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Effects of compression bandaging on leg pulsatile blood flow

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Summary. Leg external compression bandaging is the mainstay of venous ulcer treatment, yet little is known about the impact of therapeutic compression levels on arterial haemodynamics. In this study, the effect of foot-to-knee, four-layer compression bandaging on below-knee arterial pulsatile blood flow was assessed by nuclear magnetic resonance flowmetry. In 14 healthy supine subjects, bilateral flow measurements at five below-knee sites without compression, and after compressing one leg to an average malleolar sub-bandage pressure of 40·7±4·0 mmHg, revealed a potentially important new phenomenon. The forefoot-to-knee compression bandaging caused a highly significant ($P<0·001$) increase in the bandaged leg pulsatile blood flow owing to increases in both peak flow and pulse width. It is hypothesized that arteriolar vasodilatation, induced either myogenically by reduced transmural pressure or by vasodilatory substance release triggered by increased venous shear stress, produce the observed compression-related phenomenon. Whatever the mechanism(s), the finding of a compression-associated pulsatile flow increase suggests a previously undiscovered arterial linkage, which may play a role in the well-documented beneficial effects of compression bandaging in venous ulcer treatment. A possible impact of the arterial flow–pulse increase is speculated to effect venous ulcer outcome via a decrease in leucocyte effects in the distal microvasculature, as a consequence of the more vigorous haemodynamic state.

Key words: compression bandaging, leg blood flow, magnetic resonance, vascular control, venous ulcers.

Introduction

There are a number of instances in which lower limbs are subject to the effects of external compression. As a therapeutic modality, external compression of the limbs is used on an intermittent basis for oedema reduction, and sustained compression bandaging is the mainstay of effective treatment of venous ulcers. In conjunction with the latter, there has been interest and experimental work regarding the effect of compression therapy

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on venous haemodynamics. However, there is very little known with regard to its effect on arterial haemodynamics, especially leg pulsatile blood flow. Since the magnitude of pressures routinely used are about 40 mmHg, and in some cases higher, it was reasoned that, although less than arterial diastolic pressure, a possible impact on leg pulsatile blood flow might be present. Because the magnitude and pattern of leg flow pulses depend on arterial compliance and complex reflected wave phenomena, either or both of which might be influenced by the external compression, the present study was done to provide seminal data on the type and nature of compression bandaging alterations in leg pulsatile blood flow features. For this purpose, nuclear magnetic resonance flowmetry (NMRF) was used to measure pulsatile blood flow bilaterally at five below-knee sites before and after application of a four-layer compression bandage to one of the legs. The study was conducted in 14 healthy volunteer subjects.

Methods

SUBJECTS AND PRELIMINARY EVALUATIONS

Healthy volunteer subjects ($n=14$, seven women, aged $42\pm5{\cdot}3$ years) were studied after reading and signing an Institutional Review Board-approved informed consent form. No subject had diabetes, had any history of venous or arterial disease or was taking any vasoactive medication. Absence of lower extremity arterial disease was confirmed in each participant based on screening with bilateral NMRF and ankle–brachial systolic pressure indices (ABI), obtained using standard Doppler ultrasound at the posterior tibia and dorsal pedis arteries. All subjects tested normal with mean blood perfusion at the knee and ankle of $1{\cdot}68\pm0{\cdot}20$ and $1{\cdot}71\pm0{\cdot}16$ ml min^{-1} 100 cm^{-3}, respectively, and an average ankle systolic pressure and ABI of $130{\cdot}8\pm5{\cdot}5$ and $1{\cdot}02\pm0{\cdot}02$ respectively. Systemic blood pressures measured with standard blood pressure cuffs also verified that the group was normotensive (systolic $126\pm4{\cdot}7$, diastolic $84\pm3{\cdot}2$ mmHg).

LEG PULSATILE BLOOD FLOW METHODOLOGY

Pulsatile blood flow was evaluated under resting supine conditions using the method of nuclear magnetic resonance flowmetry (NMRF). With this method, the participant is placed on a moveable table, which is advanced by an operator so as to position a specific leg site within the centre of a tubular measurement section of the NMRF system (Metriflow AFM100; Milwaukee, USA). Within the measurement section a fixed magnet (0·1 Tesla) causes hydrogen nuclei of the fluids within the leg to precess at a very precise frequency and an NMR sensor detects the amount of precession. The main NMR signal detected and processed is caused by precession of hydrogen nuclei associated with intravascular water. Because the precession frequency is quite specific, it is possible to tune the detection processor finely to detect optimally the amount of hydrogen precession within the vascular compartment of the leg, which is exposed to the magnetic field.

The detected signal is proportional to the number of precessing hydrogen nuclei and is thus proportional to the amount of vascular water flowing into and out of the measurement section. Non-pulsatile flow (e.g. tissue water, venous flow) produces small contributions ,which are filtered out by the system.

The magnetic resonance technology used by this system is specially designed for the measurement of the volume of blood flowing through a limb cross-section. The flow signal arises from a flow-induced adiabatic tipping of the nuclear magnetization in all of the flows simultaneously in a cross-section, whether in major or minor arteries or collateral pathways. The NMR system's radio frequency (RF) transmitter and RF receiver are both 'on' continuously, so all pulsatile flows in the cross-section contribute to the magnitude of the real-time, continuous pulsatile flow signal induced in the receiver coil. This signal is detected in sidebands of the RF transmitter frequency, which are produced as a result of the presence of a continuous modulating field applied along the direction of the 0·1-T main field. Perfusion information is generated by dividing cross-sectional flow rate by the volume of tissue distal to the cross-section. Being specially designed for the application, the accuracy of the measurement method is not dependent upon the relationship between pixel and vessel sizes, as in conventional pulsed MRI technology.

Calibration to obtain absolute blood flow is done with a pulsatile flow pump, which drives water doped with a paramagnetic solute to simulate the NMR characteristics of blood through a phantom limb. The phantom is composed of simulated vessels, which are positioned within the NMRF measurement region. The pump pulsatile flow is registered using an electromagnetic sensor and a range of calibration flows are used (0–120 ml min^{-1}) to obtain a calibration curve. Calibration is done each day before patient use, and a calibration factor relating actual pulsatile flow to NMR magnitude is automatically determined by the system software. Further technical details and theoretical aspects regarding the NMRF and its applications may be found in the literature (Battocletti, 1986; Kerr *et al*., 1991; Kofler *et al*., 1991; Salles-Cunha & Beebe, 1994; Rice, 1994; Mayrovitz & Larsen, 1996a,b).

LEG EXTERNAL COMPRESSION

Leg compression was produced by wrapping one leg from forefoot to knee with a four-layer bandaging system (Blair *et al*., 1988; Moffat & Dickson, 1993). The compression system chosen for use in this study (Profore; Smith and Nephew) is one of several available commercially designed and used therapeutically for the treatment of venous ulcers. The four layers of the bandage system, referred to as layers 1–4, are applied sequentially to the leg with each subsequent layer overlapping the other. Layer 1 is lightly wrapped and produces no measurable compression; layer 2 secures layer 1 and produces little compression; layers 3 and 4 are the elastic components, which produce roughly equal compression pressures. In all subjects, application of the bandage was

done by the same wound care nurse, who had extensive experience with the use and application of this bandage system.

SEQUENCE

Subjects took a supine position on a moveable table, which is part of the flow measuring system, and the subject remained supine for the duration of the leg evaluation. A pressure sensor was then placed on the medial aspect of the leg 4–5 cm proximal to the malleolus to record sub-bandage pressures using an automated monitoring system (Talley Oxford Pressure Monitor, MKII). Bandage layer 1 was then applied to both legs and baseline precompression leg blood flow measurements (described below) were made bilaterally at each of the five standardized sites. By covering both legs with layer 1 (non-compression) during baseline measurements, the effects of environmental variables (room temperature, draughts, if any, etc.) on skin temperature and, possibly, blood flow between legs were minimized. Thereafter, layers 2, 3 and 4 were applied to one leg only, and bilateral leg blood flow measurements were repeated in both legs. Leg order for these measurements was randomized. The sub-bandage pressure recorded was $40{\cdot}7 \pm 4{\cdot}0$ mmHg, which is near the target level recommended for therapeutic use (40 mmHg).

BLOOD FLOW PROCEDURE AND PARAMETERS

All testing was done in a room with temperature controlled at $22{\cdot}8 \pm 1{\cdot}1$°C. Pulsatile leg blood flow (Q, ml min^{-1}) was measured at five below-knee sites by integrating each pulse waveform over a cardiac cycle and then ensemble averaging for 15–20 beats. The sites were standardized for all subjects by measuring the distance (L) between the lateral malleolus and the tibial tubercle and marking five sites located at 10%, 25%, 50%, 75% and 90% of the malleolus–tubercle distance with the zero reference point at the malleolus. Thus, flow measured at the 90% site represents the approximate pulsatile flow perfusing the lower limb. The flow measurement includes the sum of all pulsatile arterial flow passing peripherally through the leg cross-section within an axial segment 5 cm in length. The blood perfusion at each site (ml min^{-1} 100 cm^{-3}) was calculated by dividing the corresponding measured Q by the leg volume distal to the measurement site. An estimate of leg volume between knee and ankle was made by first calculating the volume of each of the four leg segments between the 90% and 10% sites using a truncated frustrum model with the measured proximal and distal circumferences being the upper and lower boundaries for the calculation. The knee–ankle volume was taken as the sum of these volume segments. Total volume was estimated by adding to this the below-ankle (foot) volume, which was determined by a standardized algorithm within the measuring system based on measured shoe size. This method of below-knee volume determination has been shown to be essentially equivalent to water displacement volumetric methods. The total below-knee blood perfusion (ml min^{-1} 100 cm^{-3}) was

determined by averaging the calculated blood perfusion values obtained at each measured site. An estimate of the relative broadness (width) of the flow pulse at each site was determined by measuring its width at one-half of the flow pulse maximum amplitude and expressing this as a percentage of the cardiac period.

FLOW COMPARISONS

Flow parameters were compared with respect to differences in before-compression bandaging and after-compression values (with compression in place) for the bandaged leg and the control uncompressed leg separately. Also, paired-leg parameter ratios (compressed leg/control leg) were compared with respect to before and after bandaging differences. Non-parametric statistical tests (Wilcoxon) were used with a level of 0·05 taken as statistically significant.

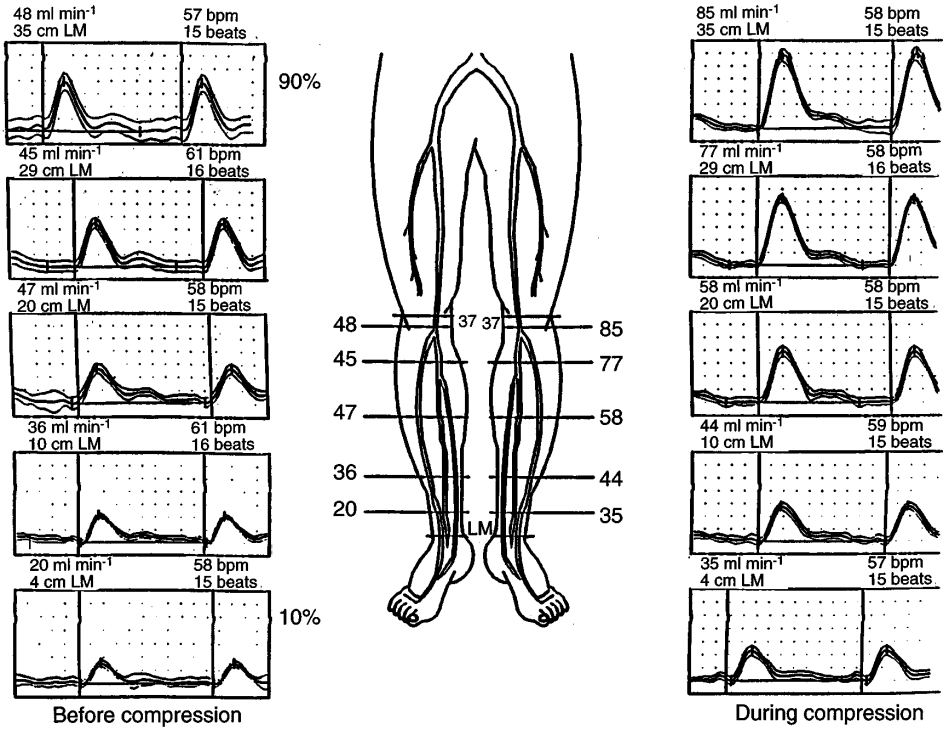

Fig. 1. Pulsatile blood flow before and after leg compression bandaging. Flow waveforms at five below-knee sites in a subject before compression (left) and during compression (right) show an increase in flow pulse amplitude and width at all sites. Flows were measured on the left leg but for clarity of presentation the before-compression flow values and sites are indicated on the right leg and the during compression flows on the left leg of the central anatomical diagram.

Results

A typical response to compression bandaging is illustrated in Fig. 1. Pulsatile flow waveforms at five below-knee sites in a test subject before compression are shown in the left panel and flows at these same sites with all layers of the four-layer compression bandage in place are shown in the right panel. It may be noted that at each site there are three contours of the flow pulse tracing. The upper and lower tracings represent one standard deviation of the ensemble averaged beats and the middle tracing the mean. The central portion of the figure contains a leg diagram with flow values at each of the sites. Although actual flows in this subject (before and during compression) were made on the same leg (left), for clarity of presentation the before-compression flows are shown on the right leg and the flow after compression on the left leg of the central diagram. As may be noted, there was a generalized increase in flow during compression with flow pulse peak and width increased at every measured site. Flows increased without an appreciable change in average heart rate (59 beats min^{-1} before and 58 beats min^{-1} after). The composite data show that flow during compression was significantly greater at all sites except the 10% site, with a tendency for a greater flow differential at the more proximal leg sites (Fig. 2). Flow ratios (bandaged leg/control leg) are also greater (Fig. 3). Because there is ordinarily a flow asymmetry in paired legs, the approximate bounds of normal ratios from 60 normal subjects is also shown by dashed lines (Mayrovitz &

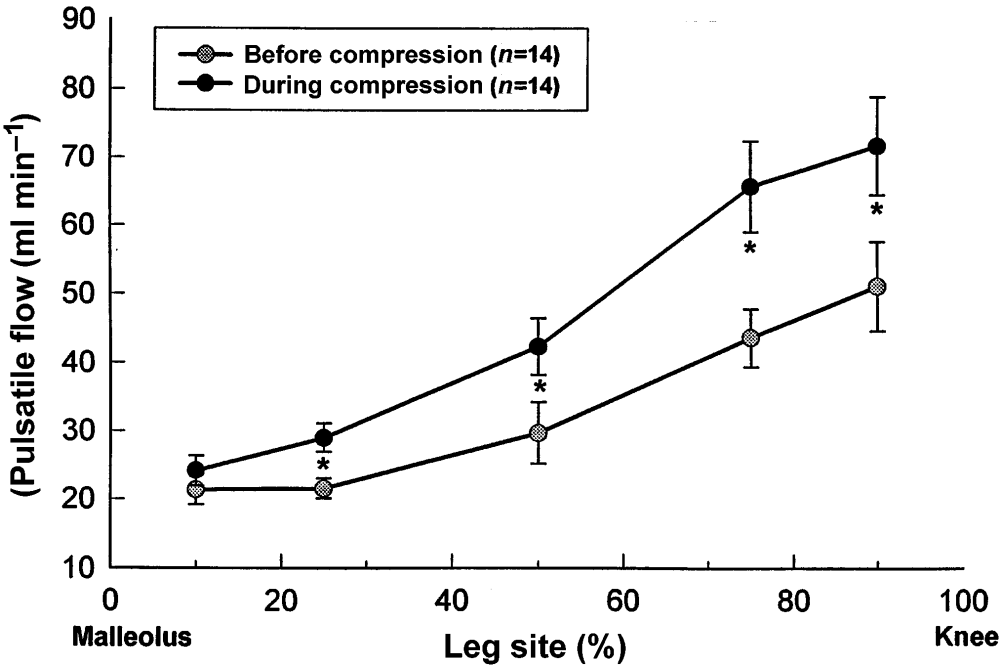

Fig. 2. Compression effect on pulsatile blood flow at each below-knee site. Except for the most distal site, compression produced a significant increase in all measured sites.

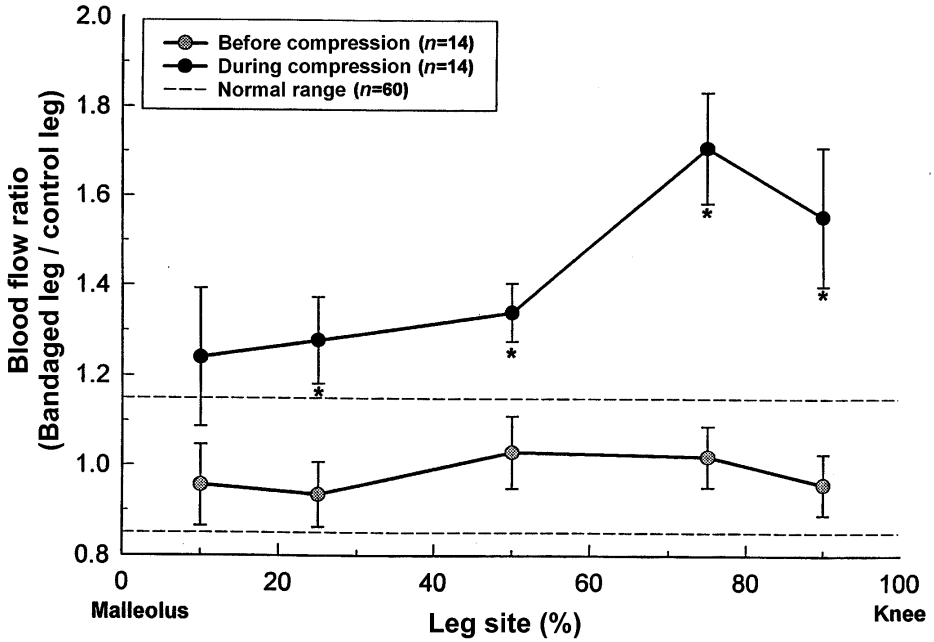

Fig. 3. Effect of compression on the leg flow ratios (bandaged leg/control leg). Before compression, paired-leg flow ratios at each site were in the normal range (horizontal dashed lines). During compression there was a significant increase in this ratio at all but one site.

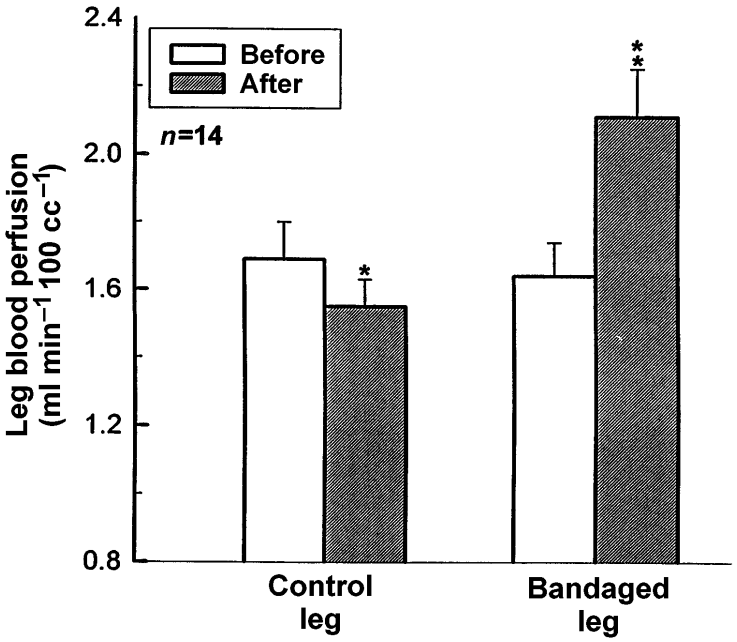

Fig. 4. Effect of compression on below-knee average blood perfusion. A highly significant increase in blood perfusion accompanies the compression bandaging, whereas a slight, but significant, decrease in the control leg perfusion is recorded. (*$P<0{\cdot}05$, **$P<0{\cdot}001$).

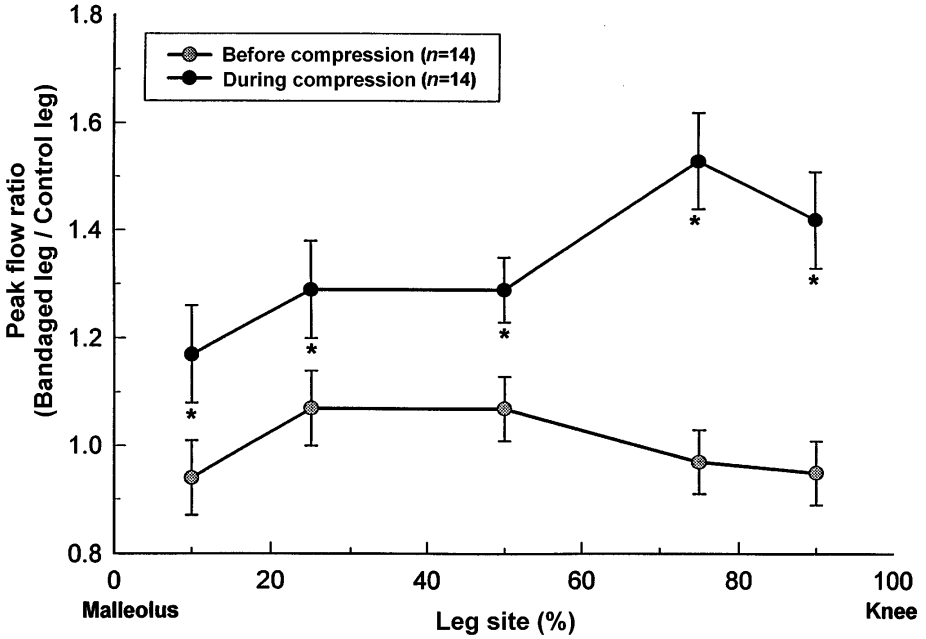

Fig. 5. Changes in peak pulsatile blood flow with compression. Peak blood flow amplitude increased at all sites during compression bandaging.

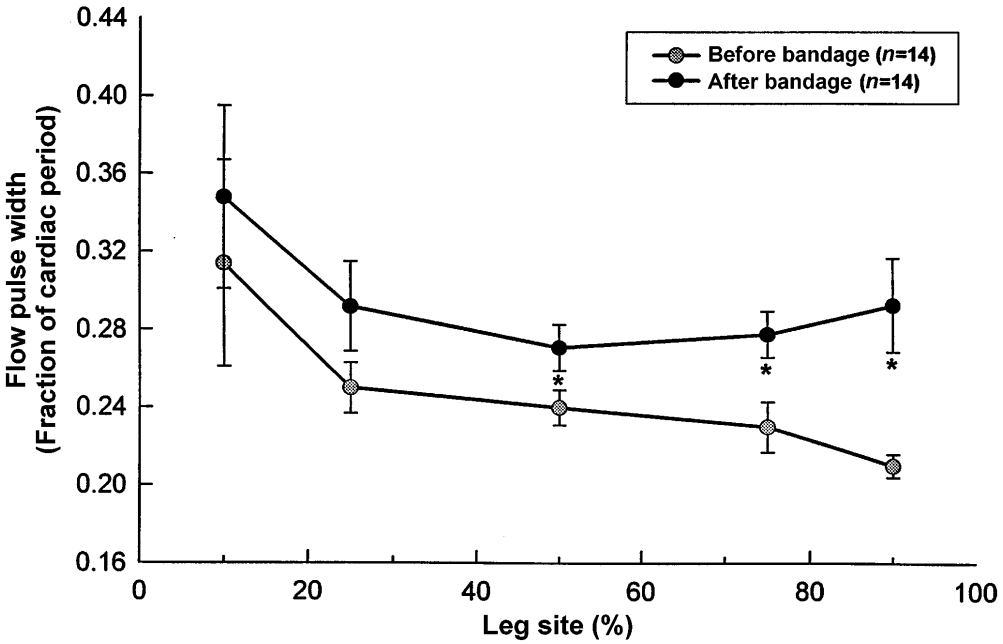

Fig. 6. Changes in flow pulse width accompanying compression bandaging. During compression the flow pulse width is significantly increased at the more proximal sites.

Larsen, 1996b). Before compression bandaging, the paired leg flow ratio falls within the normal range; with compression the bandaged leg/control leg ratio is significantly greater at all but the 10% site. An overall comparison of below-knee arterial pulsatile blood perfusion shows that compression bandaging caused a highly significant ($P<0{\cdot}001$) increase in blood perfusion (Fig. 4); absolute flow increased from $1{\cdot}64\pm0{\cdot}11$–$2{\cdot}11\pm0{\cdot}14$ ml min^{-1} 100 cm^{-3}. In contrast, a net decrease in control leg perfusion was noted; from $1{\cdot}69\pm0{\cdot}11$–$1{\cdot}55\pm0{\cdot}08$ ml min^{-1} 100 cm^{-3}. Expressed as compressed leg/control leg flow perfusion ratios (average of all sites), there was a highly significant increase from $0{\cdot}97\pm0{\cdot}05$–$1{\cdot}34\pm0{\cdot}10$ ($P<0{\cdot}01$). Separate analyses of the flow pulse peak amplitude show that the compressed leg/control leg ratio is significantly increased at all sites (Fig. 5) and the flow pulse width is significantly increased at the more proximal sites (Fig. 6).

Discussion

The present findings demonstrate a significant increase in leg pulsatile blood flow produced by forefoot to knee compression bandaging at pressure levels routinely used therapeutically. To the authors' knowledge, this is the first report of this phenomena. Based on analysis of flow pulse waveform morphology, it is apparent that the flow increase is attributable to increased peak flow and flow pulse broadening. The somewhat surprising finding that static compression consistently increases, rather than decreases, lower extremity pulsatile blood flow raises a number of physiological as well as clinically related questions. From the physiological side, there is the question of operative mechanisms and a prime clinical question is whether and how such pulsatile flow augmentation impacts on the treatment outcome of the underlying ailment.

POSSIBLE FLOW-AUGMENTATION MECHANISM

Because the measured flow waveform is dependent on multiple and complex interactive factors, the details of which were not intrinsically incorporated for study in the present series, it is not yet possible to state the specifics of the underlying mechanisms responsible for the flow increase. However, one may offer a hypothesis that is consistent with the present findings. As a prelude, it is to be noted that the flow pulse waveform at any leg cross-section depends on the summation of forward and reflected flow waves within the set of arterial vessels at the cross-section. Pulsatile flow in one of these arteries as measured by Doppler ultrasound in vascularly normal legs would generally yield triphasic flow patterns. This normal pattern is caused by an initial flow increase associated with the forwardly transmitted wave followed by the effects of reflected and possibly re-reflected waves (Strandness & Sumner, 1975; Westerhof & O'Rourke, 1995.). Under normal conditions, the leg distal vasculature presents a vascular resistance to the forward moving wave, which is high compared with the characteristic impedance of the artery (McDonald, 1974). This impedance mismatch produces a reflected flow wave nearly 180° out of phase with the incident wave, which destructively interferes with the forward wave

producing a negatively going flow component. When the distal arteriolar vasculature dilates, either as a physiological response to leg exercise or as a result of pathological conditions, such as proximal arterial disease, the reflected flow wave is significantly reduced in magnitude and altered in phase because of the reduced terminal impedance. The net effect on the measured composite flow wave pattern is to diminish or eliminate the reflected negative going component and cause waveform broadening. Arteriolar vasodilation is thus accompanied by both an increase in flow pulse peak and width. Since this pattern has been observed as a result of compression bandaging in every subject tested, it is plausible that an arteriolar vasodilation may be involved. Based on known vascular control features, one may offer two possibilities to account for this response: reduced arteriolar transmural pressure concomitant with external compression, and compression-related effects on the venous system.

Because of the small size and thick-walled structure of arterioles, compression levels as used herein will probably not reduce arteriolar lumen, as would occur in the venous system. And, whereas limb exposure to subatmospheric pressures produce an increase in transmural pressure (Cole *et al*., 1956), the increase in extravascular tissue pressure associated with external compression reduces the arteriolar transmural pressure by an amount roughly equal to the compression pressure level. In experimental models, it is well established that an increase in arteriolar transmural pressure is a stimulus for vasoconstriction and a decrease in transmural pressure is associated with arteriolar vasodilation (Bayliss, 1902; Folkow, 1962). Thus, the compression-related transmural pressure reduction may set the stage for an adaptive myogenic vasodilatory response (Mellander *et al*., 1964; Henriksen, 1976; Nielsen, 1983). Further experimental evidence for this occurring locally in humans at external pressures between 10 and 30 mmHg has also been reported (Caro *et al*., 1970; Holloway *et al*., 1976;), and older reports describe therapeutic intermittent limb compression as a method of increasing arterial flow (Collens & Wilensky, 1937). More recent measurements of popliteal blood flow before and after intermittent calf compression also demonstrate a flow augmentation (Van Bemmelen *et al.*, 1994), and a biphasic response to compression has been described (Walker *et al*., 1967). The recent finding of an increase in skin blood perfusion produced by regional leg compression in both normal subjects and patients with chronic venous insufficiency (Abu-Own *et al*., 1994) are consistent with the hypothesized mechanism. Such compression effects apparently occur without changes in either the size or the number of capillaries (Burki & Guz, 1970), thereby further suggesting an arteriolar-related phenomena.

An additional possibility, which might account for the arteriolar vasodilation, is associated with venous factors. Previous work has shown that leg compression was associated with an increase in the linear flow velocity in deep veins of the lower extremity when legs were subjected to compression pressures (Stanton *et al*., 1949; Meyerowitz & Nelson, 1964; Lawrence & Kakkar, 1980), and, more recently, in both the popliteal and common femoral veins at pressure levels between 40 and 50 mmHg (Mayberry *et al*., 1991). The increased endothelial shear stress associated with such velocity increases may

elicit the release of vasodilatory substances (Falcone & Bohlen, 1990), which subsequently impact on the arteriolar vasculature (Boegehold, 1996). Further evidence for such venous–arteriolar linkages has recently been described (Saito *et al*., 1993, 1994), as well as the impact of pulsatile flow amplitude on endothelium-derived relaxing factor (EDRF) release from endothelial cells (Hutcheson & Griffith, 1991).

The impact of such arteriolar dilation, whether owing to myogenic or venous factors, on the measured flow pulse wave would be expected to result in an increase in the peak flow associated primarily with the forwardly transmitted flow pulse into a distal region of lowered vascular resistance and a reduction in the negative reflected wave as a result of the decreased terminal impedance, thereby resulting in a broadened flow pulse. An additional factor, which cannot be discounted, is that the reduced transmural pressure causes an increase in the dynamic compliance of the arteries, thereby altering pulse wave velocity and/or local pulsatile phenomena.

POTENTIAL IMPACT ON VENOUS ULCERS

Preliminary work (Mayrovitz & Delgado, 1996) with compression bandaging of the same type as described here, but applied to patients with unilateral venous ulcers, has so far shown results paralleling those reported here for healthy limbs. The question as to the role, if any, of arterial pulsatile blood flow increase in the venous ulcer healing process is clearly unknown and speculative, but it is possible to offer a tentative hypothesis. One of the theories regarding the aetiological process whereby venous pathology and chronic venous hypertension leads to skin ulceration is related to microvascular compromise, in part secondary to capillary flow disturbances associated with leucocyte effects in skin capillaries and venules (Smith *et al*., 1988; Thomas *et al*., 1988). Transient leucocyte adherence in normal skin venules and associated short periods of flow stasis in capillaries as a result of leucocyte plugging (Mayrovitz, 1992) have been observed directly. However, there is controversy as to whether the impact of leucocytes on venous ulcer initiation and maintenance is related to plugging or cell activation following entrapment within the microvasculature (Wilkenson *et al*., 1993; Pappas *et al*., 1995). In venous ulcer patients, these events would need to be occurring even in the presence of an elevated arterial pulsatile flow in the vicinity of the venous ulcer (Mayrovitz & Larsen, 1994a), and an elevated peri-ulcer skin blood perfusion (Mayrovitz & Larsen, 1994b). It is well established that the adherence of leucocytes within the microvasculature is dependent on local haemodynamic forces. Thus, the combined effect of compression-related arteriolar vasodilation (hypothesized) and significantly increased pulsatile blood flow (demonstrated) may tend to minimize, partially clear, or reverse such white blood cell capillary-plugging effects, thereby offsetting the negative impact on venous ulcer healing. Although speculative, this hypothesis provides a self-consistent and testable explanation for a possible arterial linkage to venous ulcer healing. Clearly, further experimental work will be required to test these concepts and clarify further the mechanism of the newly discovered pulsatile blood flow augmentation.

In summary, lower extremity forefoot-to-knee compression bandaging of the type and level used here results in an increase in leg pulsatile blood flow as a consequence of increases in both peak flow and pulse width. The mechanism for this is hypothesized to be arteriolar vasodilation caused by either or both a myogenic arteriolar response or a shear-dependent venous effect. The impact of the arterial flow pulse increase is speculated possibly to impact on venous ulcer outcome via a diminution of capillary-leucocyte adherence duration and/or partial clearance of leucocytes entrapped within the microvasculature.

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