

Effect of percutaneous electrical stimulation of the sole upon lower limb blood pooling induced by protracted sitting in man

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Keywords:

Venous Pooling; Electrical Stimulation; Sole; Doppler Ultrasound; Pressor response

Introduction

Venous pooling

In tall or upright animals such as man, large hydrostatic forces exist within the venous and arterial vasculature. Pooling is induced by an increase in hydrostatic pressure (the gravitational force exerted by the column of blood between the heart and the foot) reduces blood volume within the central circulation and thereby increases the work of the heart (increased heart rate) in an attempt to maintain cardiac output.

Venous pooling within the lower limbs is all too common in individuals with impaired mobility although even those without defined pathology may experience pooling during prolonged upright standing or sitting. Furthermore, pooling within the periphery if protracted can lead to swelling (oedema) due to extremities leads to increased transcapillary filtration into the interstitial space. In fact, during prolonged standing about 600ml of blood collects within the legs. Concomitantly, the reabsorption of interstitial fluid is reduced resulting in increase extravascular fluid volume (Stick, Grau & Witzleb, 1989).

These processes can in turn induce severe discomfort or pain that may impair mobility further. In addition, protracted immobility can lead to the development of deep vein

thrombosis (DVT), particularly in the lower limb. Intravascular thrombus formation in addition to stasis has been related to primary lesions of endothelial cells, and changes of blood coagulability with risk factors including physical inactivity, occupation, work posture, and long-distance flight (economy class syndrome)(Breddin, 1989). DVT is also associated with swelling, reddening and pain that may be precipitated or exacerbated by standing or walking and may result in endothelial lesions. The most serious (and rare) complication of DVT is pulmonary embolism.

Reduction or retardation of limb pooling may occur via the induction of venous outflow from the periphery and into the central circulation. This has been demonstrated via lower limb muscular contraction and in particular the Soleus and Gastrocnemius complex of the calf that forces blood from the vasculature tethered to the muscle fibres. Such a mechanism is termed the 'muscle pump' and may be mediated via normal locomotion or a voluntary contraction. Furthermore, it has been proposed that 'fidgeting' is in fact an involuntary behaviour whose function may include activation of the muscle pump.

In healthy individuals the muscle pump is considered to play a role in the maintenance of central blood volume during rapid postural changes i.e. getting out of a chair or bed and standing up preventing loss of blood flow to the brain. Furthermore, if individuals stand still for extended periods of time they may experience reduced venous return to the heart and low blood pressure (hypotension) leading to dizziness or fainting (syncope).

The muscle pump increases muscle perfusion pressure (i.e. the arterio-venous pressure difference) via reducing venous hydrostatic pressure, whereas arterial pressure remains over 50mmHg greater than that at heart level. For the muscle pump to be effective in promoting venous return it is considered necessary that any contraction must be of moderate intensity (>20% of a maximal voluntary contraction), brief as the contraction will occlude additional venous flow. Thus, contractions should also be repetitive (preferably rhythmical) for prolongation of effects. It has been claimed that the muscle pump can lead to move about 3–5% of total blood volume (5ml/kg) which for a 75 kg human is 400 mL. The muscle pump is even operational in elevated limbs suggesting that calf veins still contain significant blood volume.

Following each contraction the veins remain empty and valves prevent backflow rendering muscle venous pressure close to (or below) zero. Negative intravenous draws blood through the microcirculation from the arterial side resulting in a large and rapid rise in conductance. Hence, it is a potent blood volume redistribution mechanism. By increasing venous flow through the one-way valves from the musculature can evoke transient increments in venous return delivered to the right-side of the heart.

Forceful calf contractions can significantly reduce calf volume (measured as calf circumference). Redistribution of blood volume appears to occur during relatively weak contractions and thus are not associated with the generation of a pressor response i.e. elevation of blood pressure and heart rate acceleration. How actual induced venous flow relates to such contractions remains unclear.

Involuntary electrical stimulation

Muscular contraction may be evoked involuntarily via magnetic stimulation of the motor cortex. However, more practically percutaneous electrical stimulation can be delivered to the nerve innervating the muscle, the muscle itself, or as recently suggested the sole of the foot in the case of the calf. Percutaneous electrical stimulation provides an opportunity to evoke muscle pump-like effects in a manner that is controllable and reproducible. However, the requirement of electrodes and trailing wires can be, particularly in those not technologically proficient, impractical and troubling, leading to non-adherence. Furthermore, it is imperative that such a system is effective without evoking pressor reflex responses and not being painful.

Hence, investigation into whether non-painful percutaneous electrical stimulation of the sole via placing the feet upon a stimulation footplate can reduce induced lower limb swelling may provide insight into a novel and convenient mechanism of pooling amelioration, without the requirement for repetitive voluntary muscular activation. A previous study demonstrated that foot and calf stimulation evoked augmentation of popliteal and femoral blood flow thereby reducing venous pooling (Kaplan et al., 2002) although issues of tolerability exist. In addition via the application of continuous wave Doppler ultrasound to the femoral vein we seek to investigate the relationship between evoked venous flow and the magnitude of swelling amelioration.

Aim

Thus, the aim of this study was to investigate whether: i). non-painful ($\approx 50\%$ pain threshold) percutaneous electrical stimulation of the sole of the foot delivered via a footplate can reduce lower limb swelling induced by sitting quietly for a period of 40 mins: ii). if any effects are independent of pressor reflex responses: iii). and if pooling reduction relates to evoked femoral vein blood flow velocity and/or subjective swelling and associated discomfort.

Methods

Eighteen (12 ♂; mean age 33 ± 8 yrs; height 175 ± 9 cm; weight 72 ± 16 kg) healthy (according to validated health questionnaire responses) naïve volunteers gave written, informed consent to participate in the study, which received local ethical committee approval.

Procedure

All subjects were required to sit in a chair (that formed part of the Perometer™) and resting recordings (see below) were obtained over a period of 5 mins (PRE). Then subjects were instructed to remain as still as possible for 40 mins (STASIS) whilst remaining in the chair with minimal talking to minimise thoracic pump effects on venous return. Following this period electrical percutaneous stimulation of the soles of both feet was performed for 10 mins (STIM)(Fig. 1). Sole stimulation required subjects to place

their bare feet onto the percutaneous electrical stimulator (Circulation Booster™) footplate. Stimulation provoked observable ankle dorsi- and plantar-flexion as a result of evoked calf contraction in addition to variable contraction of the intrinsic muscles of the feet.

Prior to the main protocol assessment of the subjects' pain threshold (PT) was performed via a repeated ramp procedure. Hence, the stimulator intensity was set to provide stimulation at 50% PT during STIM. Furthermore, subjects were required to perform a maximal right leg (irrespective of limb dominance) plantar-flexion manoeuvre on an isometric calf rig (with a force transducer in line with the vertical force). This procedure was repeated until the experimenters were satisfied that a maximal voluntary contraction (MVC) was achieved. Then subjects were required to generate a contraction equal to 10% of the MVC (visually guided) at which time right common femoral venous peak blood flow velocity via Doppler ultrasound (Sonosite 180 Plus portable handheld system) was recorded. The probe was placed in the upper groin region (approx. 1cm below the inguinal ligament) whilst the angle of insonation was maintained at 60°.

Right common femoral venous peak blood flow was also recorded with the subjects sat in the final minute of PRE, and during the final minute of STASIS and STIM. Right limb volume was obtained by horizontal placement of the limb with the foot on a holding plate using a Perometer™ (based on an optical LED array system) prior to sitting still (PRE), and immediately following STASIS, and STIM. Knee angle was maintained in the relaxed fully extended position in order to ameliorate the effect of angle upon Perometer™ recordings (Man et al, 2003a). Voluntary activation of either lower limb was not permitted at any time and the experimenters moved the limbs on behalf of the subjects so that the legs remained passive.

R-R interval (ms; standard 3 lead ECG) and digital artery blood pressure (MBP; mmHg) via a pressure cuff placed on the middle finger of the left hand (Finapres™) were recorded throughout. Subjective verbal ratings of swelling and associated discomfort were requested immediately following STASIS and STIM conditions. Furthermore, verbal assessment of stimulation intensity was performed each minute of STIM.

Data Recording & Analysis:

Heart rate, (1Khz), blood pressure (200Hz) and venous blood velocity (1Khz) signals were recorded using a CED 1401 (ADC), stored on a PC computer and analysed using Spike2 software. The Perometer™ was used to calculate volumes equating to the right foot, ankle, sub calf and calf. Mean R-R interval, mean blood pressure, femoral venous peak blood velocity and limb volumes were compared between PRE, STASIS and STIM. Analogous responses were observed for diastolic and systolic blood pressures, therefore only MBP is described. Furthermore, comparisons between the change (Δ) from PRE during STASIS and STIM were performed in order to correlate the magnitude of induced change with verbal ratings. Δ values are expressed as a % difference and for STASIS and STIM as a compound rate of change to facilitate interpretation.

Verbal ratings of lower limb swelling (0 = No swelling; 10 = Maximal tolerable) and discomfort/pain (0 = No sensation; 10 = Pain threshold) were recorded manually and compared immediately after STASIS and STIM. Stimulation intensity associated with the electrical stimulation was also assessed on a 0-10 scale (0 = No sensation; 10 = Pain threshold).

Students paired *t*-tests were performed upon autonomic and volume data between conditions and the calculated Δ responses having established data normality. The Wilcoxon signed rank test was used to test whether verbal ratings of limb swelling and discomfort differed between STASIS and STIM. Non-parameter correlation (Spearman's rho) between changes in volume, and subjective ratings were conducted to investigate the relationship between physiological and psychological responses to swelling. All statistical analyses were carried out with the SPSS v12.

Results

Limb Volume

Statistically significant swelling (cm^3) was evoked at the foot (378 ± 33 vs. 407 ± 40 ; $p = 0.006$), ankle (323 ± 38 vs. 333 ± 38 ; $p = 0.001$), sub calf (1690 ± 197 vs. 1752 ± 201 ; $p = 0.030$), and the calf itself (1323 ± 169 vs. 1338 ± 174 ; $p = 0.031$) by 40 mins quiet sitting (PRE vs. STASIS). Significant swelling was not induced at the knee (1208 ± 131 vs. 1207 ± 112 ; $p = 0.086$) or above. Significant pooling corresponded to an increase of volume of 6.7 ± 1.4 , 3.6 ± 1.0 , 4.2 ± 1.4 and 0.9 ± 0.5 % of the foot, ankle, sub calf and calf respectively. Therefore, the rate of pooling in each section was 0.158 ± 0.034 , 0.087 ± 0.023 , 0.100 ± 0.032 , and 0.023 ± 0.012 mL per min^{-1} respectively.

Following 10 minutes of sole stimulation (STIM) there was no difference vs. PRE at the foot (378 ± 33 vs. 390 ± 35 ; $p = 0.088$), sub calf (1690 ± 197 vs. 1712 ± 198 ; $p = 0.087$) and calf (1323 ± 169 vs. 1330 ± 172 ; $p = 0.142$) (PRE vs. STIM). Limited albeit significant pooling persisted at the ankle (323 ± 38 vs. 327 ± 39 ; $p = 0.044$). Remaining pooling corresponded to an increase of volume of 2.6 ± 1.3 , 1.0 ± 0.5 , 1.5 ± 0.6 and 0.4 ± 0.3 % respectively. Therefore, the rate of pooling amelioration in each section was 0.096 ± 0.027 , 0.063 ± 0.021 , 0.063 ± 0.030 , and 0.013 ± 0.008 mL per min^{-1} respectively.

Hence, the difference (Δ) in volume vs. PRE during STASIS and at the end of STIM was significantly smaller at the foot ($p = 0.015$) and ankle ($p = 0.008$) although the effect was weaker at the calf ($p = 0.049$) and not present at the lower calf, in due to profound inter-subject variability ($p = 0.117$)(Fig. 2.).

Femoral Venous Peak Velocity

Peak venous velocity (cm/s) evoked by a 10% MVC (52.9 ± 4.3 ; $p = 0.000$) and STIM (32.0 ± 5.0 ; $p = 0.000$) were both significantly greater than PRE (7.0 ± 0.6). However, the peak venous velocity difference (Δ) between PRE and 10% MVC was significantly greater than STIM ($p = 0.001$)(Fig. 3.).

Subjective Swelling & Discomfort

Following STASIS subjects reported swelling (PRE = 0; $p = 0.000$) and associated discomfort (PRE = 0; $p = 0.000$) were significantly greater than PRE. Subjective rating of swelling magnitude was significantly reduced following STIM ($p = 0.013$). A similar significant reduction in discomfort related to swelling was observed from STASIS to STIM ($p = 0.024$)(Fig. 4.).

Stimulation Intensity

Assessment of subject's pain threshold yielded a mean stimulator setting of 25.3 ± 1.9 . Mean reported stimulation (STIM) intensity was 5.1 ± 0.3 or 51% of the pain threshold.

Autonomic Responses

MBP (at the finger) was unchanged during STASIS vs. PRE ($p = 0.696$)(Fig. 5.) whilst there was a significant increase in MBP during STIM vs. PRE ($p = 0.000$) and STASIS ($p = 0.000$). R-R interval was slightly lengthened (i.e. heart rate slowing) during STASIS vs. PRE ($p = 0.179$), whilst surprisingly, there was a lengthening of R-R interval during STIM vs. PRE ($p = 0.087$) albeit again non-significant. The R-R interval lengthening evoked during STASIS and STIM were analogous ($p = 0.571$).

Correlations

Ratings of swelling correlated with Δ calf volume ($\rho = 0.512$; $p = 0.030$) and associated sensation ratings ($\rho = 0.612$; $p = 0.007$) during STASIS. In addition, STASIS sensation ratings correlated with Δ foot volume during STASIS ($\rho = 0.651$; $p = 0.003$). Ratings of swelling continued to correlate with associated sensation ratings ($\rho = 0.639$; $p = 0.004$) during STIM. Furthermore, the Δ swelling and sensation ratings between STASIS and STIM correlated ($\rho = 0.508$; $p = 0.031$). However, the Δ ratings did not correlate with the reduction in swelling observed during STIM.

Discussion

Evoked venous pooling

This study demonstrates that 40 mins of sitting without voluntary calf activation was sufficient to evoke statistically significant swelling as measured by the perometerTM from the level of the foot to the calf. Whilst the magnitude of swelling within these different anatomical compartments varied, overall the swelling was consistent with the lower limb pooling literature induced by a combination of gravity and inactivity. In fact, whilst the mean volume change of the foot and ankle combined was slightly smaller than in response to 30 mins of quiescent standing, the variability is less (Man et al, 2003b), rendering the test more reproducible. This finding in all likelihood relates to the fact that the hydrostatic difference, and therefore actual tendency to pool was weaker in the

current study but it was much more difficult, if not impossible to not to generate muscle contractions whilst stood. In fact, within the Man and co-workers (2003b) study some individuals demonstrated pre-syncope signs, which may have reflected that particular subjects adherence to the protocol i.e. producing very little muscular contraction. Hence, the ability (or willingness) to stand perfectly still provides the opportunity for significant variation.

Thus, our pooling model of 40 mins quiet sitting is valid and consistent with recommendations that, where possible, treatment and assessment of lower leg swelling should be undertaken with the leg in a non-dependent position i.e. sitting or lying supine, and not standing (Man et al, 2004b). In fact, the inherent tendency of an individual to evoke muscle contraction (fidget and or dynamic balance control) and/or the efficacy of such contractions may in part relate to their relative orthostatic tolerance. Such a relationship however is difficult to test as in the lab orthostatic tolerance (tilt) tests have relatively weak predictive power (Lamarre-Cliche & Cusson, 2001).

The current study required 40 rather than 30 mins of inactivity used elsewhere (Man et al, 2003b) and so this may have contributed to the degree of pooling. However, the actual time course of pooling remains unknown and may have in fact plateaued prior to 40 mins. We calculated a compound pooling rate similar to Stick et al., (1989) which assumes a linear (similar to compound interest) pooling accumulation and subsequent amelioration via electrical stimulation. Significant swelling was not induced at the knee. Whilst the 'gold standard' method of water volumetry was not utilised in the study the perometerTM is sufficiently sensitive to observe any evoked changes, although the methods are not interchangeable (Man et al, 2004a). Water volumetry however has a serious limitation of not permitting compartmentalisation of the limb.

Venous pooling following stimulation

Periodic electrical stimulation-induced calf muscle contractions has been demonstrated to lead to significant muscle pump-like effects i.e. improved venous circulation and reduction of blood stasis (Faghri et al., 1997, 1998) albeit not as effective as voluntary activity e.g. toe raise exercises (Christopoulos et al., 1989).

Following 10 minutes of electrical percutaneous stimulation of the soles there was no significant pooling remaining at the level of the foot, sub calf and calf itself. Thus, percutaneous sole stimulation was effective in ameliorating pooling induced by prolonged quiet sitting. Amelioration of pooling however was incomplete with the stimulation being effective to the degree of 62% at the foot, 64% at the sub calf and 54% at the calf. Surprisingly, a reduction of 66% pooling at the ankle was insufficient to obtain significance over the period of 10 mins again pointing to differences between compartments. Longer duration or greater intensity of stimulation may be more effective although the rhythmical nature of evoked contraction in our study bears great similarities with cycling, albeit with a lower muscle mass (Stick, Grau & Witzleb, 1989). Such amelioration was found to be intensity dependent (50 vs. 100W) with the greater workload, and hence contraction intensity being most effective (Stick, Grau & Witzleb, 1989). In this case decremented venous pressure may have reduced the effective filtration

pressure, increased lymph flow thereby removing fluid and osmotically active colloid proteins from the interstitial space or increase in muscle tissue pressure that may counteract intravascular pressure during contraction (Stick, Grau & Witzleb, 1989).

Whilst the stimulation was effective, the mechanism(s) of action is unknown. Possible mechanisms include those proposed by Man and co-workers by “increasing venous return, reducing venous stasis, increasing lymph flow, and increasing interstitial hydrostatic pressure, which would reduce capillary filtration and assist fluid reabsorption” (Man et al, 2003a).

Femoral Venous Peak Velocity

Peak venous velocity recorded within the femoral vein evoked by the stimulation was greater than at rest, but represented $\approx 54.6\%$ of a 10% MVC. Whilst, this suggests that the muscular contraction evoked by the stimulation was weaker than a 10% MVC (approx 5% MVC) this may not be the case. Unfortunately the force generated during stimulation could not be recorded with the rig due to the size of the stimulator and EMG acquisition during stimulation was impossible due to a substantial stimulus artifact. Thus, the relationship between evoked peak venous velocity and the strength of muscular contraction evoked voluntarily or electrically is unclear. Rather than evoking a contraction $< 10\%$ MVC it may be that the efficacy of evoking venous flow may be inferior to a voluntary contraction. Furthermore, it is plausible that the peak venous velocity recorded closer to the calf i.e. the popliteal vein formed by the joining of the posterior tibial vein and anterior tibial veins within the popliteal fossa may yield greater increments. However surprisingly, during similar stimulation greater blood flow augmentation was evoked in the femoral vs. popliteal vein (Kaplan et al., 2002).

Subjective Swelling & Discomfort

The development of swelling was associated with the subjective sensations of swelling and associated discomfort. Both symptoms were significantly reduced following stimulation thereby demonstrating stimulator effectiveness on a perceptual/subjective level. Such effects may be of greater benefit to the individuals than actual swelling reduction, particularly in those whom are unlikely to regain mobility. For instance, functional electrical stimulation with spinal cord-injured individuals may prevent orthostatic hypotension and circulatory hypokinesia during standing and tilting (Faghri & Yount, 2002).

Stimulation Intensity

Stimulation presentation over a 10 min period was reported to be equivalent to 51% of the pain threshold. Thus, stimulation was easily tolerable over protracted periods of time suggestive that greater stimulation intensities could be presented that may prove more effective at amelioration of pooling. It was noted that whilst stimulation provoked observable but easily tolerable ankle dorsi- and plantar-flexion, concurrent intrinsic foot muscle activation was on some occasions demonstrated. Such contraction was not painful

and ratings were substantially lower than 'not uncomfortable' as used by Kaplan and co-workers (Kaplan et al., 2002). The exact nature of intrinsic foot muscle activation varied and may be dependent upon exact foot placement and/or contact with the footplate.

Autonomic Responses

MBP remained unchanged during STASIS and hence the 'loss' of the muscle pump did not compromise systemic arterial blood pressure. The significant increase of MBP during STIM vs. PRE and STASIS demonstrates additional pressure generation evoked by the stimulation over and above the endogenous muscle pump. R-R interval was slightly lengthened during STASIS vs. PRE presumably due to the extreme relaxation involved in staying perfectly still. This also suggests that cardiac output was not compromised by the extent of venous pooling precipitated. Surprisingly, there was a tendency for lengthening of R-R interval during STIM albeit non-significant. These findings demonstrate that overt stimulation of the pressor reflex was not evoked. The slight R-R interval lengthening evoked during STASIS and STIM were similar, supportive of the fact that stimulation was not distressing and therefore tolerable.

Correlations

Subjective ratings of swelling correlated with actual calf volume and associated sensation ratings during both STASIS and STIM. In addition, sensation ratings correlated with foot volume but no other limb compartment. This data suggests a close relationship between the perceived magnitude of swelling and the perceived discomfort, which is perhaps unsurprising. What is more surprising is the lack of correlation between subjective and anatomical assessment of swelling. However, there was no significant relationship between ankle-foot swelling and self-assessed ankle function in the early period after ankle sprain injury (Man & Morrissey, 2007). Furthermore, the effectiveness of stimulation appears to depend upon a certain magnitude of stasis as following ankle strain (minor injury; without total immobilisation stimulation has no effect (Man et al, 2007). Thus, further work with clinical models is required to ascertain whether stimulation is as effective in these particular individuals. It may be that subjective assessment of swelling and its physical manifestation are poorly associated both in health and pathology.

Furthermore, the reduction of swelling and sensation ratings resulting from stimulation correlated suggesting that the perceptual benefits of stimulation relate to severity of swelling prior to treatment. As such individuals with the greatest discomfort stand to obtain the most relief. However, the subjective ratings failed to correlate with the magnitude of swelling reduction, stimulation intensity, or peak venous velocity observed during stimulation. The latter finding suggests that the mechanism of swelling amelioration evoked by stimulation is complex and may not dependent upon increasing peak venous velocity but rather mean venous flow.

The failure to relate the symptoms of swelling and the actual magnitude of swelling reflects profound inter-subject variability. Our cohort of young, healthy volunteers were not accustomed to swelling and may have augmented subjective responses to what was

only moderate swelling. Such responses may or may not be present during pathological states where swelling is a chronic issue in pathology, the elderly, those at risk of DVT and/or excessive adopters of a sedentary lifestyle. It may be that in these individuals even greater benefits may be attained from percutaneous stimulation of the sole.

Conclusion

In conclusion, our study extends the Kaplan study demonstrates that non-painful percutaneous stimulation of the sole is a potent ameliorator of pooling induced by our model of immobility in the young and healthy (Kaplan et al., 2002). As such provides a method of pooling amelioration in addition to physical devices such as passive exercises (27), intermittent pneumatic compression (IPC) (Flam et al., 1996), and compression hosiery (Badger et al., 2000).

Whilst the exact mechanism remains to be determined overt pressor reflexes were not elicited by the stimulation whilst evoked peak (rather than mean) femoral vein blood flow velocity is an inadequate index of swelling amelioration. Finally, whilst subjective swelling and discomfort are strongly linked and are greatly improved via sole stimulation they possess weak relationships with actual swelling magnitude.

Acknowledgements

The authors wish to thank sincerely Dr. Matt Morrissey for the use of the perometer, Dr. Katya Mileva for advice in the analysis of the Doppler ultrasound signals and Ms Lindsey Marjoram for her technical assistance.

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Figures & Legends

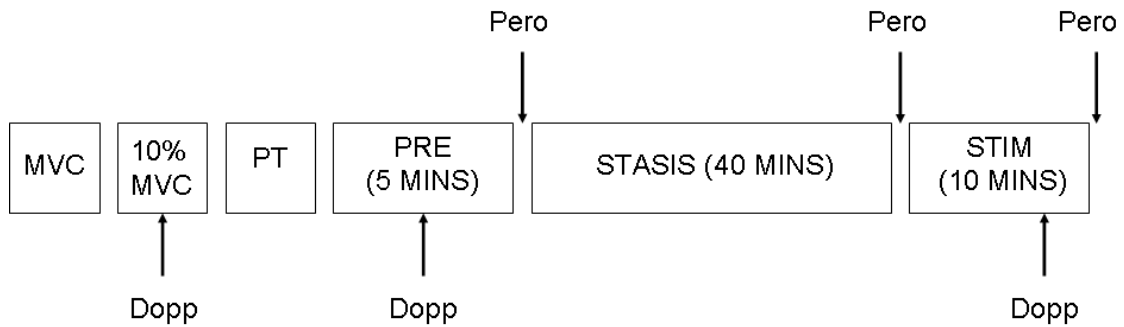


Figure. 1. Experimental Protocol. MVC = Maximum Voluntary Contraction; PT = Pain Threshold assessment; PRE = Normal sitting; STASIS = Sitting without contraction; STIM = 50% PT percutaneous electrical stimulation; Dopp = Right Femoral vein (peak) velocity recording; Pero = Right limb volume recording with Perometer™.

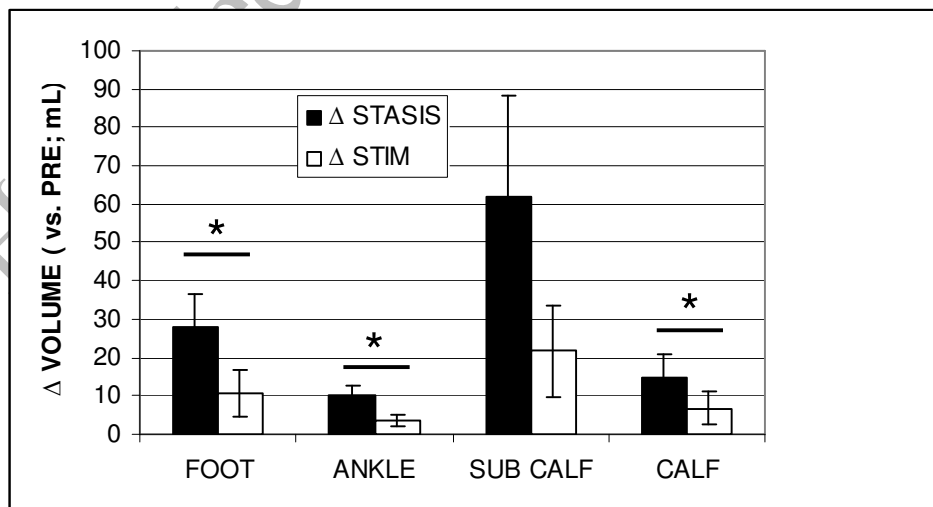


Figure 2. Mean \pm SEM change (Δ) of volume (mL) vs. PRE immediately following 40 mins of sitting (STASIS) and then 10 mins of sole stimulation (STIM). * Indicates a significant difference between conditions ($p < 0.05$).

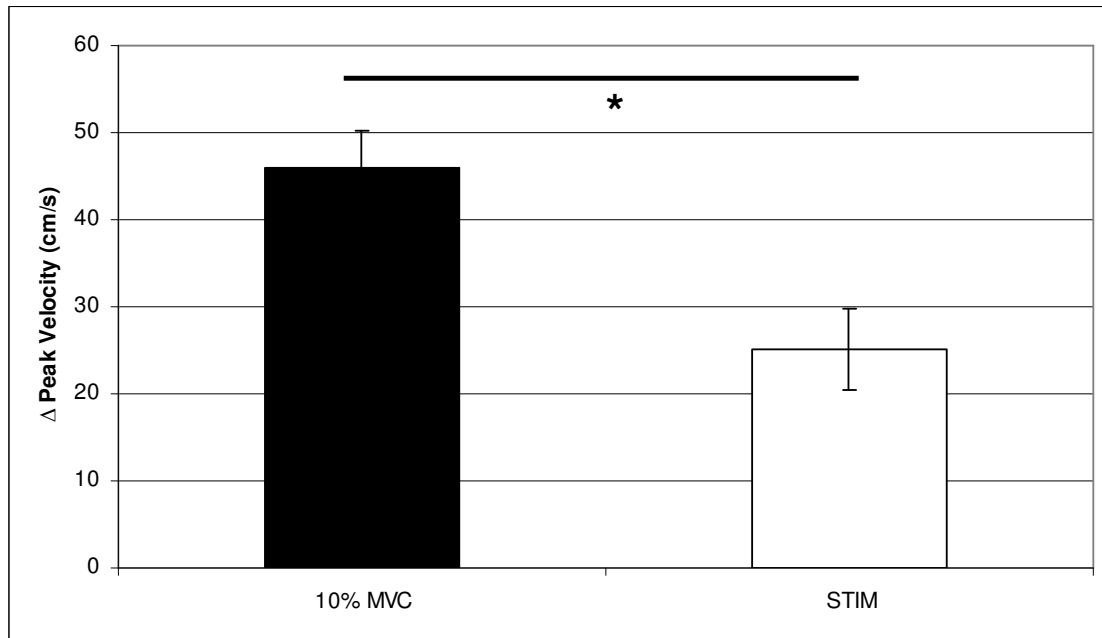


Figure 3. Mean \pm SEM change (Δ) of femoral venous peak velocity (cm/s) vs. PRE during performance of a 10% maximal voluntary contraction (10% MVC) and during minute 7 of sole stimulation (STIM). * Indicates a significant difference between conditions ($p < 0.05$).

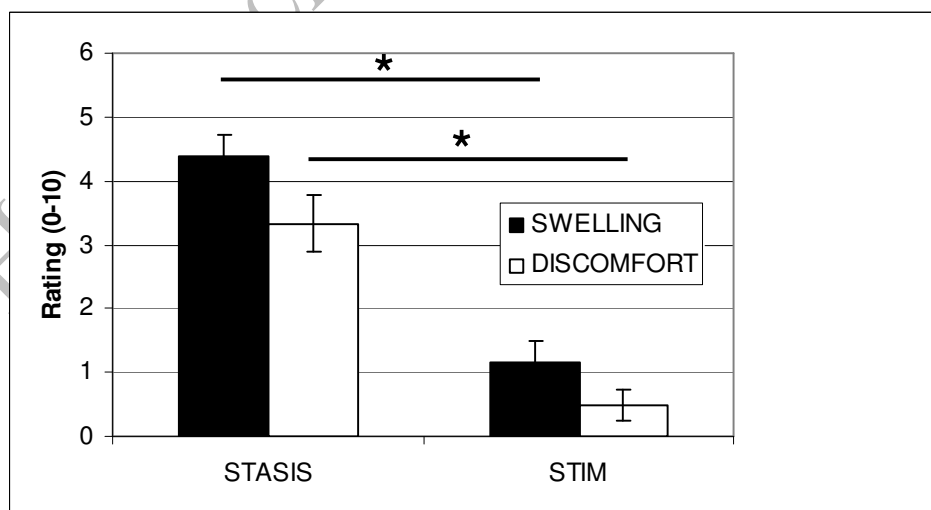


Figure 4. Mean \pm SEM subjective rating (0-10) of swelling magnitude (SWELLING) and related discomfort (DISCOMFORT) immediately following 40 mins STASIS and then 10 mins of sole stimulation (STIM). * Indicates a significant difference between conditions ($p < 0.05$).

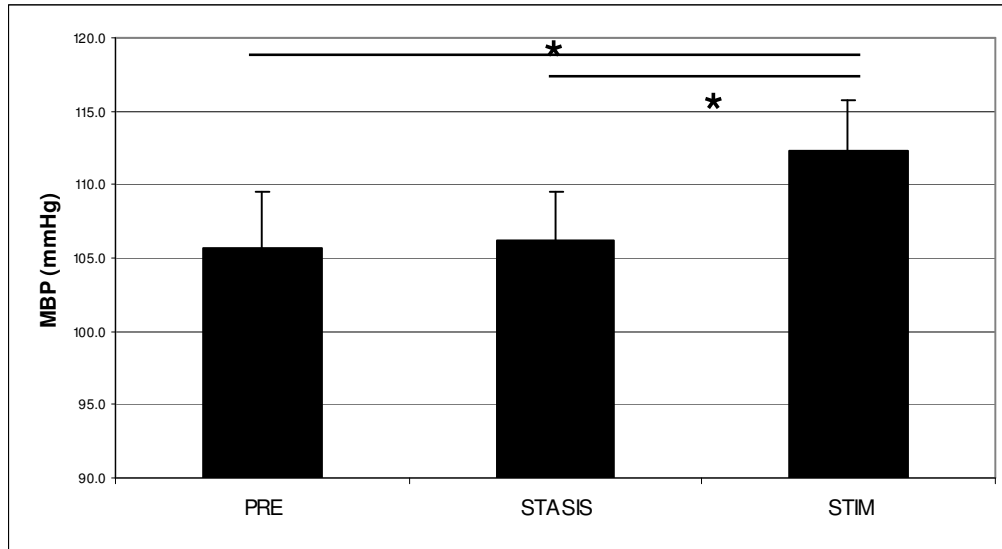


Figure 5. Mean \pm SEM mean blood pressure (MBP; mmHg) at rest (PRE), during the final 3 mins of sitting (STASIS), and during sole stimulation (STIM). * Indicates a significant difference between conditions ($p < 0.05$).

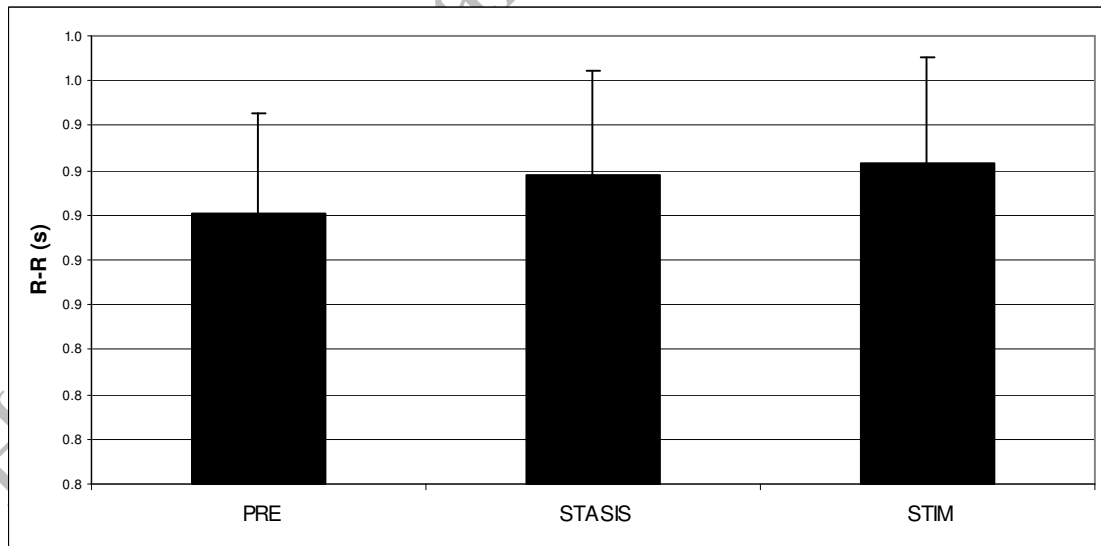


Figure 6. Mean \pm SEM R-R interval (ms) at rest (PRE), during the final 3 mins of sitting (STASIS), and during sole stimulation (STIM). * Indicates a significant difference between conditions ($p < 0.05$).