
PRACTICAL BLOOD FLOW RESTRICTION TRAINING INCREASES ACUTE DETERMINANTS OF HYPERTROPHY WITHOUT INCREASING INDICES OF MUSCLE DAMAGE

JACOB M. WILSON,¹ RYAN P. LOWERY,¹ JORDAN M. JOY,¹ JEREMY P. LOENNEKE,² AND MARSHALL A. NAIMO¹

¹Department of Health Sciences and Human Performance, The University of Tampa, Tampa, Florida; and ²Department of Health and Exercise Science, University of Oklahoma, Norman, Oklahoma

ABSTRACT

Wilson, JM, Lowery, RP, Joy, JM, Loenneke, JP, and Naimo, MA. Practical blood flow restriction training increases acute determinants of hypertrophy without increasing indices of muscle damage. *J Strength Cond Res* 27(11): 3068–3075, 2013—Vascular blood flow restriction (BFR) training stimulates muscle hypertrophy by increasing muscle activation and muscle swelling. Previous studies used expensive pneumatic cuffs, which may not be practical for regular use. The aim was to investigate the acute effects of low-intensity practical BFR (LI-pBFR) on muscle activation, muscle swelling, and damage. Twelve trained male participants completed a 30-, 15-, 15-, 15-repetition scheme at 30% of their leg press 1-repetition maximum under control and LI-BFR conditions. Under the LI-BFR trial, knee wraps were applied to the thighs at a pressure that resulted in venous, not arterial, occlusion. In the control trial, wraps were applied with zero pressure. Ultrasound-determined muscle thickness was recorded at baseline; 0 minutes post with wraps; 0, 5, and 10 minutes post without wraps. Muscle activation was recorded during warm-ups and on the final set of 15 repetitions. Indices of muscle damage (soreness, power, and muscle swelling) were also recorded. There was a condition by time effect for muscle thickness ($p < 0.0001$, effect size [ES] = 0.5), in which muscle thickness increased in the LI-pBFR condition 0 minutes post with wraps and through 5 minutes post without wraps. No changes occurred in the control. There was a condition by time effect for muscle activation ($p < 0.05$, ES = 0.2). The LI-pBFR had greater activation than the control did. There were no condition by time effects on indices of muscle damage. Our data indicate that practical BFR significantly

increases muscle activation and muscle thickness without increasing indices of damage.

KEY WORDS muscle swelling, muscle activation, occlusion, low intensity

INTRODUCTION

Resistance training has been widely recognized as an effective stimulus for increasing skeletal muscle size and strength. Traditionally, the American College of Sports Medicine recommends resistance training using intensities $>70\%$ of 1-repetition maximum (1RM) because it seems to elicit the greatest increases in skeletal muscle size and strength (2). More recently, low-intensity resistance training in combination with blood flow restriction (LI-BFR) has been shown to increase muscle size and strength using only 20–30% of an individual's 1RM (15,27,35,36). The LI-BFR resistance training seems to be an effective, safe alternative to training at higher intensities (25), which may have a potential for increased injury and the possibility of leading to overreaching (9). There are 3 primary mechanisms through which LI-BFR resistance training is thought to operate: increased cellular swelling, enhanced metabolic stress, and increased muscle fiber recruitment (18). Although the mechanisms behind LI-BFR resistance training are not totally understood, Loenneke et al. (18) recently suggested that cell swelling may occur through blood pooling, an accumulation of metabolites, and reactive hyperemia. Cellular swelling is thought to activate an intrinsic volume sensor, which may lead to the stimulation of various anabolic-signaling pathways (10,11,13,18). Research also demonstrates that LI-BFR resistance training increases metabolic stress (32), thus leading to greater increases in growth factors, epinephrine (E), and norepinephrine (NE) (16). In addition, the accumulation of metabolites can increase muscle fiber recruitment through the stimulation of group III and group IV afferents (37). It is postulated that this may increase fast-twitch fiber recruitment by inhibiting the alpha motor neuron, which ultimately supplies slow-twitch fibers (37).

Address correspondence to Jacob M. Wilson, jmwilson@ut.edu.
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The purpose of LI-BFR resistance training is to fully occlude venous but not arterial blood flow (18). The LI-BFR resistance training involves applying a wrapping device, typically a pneumatic restriction cuff, proximal to the muscle being trained (6,8,30). However, this may not be a practical approach for most populations because of cost and accessibility. Recently, because of its accessibility and relative cost effectiveness, practical blood flow restriction (LI-pBFR) resistance training has been a rising topic in our field. Loenneke et al. (17,21,22,24) were the first to propose pBFR training. Specifically, these researchers applied knee wraps proximally around participants' thighs until they were snug, but the wraps did not cause pain (17,21,22,24). However, these researchers did not quantify the tightness of the wrap. Additionally, they did not verify if wrapping resulted in venous and arterial occlusion. Moreover, no research has identified if LI-pBFR resistance training can acutely elicit the 3 mechanisms of action through which the restriction of blood flow is thought to operate. Finally, it is unknown whether or not LI-pBFR resistance training increases the indices of muscle damage. Therefore, the purpose of this study was to investigate the effects of moderate pBFR on metabolic stress, muscle swelling, skeletal muscle activation, and indices of muscle damage after a low-intensity resistance training bout. The second purpose of this study was to validate a practical alternative to traditional BFR.

METHODS

Experimental Approach to the Problem

The participants completed a total of 5 testing sessions separated by a minimum of 72 hours' rest over a 2- to 3-week period. No adverse events occurred throughout the protocols, and all the participants were able to complete both exercise interventions. All the participants were directed to refrain from performing lower-body exercises for a minimum of 72 hours before each experimental trial for the duration of the study. During each testing session, the participants wore the same clothing and shoes worn on the first testing day to control any effects that this may have. The first session consisted of assessment of participants' concentric 1RM strength in the leg press, and familiarization with a force plate. We also determined the presence of blood flow via ultrasonography at the following perceived pressures: control (0 out of 10),

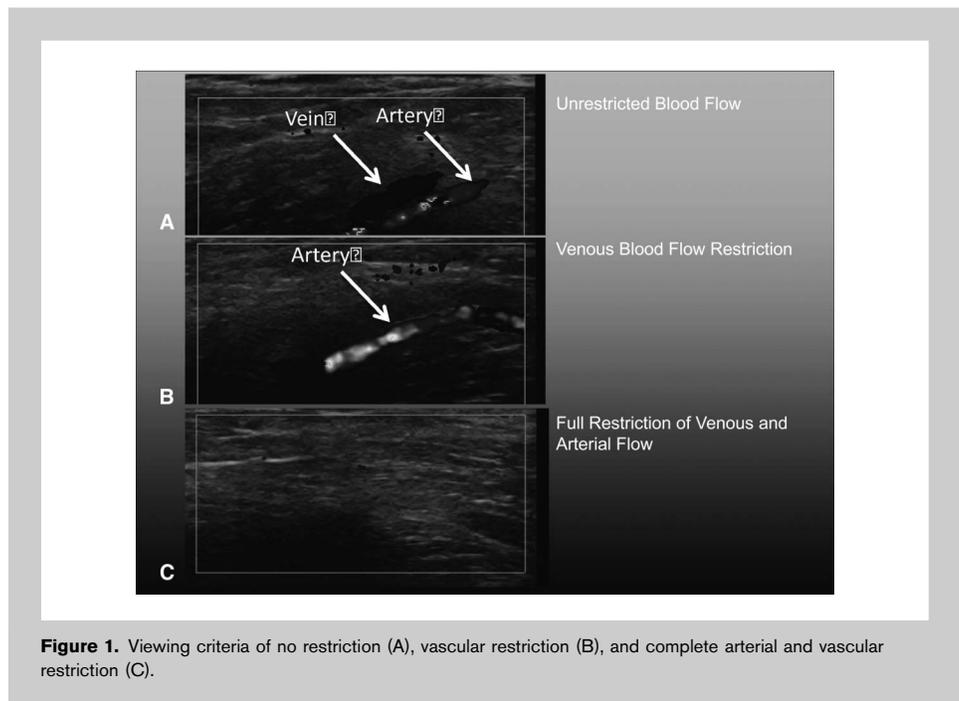
moderate (7 out of 10), and tight (10 out of 10). The moderate condition was chosen as a way to quantify Loenneke et al.'s (17,21,22,24) description of snug, but not painful pressure. The participants were randomly assigned to which condition (control or moderate pressure) they performed first. The experimental conditions required participants to perform the leg press using a low-intensity load (30% 1RM) for a scheme of 30–15–15–15 repetitions. Thirty seconds of timed rest occurred in between each set. After each exercise session, the participants returned to the laboratory for testing (24 hours post).

Subjects

Twelve college-aged male participants aged 21 ± 3 years (body mass 84.5 ± 14.1 kg, height 178.6 ± 4.2 cm) with a minimum of 1 year of resistance training experience were recruited for this study. All the participants were thoroughly informed of the purpose, nature, practical details, and possible risks associated with the experiment, and the right to terminate participation at will, before they gave their voluntary informed consent to participate. The study was approved by the University's Institutional Review Board.

Laboratory Visit 1 Blood Flow and Perceived Pressure, Strength Testing, and Familiarization

Vascular blood flow restriction occurs when the target veins, but not arteries are completely occluded to blood flow. We therefore began day 1 by determining whether a moderate pressure applied to each participant would result in the desired outcome. Upon arriving to the laboratory on day 1, the participants rested prone for 10 minutes. After participants' blood flow assessment was determined using a GE Logic e ultrasound system (General Electric Medical Systems,



Milwaukee, WI, USA). The unit was placed in the Doppler mode and used to locate the femoral artery and vein. The participants were first measured with elastic knee wraps (Harbinger Red-Line, Fairfield, CA, USA; 76 mm wide) applied by the same investigator on each day. Before wrapping, the participants were introduced to the perceived pressure scale. It was explained that a 0 out of 10 pressure meant no pressure, a 7 out of 10 pressure was described as moderate pressure with no pain, and a 10 out of 10 pressure was described as intense pressure with pain. After the explanation of the perceived pressure scale, the participants were asked if they understood, and if they did not understand, the scale was reviewed until comprehension was attained. The wrapping process involved wrapping the knee wraps proximally on the femur near the inguinal crease. The length of the knee wraps allowed for several wraps around the femur. After each wrap around the femur, the participants were asked to rate the perceived pressure of the wrap on a scale of 0–10. Wrapping ceased when 1 of 3 pressures were reached: a light (control) pressure (0 out of 10), a moderate (7 out of 10) pressure, and tight (10 out of 10) pressure. The ultrasound probe was placed in the popliteal region, because this is the closest to the femoral blood vessels we could obtain because of the wraps being placed around the upper thigh. Complete arterial or venous restriction was determined when flow had completely ceased during a wrapping

protocol in a given vessel (Figure 1). This outcome was verified using color flow mode.

After blood flow measurements, the concentric 1RM test for the leg press began with a warm-up at a light resistance 50% 1RM (5–10 repetitions). The load was then increased in 13.64- to 18.18-kg increments until only 1 successful repetition could be completed (4). Each participant’s 1RM was determined in approximately 5 attempts because all 1RMs were found within these attempts. A lift was deemed successful when the subject’s leg descended to a point where the angle at the knee was $<90^\circ$ and the subject could ascend to the starting position without assistance. Participants’ foot placement was controlled, as all participants’ heels were placed in the same location during each session. In the event of a failed 1RM attempt, the weight was decreased by 4.54–9.09 kg until completion of a successful lift.

Laboratory Visits 2–5: Resistance Exercise and Muscle Damage Testing Protocols

Upon arriving to the laboratory, the participants rested for 5 minutes in a supine position before baseline muscle thickness measures were performed to account for any confounds. Total muscle thickness was recorded midway between the greater trochanter and lateral epicondyle of the femur using ultrasonography by the same investigator

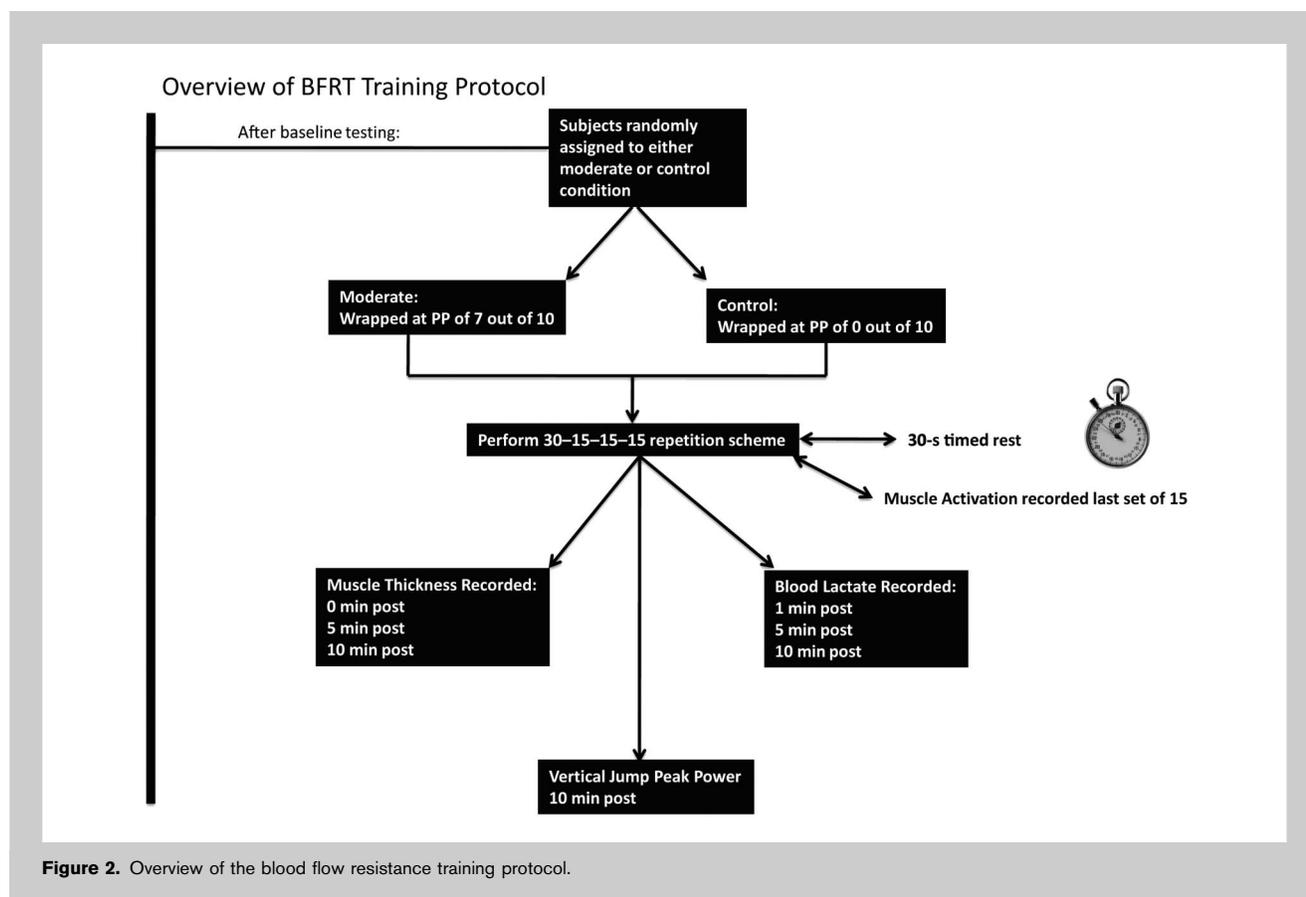


Figure 2. Overview of the blood flow resistance training protocol.

(A Pearson product moment correlation determined reliability of day-to-day muscle thickness as $r = 0.99$). Simultaneously, baseline blood lactate samples approximately $0.7 \mu\text{l}$ by volume were obtained from the subject's fingertips. Values were recorded using a handheld analyzer (Lactate Plus; Nova Biomedical Corporation, Waltham, MA, USA). Baseline leg soreness was also recorded using a visual analog scale (VAS; 0–10) (28). The participants were instructed to lay in a supine position with their leg extended while a laboratory assistant gently applied pressure to the participants' quadriceps muscle with 2 fingers. After palpation, the participant placed a mark on the VAS according to their level of soreness, where 10 was "very sore" and 0 was "no soreness." The same laboratory assistant applied gentle pressure during every testing session for consistency. After these tests, the participants performed 3 baseline jumps on a force plate to record peak vertical jump power. All the jumps were performed on a multicomponent AMTI force platform (Advanced Mechanical Technology, Inc., Watertown, MA, USA) that interfaced with a personal computer at a sampling rate of 1,000 Hz. Data acquisition software (LabVIEW, version 7.1; National Instruments Corporation, Austin, TX, USA) collected values for vertical jump power. Peak power was calculated as the peak combination of ground reaction force and peak velocity during the accelerated launch on the platform (A Pearson product moment correlation determined reliability of day-to-day vertical jump as $r = 0.97$). Changes in soreness were examined before, and 24 hours

after exercise. Power was measured before, 10 minutes, and 24 hours postexercise. These were used as indirect indices of muscle damage (5).

After 5 minutes of rest, the participants performed a warm-up set of 15 repetitions at 30% of their 1RM with no wraps applied. An electromyography (EMG; Delsys Trigno Wireless EMG systems, Boston, MA, USA) sensor was applied to the belly of the vastus lateralis of the dominant leg to get baseline muscle activation during exercise. Before sensor placement, the leg was shaved and sterilized with alcohol to ensure optimal electrical conductance. The sensor was applied using specialized, double-sided adhesive (Delsys Trigno adhesive, Boston, MA, USA). Surface EMG signals were preamplified ($\times 100$), amplified ($\times 2$), band-pass filtered (10–1,000 Hz), and sampled at 2,500 Hz with EMG works software (version 4.01, Boston, MA, USA). All EMG data are expressed as root mean squared values for the average activation of the final 5 repetitions of the set.

After baseline testing, the participants were randomly assigned to control and moderate perceived pressure conditions. The 2 experimental conditions required the participants to perform the leg press at 30% of their 1RM. Under both conditions, the participants were required to first perform 1 set of 30 repetitions followed by 3 sets of 15 repetitions (30–15–15–15). A timed rest period length of 30 seconds was used between all sets. Muscle activation was recorded again on the final set of 15 repetitions. The participants were instructed to descend the weight until

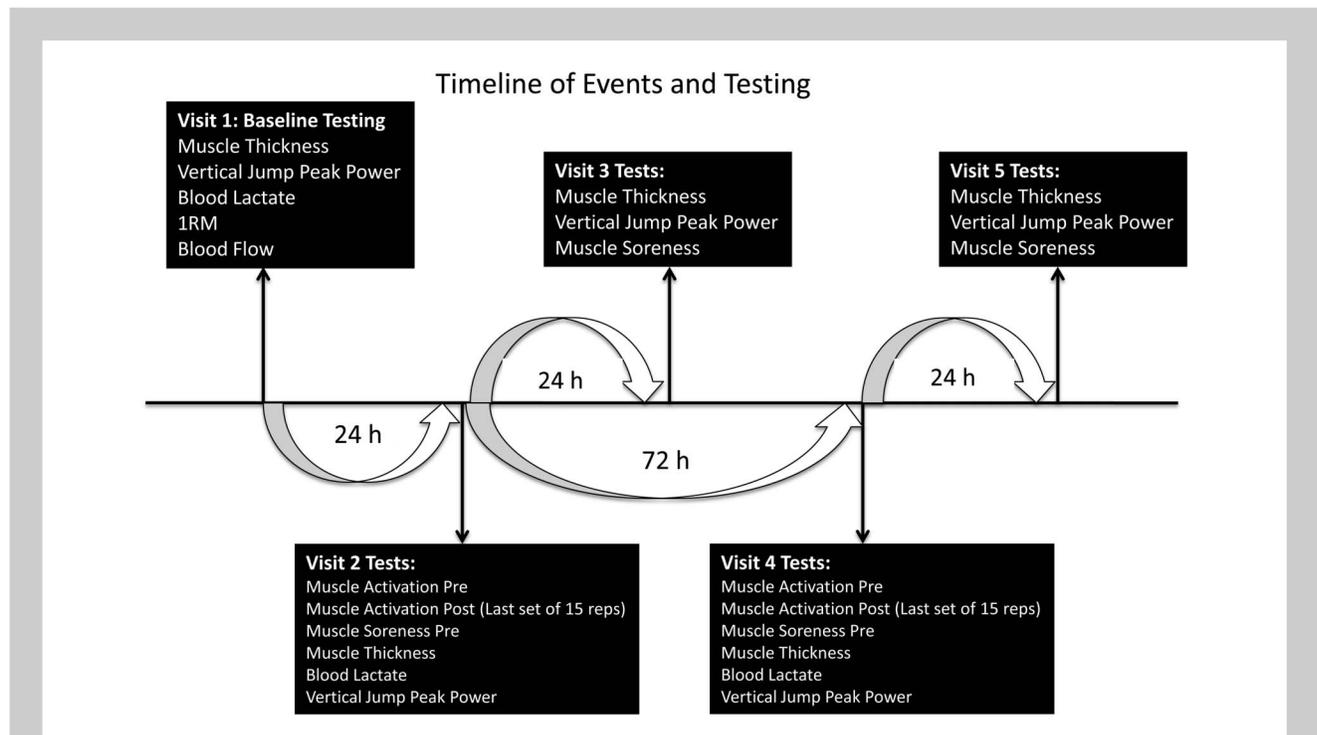


Figure 3. Timeline of the tests and measurements.

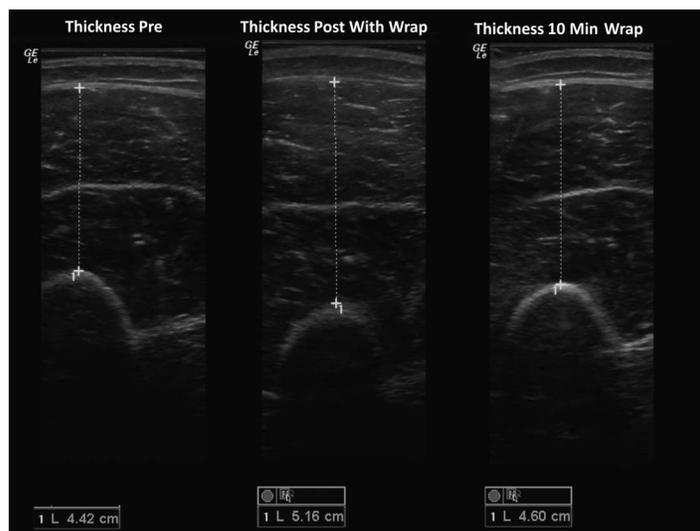


Figure 4. Sample subject response to moderate blood flow restriction at pre, immediately postexercise with wraps, and 10 minutes postexercise without wraps.

the participants returned and performed the same protocol (visit 4) but under the opposite condition as in visit 2. On visit 5 (24 hours after visit 4), the participants returned and measurements were taken identical to that in visit 3 (Figure 3).

Muscle Thickness and Blood Flow Assessment

Participants’ muscle thickness was determined via the ultrasound by measuring the total muscle thickness of the vastus lateralis, vastus intermedialis, and the fascia between the 2 muscles located midway between the greater trochanter and lateral epicondyle of the dominant leg (Figure 4). To ensure accuracy, we took 3 measurements per subject and recorded the average. All 3 val-

ues were within a 0.10-cm variation for each subject. To ensure that a precise location was kept across visits, participants were marked daily with a permanent marker to maintain the same measuring spot. In total, there were 6 recorded measures taken for muscle thickness occurring at baseline, 0 minutes post with wraps, 0 minutes post without wraps, 5 minutes post, 10 minutes post, and 24 hours post. The measure 24 hours later was used as indices of muscle damage (31).

there was a <90° angle at the knee to ensure a full range of motion. After the exercise bout, muscle thickness tests were recorded at 0, 5, and 10 minutes post. Blood lactate was taken at 1, 5, and 10 minutes post removal of the wrap (Figure 2). The participants returned to the laboratory 24 hours later for measures of muscle thickness, vertical power, and soreness (visit 3). A minimum of 72 hours later,

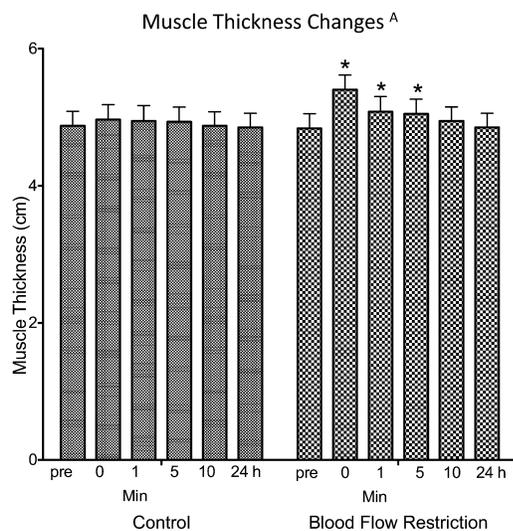


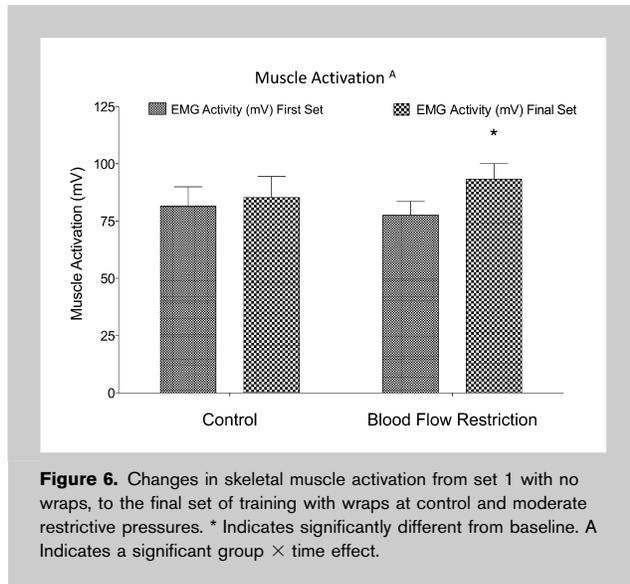
Figure 5. Changes in muscle thickness before and up to 24 hours postexercise. * Indicates significantly different from baseline. A indicates a significant group × time effect.

Statistical Analyses

Repeated measure analysis of variance was run to assess group, time, and group by time interactions. If any main effects were found, a Tukey post hoc was employed to locate differences. For effect size (ES), the partial eta squared (η^2) statistic was calculated, and according to Green et al. (12) η^2 of 0.01, 0.06, and 0.14 represents small, medium, and large ESs, respectively. To compare differences in the perceptual response (VAS), the Wilcoxon related samples nonparametric test was used to determine if significant differences existed between conditions at different time points (Pre vs. 24 hours). Values for VAS are presented as 25th–50th–75th percentiles for each time point. An alpha of $p \leq 0.05$ was established a priori. Statistica (StatSoft, Tulsa, OK, USA) was used for all statistical analyses. Variability is represented in SDs.

RESULTS

Results with varying perceived pressures indicated no blood flow restriction in the control condition (Figure 1). There was complete restriction of the femoral vein but not artery in all the participants at a perceived pressure of 7 out of 10. At a perceived pressure of 10 out of 10, 67% of the participants experienced complete arterial restriction. There was a condition effect for



blood lactate ($p < 0.05$, $ES = 0.2$) in which the average session blood lactate was higher after exercise in the moderate (6.2 ± 2.8 mmol/L) vs. control (4.7 ± 1.8 mmol/L) pressure condition. There was a condition by time effect for muscle thickness ($p < 0.0001$, $ES = 0.5$), in which muscle thickness was significantly elevated above baseline in the moderate pBFR condition 0 minutes post with wraps and 0 minutes through 5 minutes post without wraps (Figure 5). No changes were observed in the control condition. By 24 hours post, no swelling existed in either condition, indicating no effect of pBFR on muscle damage (Figure 5). There was a condition by time effect for muscle activation ($p < 0.05$, $ES = 0.2$) in which the moderate pBFR condition had significantly greater muscle activation than did the control (Figure 6). There were no median differences (25th–50th–75th percentile) between groups in perceived soreness at baseline (pBFR [0–1–1 cm] vs. Control [0–1–1 cm], $p = 0.564$) or 24 hours postexercise (pBFR [1–1–2.8 cm] vs. Control [0–1–2.7 cm], $p = 0.774$). Similarly, there was a time effect for peak power, which decreased from pre ($5,018.9 \pm 279$ W) to 24 hours posttraining ($4,718.8 \pm 260.4$ W), but no differences existed between conditions.

DISCUSSION

The purpose of this study was to investigate the effects of LI-BFR on metabolic stress, muscle swelling, skeletal muscle activation, and indices of muscle damage. The second purpose of this study was to validate a practical alternative to BFR. The primary findings of this research were that moderate pBFR resulted in greater indices of metabolic stress, muscle swelling, and muscle activation than did a work-matched control, without increasing indices of muscle damage. In addition, moderate pBFR resulted in venous, but not arterial occlusion in all the participants.

Previous research using a pneumatic cuff has demonstrated that using a 30% 1RM load resulted in similar metabolic stress

to high-intensity (65% 1RM) non-BFR resistance exercise (33). However, pneumatic cuffs may not be practical for the majority of the population. For this reason, Loenneke and Pujol (22) suggested the use of knee wraps, which are similar in width to the well-studied KAATSU device. Specifically, these researchers applied knee wraps proximally around participants' thigh until they were snug, but the wraps did not cause pain. However, these researchers did not quantify the tightness of the wrap. Additionally, they did not verify if wrapping resulted in venous and arterial BFR. For this reason, we chose to wrap the participants at a moderate perceived pressure (7/10), and we verified venous but not arterial occlusion in all the participants examined. Low-intensity resistance exercise with moderate LI-pBFR resulted in greater metabolic stress than in the control condition. This metabolic accumulation with LI-BFR is likely produced from the reduction in oxygen from applying the wraps. Mechanistically speaking, metabolic accumulation may increase the recruitment of higher threshold (type II) fibers through the stimulation of group III and IV afferent fibers (37). This increased activation is important for muscle hypertrophy because it is thought that there is a close relationship between increased activation and muscle protein synthesis (20). In addition, that accumulation of metabolites may also facilitate the increase in growth hormone observed after resistance exercise with BFR (34), although the muscle anabolic effect of growth hormone in adults is largely unfounded (29).

According to Haussinger et al. (14), cell swelling shifts protein balance toward anabolism and thus induces hypertrophy. More recently, Loenneke et al. (18) postulated that LI-BFR results in increased water content of the muscle cells, which induces a cascade of anabolic intracellular signaling to occur. This postulation is supported in part by Fry et al. (10) who observed greater increases in muscle size (measured by circumference) with LI-BFR compared with low-intensity resistance exercise without BFR. The authors suggested that this acute swelling might mechanistically explain part of the increase in muscle protein synthesis observed after LI-BFR (10,11,13). Our results indicated that LI-pBFR may have resulted in an acute increase in muscle swelling. It is probable that the initial increase in muscle thickness was mostly because of venous pooling and not necessarily a fluid shift into the muscle cells. However, at some point during the protocol, it is probable that a fluid shift into the muscle cells did occur. If the acute change in muscle thickness was solely because of venous pooling, the muscle thickness value would have returned to baseline after the removal of the knee wrap. In fact, the changes in muscle thickness remained elevated 5 minutes after the removal of the wrapping device and did not begin to return to baseline until 10 minutes. Our results agreed with those of Loenneke et al. (19) who found an acute increase in muscle swelling and a decrease in plasma volume using the KAATSU device. That study was completed in the absence of exercise, but it does support the hypothesis that acute changes in muscle

cell swelling are likely occurring with this stimulus. Although acute increases in muscle thickness were observed and maintained after the removal of the wrapping device, indicating a fluid shift did occur, we are unable to definitively determine from this study whether or not the fluid was shifted into the actual muscle cell.

Recruitment of higher threshold motor units is important for the stimulation of muscle hypertrophy (7). It is commonly suggested that external load dictates changes in motor unit recruitment (2). However, results from LI-BFR training suggests that intensity determined by external load is of less importance than changes in the intramuscular environment (1). Through the application of blood flow restriction, the intensity of exercise can be increased, without altering the external load (1). Our results indicated that LI-pBFR increased skeletal muscle activation. These findings agreed with those of Yasuda et al. (38) who reported increases in EMG activity with LI-BFR using the KAATSU device and a similar protocol to our own. However, it should be noted that the Yasuda et al. (38) study investigated the elbow flexors. Regardless, the mechanism underlying increased motor unit recruitment is likely tied to the accumulation of metabolites, which can increase muscle fiber recruitment through the stimulation of group III and group IV afferents (37).

Skeletal muscle damage can be measured in various ways. Armstrong et al. (3) suggested that the most accurate indirect measure of muscle damage was a decline in performance. Moreover, his research also indicates that peak power has the greatest sensitivity to changes in skeletal muscle damage (3). In addition, Clarkson and Hubal (5) has also indicated that at 24–72 hours postexercise, muscle swelling and soreness are noninvasive, indirect measures of muscle damage. Although not taken at the fiber level, our results indicated that both the pBFR and work-matched control conditions decreased 24-hour peak power (5% decline) and increased muscle soreness. No changes in 24-hour muscle swelling were noted. There were no differences between conditions for any variable, suggesting that BFR does not augment the muscle damage response to resistance exercise. These results agree with those of the studies measuring serum markers of muscle damage, which show no significant elevation with LI-BFR (26). In addition, the return of peak power to within 5% of baseline at 24 hours post suggests that minimal to no muscle damage took place, which is in agreement with a recent study on LI-BFR, which used a similar protocol (23). Collectively, these results suggest that neither traditional nor pBFR augment training induced skeletal muscle damage.

PRACTICAL APPLICATIONS

Our results suggest that moderate pBFR can acutely increase hypertrophic stimuli such as metabolic stress, skeletal muscle swelling, and EMG determined muscle activation. We also found that a perceived pressure of 7 out of 10 consistently

resulted in complete occlusion of the veins, but not arteries. Therefore, the use of pBFR may serve as a less expensive alternative to pneumatic cuffs in resistance trained populations when wrapping at a moderate pressure. Future research should investigate the long-term effects of pBFR on skeletal muscle strength and hypertrophy.

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All the authors contributed to the study design, data collection, and article preparation.

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