect of intermittent pneumatic limb compression (IPC) on arterial calf inflow has been well documented, yet its effect on the other limb of the circulatory system requires further investigation. Studies using duplex ultrasonography[1–5] and air-plethysmography[6] have shown that volume flow in the leg increases significantly when IPC is applied to the foot (IPC_{foot}), calf (IPC_{calf}) or both simultaneously ($IPC_{foot+calf}$). The effect of these modes on popliteal artery volume flow in normals and arteriopaths has been evaluated comparatively.[3] In both groups $IPC_{foot+calf}$ was the most efficacious. Flow augmentation with IPC is characterised by a significant increase in the end diastolic velocity and concomitant decrease in the pulsatility index, indicating marked attenuation of peripheral resistance to flow. A recent prospective controlled study[7] exploring the therapeutic potential of IPC_{foot} in patients with intermittent claudication, when used long-term (4 hours/day for 4.5 months), demonstrated a pain-free walking distance improvement of more than 100%. The associated increases in the resting (r-ABI) and post-exercise (p-eABI) ankle–brachial indices and popliteal artery volume flow by 18%, 107% and 36%, respectively, suggested that the therapeutic effect, which was still efficacious a year after the withdrawal of the stimulus, is most likely secondary to the development of collateral circulation.

Although the natural history of intermittent claudication due to peripheral vascular disease (PVD) is benign with less than 10% of patients progressing to critical limb ischaemia during their lifetime,[8,9] quality of life is greatly impaired. Intermittent claudication affects the physical mobility and stamina of the patients as well as their psychiatric well-being.[10,11] The currently available treatment options are significantly limited by their low efficacy and cost-effectiveness. Current medications produce poor medium and long-term results.[12–15] Percutaneous transluminal angioplasty is frequently inapplicable,[16] costly[17] and yields poor long-term patency rates.[18,19] As surgical intervention is only

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indicated in cases of severe disabling claudication or critical limb ischaemia, supervised exercise programmes, with control of medical risk factors, are the only presently efficacious treatment option. Unfortunately, such programmes are expensive to run and frequently unavailable and are inconvenient for the patient, as they require regular transportation and attendance. In view of the paucity of the treatment options available, impulse technology is currently emerging as an extremely promising therapeutic modality in the management of intermittent claudication.

Three mechanisms have been postulated to explain the augmentation of flow with IPC: (a) increase in the arteriovenous pressure gradient secondary to venous emptying,[1,2,20] (b) production of endothelial vasodilators in response to the increase in shear stress[21–24] and (c) suspension of the veno-arteriolar response (VAR) with the decrease of venous pressure as lower-limb veins are emptied.[25] The VAR is a vasoconstrictive phenomenon, based on a local sympathetic axon reflex, which, on venous pressure elevation, triggers precapillary muscle contraction and increase in resistance to flow.[26,27] Despite the cardinal role that venous pressure plays in two of these mechanisms, the effect of the three IPC modes (IPC_{foot}, IPC_{calf} and $IPC_{foot+calf}$) on lower-limb venous haemodynamics and the conditions under which this is optimised have never been comprehensively evaluated.

The aim of this study was to determine the optimal combination of frequency, applied pressure, mode of compression and proximal inflate delay time [PIdelay] (time delay of calf to foot impulse with $IPC_{foot+calf}$) that enables IPC, by emptying the veins of the lower limb, to minimise venous pressure. Optimal setting was defined as the combination of lowest pressure, frequency and time delay that, under the simplest possible mode of IPC, could achieve an almost complete and well-sustained decrease in lower-limb venous pressure.

Material and Methods

The effect of three IPC modes (IPC_{foot}, and IPC_{calf} and $IPC_{foot+calf}$) under all following combinations of frequencies (2, 3, 4 impulses/minute), applied pressures (60, 80, 100, 120 and 140 mmHg) and proximal inflate delay times (0, 0.5 and 1 second; only with $IPC_{foot+calf}$) on lower-limb venous haemodynamics was determined in six legs of six normal subjects. All were physically fit male medical personnel at our institution with a median (range) age of 30 (24–35) years. Past medical history was unremarkable for superficial- or deep-vein thrombosis, chronic venous insufficiency (CVI), peripheral vascular disease and lower-limb surgery. Prior to their inclusion into the study, subjects gave informed verbal and written consent. Assessment of the lower-limb arterial and venous systems was performed using colour-flow duplex imaging (CFDI), as previously described.[28,29]

IPC was delivered to the limb using the Art Assist AA-1000 system (ACI Medical Inc., San Marcos, CA, U.S.A.) consisting of a pneumatic impulse generator and two inflatable cuffs, one applied firmly to the foot and the other to the calf. The generator comprises an electrically driven air compressor and an air reservoir which vents intermittently into the cuffs through a pair of large-bore tubings. The equipment offers the flexibility of inflating the cuffs individually or simultaneously, with a variable PIdelay (0, 0.5 or 1 second), at different pressure levels (50–140 mmHg) and frequencies (2 impulses/minute or more).

Lower-limb venous pressure was obtained directly using an accurately calibrated pressure transducer (S & W Medico Teknik A/S Alberslund, Denmark) attached to a cannulated dorsal vein of the foot. Cannulation was performed under local anaesthesia (lignocaine 1%), allowing a well-heparinised 22 gauge plastic catheter (Abbocath®, Ohmeda, Heisinborg, Sweden) to be placed in the largest-calibre superficial dorsal foot vein, punctured as far posterolaterally as possible to ensure non-interference with pressure monitoring.

Interference of foot compression delivery with the direct intravenous measurements was prevented by means of a specially designed slipper-like pneumatic foot cuff. Being held in position with two dorsal straps embracing the forefoot and midfoot respectively, and another one posteriorly wrapping the heel, this cuff enabled delivery of compression mainly over the plantar aspect of the foot with its inflatable sole part. A flexible Silastic interconnecting tube transferred venous foot pressure from the cannula to the drum of the transducer. The drum was strapped over the distal ankle level with the cannulated vein site. A three-way tap placed next to the drum of the transducer enabled flushing of the cannulated vein, cannula and its interconnecting silastic tube, in addition to offering constant access to atmospheric pressure, taken as zero mmHg. This was essential for ensuring that the calibration of the measuring set-up would be maintained throughout the investigation. After every two or three direct venous pressure measurements the i.v. line was flushed with heparinised saline and the system was recalibrated. Measurements continued as long as flushing of and backflow from the cannulated vein were both unimpaired. Return to the same resting sitting venous pressure level each time the pneumatic compression pump was switched off, on completion of a single set

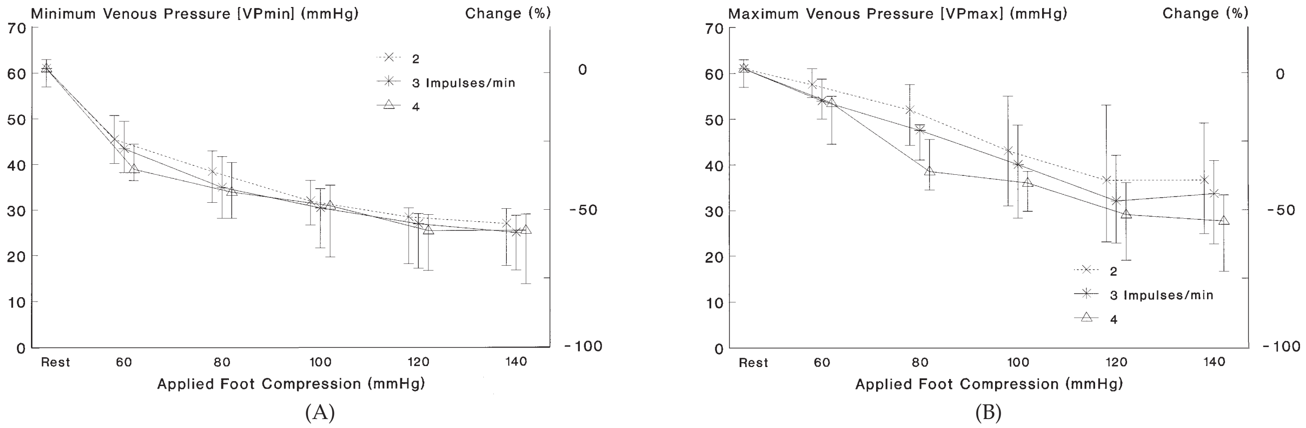


Fig. 1. Effect of intermittent pneumatic foot compression (IPC_{foot}) at applied pressures of 60, 80, 100, 120 and 140 mmHg and frequencies of 2, 3 and 4 impulses/min on the (A) minimum (VPmin) and (B) maximum (VPmax) venous pressures generated at the dorsum of the foot. (A) The VPmin generated with applied pressures of 120 and 80 mmHg was statistically lower than that with 100 and 60 mmHg ($p=0.036$) respectively, for the three examined frequencies. There was no difference in the VPmin produced either between applied pressures of 140 mmHg and 120 mmHg ($p=0.09$) or between 80 mmHg and 100 mmHg ($p=0.1$). VPmin decreased with increasing impulse frequency (from 2 to 3 or 4 impulses/min) at all applied pressure levels. (B) Applied pressures of 120 and 80 mmHg generated significantly lower VPmax than 100 mmHg ($p=0.036$) and 60 mmHg ($p=0.036$) respectively. There was no significant difference in the VPmax between either 140 and 120 mmHg ($p=0.09$) or 100 and 80 mmHg ($p=0.1$). A frequency of 3 or 4 impulses/minute generated lower VPmax than that of 2 impulses/min at each applied pressure level. Y2 axis represents the percentage changes in VPmin and VPmax with IPC_{foot}.

of measurements, provided additional monitoring information on the quality of retrieved data. The accuracy of the measuring set-up was assessed on every limb examined by comparing the recorded pressure values with progressively increasing levels of external compression (from 5 mmHg to 70 mmHg in increments of 5 mmHg), applied in the horizontal position using a well-calibrated sphygmomanometer wrapped around the distal calf, just proximal to the tip of the plastic cannula. Measurements were performed only when the pressure discrepancy between the sphygmomanometer and the transducer, throughout the range of externally applied pressures, was less than 4 mmHg.

The examination protocol entailed a resting period of 20 min prior to the application of IPC. The subject maintained the sitting position throughout the investigation, with his back thoroughly supported and his legs resting comfortably on a flat stool. Seconds after the delivery of a pneumatic impulse to the leg, venous pressure declined to a minimum, followed by a rise to a maximum until the next impulse was delivered. All these pairs of pressure readings were recorded impulse by impulse until a steady state was reached. At this stage the minimum (VPmin) and maximum venous pressures (VPmax), which could not be reduced any further by the delivery of more impulses, were used in our analysis as characteristic of the corresponding combination of presets and pneumatic impulse mode. The pneumatic impulse system was then turned off and further investigation of lower-limb venous pressure changes under different presets or modes was not resumed until venous pressure had fully returned to the resting level and a time break of five minutes had elapsed. Examination of each leg was completed in two to three sessions (3–5 h per session). Crucial measurements, i.e. those obtained from the most effective IPC settings and modes, were re-evaluated at every investigation session and, unless same values were reached, the finally recorded values were the average of all these individual estimations. With optimisation of the pressure measuring set-up, recorded discrepancies were less than 2 mmHg for the VPmin and less than 3 mmHg for the VPmax. Measurements with discrepancies exceeding these limits were repeated following optimisation of the measuring system. The above limits were always maintained under these optimised conditions.

Data are presented as median and interquartile range (IQR). Analysis of results was performed with nonparametric paired statistics (Wilcoxon signed-ranks test) using Minitab.

Results

Optimisation of lower-limb venous emptying using IPC is presented separately for each mode (IPC_{foot}, IPC_{calf} and $IPC_{foot+calf}$) and finally as a comparison between the modes, to enable determination of the optimum intermittent pneumatic compression stimulus:

IPC_{foot}

The effect of impulse frequency (2, 3 or 4 impulses/min) at different levels of applied pressure (60, 80, 100, 120 and 140 mmHg) on the VPmin and VPmax upon application of $\mathbf{IPC_{foot}}$ is depicted in Figures 1a

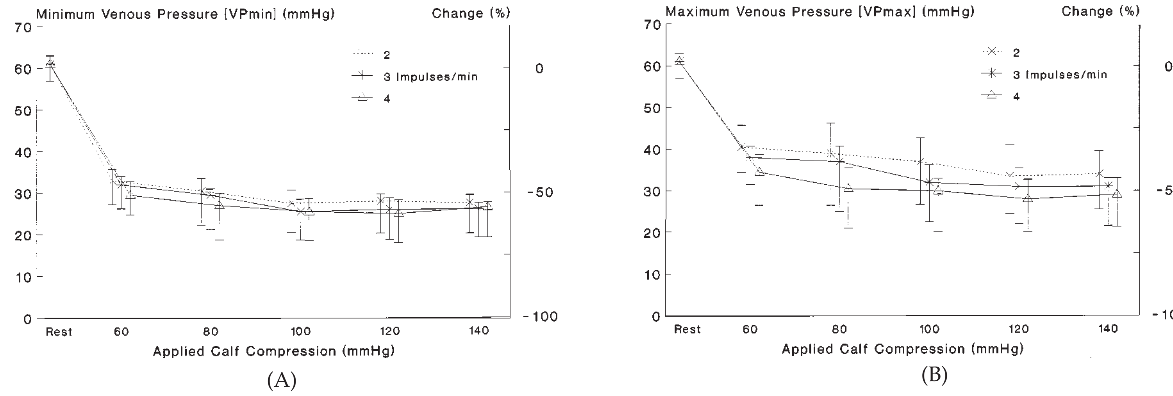


Fig. 2. Effect of intermittent pneumatic calf compression (IPC_{calf}) at applied pressures of 60, 80, 100, 120 and 140 mmHg and frequencies of 2, 3 and 4 impulses/min on the (A) minimum (VPmin) and (B) maximum (VPmax) venous pressures generated at the dorsum of the foot. (A) The VPmin generated with 80 mmHg was statistically lower than that with 60 mmHg ($p=0.036$) for the three examined frequencies. There was no significant difference in the VPmin achieved either between applied pressures of 140 mmHg and 100 mmHg ($p=0.5$) or between 120 mmHg and 80 mmHg ($p=0.2$). VPmin decreased with impulse frequency (from 2 impulses/min to 3 or 4) at all applied pressure levels, although differences were small. (B) Applied pressure of 80 mmHg generated a significantly lower VPmax than 60 mmHg ($p=0.036$) for the three examined frequencies. Similar levels of VPmax were produced with applied pressures of 80, 100, 120 and 140 mmHg. A frequency of 3* or 4 impulses/min generated lower VPmax than that of 2 impulses/min (*$p=0.036$ for applied pressures of 100, 120 and 140 mmHg). Four impulses/min achieved lower VPmax than 3 impulses/min at each applied pressure, however the difference was insignificant ($p=0.1$) at applied pressures of 100, 120 and 140 mmHg. Y2 axis represents the percentage changes in VPmin and VPmax with IPC_{calf}.

and 1b, respectively. The VPmin and VPmax generated with applied pressures of 120 and 80 mmHg were statistically lower than those with 100 and 60 mmHg ($p=0.036$) respectively, for the three examined frequencies. There was no significant difference either between applied pressures of 140 mmHg and 120 mmHg or between 80 mmHg and 100 mmHg. VPmin and VPmax decreased with increasing impulse frequency (from 2 to 3 or 4 impulses/minute) at all applied pressure levels.

IPC_{calf}

The VPmin and VPmax generated at different applied levels of **IPC_{calf}** over the range of examined frequencies (2, 3 and 4 impulses/min) are demonstrated in Figs 2a and 2b, respectively. The VPmin and VPmax generated with 80 mmHg were statistically lower than those with 60 mmHg ($p=0.036$) for the three examined frequencies. There was no significant difference in the VPmin and VPmax achieved either between applied pressures of 140 mmHg and 100 mmHg or between 120 mmHg and 80 mmHg. Venous pressure decreased with impulse frequency (from 2 impulses/minute to 3 or 4) at all applied pressure levels.

$IPC_{foot+calf}$

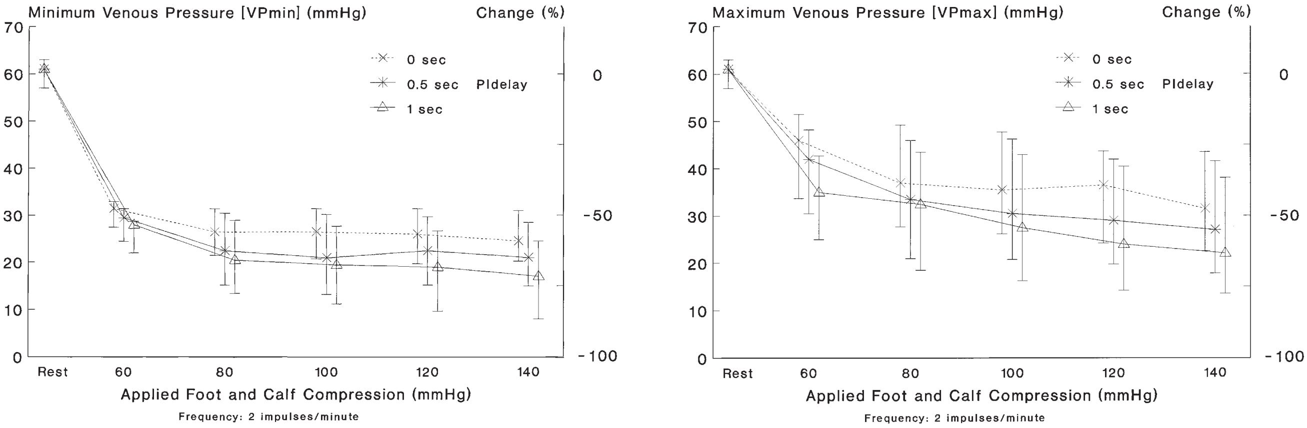
Figures 3a to 5b show the effect of different applied pressures (60–140 mmHg), frequencies (2–4 impulses/min) and proximal inflate delay times (0, 0.5, 1 s) on VPmin and VPmax when **$IPC_{foot+calf}$** is delivered to the limb. A delay time of 1 s gave superior results to that of 0.5 s and this was more effective than no delay, at each of the examined applied pressures and frequencies of $IPC_{foot+calf}$. Applied pressures of 120 mmHg and 140 mmHg delivered the lowest VPmin and VPmax when the proximal inflate delay time was 1 second, at all frequencies examined (2–4 impulses/min).

Figures 6a and 6b show the effect of altering the frequency of $IPC_{foot+calf}$ on the VPmin and VPmax delivered with a proximal inflate delay time of 1 second. A frequency of 3 or 4 impulses/min was more effective than 2 impulses/min at each of the examined applied pressures. Although a frequency of 4 impulses/min generated lower VPmin and VPmax than 3 impulses/min, the difference was small ($p \geq 0.06$).

The optimal effect of the three investigated modes of IPC on VPmin and VPmax is depicted in Figs 7a and 7b, respectively. At the applied pressures examined with a frequency of 4 impulses/min $IPC_{foot+calf}$ was more effective on the VPmin and VPmax than IPC_{calf} ($p<0.036$). IPC_{calf} generated lower venous pressures than IPC_{foot} over the lower range of applied pressures (60–100 mmHg), particularly on the VPmax, but there was practically no difference between the two modes over the upper applied pressure range (120–140 mmHg).

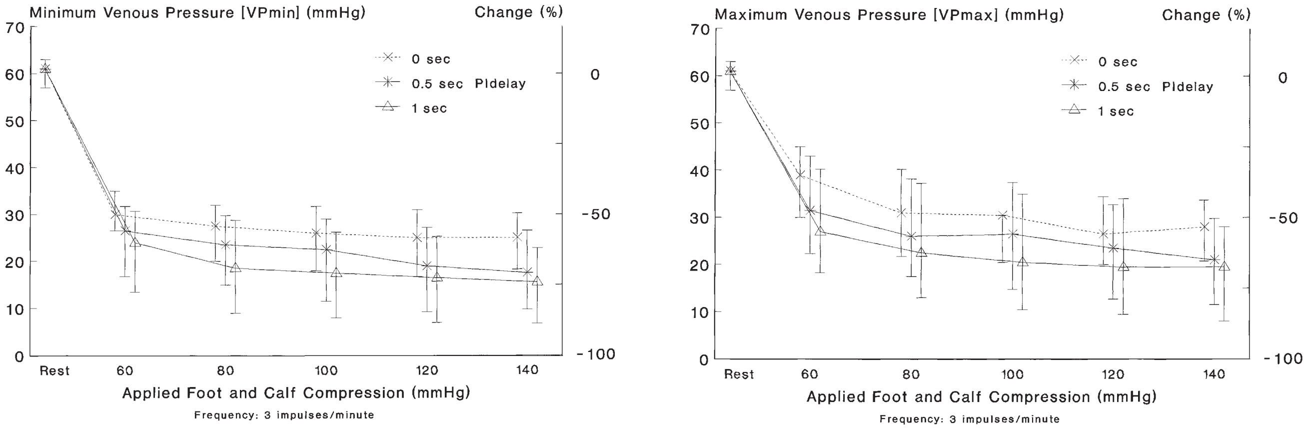
Discussion

The arteriovenous pressure gradient is one of the main factors that determine the level of arterial volume flow



(A) (B)

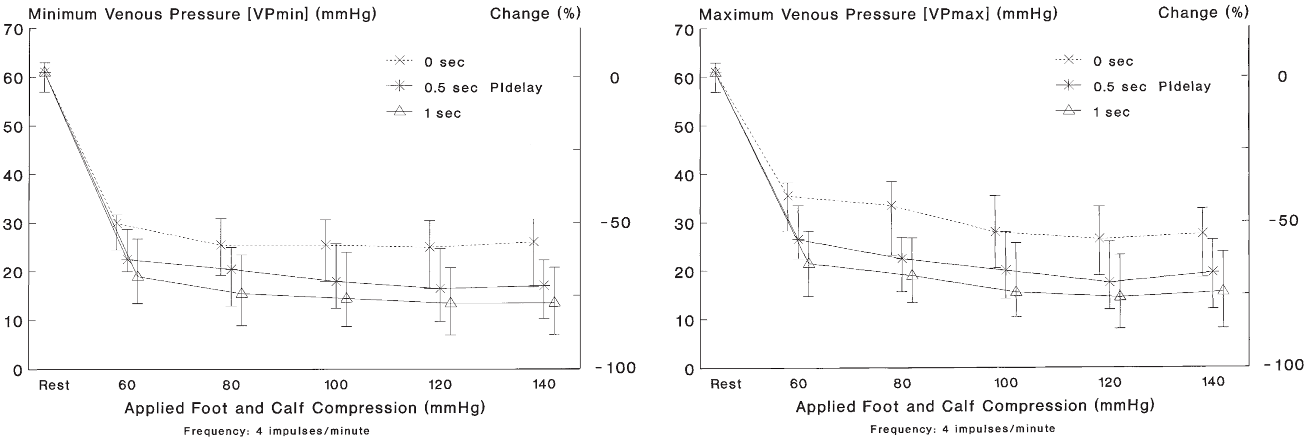
Fig. 3. Effect of different proximal inflate delay times (PIdelay) [0, 0.5 and 1 s] of intermittent pneumatic foot and calf compression ($IPC_{foot+calf}$) delivered at applied pressures of 60, 80, 100, 120 and 140 mmHg and a frequency of **2 impulses/min** on the (A) minimum (VPmin) and (B) maximum (VPmax) venous pressures at the ankle. (A) PIdelay of 1 s generated lower VPmin than PIdelay of 0 s ($p=0.036$) at each examined applied pressure (60–140 mmHg). Lower VPmin was produced with increasing applied pressures; however, the differences were small. VPmin with a PIdelay of 1 s was lower than with a PIdelay of 0.5 s; however, the differences were small for each of the examined applied pressures. (B) PIdelay of 1 s generated significantly lower VPmax than PIdelay of 0.5 s ($p=0.036$) in all the applied pressure range (except 80 mmHg [$p=0.06$]). Similarly, PIdelay of 0.5 s achieved lower VPmax than PIdelay of 0 s, throughout the applied pressure range. Lower VPmax was produced with increasing levels of applied pressure; however, the differences were small. Y2 axis represents the percentage changes in VPmin and VPmax with $IPC_{foot+calf}$ for the above settings.



(A) (B)

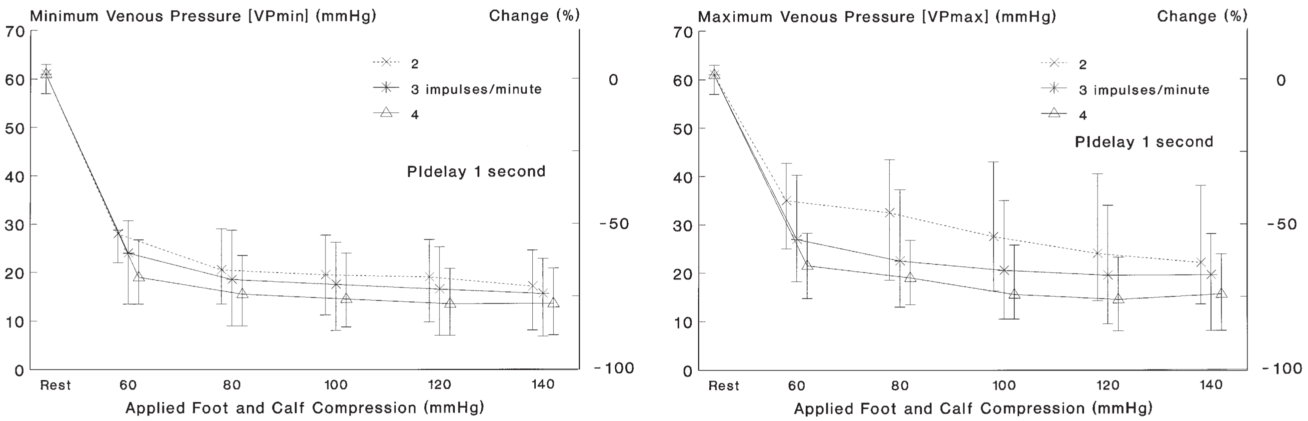
Fig. 4. Effect of different proximal inflate delay times (PIdelay) [0, 0.5 and 1 s] of intermittent pneumatic foot and calf compression ($IPC_{foot+calf}$) delivered at applied pressures of 60, 80, 100, 120 and 140 mmHg and a frequency of **3 impulses/min** on the (A) minimum (VPmin) and (B) maximum (VPmax) venous pressures at the ankle. (A) PIdelay of 1 s generated lower VPmin than PIdelay of 0.5 s ($p=0.036$), at each of the examined applied pressures (60–140 mmHg). Lower VPmin were produced with increasing applied pressures; however, the differences were small. VPmin with PIdelay of 0.5 s was lower than with PIdelay of 0 s for each of the examined applied pressures. (B) PIdelay of 1 s generated significantly lower VPmax with PIdelay of 0.5 s ($p=0.036$) at each of the examined applied pressures (except 80 mmHg [$p=0.06$]). Similarly, PIdelay of 0.5 s achieved lower VPmax than PIdelay of 0 s. Lower VPmax was produced with increasing levels of applied pressure; however, the differences were small. Y2 axis represents the percentage changes in VPmin and VPmax with $IPC_{foot+calf}$ for the above settings.

in the lower limb.[30] In the supine position, the venous pressure of the legs, which are at the level of the right atrium, is approximately 4–5 mmHg.[31] When the foot is lowered below the level of the heart the pressure in the arteries and veins increases by an amount determined by the hydrostatic pressure of column of blood between the heart and the foot. In an average-sized man in the sitting position, the venous foot pressure is approximately 60 mmHg and increases to about 90 mmHg on standing.[32] As the arterial systolic blood pressure at the ankle in the sitting position is at least 170 mmHg, application of IPC at 60 mmHg to 140 mmHg for 4 s at a frequency of 2–4 impulses/min (impulse frequency range used in this study) does not affect the overall



(A) (B)

Fig. 5. Effect of different proximal inflate delay times (PIdelay) [0, 0.5 and 1 s] of intermittent pneumatic foot and calf compression ($IPC_{foot+calf}$) delivered at applied pressures of 60, 80, 100, 120 and 140 mmHg and a frequency of **4 impulses/min** on the (A) minimum (VPmin) and (B) maximum (VPmax) venous pressures at the ankle. (A) PIdelay of 1 s generated lower VPmin than PIdelay of 0.5 s ($p=0.036$), at each of the examined applied pressures (60–140 mmHg). Lower VPmin was produced with increasing applied pressures. VPmin with a PIdelay of 0.5 s was lower than with a PIdelay of 0 s at each of the examined applied pressures. (B) PIdelay of 1 s generated significantly lower VPmax than PIdelay of 0.5 s ($p=0.036$) at each of the examined applied pressures. Similarly, PIdelay of 0.5 s achieved lower VPmax than PIdelay of 0 s. Lower VPmax was produced with increasing levels of applied pressure. Y2 axis represents the percentage changes in VPmin and VPmax with $IPC_{foot+calf}$ for the above settings.



(A) (B)

Fig. 6. Effect of frequency of intermittent pneumatic foot and calf compression ($IPC_{foot+calf}$) delivered at a proximal inflate delay time (PIdelay) of 1 s and applied pressures of 60, 80, 100, 120 and 140 mmHg on the (A) minimum (VPmin) and (B) maximum (VPmax) venous pressures at the ankle. A frequency of 3 impulses/min generated significantly lower VPmin ($p=0.036$) and VPmax ($p=0.036$) than 2 impulses/min at each of the examined applied pressures (60–140 mmHg). Although the lowest venous pressures were achieved at a frequency of 4 impulses/min, when compared to the venous pressures produced at 3 impulses/min differences were not significant ($p>0.1$). Y2 axis represents the percentage changes in VPmin and VPmax with $IPC_{foot+calf}$ for the above settings.

arterial pressure level. However, the results of this and previous studies[20,33] show that IPC can significantly reduce the lower-limb venous pressure and consequently the arteriovenous pressure gradient and thus improve arterial calf inflow. The contribution of this study was to identify and quantify pressure changes imposed on the venous circulation of the foot on application of different compression stimuli and to determine the optimal combination of applied pressure, frequency and mode of compression that enhances lower-limb venous emptying in order to optimise the clinical effect of IPC.

The results of this study show that applied pressures of 120 mmHg and 140 mmHg were more effective in emptying lower-limb veins than 60–100 mmHg, both with IPC_{foot} and $IPC_{foot+calf}$. With IPC_{calf} a pressure level of 80–140 mmHg was more effective than 60 mmHg. In the sitting position, resting venous pressure is 60 mmHg on the dorsum of the foot and is lower in the calf. The

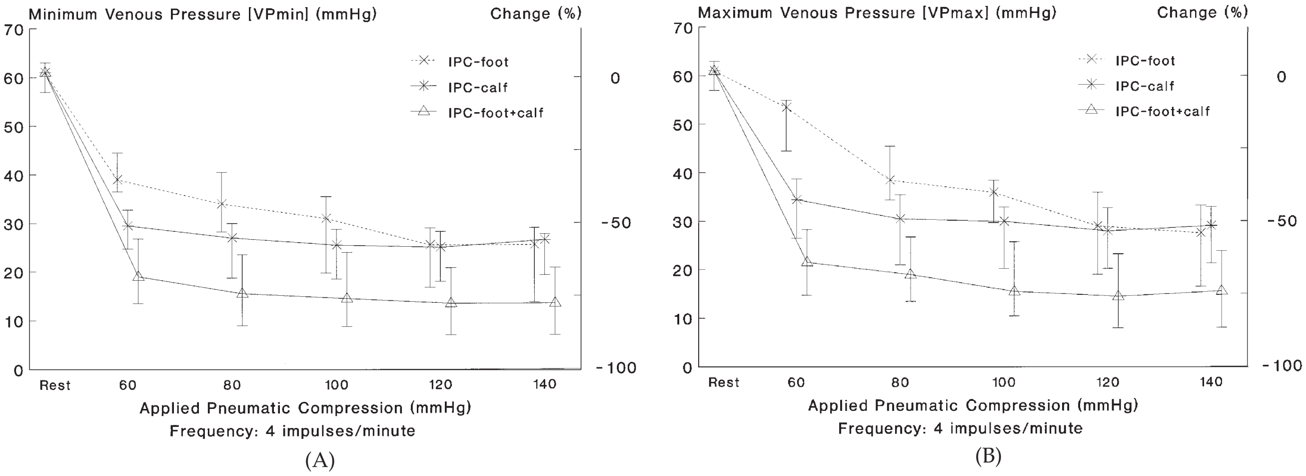


Fig. 7. Comparison of the optimal effects of the three compression modes (IPC_{foot}, IPC_{calf} and $IPC_{foot+calf}$ [PIdelay of 1 s]) delivered at a frequency of 4 impulses/min and at applied pressures of 60, 80, 100, 120 and 140 mmHg, on the (A) minimum (VPmin) and (B) maximum (VPmax) venous pressures at the ankle. At all applied pressure levels $IPC_{foot+calf}$ achieved significantly lower VPmin ($p=0.036$) and VPmax ($p=0.036$) than IPC_{calf}. Although IPC_{foot} generated lower venous pressures than IPC_{calf} with applied pressures of 60, 80 and 100 mmHg, differences were negligible at the higher spectrum (120 and 140 mmHg). Y2 axis represents the percentage changes in VPmin and VPmax with IPC for the above settings.

higher level of applied pressure required to cause lower-limb vein walls to collapse may be attributed to the dissemination of a substantial part of the delivered impulse energy, in the skin, subcutaneous fat, muscle or other tissues, before the vessel walls are reached. The inherent inefficiency in the design of the limb cuffs that transfer the mechanical energy load to the limb, including their elastic characteristics and contact surface, contribute inevitably to these losses. It appears that approximately 50% of the overall energy delivered from the inflatable cuffs to the leg is lost due to the above-mentioned factors. This is in agreement with the data of Gaskell and Parrott[20] who reported that compression much higher than the venous pressure at the foot was necessary to obtain an efficient venous pressure reduction. These findings are further supported by Baumann *et al.*[34] who demonstrated that muscle contraction in the calf, which is the main mechanism of natural lower-limb venous pumping, can generate intramuscular pressures of up to 107 mmHg, indicating that the function of calf venous pumps (proximal and distal) occurs at pressures that significantly exceed those in the leg veins. Both the foot and the calf pumps have been shown to be powerful enough to overcome a cuff inflated to 100 mmHg during normal locomotion and hence displace a column of blood to the heart.[35]

The improvement in lower-limb venous emptying, which was documented in the three different modes of compression at all levels of applied compression, when the frequency was raised from 2 to 3 or 4 impulses per min may be explained by considering the time normally taken for lower-limb veins to refill. Based on direct pressure estimations following a standard exercise of 10 tip–toe movements (1 movement/second), Nicolaides and Zukowski[36] showed that the 90% venous refilling time in normal limbs is 18–40 s (95% range). Gaskell and Parrott[20] using an inflatable foot and ankle boot to expel lower-limb venous blood and measuring pressure in the foot directly, reported a refill time of 16–20 s. The discrepancy in the upper range is due to the different ejected venous volumes in the two methodology settings, being higher in the former study. The results of Gaskell and Parrot[20] are in agreement with the data of this study (Figs 1a, 1b, 2a, 2b, 6a and 6b). By increasing the frequency of delivered pneumatic impulses from 2 to 3 or 4 per min the deflation time is reduced from 26 to 16 and 11 s, respectively. A frequency of 2 impulses per min, based on the aforementioned venous refill times, is not sufficient to maintain the lower-limb veins empty of blood and thus a low level of venous pressure. By inference a frequency of 3 impulses per min is theoretically inferior to 4 per min, provided that refilling starts with the end of compression. Based on our data, however, the difference between a frequency of 3 and 4 impulses/min, irrespective of mode of leg compression, is too small to be significant.

It was not surprising that when $IPC_{foot+calf}$ was applied, a calf inflate delay time of 0.5 or 1 s was more effective in emptying lower-limb veins than no proximal inflate delay, at all applied pressure levels and all three different examined frequencies (2, 3 and 4 impulses per min). As venous pressure in the calf is lower than in the foot on sitting, application of the same external compression to the foot and the calf simultaneously, at a level above the resting lower-limb venous pressure, would result in an earlier collapse of the veins in the calf than in the foot. This would cause the venous volume below the calf cuff to be trapped for a time period equivalent to the inflation time, since the pressure generated in the foot on pneumatic compression is lower than the transmural pressure in the calf veins that maintains them collapsed (as calf compression is exerted), by a gradient which theoretically should equal the resting venous pressure differential between the foot and the calf. Our results are in agreement with those by Kamm *et al.*,[37] who maintained that sequential compression proceeding from the foot upwards in a wave-like manner is more effective than simultaneous, undelayed, multi-level leg compression. They demonstrated that this uniform mode is severely compromised by the formation of a flow-limiting occlusion throat at the proximal end of the compression cuff that reduces both the rate at which blood is expelled and the total blood volume ejected from the lower limb. This was further confirmed by isotopic studies on healthy volunteers.[38] In our study, the improvement of venous emptying by increasing the calf inflate delay time from 0.5 to 1 s is in accord with the data of Kamm *et al.*,[38] who suggested that the delay time of the proximal applied compression should be a little longer than the rate of inflation of the preceding more distal impulse. The rate of inflation of the cuffs used in this study was 0.5–0.6 s (Art Assist 1000).

Comparative Figs 7a and 7b demonstrate that $IPC_{foot+calf}$ in all the applied pressure range is more powerful than IPC_{calf} and, except in the higher pressure range (120–140 mmHg), the latter is better than IPC_{foot}. This may be explained by the different venous volumes expelled by each of the three compression modes. The plantar venous plexus is believed to have a capacitance of 20–30 ml, whereas the calf an overall capacitance of 70–100 ml. Assuming a similar rate of arterial calf and foot inflow, it would take twice as long for the veins in the former to refill, and for resting venous pressure to be restored. On the other hand, a similar venous refill time after foot or calf venous emptying would require a much higher arterial calf inflow, which could be achieved by an increased arteriovenous pressure gradient, a reduced peripheral resistance or both. Under optimal conditions (frequency, applied pressure) there might be no differences between IPC_{foot} and IPC_{calf} (Figs 7a and 7b), but at lower frequencies and applied pressures the results are in favour of the latter mainly due to the lower VPmax generated.

As regards the relative importance of the two pressure levels recorded at the steady state, VPmin, the lowest pressure generated immediately after the delivery of a pneumatic impulse, reflects mainly the impact of the level of applied pneumatic pressure (the drive for venous emptying) for a certain impulse mode, frequency and proximal inflate delay. VPmax, the highest recorded venous pressure just prior to the delivery of the next pneumatic impulse, reflects mainly the degree of venous priming allowed between consecutive impulses (frequency of the impulse), for a certain level of applied pressure. VPmax also reflects the mode of IPC, and the proximal inflate delay time for a certain level of applied pressure. Consideration of their average, rather than the VPmin and VPmax individually, would offer a simpler approach to the clarification of venous haemodynamics generated on continuous application of IPC, at the expense of haemodynamic accuracy and detail.

Although the results of this study are applicable to healthy limbs, the reported data can be extended to claudicants without venous incompetence. Patients with intermittent claudication are known to have decreased levels of peak leg inflow enhancement with maximal exercise, generating only a six-fold maximal flow increase compared with a ten-fold increase amongst normals. However, the similar maximal flow levels documented with IPC between the two groups[3] indicate an insignificant inflow discrepancy with pneumatic compression challenge and, in the absence of venous incompetence, the results of the current study representing healthy limbs should also be applicable to limbs with claudication.

In the presence of chronic venous disease (without critical limb ischaemia), the time taken for lower-limb veins to refill is a direct function of the severity of venous incompetence and venous outflow obstruction. Assuming that outflow obstruction is absent, venous refill time depends on the amount of reflux, and possibly the pattern of venous incompetence. As a result of the decreased refill times in limbs with venous incompetence, any of the IPC modes investigated in the current study, on any setting should be expected to result in a significantly higher level of venous pressure (both VPmin and VPmax) than those in healthy limbs. Of the two venous pressures recorded at the steady-state condition, VPmax should be the one more significantly affected, as it reflects the refilling of the venous system between two consecutive pneumatic impulses. Higher IPC frequencies should be required to prevent the leg veins from refilling before the delivery of the next impulse. Optimisation of IPC frequency in limbs with venous incompetence could be achieved by quantification of the amount of reflux. Once optimisation of the IPC frequency is counterbalanced for decreased refill times, the range of applied pressures used in the current study should be sufficient to enable a satisfactory emptying of the lower-limb veins.

In conclusion, of the three different modes of IPC investigated in this study, $IPC_{foot+calf}$ is the most effective in emptying the leg veins. The optimum stimulus is achieved when an applied pressure level of 120 mmHg to 140 mmHg is combined with a frequency of 3 or 4 impulses/min and a proximal inflate delay time of 1 second.

References

1 Morgan RH, Carolan G, Psaila JV *et al*. Arterial flow enhancement by impulse compression. *Vasc Surg* 1991; **25**: 8–15.

2 van Bemmelen PS, Mattos MA, Faught WE *et al*. Augmentation of blood flow in limbs with occlusive arterial disease by intermittent calf compression. *J Vasc Surg* 1994; **19**: 1052–1058.

3 Delis K, Labropoulos N, Nicolaides AN *et al*. The acute effect of intermittent pneumatic foot vs calf vs simultaneous foot and calf compression on popliteal artery haemodynamics: a comparative study. [Abstract]. *Int Angiol.* 1996; **15** (Suppl. 1): 6.

4 Delis K, Labropoulos N, Nicolaides AN *et al*. Arterial calf inflow augmentation in peripheral vascular disease using intermittent pneumatic foot compression (IPFC): effects on popliteal artery haemodynamics. [Abstract]. *Br J Surg* 1997; **84** (Suppl. 2): 159.

5 Eze AR, Comerota AJ, Cisek PL *et al*. Intermittent calf and foot compression increases lower extremity blood flow. *Am J Surg* 1996; **172**: 130–135.

6 Banga JD, Idzerda HD, Schurman JG *et al*. Intermittent pneumatic compression therapy in patients with leg ischaemia. [Abstract]. *Int Angiol* 1995; **14 (Suppl. 1)**: 202.

7 Delis K, Nicolaides A, Stansby G *et al*. Intermittent pneumatic impulse compression of the foot can improve the condition of patients with stable intermittent claudication: a prospective controlled study. [Abstract]. *Br J Surg* 1997; **84**: 577–578.

8 Hertzer NR. The natural history of peripheral vascular disease. Implications for its management. *Circulation* 1991; **83**: I12–I19.

9 O'Riordain DS, O'Donnell JA. Realistic expectations for the patient with intermittent claudication. *Br J Surg* 1991; **78**: 861–863.

10 Khaira HS, Hanger R, Shearman CP. Quality of life in patients with intermittent claudication. *Eur J Vasc Endovasc Surg* 1996; **11**: 65–69.

11 Currie IC, Wilson YG, Baird RN, Lamont PM. Treatment of intermittent claudication: the impact on quality of life. *Eur J Vasc Endovasc Surg* 1995; **10**: 356–361.

12 Porter JM, Cutler BS, Lee BY *et al*. Pentoxifylline efficacy in the treatment of intermittent claudication: multicenter controlled double-blind trial with objective assessment of chronic occlusive arterial disease patients. *Am Heart J* 1982; **104**: 66–72.

13 Balsano F, Coccheri S, Libretti A *et al*. Ticlopidine in the treatment of intermittent claudication: a 21-month double blind trial. *J Lab Clin Med* 1989; **114**: 84–91.

14 Solomon SA, Ramsay LE, Yeo WW, Parnell L, Morris Jones W. Beta blockade and intermittent claudication: placebo controlled trial of atenolol and nifedipine and their combination. *BMJ* 1991; **303**: 1100–1104.

15 Fagler B. Long term effects of ticlopidine on lower limb blood flow, ankle/brachial index, and symptoms in peripheral atherosclerosis. A double blind study. The STIMS Goup in Lund. Swedish Ticlopidine Multicenter Study. *Angiology* 1994; **45**: 777–788.

16 Whyman MR, Fowkes FG, Kerracher EM *et al*. Randomised controlled trial of percutaneous transluminal angioplasty for intermittent claudication. *Eur J Vasc Endovasc Surg* 1996; **12**: 167–172.

17 Rudofsky G, van Laak HH. Treatment costs of peripheral occlusive disease in Germany: a comparison of costs and efficacy. *J Cardiovasc Pharmacol* 1994; **23** (Suppl. 3): S22–S25.

18 Capek P, McLean GK, Berkowitz HD. Femoropopliteal angioplasty. Factors influencing long term success. *Circulation* 1991; **83**: I70–I80.

19 Kokesh J, Kazmers A, Zierler RE. Pentoxifylline in the nonoperative management of intermittent claudication. *Ann Vasc Surg* 1991; **5**: 66–70.

20 Gaskell P, Parrott JCW. The effect of a mechanical venous pump on the circulation of the feet in the presence of arterial obstruction. *Surg Gyn Obst* 1978; **146**: 583–592.

21 Frangos JA, Eskin SG, McIntire LV, Ives CL. Flow effects on prostacyclin production by cultured human endothelial cells. *Science* 1985; **227**: 1477–1479.

22 Editorial. Yin and yang in vasomotor control. *Lancet* 1988; **2**: 19–20.

23 Editorial. Endothelins. *Lancet* 1991; **337**: 79–80.

24 Ranjan V, Xiao Z, Diamond SL. Constitutive NOS expression in cultured endothelial cell is elevated by fluid shear stress. *Am J Physiol* 1995; **269**: H550–H555.

25 Michel CC. Microcirculation in the limbs in venous hypertension. *Medicographia* 1989; **11**: 40–42.

26 Henriksen O. Orthostatic changes of blood flow in subcutaneous tissue in patients with arterial insufficiency of the legs. *Scand J Clin Lab Inves* 1974; **34**: 103–109.

27 Henriksen O. Local nervous mechanism in regulation of blood flow in human subcutaneous tissue. *ACTA Phys Scand* 1976; **97**: 385–391.

28 Delis KT, Ibegbuna V, Nicolaides AN, Lauro A, Hafez H. Prevalence and distribution of incompetent perforating veins in chronic venous insufficiency. *J Vasc Surg* 1998; **28**: 1–11.

29 Kohler TR. Duplex scanning for the evaluation of lower limb arterial disease. In: Bernstein EF, ed. *Vascular Diagnosis.* St Louis: Mosby, 1993: 520–526.

30 Samner DS. Haemodynamics in the lower limb. In: Myers KA, Nicolaides AN, Sumner DS, eds. *Lower Limb Ischaemia.* London: Med-Orion, 1997: 1–29.

31 Rhoads R, Pflanzer R. Circulation. In: Rhoads R, Pflanzer R, eds. *Human Physiology.* Orlando: Saunders College Publishing, 1996: 575–615.

32 Pollack AA, Wood EH. Venous pressure in the saphenous vein at the ankle in man during exercise and changes in posture. *J Appl Physiol* 1948; **1**: 649–662.

33 McMullin GM, Scott HJ, Coleridge Smith PD. An assessment of the effect of the foot pump on venous emptying in chronic venous insufficiency. *Phlebol* 1989; **4**: 75–82.

34 Baumann JU, Sutherland DH, Hanggi A. Intramuscular pressure during walking: an experimental study using the wick catheter technique. *Clin Orthop* 1979; **145**: 292–299.

35 Gardner AMN, Fox RH. Peripheral venous physiology. In: Gardner AMN, Fox RH, eds. *The Return of Blood to the Heart.* London: John Libbey 1993; 61–88.

36 Nicolaides AN, Zukowski AJ. The value of dynamic venous pressure measurements. *World J Surg* 1986; **10**: 87–95.

37 Kamm RD. Bioengineering studies of periodic external compression as prophylaxis against deep vein thrombosis – part one: numerical studies. *J Biomech Eng* 1982; **104**: 87–95.

38 Kamm R, Butcher R, Froelich J *et al*. Optimisation of indices of external pneumatic compression for prophylaxis against deep vein thrombosis: radionuclide gate imaging studies. *Cardiovasc Res* 1986; **20**: 588–596.

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