

Increase in calf post-occlusive blood flow and strength following short-term resistance exercise training with blood flow restriction in young women

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Abstract The response of calf muscle strength, resting (R_{bf}) and post-occlusive (PO_{bf}) blood flow were investigated following 4 weeks resistance training with and without blood flow restriction in a matched leg design. Sixteen untrained females performed unilateral plantar-flexion low-load resistance training (LLRT) at either 25% ($n = 8$) or 50% ($n = 8$) one-repetition maximum (1 RM). One limb was trained with unrestricted blood flow whilst in the other limb blood flow was restricted with the use of a pressure applied cuff above the knee (110 mmHg). Regardless of the training load, peak PO_{bf} , measured using venous occlusion plethysmography increased when LLRT was performed with blood flow restriction compared to no change following LLRT with unrestricted blood flow. A significant increase ($P < 0.05$) in the area under the blood time–flow curve was also observed following LLRT with blood flow restriction when compared LLRT with unrestricted blood flow. No changes were observed in R_{bf} between groups following training. Maximal dynamic strength (1 RM), maximal voluntary contraction and isokinetic strength at 0.52 and 1.05 rad s^{-1} also increased ($P < 0.05$) by a greater extent following resistance training with blood flow restriction. Moreover, 1 RM increased to a greater extent following training at 50% 1 RM compared to 25% 1 RM. These results suggest that 4 weeks LLRT with blood flow restriction provides a greater stimulus to increase peak PO_{bf} as well as strength parameters than LLRT with unrestricted blood flow.

Keywords Ischaemia · Vascular occlusion · Strength training

Introduction

It is well known that heavy resistance exercise has a potent effect to increase the size and strength of skeletal muscle. The load required to achieve these responses should generally exceed 70% one-repetition maximum (1 RM) (ACSM 2002). It is, therefore, interesting that several studies have demonstrated that resistance training at relatively low levels of force (20–50% 1 RM) when combined with blood flow restriction results in gains in strength and hypertrophy that are commensurate with traditional high-load resistance training (Burgomaster et al. 2003; Takarada et al. 2002). For example, Takarada et al. (2002) demonstrated a 14% increase in knee extensor strength of young subjects when low-load resistance training (LLRT) at an intensity of 50% 1 RM was combined with blood flow restriction compared with no change in strength with resistance training alone. In another study, Takarada et al. (2000a) demonstrated in the elbow flexors of older women that LLRT combined with blood flow restriction resulted in a similar increase in strength as that resulting from high-load training (80% 1 RM) without occlusion. Several other studies (Burgomaster et al. 2003; Takarada et al. 2002) show favourable increases in muscle size and strength during LLRT with blood flow restriction compared to conventional heavy resistance training alone using a variety of exercise modalities including the so-called Kaatsu walking (Abe et al. 2006). Indeed, some observations of increases in strength as a result of muscle hypertrophy, following LLRT with blood flow restriction have been made within short timescales such as 2 weeks (Abe et al. 2005).

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Along with increases in strength, it is also of interest that recent work has demonstrated that resistance training exercise has also been shown to enhance peak PO_{bf} (Rakobowchuk et al. 2005). Alomari and Welsch (2007) have also shown that 4 weeks handgrip resistance training increased peak PO_{bf} in the trained arm. These findings combined with the observation that athletes who are specifically trained to perform ischaemic contractions have significantly enhanced vascular capacity (Ferguson and Brown 1997) suggest that LLRT with blood flow restriction may also increase PO_{bf} to a greater extent compared to LLRT alone. However, not all studies show an increase in PO_{bf} following ischaemic contractions. McGowan et al. (2006, 2007) found that PO_{bf} was reduced following handgrip isometric contractions in both normotensive and hypertensive individuals. The differences seen between studies could be due to different contractions performed during training. Alomari and Welsch (2007) had their participants perform dynamic contractions with one contraction every 4 s for 20 min duration compared to 2 min isometric contractions at 30% maximal voluntary contraction (MVC) (McGowan et al. 2006, 2007). These contractions will provide very different blood flow patterns.

Although research in the area of LLRT with blood flow restriction has been increasing in interest, the studies thus far have used varying protocols making it difficult to establish an optimum training regime. This is especially true for the workloads used during exercise, with investigators using loads ranging between 20 and 80% 1 RM (Burgomaster et al. 2003, Laurentino et al. 2008, Moore et al. 2004, Reeves et al. 2006). Work by Cook et al. (2007) investigated the effect of varying protocols for exercise load, occlusion pressure and occlusion duration. They suggested that the most potent stimulator for muscle growth was one that resulted in the greatest fatigue and thus concluded that training at a load equating 20% maximum with partial but continuous restriction of blood flow was the most fatiguing, therefore, resulting in the most growth. This study, however, only investigated the acute effects of resistance training with blood flow restriction, with longer term changes unknown for lighter workloads. Until recently, it was not clear if training at higher workloads with blood flow restriction further enhanced strength and hypertrophy gains, however, Laurentino et al. (2008) investigated the effect of heavy (60–80% 1 RM) resistance training with and without blood flow restriction and did not observe any changes in size or strength between groups.

Therefore, we currently know that: (i) resistance training without external blood flow restriction can increase PO_{bf} , (ii) blood flow restriction does not enhance strength gains if high-load training is used, (iii) LLRT without blood flow restriction does not enhance strength and (iv) LLRT with

blood flow restriction evokes similar increases in the strength and size of a muscle when compared to high-load training without restriction. However, it is currently unknown if low (25% 1 RM) and moderate (50% 1 RM) load resistance training with blood flow restriction may improve PO_{bf} and secondly what the load needs to be to induce a gain in strength when combined with blood flow restriction. Therefore, we hypothesised that PO_{bf} would be increased by a greater extent following LLRT with blood flow restriction compared to LLRT alone. We also hypothesised that strength parameters will also increase by a greater extent following resistance training with blood flow restriction at 50% 1 RM when compared to training at 25% 1 RM. We have used the calf muscle as this provides a suitable model for the study of both strength and blood flow parameters using well-defined techniques.

Methods

Participants

Sixteen young healthy females volunteered to participate in the study. They were assigned to one of two groups and matched for maximal dynamic plantar-flexion strength determined from a 1 RM. These were 25% 1 RM ($n = 8$; age 23 ± 3 year, height 168.6 ± 6.8 cm, body mass 62.6 ± 8.5 kg) or 50% 1 RM ($n = 8$; age 22 ± 3 year, height 162.6 ± 5.8 cm, mass 61.3 ± 6.2 kg). Within each group, participants were counterbalanced with four participants performing LLRT with blood flow restriction on their dominant limb, whilst four performed LLRT with blood flow restriction with their non dominant limb. All participants were habitually physically active, but none specifically performed resistance exercise training. The participants were fully informed of the purposes, risks and discomfort associated with the experiment before providing written, informed consent. This study conformed to current local guidelines and the Declaration of Helsinki and was approved by Loughborough University Ethics Committee.

Overview of experimental procedures

Participants initially performed a familiarisation trial before the experimental protocol in order to become accustomed to all testing procedures and training devices. Participants were instructed in proper use of the resistance exercise equipment and also performed several plantar-flexions using a light load ($<25\%$ 1 RM) in order to mimic the type of actions performed during the training.

The experimental protocol consisted of (i) baseline measurement of resting limb blood flow (R_{bf}) and blood

flow following 5 min occlusion (PO_{bf}) as well as baseline measurements of plantar-flexor strength, (ii) a 4-week plantar-flexor resistance training programme with and without blood flow restriction and (iii) post-training blood flow and strength measurements that were conducted in an identical manner to the baseline measurements. All pre- and post-testing and training procedures were performed on both limbs. In the “restricted blood flow” condition all training was performed with an occlusion cuff, whereas the contralateral limb training was performed without restriction. It has been recently demonstrated that changes in vascular capacity are limited to the trained region following resistance training (Alomari and Welsch 2007) and there are no cardiovascular effects on the contra-lateral limb (Mourtzakis et al. 2004; Saltin et al. 1976). All pre-training tests were performed 3–5 days prior (baseline) to the commencement of the resistance training programme and post-training measurements performed 3–5 days after the final training session.

Limb blood flow

Calf blood flow measurements were carried out in a supine position using venous occlusion strain-gauge plethysmography, using mercury-in-rubber strain gauges (Hokanson, Bellvue, WA, USA). Mercury strain gauges were placed on the widest circumference of the calf. Inflation cuffs (CC17RB and SC10RB, Hokanson, Bellvue, WA, USA) were positioned 2–3 cm above the knee and around the ankle. Strain gauges were attached to a dual channel plethysmograph (EC6 Plethysmograph, Hokanson, Bellvue, WA, USA) with blood flow traces being sampled on line at 100 Hz (Powerlab, AD Instruments, NSW, Australia). Venous drainage was facilitated by placing a 15-cm foam block under the ankle and a 7-cm foam block under the knee and ensuring the limb was positioned in line with the heart. Rapid inflation of collection cuffs occurred by connecting the thigh cuff to a pneumatic air source (E20 Rapid cuff inflator and AG101 Cuff Inflator Air Source, Hokanson, WA, USA). R_{bf} and PO_{bf} were measured in each limb in a counterbalanced order. Blood flow was calculated from the slope of the volume change over the first cardiac cycle (Tschakovsky et al. 1995), using Chart version 5 software (ADInstruments, NSW, Australia) and expressed in ml/min/100 ml of tissue. It should be noted that the use of venous occlusion results in congestion, and the compliance and capacitance of the venous system can, therefore, affect the inflow during congestion. Figure 1 demonstrates typical plethysmographic tracings of blood flow following cuff inflation to 50 mmHg. The coefficient of variation (CV) over repeated measurements of R_{bf} and PO_{bf} for the investigator was 10–11 and 7–10%, respectively. These correspond with values obtained from previous studies (Thijssen et al. 2005).

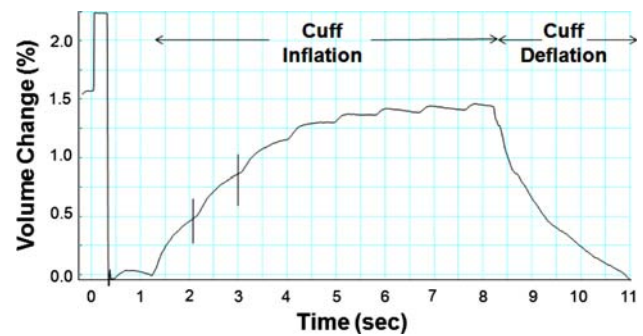


Fig. 1 Strain gauge calf volume profile during occlusion cuff inflation to 50 mmHg. Vertical solid lines indicate calculated blood flow from first beat. Horizontal arrows indicate cuff inflation and deflation. Change in tracing observed prior to cuff inflation was due to resetting the strain gauge prior to measurement

Resting limb blood flow (R_{bf})

Following instrumentation participants rested for 20 min in a supine position. Thirty seconds prior to the measurement of blood flow, arterial blood flow to the foot was occluded by inflating the ankle cuff to 200 mmHg. The measurement of blood flow was performed by inflating the thigh cuff to a venous occlusion pressure of 50 mmHg for 7 s after which the cuff was deflated. This process was repeated thrice, with approximately 30 s between each measurement, and the average taken. The ankle cuff was deflated immediately after the final blood flow measurement was obtained.

Post-occlusion reactive hyperaemia (PO_{bf})

After R_{bf} , the measurement of PO_{bf} was performed while participants remained in the supine position by inflating a thigh blood pressure cuff to 200 mmHg to induce arterial occlusion for 5 min. With 30 s left of arterial occlusion, an ankle cuff was inflated to 200 mmHg. Following rapid deflation of the thigh cuff, blood flow measurements were obtained within 15 s following arterial occlusion and every 15 s thereafter for 2 min. PO_{bf} was taken as the highest value obtained after occlusion. Total blood flow following 5-min occlusion was expressed in absolute terms as area under the time–flow curve (AUC) calculated by the trapezoid method (Meeking et al. 2000).

Muscle strength

Plantar-flexion torque was recorded on both limbs with the subjects lying prone, and the foot firmly secured to the foot adapter of an isokinetic dynamometer (Cybex Norm, Cybex International, New York, NY). This resulted in the leg being in the same (extended) position it was in during the blood flow measurements and training. Straps were used about the hip to prevent forward displacement of the

body during maximal plantar-flexions. Participants were placed with the knee at full extension and the lateral malleolus aligned with the axis of rotation identified on the dynamometer. Before measurements of MVC subjects performed five submaximal isometric plantar-flexion contractions as a warm up. Three isometric MVCs were performed at a joint angle of 0° (the sole of the foot at 90° with respect to the tibial axis). The participants were asked to gradually but quickly attain MVC and hold for ~ 2 – 3 s during which constant verbal encouragement and feedback was provided by the investigator. The value for MVC during each contraction was determined as the highest value obtained.

Isokinetic torque was measured in the same position as described during isometric MVC. Isokinetic torque was assessed by measuring maximal plantar-flexion torque during three, single maximal repetitions. Prior to the maximal repetitions, five warm up contractions were performed to accustom the participant to the required velocity. Torque production was assessed during the concentric phase of the movement only, at three different contraction velocities (0.52 , 1.05 and 2.09 rad s^{-1}). The highest torque value recorded during any of the three repetitions was taken as peak torque. The performance of each velocity was randomised and 1-min rest was given between each maximal effort.

After 15 min rest, dynamic plantar-flexion 1 RM of each limb was assessed in a supine position on a leg press machine. After warming up, the load was set at 80% of the predicted 1 RM. Following each successful lift, the load was increased by $\sim 5\%$ until the subject failed to lift the load through the entire range of motion. A test was only considered valid when the participant used proper form and completed the entire lift in a controlled, unassisted manner. Approximately 2–3 min of rest was allowed between each attempt to ensure recovery.

Training protocol

The 4-week training programme consisted of three sessions per week of supervised resistance training. Training consisted of unilateral plantar-flexion resistance exercise using one of the two respective loads (25 or 50% 1 RM). Following a warm up involving 5-min cycling at 50 W, participants performed single leg plantar-flexion exercise in a supine position using the same device employed for the dynamic 1 RM strength test. For all training sets, the restricted blood flow limb was trained first in which participants completed three sets of exercise to the point of failure, at a cadence of 1.5 s lifting and 1.5 s lowering the weight, with 1 min rest interval between sets. Vascular occlusion was maintained at an occlusion pressure of 110 mmHg as this has been shown to compress underlying

arteries and veins causing a pooling of blood (Takarada et al. 2000a). This pressure was maintained for the entire three sets (including rest periods), which resulted in a duration of ~ 5 – 8 min. The number of repetitions performed by the unrestricted blood flow leg was matched to that completed by the restricted condition. The participants performed each set to the point of failure, therefore, the average number of repetitions performed varied for each individual. The average number of repetitions performed by both groups during their first training session was 34, 13 and 9 for the first, second and third sets, respectively. This increased over the period of training to 92, 33 and 21 repetitions for each of the three sets by the final training session. One RM of each limb was reassessed after 2 weeks of training and loads were adjusted to maintain the required training intensity.

Statistical analysis

Results are expressed as means \pm standard deviation (SD) for all variables. There were no significant differences between resting values for any of the variables measured. Changes in R_{bf} , PO_{bf} , 1 RM, MVC and isokinetic strength were examined using a two-way (load (25 vs. 50% 1 RM) \times condition (restricted vs. normal)) mixed ANOVA with repeated measures design. The absolute response for R_{bf} , PO_{bf} , blood flow AUC were analysed using a three-way (time (pre vs. post) \times load (25 vs. 50%) \times condition (restricted vs. normal)) mixed ANOVA with repeated measures design. R_{bf} was not normally distributed, therefore, statistical analysis was performed on the logarithmic transformation of the data. Where significant interactions between load and condition used have been found they are reported. If the interaction between load and condition was non-significant but a significant main effect for load or main effect for condition was found, the main effects are only reported. Statistical significance was accepted at $P < 0.05$.

Results

All the participants in both training groups were able to successfully complete all training sessions with 100% compliance and free of injury. No differences were found in any baseline variables between the restricted blood flow condition and unrestricted blood flow condition.

Changes in limb blood flow

Absolute values of R_{bf} did not change with resistance training either with or without blood flow restriction (Table 1). Regardless of training load, peak PO_{bf} following

Table 1 Resting (R_{br}), post-occlusion reactive hyperaemia blood flow (PO_{br}) and area under the blood flow curve (AUC) before and following 4 weeks resistance training with and without blood flow restriction at 25 and 50% 1 RM

	25% 1 RM				50% 1 RM			
	Normal		Restricted		Normal		Restricted	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
R_{br}	2.3 ± 1.1	1.8 ± 0.5	1.9 ± 0.7	1.9 ± 0.7	2.4 ± 0.9	2.3 ± 0.7	2.5 ± 1.6	2.7 ± 1.4
PO_{br}	20.3 ± 4.5	21.4 ± 5.3	19.8 ± 3.6	27.4 ± 5.3*	23.0 ± 3.3	24.1 ± 4.4	20.3 ± 5.9	29.9 ± 7.8*
AUC	347 ± 81	388 ± 93	310 ± 91	412 ± 88*	407 ± 110	462 ± 120	391 ± 192	523 ± 186*

Values of blood flow and AUC are in ml/min/100 ml and ml/100 ml, respectively

* Significant ($P < 0.05$) time × condition interaction for restricted vs normal (i.e. data for training groups are collapsed and combined). Following LLRT blood flow restriction values were significantly greater than following training with unrestricted blood flow

LLRT with blood flow restriction absolute increased ($P < 0.05$) by a greater extent when compared to LLRT with unrestricted blood flow (Table 1, Fig. 2). Changes in peak PO_{br} were greater ($P < 0.05$, main effect for condition) following LLRT with blood flow restriction when compared to LLRT with unrestricted blood flow (Fig. 3). Similarly, absolute AUC increased ($P < 0.05$, group × time interaction) to a greater extent following LLRT with blood flow restriction compared to LLRT with unrestricted blood flow (Table 1).

Changes in muscle strength

Regardless of the training condition (unrestricted or restricted blood flow) training at 50% 1 RM resulted in a greater ($P < 0.05$, main effect for load) increases in 1 RM compared to 25% 1 RM (Fig. 4). Furthermore, when LLRT was performed with blood flow restriction, delta values of 1RM increased ($P < 0.05$, main effect for condition) by a greater extent ($30 \pm 11\%$) when compared to LLRT with unrestricted blood flow ($23 \pm 12\%$) (Fig. 4). Likewise, changes in MVC increased ($P < 0.05$, main effect of condition) by a greater extent following resistance training with blood flow restriction ($13 \pm 12\%$) compared to LLRT with unrestricted blood flow ($4 \pm 8\%$) (Fig. 5), as did isokinetic torque at 0.52 and 1.05 rad s^{-1} (Fig. 6a, b). However, there was no effect of either condition or load on isokinetic torque at 2.09 rad s^{-1} (Fig. 6c).

Discussion

The main finding of the present study was that 4 weeks calf resistance training with partial blood flow restriction enhanced the increase in calf PO_{br} compared to resistance training alone. Furthermore, plantar-flexor 1 RM, MVC and isokinetic torque at 0.52 and 1.05 rad s^{-1} were also enhanced when training was performed with blood flow restriction when compared to resistance training alone.

This is the first study to show an enhanced increase in PO_{br} following LLRT with blood flow restriction. The major limitation within this study is that venous occlusion strain-gauge plethysmography does not allow us to elucidate the exact mechanisms behind changes within the vasculature. The exact mechanisms that determine peak reactive hyperaemia are currently unknown, although NO-dependent endothelial function is only likely to have a modest, if any, effect (Engelke et al. 1996; Tagawa et al. 1994) and is more likely a myogenic and metabolic phenomenon (Carlsson et al. 1987). Therefore, it is possible that an enhanced metabolite accumulation created by the blood flow restriction during training (Suga et al. 2009; Takarada et al. 2000b), including vasoactive metabolites such as adenosine, contributed to the enhanced PO_{br} .

Another possibility is that blood flow restriction resulted in an increased capillarity. The potential contribution of angiogenesis to an increased blood flow with exercise training remains equivocal. The influence of muscle fibre recruitment may play an important role, as it has been observed that a preferential capillarisation occurs amongst FT fibres (Adair et al. 1990). Low-intensity exercise tends to recruit mainly slow twitch (ST) oxidative fibres, whereas more intense exercise requires more fast-twitch (FT) glycolytic fibre recruitment (Vollestad and Blom 1985). However, the addition of blood flow restriction favours additional recruitment of FT fibres even at relatively low workloads (Krustrup et al. 2009) and would, therefore, provide an additional stimulus for angiogenesis. However, the evidence for this increased recruitment is equivocal, with some investigators showing a recruitment pattern during LLRT with blood flow restriction that is similar to heavy load resistance training (Takarada et al. 2000a), whilst others show that although higher than LLRT alone, the recruitment is less than heavy load resistance training (Manini and Clark 2009). The additional fibre recruitment and associated metabolic consequences of this would also support the role of the important regulator of angiogenesis, vascular endothelial growth factor (VEGF) whereby local

Fig. 2 Individual peak PO_{bf} responses, before and following 4 weeks resistance training with and without blood flow restriction (25% 1 RM, $n = 8$; 50% 1 RM, $n = 8$). *Significant ($P < 0.05$) time \times condition interaction for restricted versus normal (i.e. data for training groups are collapsed and combined)

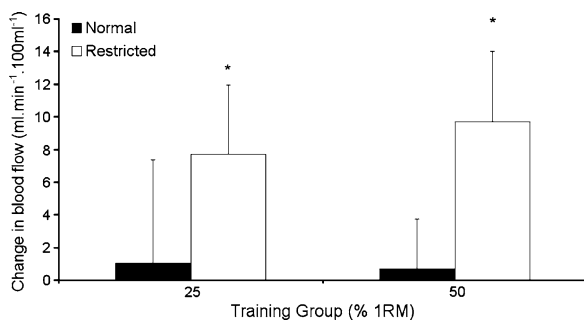
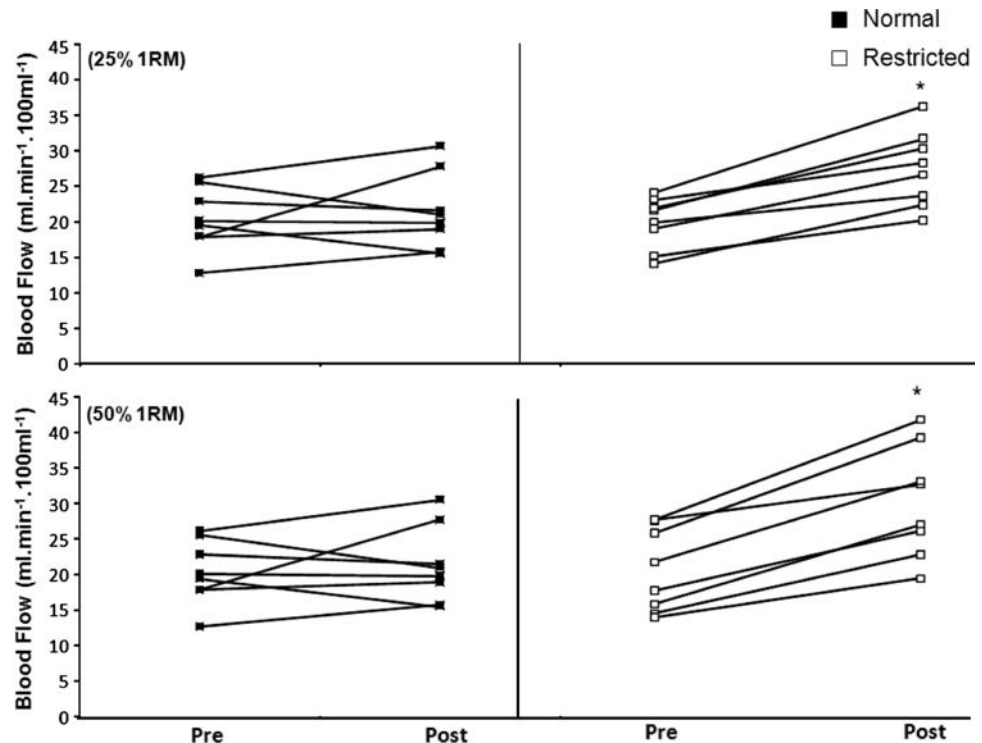


Fig. 3 Change in peak PO_{bf} following 4 weeks resistance training with and without blood flow restriction. Values are means \pm SD (25% 1 RM, $n = 8$; 50% 1 RM, $n = 8$). *Significant ($P < 0.05$) main effect for restricted versus normal (i.e. data for training groups are combined)

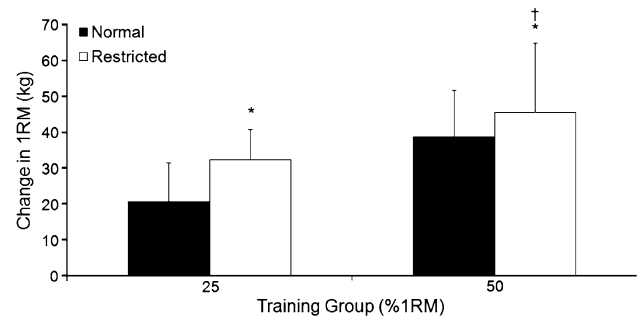


Fig. 4 Change in 1 RM following 4 weeks resistance training with and without blood flow restriction. Values are means \pm SD. (25% 1 RM, $n = 8$; 50% 1 RM, $n = 8$). *Significant ($P < 0.05$) main effect for restricted versus normal (i.e. data for training groups are combined). †Significant ($P < 0.05$) main effect for 25% 1 RM versus 50% 1 RM (i.e. data for restricted and normal are collapsed and combined)

metabolic changes occurring in response to exercise seem to be an important signal for VEGF up-regulation (Roca et al. 1998) possibly initiated through the VEGF/NO cascade (Milkiewicz et al. 2005). Indeed, serum VEGF has previously been shown to significantly increase in response to resistance training with blood flow restriction (Takano et al. 2005). In a rat model, Kawada and Ishii (2008), demonstrated that expression of skeletal muscle VEGF₁₈₈ increased, with no changes being observed in VEGF₁₆₄ and hypoxia inducible factor-1 (HIF-1), following 2 weeks of blood flow restriction. Of interest, though is the fact muscle capillary supply did not change following blood flow restriction and indeed muscle capillary density

actually decreased. However, these changes were following 2 weeks of total blood flow restriction and are, therefore, hard to interpret with respect to human training studies.

One other possible suggestion for the change in peak PO_{bf} following LLRT with blood flow restriction is an increased venous compliance such that the impact of venous congestion on impeding arterial inflow is reduced, which could, therefore, explain the differences in the increase of peak PO_{bf} . Although not measured in the current study, it is possible that pooling of blood flow associated with this type of training may result an increased compliance (Convertino et al. 1988). This is a similar response to that seen following

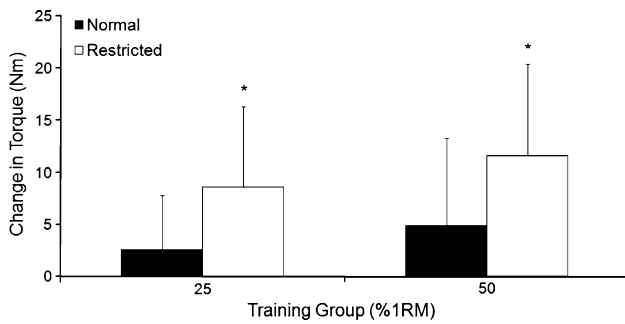


Fig. 5 Change in MVC following 4 weeks resistance training with and without blood flow restriction. Values are means ± SD. (25% 1 RM, $n = 8$; 50% 1 RM, $n = 8$). *Significant ($P < 0.05$) main effect for restricted versus normal (i.e. data for training groups are collapsed and combined)

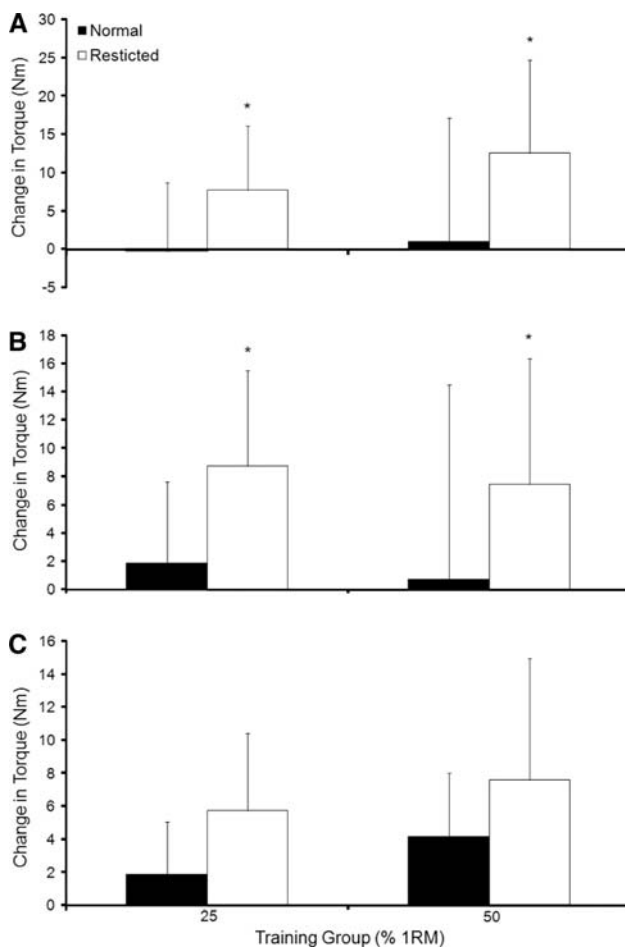


Fig. 6 Change in isokinetic torque at (a) 0.52, (b) 1.05 and (c) 2.09 rad s⁻¹ following 4 weeks resistance training with and without blood flow restriction. Values are means ± SD (25% 1 RM, $n = 8$; 50% 1 RM, $n = 8$). *Significant ($P < 0.05$) main effect for restricted vs normal (i.e. data for training groups are collapsed and combined)

endurance training where venous congestion is increased following training with no decrement on tolerance to orthostatic stress (Hernandez and Franke 2005). What is

clear is that further research is needed to investigate the exact mechanisms behind the increase in peak PO_{bf} found following LLRT with blood flow restriction.

Like previous studies, we have observed greater increases in strength when resistance training was performed with blood flow restriction compared to resistance training alone. For example, Abe et al. (2005) and Kubo et al. (2006) reported greater gains in strength of the quadriceps muscle at loads <50% 1 RM when blood flow was restricted. Although in the present study there were no significant interactions between the load used and the use of blood flow restriction on any of the strength or blood flow measurements, it is perhaps not surprising that there was a significant main effect for 1 RM in the 50% compared to the 25% group irrespective of the condition used to train. It is well known that intensities of 50% 1 RM can result in a sufficient stimulus for improved strength, most likely due to the specificity of this measure in relation to the training manoeuvre. Indeed, Moore et al. (2004) found that resistance training at an intensity of 50% 1 RM was effective in improving 1 RM independent of the application of blood flow restriction.

Regardless of the workload, resistance training in combination with blood flow restriction was also effective in increasing strength in non-training specific manoeuvres, as shown by the greater increases in MVC and isokinetic strength at 0.52 and 1.05 rad s⁻¹. The greater changes in strength with blood flow restriction were probably due both to neural adaptations, and possibly muscle hypertrophy. As described previously, the addition of blood flow restriction results in additional recruitment of FT fibres (Krustrup et al. 2009), which would facilitate an enhanced recruitment of fast motor units as a result of training (Takarada et al. 2000a). Although we have not measured muscle size in the present study, hypertrophy is not typically thought to occur so early in a traditional resistance training programme, as neural factors are thought to influence the early changes in strength (Hakkinen et al. 1996; Sale 1988). However, numerous studies of LLRT with blood flow restriction have clearly shown significant hypertrophy to occur, even after 14 days (Abe et al. 2005). It is thought that growth factors such as IGF-1 are important for skeletal muscle hypertrophy. Serum levels of IGF-1 and growth hormone (GH) are known to significantly increase following resistance training with blood flow restriction compared to exercise with unrestricted blood flow (Abe et al. 2005; Reeves et al. 2006; Takarada et al. 2000b). However, systemic levels of GH or IGF-1 may not actually play a role in increasing skeletal muscle size as it has been recently shown that neither contributes to stimulating protein synthesis or hypertrophy (West et al. 2009). It is more likely that changes at the local level are important for hypertrophy. Increases in local IGF-1/MGF have been

observed following acute bouts of high-load resistance training (Hameed et al. 2004; Petrella et al. 2006), however, the effect of resistance training with blood flow restriction on local growth factor responses is not known. Fujita et al. (2007) observed that S6K1, a key downstream effector of the mTOR signalling pathway (one of the two signalling pathways thought to be activated by IGF-1), became phosphorylated and muscle protein synthesis was stimulated following an acute bout of resistance training with blood flow restriction, suggesting a role of local IGF-1 in the hypertrophy response.

Although we cannot confidently suggest that 50% 1 RM provides a greater stimulus for increasing strength and blood flow than 25% 1 RM, what is clear is that loads as low as 25% 1 RM when combined with blood flow restriction does provide sufficient stimulus for these improvements as shown by the changes in this current study. Further evidence for using workloads as low as 20% comes from the increases in strength seen by Abe et al. (2005) as well as the positive hormonal changes seen following acute bouts of exercise with blood flow restriction (Pierce et al. 2006). Fujita et al. (2007) also found that a workload of 20% combined with blood flow restriction was enough to stimulate protein synthesis. Moreover, the increase in blood flow may enhance the endurance capacity of the muscle trained thus improving the exercise tolerance of the muscle by helping reduce fatigue. For example, Takarada et al. (2002) have shown that the endurance capacity of the knee extensor muscles can increase following 8 weeks resistance training with blood flow restriction. The evidence, therefore, suggests that this type of training may be a useful exercise to improve both muscular strength and endurance for individuals who are unable to lift such relatively heavy loads such as those recovering from an injury or older people.

One limitation of the current study is that hormonal status was not measured in our female participants. However, evidence suggests that strength is not influenced by the menstrual cycle (de Jonge 2003). Recent evidence also suggests that menstrual cycle phase has no effect on hemodynamics. For example, Cooper et al. (2006) found that suppression of ovarian hormones associated with the menstrual cycle does not affect resting calf blood flow. Finally, although hormonal status was not tracked, all females reported normal cycles (28–30 days). Taking this into account and the fact that the training intervention lasted 4 weeks, it is likely that all participants were at on the same phase of their menstrual cycle during the pre- and post-training measurements.

Although the changes seen in the current study are positive, there are many unanswered questions, specifically surrounding the safety of this type of training. We have

shown that PO_{bf} and AUC are both increased following a short period of LLRT with blood flow restriction, however, the effect on the veins are unknown. Concern surrounds the fact that the veins are congested and distended and this may cause problems for normal blood flow by causing damage to the valves within the vein. Preliminary data from Manini and Clark (2009) suggest that LLRT with blood flow restriction does not affect blood clotting time or ankle brachial index. Though this work, like ours, was following 4 weeks training thus not long enough to provide long-term effects and was in young healthy individuals. Further research is needed on the long-term safety aspects as well as its applicability to be used in other non-healthy population groups.

In conclusion, this study is the first to demonstrate enhancements in the blood flow capacity following resistance training with blood flow restriction compared to resistance training alone. Resistance training with blood flow restriction also increased plantar-flexor 1 RM, MVC and isokinetic strength to a greater extent than following resistance training alone.

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