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Acute Muscular, Metabolic, Cardiovascular, and Perceptual Responses to Low Cuff Pressure-small Cuff Width Blood Flow Restricted Exercise Prescription

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Abstract

Low-load blood flow restricted (BFR) exercise represents a novel method of rehabilitative exercise, however, little is known about variables that may influence the acute physiological response to BFR exercise prescription. This study explored the muscular, metabolic, cardiovascular, and perceptual responses to acute blood flow restricted exercise and compared it to traditional exercise using a Biodex dynamometer. Fourteen resistance trained, male participants (age: 22.1 ± 3.3 years; height: 177.8 ± 6.4 cm; body mass: 85.8 ± 11.9 kg) were randomized to complete 4 sets of isotonic knee extension-flexion resistance exercise under two conditions: 1) control; and 2) BFR exercise. Both control and BFR exercise used training loads of 20% of maximal voluntary contraction, however, control had free limb blood flow and BFR exercise was implemented using a 5 cm external cuff around the proximal thigh inflated to 140 mmHg. Muscle cross-sectional area (an index of muscle swelling) was significantly increased from baseline by 11.3% and 12.4% in control and BFR, respectively ($p = 0.001$). Similarly compared to baseline, lactate (control = 6.1 ± 1.3; BFR = 5.9 ± 0.9 mmol; $p < 0.001$), heart rate (control = 140.1 ± 18.8; BFR = 144.3 ± 12.6 bt · min-1; $p < 0.001$), RPE (control = 5.8 ± 2.8; BFR = 6.3 ± 2.4 arbitrary units; $p < 0.001$), and pain (control = 6.71 ± 18.4; BFR = 16.8 ± 29.2 mm; $p = 0.003$) significantly increased, however no differences could be detected between exercise types. Low cuff pressure-small cuff width BFR exercise does not result greater muscular swelling or alter metabolic, cardiovascular, or perceptual responses relative to low-intensity exercise alone. If rapid strength and mass gains can be achieved using low cuff pressure-small cuff width BFR methods it represents an intriguing rehabilitation strategy for disuse, injury, and some muscular disease treatments with less concern for patient safety.

Keywords: Blood flow restricted exercise; Muscle swelling; Ultrasound; Whole blood lactate

Introduction

There is strong evidence to support low-load (20-30% maximum strength) blood flow restricted resistance exercise as a training method to increase muscle cross-sectional area (CSA) and strength [1,2]. This type of exercise training may be an alternative to traditional high-load resistance training and have significant clinical viability [3]. For example, blood flow restricted exercise has shown efficacy in treatments for knee osteoarthritis [4], osteochondral fracture [5], inflammatory myositis [6], muscular weakness from disuse [7], anterior cruciate ligament reconstruction [8], and sarcopenia [9]. The synergistic mechanisms that appear to facilitate blood flow restricted exercise training adaptations include increased anabolic hormone production [10,11], increased cell-signaling for pathways muscle protein synthesis [12,13], suppressed negative growth regulators [14], decreased cell-signaling for pathways resulting in muscle protein breakdown [15], altered muscle fiber recruitment leading to an accumulation of metabolites [13], and acute skeletal muscle swelling [16,17].

Interestingly, blood flow restricted exercise prescription is quite variable [18,19]. For example, previous studies have prescribed inflation cuff pressure based on systolic blood pressure [1,7,15,20], limb circumference [21,22], initial restrictive pressure [23] or a predetermined static pressure [12,13]. Further, wider cuffs (13.5 cm) also have been shown to restrict arterial blood flow to a greater extent compared to narrow cuffs (5 cm) [21]. Practitioners or recreational exercisers using this exercise tool need to be aware of the interaction between pressure and width [18]. For example, facilitating mechanistic growth indicators (e.g., muscle swelling) during blood flow restricted exercise prescription by utilizing large cuff widths and high pressure; may be problematic if arterial flow is occluded and clotting factors (e,g. thrombin) are upregulated [24]. Further, long term ramifications of chronic blood flow restricted exercise training are unknown relative to more traditional exercise methods [25] and there are more recent concerns related to the amount of vascular occlusion (combination of cuff pressure and width) and the subsequent stress placed on the heart and blood vessels (e.g. reduced preload, pressor reflex) [20,26]. As a result, lower cuff pressures and small cuff widths may be generally safer than high cuff pressures and larger cuff widths. Therefore, the purpose of this study was to determine if low cuff pressure (140 mmHg) and small cuff width (5 cm) blood flow restricted exercise prescription would induce acute changes in muscle CSA (an index of muscle swelling) or accompanying metabolic, cardiovascular, and perceptual indicators to a greater extent than exercising at low-loads with free limb blood flow.

Methods

Fourteen healthy males with resistance exercise training experience were recruited to participate (age: 22.1 ± 3.3 years; height: 177.8 ± 6.4

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cm; body mass: 85.8 ± 11.9 kg; thigh circumference: 58.9 ± 3.9 cm; thigh length: 45.4 ± 9.5 cm; systolic blood pressure: 135.7 ± 10.9 mm Hg; diastolic blood pressure: 77.7 ± 6.9 mm Hg, isometric knee extension: 336.9 ± 88.5 N, isometric knee flexion: 134.9 ± 28.1 N).

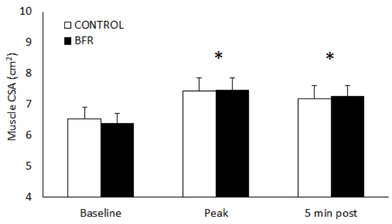

Figure 1: Change in muscle CSA (index of swelling) from baseline to 5-min post-exercise. Main effects for time with Sidak post-hoc corrections. *significant change from baseline.

	Baseline	Peak	5 min Post
Control	76.8 ± 11.9	140.1 ± 18.8*	87.3 ± 15.5*†
BFR	82.1 ± 12.1	144.3 ± 12.6*	91.5 ± 13.3*†

Main effects for time with Sidak post-hoc corrections.
*significant change compared to baseline;
†significant change from peak exercise response. Mean + SD.

Table 1: Heart rate responses with control and BFR exercise.

Health status was determined by Physical Activity Readiness and Health History Questionnaires. The definition of resistance training experience used was having lifted weights, or participated in resistance exercise, for a minimum of two days per week for the past six months. Additional exclusion criteria included previous nicotine or anabolic steroids use, or abnormally low blood pressure. All procedures were conducted according to the Declaration of Helsinki. Each participant provided written informed consent and the study was approved by the North Dakota State University Institutional Review Board.

Study design

Participants completed two unilateral, concentric, lower body resistance exercise sessions on the Biodex System 4 Pro (Shirley, NY, USA) a minimum of 48 hours apart and were performed in a randomized order. A standard warm-up was provided at each session which included 5 minutes on standard cycle ergometer at 50 watts as well as standing hamstring and quadriceps stretches. At the first session, (control or BFR) participants completed maximal isometric knee extension-flexion strength testing [27]. During this process, several (5-10) repetitions at a submaximal intensity (~50-90% effort) were performed on the left leg to get familiar with the device. Next, three maximal isometric knee extension-flexion contractions were performed. Twenty percent of the peak maximal isometric knee extension and flexion of the left limb was used to set both control and BFR exercise load for the right limb. The control session consisted of unilateral, knee extension-flexion exercise at 20% maximal voluntary contraction with free limb blood flow. The BFR session consisted of unilateral, knee extension-flexion exercise at 20% maximal voluntary contraction with a 5 cm inflation cuff set to 140 mmHg using rapid cuff inflator (D.E. Hokanson, Inc, E20 Rapid Cuff Inflator, Bellevue, WA, USA). During the BFR session, the external cuff was slowly inflated and deflated until the desired pressure was reached as described by Fujita et al. [13]. Both BFR and control sessions consisted of 4 sets, with the first set containing 30 repetitions, and sets 2-4 containing 15 repetitions. There was 30 seconds of rest between each set. During BFR, the cuff remained inflated during the rest interval [13].

Prior to the first session, descriptive measures were obtained on each participant which included age, height, body mass, systolic and diastolic blood pressure, thigh length, thigh size, and isometric knee extension-flexion strength. Resistance exercise on the Biodex consisted of one session of low-load knee extension-flexion exercise with free limb blood flow (control), and a second session with blood flow restriction (BFR). To investigate the metabolic, cardiovascular, and perceptual response to BFR exercise, whole blood lactate, muscle CSA, heart rate, perceived exertion, and pain were evaluated before exercise (baseline), immediately after sets 1, 2, 3, and 4 to determine the greatest response (peak) and five minutes post-exercise (5 min-post). Indices of fatigue were also determined from knee extension peak contraction velocity and total work during sets 1, 2, 3, and 4.

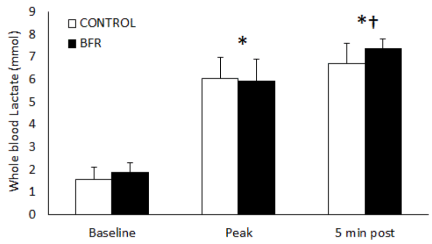

Figure 2: Whole blood lactate response from baseline to 5-min post-exercise. Main effects for time with Sidak post-hoc corrections. *significant change from baseline; $p < 0.001$; †significant change from peak to 5 min post.

Descriptive measures

Age was self-reported by participants on the health history questionnaire. Height (cm) and body mass (kg) were measured using a stadiometer (Seca 213, Chino, CA) and digital scale (DA series, Denver Instruments, Bohemia, NY), respectively. Systolic and diastolic blood pressures (mm Hg) were assessed with the subject in a standard seated position using an inflation cuff, sphygmomanometer, and stethoscope (Littman Lightweight II SE, 3M, Maplewood, Minnesota). Thigh size was evaluated according to the methods of The United States Department of Health and Human Services [28]. Briefly, the midpoint of the thigh was determined by placing a mark halfway between the anterior superior iliac spine and proximal patella on the right limb. The midthigh circumference (cm) was assessed standing with knee slightly flexed using a measuring tape. The average of three measurements was calculated and reported.

Skeletal muscle, metabolic, and cardiovascular measures

The rectus femoris (RF) was selected to be examined because it is a knee extensor muscle that is active during knee extension exercise and

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has been previously shown to be a responsive to measure during acute muscle swelling [16]. An image of the RF muscle was captured with the knee joint at 90° flexion in the Biodex system 4 Pro dynamometer (Shirley, New York, USA) using a Phillips HD11XE ultrasound scanner and 12-5 MHz linear probe (Phillips Ultrasound, Bothell, WA, USA) in panoramic mode [29].

A 2 cm × 2 cm calibration square was also traced using the internal ultrasound software and saved on all muscle images. All images were also coded and transferred to a personal computer where the RF and calibration image were analyzed for area (cm^2) using Image J software (National Institutes of Health, Bethesda, Maryland, USA) [30].

The calculated area of the RF was then normalized to the calculated area of the calibration image to obtain a measure of muscle cross-sectional area (CSA). A single investigator performed all image analysis and was blinded to the exercise type and time points. The test-retest reliability of this technique using the intraclass correlation coefficient was 0.998. A permanent marker was used to mark the site where the measure would be taken by the ultrasound probe.

This position was recorded in cm in order to replicate during the second session. Whole blood lactate was measured using a finger stick blood sample and a portable analyzer (Lactate Plus, Nova Biomedical, Waltham, MA, USA). Heart rate was determined continuously using a heart rate monitor (Polar, Polar Electro Inc, New York, USA).

Perceptual and fatigue measures

Perceptual responses were evaluated by rate of perceived exertion (RPE) and visual analog scales (VAS) discomfort scales due to their reliability and ease of use [31,32].

The RPE scale was on a 0-10 scale regarding the intensity of the exercise (muscle fatigue, physical exertion). For example, scores of 0, 5, or 10 represented intensity ratings of nothing at all, hard, and very, very hard.

The VAS scale provided a way for the subjects to communicate their perceived pain or discomfort (localized discomfort from the cuff pressure) by pointing to a spot on a 100 millimeter ruler. Movement velocity and total work were calculated from the internal software within the Biodex System 4 Pro dynamometer (Shirley, New York, USA).

	Baseline	Peak	5 min Post
RPE (0-10)			
Control	0.0 ± 0.0	5.8 ± 2.8*	0.6 ± 1.2†
BFR	0.0 ± 0.0	6.3 ± 2.4*	1.0 ± 1.7†
Pain via VAS (mm)			
Control	0.2 ± 0.8	28.7 ± 36.8*	6.7 ± 18.4†
BFR	0.2 ± 0.8	39.4 ± 39.4	16.9 ± 29.1†
Main effects for time with Sidak post-hoc corrections *significant change from baseline; †significant change from peak; Mean + SD.			

Table 2: Perceptual responses for control and BFR exercise.

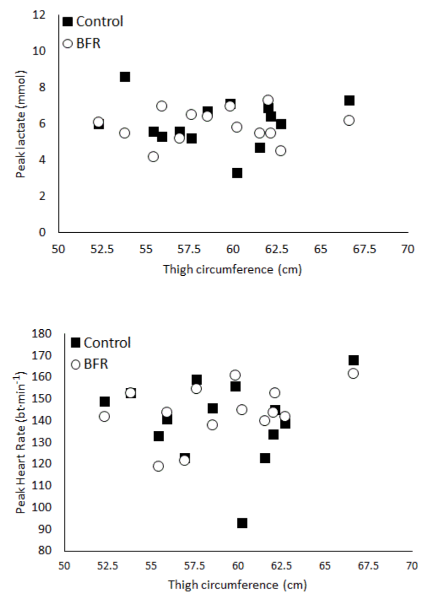

Figure 3: Association between thigh circumference (cm) and indicators of control and BFR exercise intensity/stress: A) peak lactate or B) peak heart rate. A negative correlation was expected, which would have suggested less intensity/stress with greater thigh circumferences at the same cuff pressure (140 mm Hg). However, no strong associations between thigh circumferences in peak lactate or peak heart rate were observed.

	Set 1(30 reps)	Set 2(15 reps)	Set 3(15 reps)	Set 4(15 reps)
Peak Velocity Knee Extension (deg · sec^{-1})				
Control	426.0 ± 36.9	407.7 ± 35.8*	391.5 ± 39.6*†	381.8 ± 42.7 *†‡
BFR	434.2 ± 24.0	402.9 ± 38.0*	385.3 ± 38.2*†	376.4 ± 41.2*†‡
Total Work Knee Extension (J)				
Control	3597.9 ± 498.9	1721.7 ± 284.7*	1626.8 ± 306.7*†	1580.2 ± 296.3*†‡
BFR	3641.9 ± 577.6	1646.9 ± 235.6*	1530.6 ± 240.9*†	1510.8 ± 239.6*†‡
Main effects for time with Sidak post-hic corrections: *significant change compared to set 1; †significant change compared to set 2; ‡significant change compared to set 3. Rep= repetitions completed. Mean ± SD.				

Table 3: Indicators of fatigue from set 1 to set 4 of knee extension-flexion exercise.

Statistical Analyses

Means and standard deviations (SD) were calculated for descriptive measures. Muscle CSA, heart rate, whole blood lactate, RPE and pain were analyzed using separate 2 × 3 (exercise: control and BFR × time:

baseline, peak, and 5 min-post) ANOVAs with repeated measures. Contraction velocity and total work were examined using a 2 × 4 (exercise type by set) repeated measures ANOVA. For all ANOVAs, when Mauchly's sphericity assumption was not met, the Greenhouse-Geisser correction was applied. An alpha level of $p<0.05$ was utilized for all statistics and effect size (ηp^2) is also reported below. Too reduce the change of a type I error, when a significant ANOVA interaction or main effect was discovered Sidak post-hoc tests were used to determine differences. Further, Pearson correlations between thigh size, peak lactate, and peak heart rate were calculated. All statistical analysis was performed using IBM SPSS software version 22 (Armonk, New York, USA).

Results

There were no exercise type × time interactions or main effects for exercise type for any of the dependent variables ($p>0.05$, ηp^2 range = 0.008-0.18). However, significant main effects of time were found for muscle CSA ($p = 0.001$, $\eta p^2 = 0.47$, Figure 1), whole blood lactate ($p<0.001$, $\eta p^2 = 0.95$, Figure 2), heart rate ($p < 0.001$, $\eta p^2 = 0.94$, Table 1), RPE ($p<0.001$, $\eta p^2 = 0.84$, Table 2), pain ($p = 0.003$, $\eta p^2 = 0.47$, Table 2), knee extensor contraction velocity ($p<0.001$, $\eta p^2 = 0.76$) and knee extensor total work ($p<0.001$, $\eta p^2 = 0.98$). Knee extension contraction velocity and total work declined during the exercise session (Table 3). Overall, there were no significant correlations between thigh circumference and peak lactate (R= -0.001, p=0.99) or thigh circumference and peak heart rate (R= 0.394, p=0.16) in BFR (Figure 3).

Discussion

The purpose of this study was to determine if low cuff pressure (140 mmHg) and small cuff width (5 cm) blood flow restricted exercise prescription would induce acute changes in muscle CSA (an index of muscle swelling) or accompanying metabolic, cardiovascular, and perceptual indicators to a greater extent than exercising at low-loads with free limb blood flow.

The anabolic benefits of acute shifts in muscle CSA as a result swelling from blood flow restricted exercise was recently proposed by Loenneke et al. [33]. Based on Haussinger's model of hepatocyte swelling [34], it is suggested that low load resistance exercise with blood flow restriction increases muscle cell size via intracellular water flux and reperfusion upon cuff pressure release [33]. Further, the increased muscle cell volume is then sensed, resulting in activation of anabolic cell-signaling pathways [33]. However, given the nature of blood flow restricted exercise, it is apparent that acute alterations in muscle water content would be a dynamic process as also shown with traditional exercise [35]. For instance, pressure due to initial inflation of the external cuff may force water out of the muscle cell, while the demands of working muscles may lead to the return of water via arterial blood flow and increased venous pooling. Further, once the cuff is released rapid reactive hyperemia results in a high velocity surge of arterial blood flow to the muscle [20,36]. In our study, muscle CSA, an index of muscle swelling, increased following low-load resistance exercise both with and without blood flow restriction (11.3% vs. 12.4%, respectively); however, no differences could be detected between the two exercise methods. These results are in slight contrast to Wilson et al. [17] who showed muscle thickness was enhanced 5 min post BFR leg press exercise (30% 1RM, 4 sets, 30,15, 15, 15 repetitions, 7.6 cm wide elastic knee wraps at a moderate perceived pressure) compared to control exercise and Thiebaud et al. [37] who reported a 15% increase in acute muscle swelling immediately following concentric arm flexor exercise with a similar exercise prescription (30% 1RM, 4 sets, 75 total repetitions, 30 sec rest between sets, 160 mmHg cuff pressure, 3 cm wide cuff). It is suggested that acute increases in muscle fluid may activate anabolic signaling (e.g. mammalian target of rapamycin or mitogen activated protein kinase) through osmosensing [33,38], however, a direct relationship between acute muscle swelling and anabolic cell signaling has yet to been determined [36]. Further, there is also concern that prolonged or excessive vascular occlusion in effort to enhance acute muscle swelling, can increase the strain on the cardiovascular system via reduced preload and stroke volume [20,26]. Therefore, it appears there is debate over the importance of acute muscle swelling as it pertains to BFR exercise. In this capacity, using a low cuff pressure and small cuff with BFR exercise prescription appeared to stimulate some muscle swelling when compared to baseline, but not to a greater extent that low-intensity exercise alone. Thus, this may be a beneficial response for potential hypertrophy mechanism but also the safety of a subject performing BFR exercise.

Elevations in whole blood lactate concentrations occur because of increased rates of fast glycolysis in ischemic muscle and may facilitate an increase in growth hormone following BFR exercise [10,11]. In the present study, the lack of difference in whole blood lactate responses between the control (6.7 mmol) and BFR (7.4 mmol) 5 min post-exercise further suggests the interaction between the low cuff pressure and small cuff width was not potent enough to significantly challenge muscle metabolism to a greater degree than low-intensity exercise alone. However, there was a strong metabolic perturbation that further increased at the 5 min post exercise time point. Interestingly, although efforts are underway to optimize and/or individually prescribe the optimal cuff pressure based on leg circumference and/or systolic blood pressure [22], we did not observe a strong correlation between thigh circumference and indicators of exercise intensity, such as the change in whole blood lactate (R=-0.001) or heart rate (R=0.394) using a static low pressure (140 mm Hg). We found this surprising given we would have hypothesized a negative correlation, suggesting that the larger the participant's leg size is the easier the exercise would be given a static pressure. For instance, according to Scott et al. [19], a greater occlusion pressure (150-210 mmHg) may be required when using a 5 cm inflation cuff with larger thigh circumferences in order to initiate significant metabolic stress (~60% of full arterial occlusion pressure). However, implementing the safest and most comfortable exercise prescription for BFR exercise is paramount for long term adherence [1,21,22]. Wider cuffs and larger pressures may result in greater metabolic stress, but they also result in greater RPE and pain responses, which may not be important for adaptation. In our investigation, RPE and pain ratings in this study peaked during exercise and returned toward baseline levels 5 minutes post-exercise, with no significant differences between the exercise types. Peak heart rates in BFR exercise were only ~4 bpm greater (non-significant) on average compared to control. Collectively, these data suggests that there is a complex interplay between the amount of "setting related" (cuff pressures, width, load, etc.) stress placed on the exercise limb; whereby the settings need to be intense enough to drive motor unit recruitment, facilitate whole blood lactate production, and initiate some degree of muscle swelling, yet not too intense so that it places excessive strain on the cardiovascular system (i.e., decreased preload, pressure reflex) or cause significant pain [26]. This concept was recently demonstrated by Counts et al. [39], who showed that the increases in muscle size and strength were similar when training at 90% of arterial occlusion pressure compared to 40% of arterial occlusion pressure [39]. Further, Downs et al. [20] showed cuff pressures as low as 95 ± 2 mm Hg could stimulate hypoxia in the muscle tissue without reductions in stroke volume, cardiac output or elevations in diastolic blood pressure. Thus, for future BFR exercise prescription, understanding the interactions amongst novel programming variables such as cuff pressure, cuff width, cuff inflation duration, pre-inflation cuff pressure, participant blood pressure, and participant limb size will be critical for safety [19].

Conclusion

As BFR exercise paradigms become more popular in clinical, recreational, and athletic settings, it is important to gain further understanding of variables associated with exercise prescription. Most notably, for safety and to foster the desired exercise training adaptations a scientific consensus on how cuff pressure should be prescribed given the multilevel interactions amongst cuff size, cuff type, initial cuff pressure, thigh circumference, blood pressure, and individual differences. Although muscle hypertrophy determinants such as muscle swelling may be important for muscle growth and strength; other indicators such as heart rate, lactate, and pain are equally important for safety. Data presented here show resistance exercise with a low-moderate standardized cuff pressure of 140 mm Hg combined with a small cuff width of 5 cm did not facilitate greater acute training stress (muscle CSA changes, heart rate, lactate, RPE, pain) than resistance exercise with free blood flow. Whether greater acute stress is actually required for chronic increases in muscle CSA, strength, or endurance has yet to be firmly established. Until further training studies are performed on strength and conditioning professionals should limit protocols to those outlined in the evidence based-blood flow restricted exercise recommendations provided by Scott et al. [19]. If rapid strength and mass gains can be achieved using low cuff pressure-small cuff width BFR methods it represents an intriguing rehabilitation strategy for the treatment of disuse, injury, and some muscular diseases.

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