Similar Morphological and Functional Training Adaptations Occur Between Continuous and Intermittent Blood Flow Restriction

Brief Running Head: Intermittent BFR Promotes Muscular Adaptations

Charlie J Davids[1, 2, 4], Truls Raastad[3], Lachlan James[4], Trishan Gajanand[1], Emily Smith[1], Mark Connick[1], Hamish McGorm[1,2], Shelley Keating[1], Jeff S Coombes[1], Jonathan M Peake[2, 5] and Llion A Roberts[1, 2, 6]

[1]School of Human Movement and Nutrition Sciences, The University of Queensland, Brisbane, Australia; [2]Queensland Academy of Sport, Nathan, Australia; [3]Department of Physical Performance, Norwegian School of Sport Science, Oslo, Norway; [4]School of Allied Health, Human Services and Sport, La Trobe University, Melbourne, Australia; [5]School of Biomedical Sciences and Institute of Health and Biomedical Sciences, Queensland University of Technology, School of Biomedical Science, Brisbane, Australia; [6]Griffith Sports Physiology and Performance, School of Allied Health Sciences, Griffith University, Gold Coast, Australia.

Corresponding author: Dr Charlie Joseph Davids

School of Human Movement and Nutrition Sciences

The University of Queensland

St. Lucia, Brisbane, QLD, 4067

Email: c.davids@uq.edu.au

Tel: +61 (07) 3365 6240

ORCID ID: 0000-0002-6370-9434

ABSTRACT

The aim of the study was to compare skeletal muscle morphological and functional outcomes after low-load resistance training using two differing blood flow restriction (BFR) protocols. Recreationally active males and females (n=42 [f=21], 24.4±4.4yrs) completed 21 sessions over 7-weeks of load- and volume-matched low load resistance training (30% one-repetition maximum [1RM]) with either: a) no BFR (CON), b) continuous BFR (BFR-C, 60% arterial occlusion pressure [AOP]) or c) intermittent BFR (BFR-I, 60% AOP). Muscle mass was assessed using peripheral quantitative CT (pQCT) before and after training. Muscular strength, endurance and power were determined before and after training by assessing isokinetic dynamometry, 1RM, and jump performance. Ratings of pain and effort were taken in the first and final training session. An alpha level of $p<0.05$ was used to determine significance. There were no between-group differences for any of the morphological or functional variables. Muscle cross sectional area (CSA) increased pre-post training ($p=0.009$; CON: 1.6%, BFR-C: 1.1%, BFR-I: 2.2%). Maximal isometric strength increased pre-post training ($p<0.001$; CON: 9.6%, BFR-C: 14.3%, BFR-I: 19.3%). Total work performed during an isokinetic endurance task increased pre-post training ($p<0.001$, CON: 3.6%, BFR-C: 9.6%, BFR-I: 11.3%). Perceptions of pain ($p=0.026$) and effort ($p=0.033$) during exercise were higher with BFR-C; however, these reduced with training ($p=0.005$-0.034). Overall, these data suggest that when 30% 1RM loads are used with a frequency of three times per week, the addition of BFR does not confer superior morphological or functional adaptations in recreationally active individuals. Furthermore, the additional metabolic stress that is proposed to occur with a continuous BFR protocol does not appear to translate into proportionally greater training adaptations. The current findings promote the use of both intermittent BFR and low-load resistance training without BFR, as suitable alternative training methods to continuous BFR. These approaches may be practically applicable for those less tolerable to pain and discomfort associated with ischemia during exercise.

Key Words: OCCLUSION, ISCHEMIA, HYPOXIA, KAATSU, HYPERTROPHY

LIST OF ABBREVIATIONS

ANOVA: Analysis of variance

APSS: Australian pre-exercise screening system

BFR: Blood flow restriction

BFR-C: Continuous blood flow restriction

BFR-I: Intermittent blood flow restriction

CMJ: Countermovement jump

CON: Control

CSA: Cross-sectional area

CV: Coefficient of variation

DEXA: Dual energy x-ray absorptiometry

MVC: Maximal voluntary contraction

pQCT: Peripheral quantitative computed tomography

RFD: Rate of force development

SD: Standard deviation

1RM: One repetition maximum

INTRODUCTION

Obtaining and maintaining adequate skeletal muscle mass is a goal shared by many populations, ranging from athletic cohortsto elderly individuals. Along with muscle hypertrophy, functional adaptations in muscle, such as strength, power and muscular endurance, are also sought after by such populations, to maximize performance and to minimize risk of falls and improve quality of life, respectively (2, 33). Previous guidelines from the American College of Sports Medicine (ACSM) recommended loads ≥70% of an individual's one-repetition maximum (1RM) to maximise hypertrophy and functional adaptations in muscle (2). However, more recent evidence suggests much lower-loads (e.g., 20-30% 1RM) may be capable of maximising these hallmark adaptations to resistance training, providing sets are completed close to, or at, muscular failure (11).

Blood flow restriction (BFR) combined with low-load resistance exercise is another training strategy that has gained popularity in recent times, owing to the fact that it can elicit various adaptations in skeletal muscle with reduced exercise volume (35). Indeed, this style of training is a valid alternative to high-load resistance exercise training (>70% 1RM) to induce skeletal muscle hypertrophy (20). Similarly, marked improvements in muscular strength and endurance also occur with low-load resistance training with BFR; these improvements may exceed those observed with low-load resistance training alone (35). Such benefits of BFR have been observed both in healthy athletic populations (4, 8, 25), and in elderly individuals (41), although it has been reported that perceptions of pain and effort may be elevated with this style of exercise (42). Although there is a substantial body of research supporting the efficacy of BFR exercise, evidence-based guidelines informing practitioners and coaches on how to best manipulate training variables (e.g., cuff pressure, duration, exercise type and intensity etc.) have only recently been provided (31). One important variable that is lacking is how the BFR cuffs are applied. Typically, cuffs either remain inflated during the entire exercise session (continuous application), or they are removed or deflated during the rest intervals between sets (intermittent application) (27). Evidence suggests that an intermittent application can reduce perceptions of pain and effort during BFR exercise (12, 27), which may make this mode of training more suitable for those who are less tolerable to exercise-induced discomfort (e.g., clinical or elderly populations).

However, it is not clear if applying BFR intermittently dampens the stimuli for muscle adaptation. By releasing the compression during the rest interval between sets, venous blood flow from the exercising muscles is restored, which consequently alleviates the accumulation of metabolites (30, 38). Thus, it may be that intermittent BFR poses no additional benefit over unrestricted low-load exercise. On the other hand, continuous

BFR is reported to promote a greater accumulation of inorganic phosphate and decline in intramuscular pH, compared with intermittent BFR and unrestricted low-load exercise when multiple sets are performed (30, 37, 38). Given that metabolite accumulation is outlined as a primary mechanism that underpins the favorable chronic adaptations that occur after BFR resistance exercise (32), it would seem counterintuitive to apply BFR intermittently. Indeed, a robust correlation (r=~0.85) between acute metabolic stress and chronic hypertrophy with ischemic exercise has been reported (39). Conversely, it has been postulated that the anabolic effects of metabolites may simply be achieved through an increased motor unit recruitment, and consequently mechanical tension being experienced in a greater number of muscle fibres (43). If such a theory is true, then a threshold of metabolic stress which permits the recruitment of the highest threshold motor units would only be necessary, and any additional metabolite accumulation would not promote proportionally greater adaptations to training. Instead, excessive metabolite accumulation may augment pain and effort signals during exercise via activation of group III/IV afferents (43). In support of this alternative theory, recent evidence indicates that more metabolically demanding BFR protocols (that involve higher volumes of exercise or training to muscular failure) may not necessarily promote greater adaptations, and may instead prolong fatigue and delay subsequent adaptation (5, 26, 29, 34).

In the only study where the effects of continuous versus intermittent BFR were compared directly over a resistance training period, no differences were found between protocols, or an unrestricted low-load training group, for increases in isokinetic strength and fat-free mass following a 5-week period (12). However, the use of dual energy x-ray absorptiometry (DEXA) alone (which only provides a global measure of lean muscle mass) to quantify skeletal muscle hypertrophy, and the relatively short training period (15 sessions), limit the validity of the findings. It is unclear if the negligible differences between groups were due to the BFR protocols *per se*, or simply that the measurement tools lacked sensitivity to discern any differences that may have existed between groups. Moreover, the comparison of a wider range of functional outcomes, such as isometric strength, muscular power and endurance between continuous and intermittent BFR is necessary to evaluate the efficacy of each protocol.

The results from acute studies suggest that continuous BFR may provide a stronger stimulus for muscle adaptation, however this has not yet been corroborated by a chronic training study. Therefore, the primary aim of this study was to compare chronic muscle hypertrophy and functional outcomes including strength, power and muscular endurance between continuous and intermittent BFR protocols, and low-load resistance training in recreationally active males and females. Our primary hypothesis was that all groups would improve lower limb skeletal muscle hypertrophy and functional outcomes. However, we further hypothesized that continuous BFR would be the most effective, and low-load training without BFR would be the least effective protocol for developing muscular hypertrophy and functional outcomes.

METHODS

Subjects

Fifty-one recreationally active males and females volunteered to participate in the study after procedures and risks were explained to them and they provided their written informed consent. Subsequently, participants were screened using the Adult Pre-Exercise Screening System (APSS) tool. Participants were considered eligible to participate if they had consistently performed lower body resistance training at least once per week for the last six months. Further exclusion criteria included cardiovascular disease, musculoskeletal injury, pregnancy, or those taking medications known to enhance blood clotting risk, as specified by Brandner et al. (6). This study was approved by the Human Research Ethics Committee of The University of Queensland. Baseline participant characteristics are reported in Table 1.

[Table 1 About Here]

Experimental Design

Participants completed three baseline and familiarization visits prior to training to conduct baseline assessments of muscle mass and function, and familiarize themselves with the requirements of the study. Following these visits, participants were assigned to one of three groups in a counter-balanced yet random manner. Initially, participants were ranked in order of their pre-training leg press 1RM score, multiplied by their lower body lean mass, which was determined by DEXA (Hologic Delphi, Hologic Inc, Bedford, USA). Subsequently, participants were counterbalanced into the three groups from highest to lowest rank, to ensure an even distribution of muscle mass and strength at baseline. Additionally, female participants were counterbalanced between groups based on contraceptive use. Groups were then randomly allocated to a training protocol by another researcher not involved in the study using computer software (www.randomizer.org).

The training protocols consisted of seven weeks (21 sessions) of low load resistance training with continuous BFR (BFR-C), intermittent BFR (BFR-I), or a non-BFR (CON) control protocol. Nine participants withdrew from the study after training protocol allocation was undertaken citing reasons unrelated to the study. Their data were subsequently excluded from the analysis. Assessments of muscle mass and function were repeated 5-7 days following the final training session to promote recovery and to prevent post-exercise swelling from being mistakenly measured as an increase in cross-sectional area (41).

Procedures

Resistance Training Protocol

The study involved 7 weeks of lower body resistance training, three times per week with ~48 h between sessions. This moderate training frequency has been employed in previous BFR studies that are shorter in duration (5–7 weeks) to ensure there is an adequate stimulus for adaptation (16, 19, 26). Each session involved four sets of bilateral incline leg press and four sets of bilateral leg extension exercise at an initial load of 30% 1RM. All groups were matched for training load and volume, following a similar set/rep protocol that is frequently adopted in the literature (23). Specifically, the protocol involved four sets of each exercise, consisting of one set of 30 repetitions, followed by three sets of 15 repetitions. Each set was separated by 45 s of passive seated rest. Rest intervals between exercises were 3 min. After every fourth session, leg press weight was increased by 3% and leg extension by 1.5% of the original 1RM values. These increments were chosen as they were calculated to correspond to the anticipated increases in 1RM values throughout the program (as 1RM testing was not repeated during the training), and to adhere to the progressive overload principle (2). If participants were unable to perform all 75 repetitions for each exercise, the load was reduced for the subsequent session.

Pneumatic nylon cuffs were used for both BFR-C and BFR-I (10cm width, Sports Rehab Tourniquet, QLD, Australia), and were placed on the same proximal region of both thighs (approximately 3 cm below the inguinal fold). The CON group had no cuffs applied. All participants were encouraged to consume a protein-rich diet ($2g\cdot kg^{-1}$ body mass) during training. To aid this request, the participants were provided with 30 g of whey protein isolate (Bulk Nutrients®, VIC, Australia) each day during the training block to consume before and after each training session. The participants were also provided with individual servings of whey protein to take home and consume on non-training days. They were asked to maintain their regular physical activities, but refrain from any lower-body resistance exercise outside the study.

Blood Flow Restriction Protocols

The BFR cuff pressures to be used during training were individualised to each participant using Doppler ultrasound (uSmart3300, Terason, USA) of the posterior tibial artery, as previously advocated by Loenneke et al. (22) to determine 100% arterial occlusion pressure (AOP). Determination of arterial occlusion pressure (AOP) was performed at rest while seated in an upright position. The BFR cuffs used during the training intervention were attached to the rapid cuff inflator (E20, Hokanson, Bellevue, WA) during the AOP assessment to enhance the specificity of the cuff pressure prescription. Cuffs were applied and inflated to 50% AOP before the first set of exercise for BFR-C and BFR-I. Previous research suggests that moderate restriction pressures such as this are appropriate if the exercise load used is slightly higher (e.g., 30–40% vs 10–20% 1RM) (9, 21). Pressure was increased to 60% AOP after 10 sessions, with the aim of increasing the metabolic stimulus of BFR during training. Mean absolute cuff pressure corresponding to 60% AOP was 104 mmHg. The cuffs for both BFR groups were inflated immediately before the first exercise set. The cuffs remained inflated during all sets in the BFR-C group, whereas they were deflated immediately following the final repetition of each set in the BFR-I group. Cuffs were inflated again after 20–30 s of the rest period, to ensure rest periods remained at 45 s across all groups. In both BFR-C and BFR-I protocols, cuffs were deflated for a ~3-minute period between exercises. All participants were familiarized with BFR-C during a baseline visit prior to beginning training.

Muscle Mass Assessments

Muscle mass was measured using full-body DEXA (Hologic Delphi, Hologic Inc, Bedford, USA), whereas localized muscle cross-sectional area (CSA) from the dominant thigh at five locations was measured by peripheral quantitative computed tomography (pQCT; XCT 3000, Stratec Medizintechnik GmbH, Germany). The five CSA measurement sites were 25, 40, 50, 60 and 70% of the distance between the femoral condyles and the greater trochanter. The CSA value in mm2 from each site were combined to provide a total thigh CSA value, which was used for analysis. The same technician performed and analyzed all scans. In our laboratory, test-retest coefficient of variation (CV) for mid-thigh CSA was 0.4%, and lower body lean mass by DEXA was 0.7%.

Strength and Endurance Testing

Maximal voluntary isometric and isokinetic contraction (MVC) strength of the quadriceps from the dominant leg was assessed on an isokinetic dynamometer (Biodex 3, Biodex Medical Systems, USA). Isometric knee extension MVCs were measured from three 3-s contractions at 70 degrees of knee flexion (full extension as 0 degrees). Subsequently, isokinetic knee extension MVCs were measured from three contractions at both $60^{\circ}\cdot s^{-1}$ and $150^{\circ}\cdot s^{-1}$ speeds. Range of motion for isokinetic contractions was set to 90 degrees of knee extension. Rest between each isometric and isokinetic contraction was 90 s. Participants were instructed to apply force as rapidly and hard as possible for the entire contraction. The best contraction was identified as that which produced the highest torque. Rate of force development (RFD) was also determined from the initial 250 ms of best isometric knee extensor MVC. The participants also completed an isokinetic knee extensor endurance task involving 50 sequential maximal isokinetic knee extension contractions (1 Hz, $90^{\circ}\cdot s^{-1}$). Knee flexion speed was set at $300^{\circ}\cdot s^{-1}$. All data were collected at 1,000 Hz (LabVIEW, National Instruments Corp., Texas, USA), and analyzed using a custom-written script (MATLAB R2016b, MathWorks, Natick, MA). Test-retest CV values were 4.7% for peak torque during isometric contractions and 4.1% for total work during the isokinetic endurance task.

Bi-lateral isotonic one-repetition maximum (1RM) testing was performed on leg press and knee extension machines (TechnoGym®, Gambettola, Italy) following the 1RM assessment protocol endorsed by the National Strength and Conditioning Association (NSCA) (3). The highest load that was successfully completed (90° through to full extension of the knees) was recorded as the 1RM score.

Countermovement Jump Assessment

To obtain information on lower body power and velocity characteristics, participants completed countermovement jumps on a force plate (9286BA, Kistler, Ostfildern, DE). To standardize jumping performance, participants were asked to set up on the plate with their feet shoulder-width apart, and to keep their hands on their hips throughout the jump. After a standardized warm up, participants were instructed to jump for maximal height, for three attempts, each separated by a brief 30 s rest period of quiet standing. The jump with the greatest peak power value was selected for subsequent analysis. All data were collected at 1,000 Hz (LabVIEW, National Instruments Corp., Texas, USA), and analyzed using a custom-written script (MATLAB R2016b, MathWorks, Natick, MA). Jumping performance was assessed by recording average velocity, average power, peak velocity, peak power and peak displacement values. Test-retest CV for the determination of peak power during counter-movement jump was 1.5%.

Perceptions of Pain and Effort

Perceptions of both pain and exertion were recorded following each set of exercise during the first and final sessions. Perceptions of pain were recorded using a pain (CR-10+) visual analogue scale, whereas perceived exertion was recorded using a modified Borg exertion (CR-10) scale. During the familiarisation, the participants were instructed on how to distinguish between, and attribute values for pain and effort as previously described by Hollander et al. (13). Additionally, the participants were reminded that pain and exertion are different sensations. In particular, exertion should relate more to fatigue, whereas pain should be considered as unpleasant feelings within the exercising muscles. The participants were asked to confirm that they recognise the differences in the ratings. Pain and effort ratings for all sets and exercises were averaged to provide a single value for each in the first and final session of the training block.**Statistical Analyses**

Statistical analyses were performed using GraphPad Prism Software (Version 7.0; GraphPad Software Inc., La Jolla, CA). Data were checked for normality and equality of variances using the Shapiro-Wilk, and Levene's test, respectively. Differences between groups at baseline for all dependent variables were first examined by one-way analysis of variance (ANOVA). When no significant differences were detected at baseline, two-way, group (BFR-C, BFR-I and CON) and time (e.g. PRE and POST) ANOVA tests were conducted on all dependent variables. Significant interactions were followed up by group and time post-hoc testing, whilst significant group or time main effects were followed up with main effect specific post-hoc testing. All post-hoc testing were subject to Bonferroni correction. Cohen's *d* standardised effect sizes (presented as $d \pm 90\%$ confidence intervals) were calculated to evaluate the magnitude of changes after training and differences between groups. Effect sizes were also computed to compare the magnitude of changes after training between sexes. The effect sizes were interpreted as $d<0.2$ = null effect, $d<0.5$ = small effect, $d<0.8$ = moderate effect, and $d>0.8$ = a large effect (7). Data are presented as mean ± standard deviation (SD), with significance accepted at an alpha of ≤0.05.

RESULTS

Muscle Mass

Figure 1 displays group mean and individual changes in thigh muscle CSA by pQCT (A) and lower body lean mass by DEXA (B). No differences in CSA or lower body lean mass existed between groups at baseline. There was no significant group effect (p=0.610), or a time*group interaction (p=0.285) for thigh muscle CSA measured by pQCT. However, a main effect of time (p=0.009) was observed. Further analyses indicated that muscle CSA increased pre-post training with BFR-I (2.2±3.7%, d=0.14±0.60), BFR-C (1.1±3.1%, d=0.03±0.58) and CON (1.6±2.6%, d=0.05±0.78). Upon examination of sex-specific responses, males CSA changed pre-post training with BFR-I (5.0±2.0%, d=0.69±0.92), BFR-C (-0.1±3.3%, d=-0.01±0.77) and CON (-0.2±1.3%, d=-0.01±1.34). Females changed pre-post training with BFR-I (0.4±3.3%, d=0.03±0.78), BFR-C (2.1±2.7%, d=-0.16±0.88) and CON (2.7±2.5%, d=-0.1±0.95).

For lower body lean mass measured by DEXA, there was no main effect for group (p=0.623), or a time*group interaction (p=0.422). However, a time main effect (p=0.029) was observed. Further analyses revealed marginal increases in lower body lean mass pre-post training with BFR-I (2.1±4.4%, d=0.11±0.58) BFR-C (1.4±3.1%, d=0.05±0.58) and with CON (1.9±4.2%, d=0.05±0.74).Sex-specific responses for DEXA are provided in Supplementary Material 1.

[Figure 1 About Here]

Muscle Strength

Group mean and individual changes for isometric MVC peak torque (A), 60°·s^{-1} isokinetic (C) and 150°·s^{-1} isokinetic (D) MVC peak torque, leg press (E) and leg extension (F) 1RM strength are displayed in Figure 2. No differences in isometric, isokinetic or 1RM strength existed between groups at baseline. There were no significant group effects (p=0.414) or time*group interaction (p=0.386) for isometric MVC peak torque. However, a time main effect was observed (p<0.001). Isometric MVC peak torque increased pre-post with BFR-I (19.3± 20.1%, d=0.49±0.68), BFR-C (14.3±10.4%, d=0.21±0.74), and CON (9.6±13.8%, d=0.23±0.78). Upon examination of sex-specific responses, males changed MVC pre-post training with BFR-I (19.8±21.1%, d=1.47±1.28), BFR-C (14.5±13.2%, d=-0.53±0.96) and CON (6.9±7.3%, d=-0.28±1.17). Females changed pre-post training with BFR-I (19.1±21.0%, d=0.75±0.85), BFR-C (14.0±5.5%, d=-0.57±0.1.18) and CON (11.5±17.4%, d=-0.5±0.96).

Similarly, only a main effect for time existed for isokinetic MVC peak torque during knee extension at 60°·s^{-1} (p<0.001), with no main effects for group (p=0.4533), or time*group interaction (p=0.247). Isokinetic MVC peak torque at 60°·s^{-1} increased with BFR-I (21.3±26.9%, d=0.56±0.68), BFR-C (9.2±13.5%, d=0.18±0.74) and CON (6.5±9.6%, d=0.18±0.78). There were no significant main effects for group (p=0.426), time (*p*=0.060), or a time*group interaction (*p*=0.543) for isokinetic MVC peak torque during knee extension at 150°·s^{-1}. Sex-specific responses for isokinetic peak torque are provided in Supplementary Material 1.

For leg press and knee extension 1RM, there were no main effects for group (*p*=0.885) or time*group interaction (*p*=0.458). However, main effects for time were noted for both leg press and knee extension 1RM (both *p*<0.001). Leg press 1RM increased pre-post training with BFR-I (19.8±13.8%, *d*=0.68±0.6), BFR-C (27.1±20.1%, *d*=0.83±0.62) and CON (25.2±23.1%, *d*=0.35±0.74). Similar increases in knee extension 1RM occurred following training with BFR-I group (23.1±19.7%, *d*=0.57±0.59), BFR-C (22.9±13.5%, *d*=0.58±0.59), and CON (27.3±27.7%, *d*=0.45±0.74). Upon examination of sex-specific responses, males increased leg press 1RM pre-post training with BFR-I (26.1±13.1%, *d*=1.05±0.93), BFR-C (21.8±14.7%, *d*=1.20±0.84) and CON (15.1±9.2%, *d*=-0.44±1.17), and leg extension 1RM pre-post training with BFR-I (23.4±20.6%, *d*=0.54±0.89), BFR-C (20.4±6.2%, *d*=0.83±0.81) and CON (13.4±19.5%, *d*=0.63±1.18). Females increased leg press 1RM pre-post training with BFR-I (14.9±12.9%, *d*=0.70±0.80), BFR-C (35.1±25.6%, *d*=0.94±0.99) and CON (31.9±29.9%, *d*=0.50±0.96) and leg extension 1RM pre-post training with BFR-I (22.9±20.2%, *d*=0.72±0.80), BFR-C (26.2±19.5%, *d*=0.96±0.92) and CON (36.7±29.9%, *d*=0.67±0.97).

[Figure 2 About Here]

Rate of Force Development

Percentage changes and effect sizes are reported in Table 2. No differences rate of force development (RFD) existed between groups at baseline. There were no main effects for group or time for the peak rate of RFD, or the RFD calculated over 0–50, 0–100 or 0–250 ms intervals in the isometric MVC (all *p*>0.05).

Muscular Endurance

Group mean and individual changes in total isokinetic work are displayed in Figure 2B. No differences in total isokinetic work existed between groups at baseline. There were no main effects for group (*p*=0.559) or time*group interaction (*p*=0.336). However, a time main effect (*p*<0.001) existed for the total work produced over the 50 consecutive maximal contractions during the isokinetic fatigue task. Total work increased pre-post training in the BFR-I group (11.3±15.6%, *d*=0.33±0.68), the BFR-C group (9.5±12.2%, *d*=0.21±0.74), and the CON group (3.6±9.8%, *d*=0.08±0.78). Upon examination of sex-specific responses, males changed total work pre-post training with BFR-I (20.7±18.1%, *d*=0.71±1.19), BFR-C (10.1±5.8%, *d*=0.30±0.95) and CON

(5.9±8.5%, d=0.16±1.16). Females changed pre-post training with BFR-I (6.6±12.8%, d=0.19±0.82), BFR-C (8.7±19.7%, d=-0.70±1.19) and CON (1.7±11.3%, d=0.09±1.04).

Countermovement Jump

Percent changes and effect sizes are displayed in Table 2. No differences in power or velocity existed between groups at baseline. No main effects for group or time existed for average velocity, peak velocity, or average power, during the countermovement jump (CMJ) test (all p>0.05). There was only a significant time effect (p=0.002) for peak power. Further analyses revealed peak power increased pre-post training in all groups. A group main effect (p=0.024) existed for peak displacement, but this was not accompanied by any main effect for time (p=0.929) or a time*group interaction (p=0.510). Post-hoc analyses revealed that peak displacement during CMJ at post-testing was significantly higher in BFR-C than CON (p=0.016).

[Table 2 About Here]

Perceptions of Pain and Effort

Group mean and individual ratings for pain and effort are displayed in Figure 3. There was no significant time*group interaction (p=0.533) for perceptions of pain during exercise. However, main effects of group (p=0.033) and time (p<0.001) were observed. Further analyses indicated that pain ratings were greater with BFR-C than CON (p=0.026) during the first session. Pain ratings were similar between BFR-C and BFR-I (p=0.098). During the last session, there were no differences in pain ratings between groups (p=0.207-0.813). Pain ratings significantly decreased from the first to the last session with BFR-C (p=0.005).

There was no significant time*group interaction (p=0.973) for perceptions of effort during exercise. However, main effects of group (p=0.001) and time (p<0.001) were observed. Further analyses indicated that effort ratings were greater with BFR-C than CON (p=0.032) during the first session. Effort ratings were similar between BFR-C and BFR-I (p=0.078). During the last session, effort ratings were greater with BFR-C than both CON (p=0.025) and BFR-I (p=0.035). Effort ratings significantly decreased from the first to the last session with BFR-C (p=0.034) and BFR-I (p=0.009).

[Figure 3 About Here]

DISCUSSION

The aim of this study was to compare the effectiveness of continuous and intermittent BFR protocols in eliciting hypertrophic, and muscle function adaptations to a period of low-load resistance training. In contrast to our hypothesis, we report that both continuous and intermittent BFR protocols were equally effective. Furthermore, neither continuous nor intermittent BFR appeared to be any more effective than LL-RT alone, without BFR. Thus, the additional metabolic stress that is reported to occur with an acute bout of continuous BFR (34), may not be necessary in less-trained individuals, who possess a larger ‘ceiling’ for adaptation (33).

In the only previous study that has directly compared the chronic use of continuous and intermittent BFR protocols with resistance training, Fitschen et al (12) reported no significant changes (p=0.900; d=0.03) in lower body lean mass (determined by DEXA) following five weeks of training in either group. While we reported a significant time effect (p=0.029) for lower body lean mass, suggesting muscle mass increased with training, this was to a small, and likely practically insignificant degree (d=~0.1). Moreover, the lack of time*group interaction implies that the mode of training did not have a significant influence on such increases. Alongside DEXA, the present study also utilized a more sensitive measure of hypertrophy using pQCT, which has been demonstrated to detect smaller changes in muscle mass, also occurring with shorter durations of resistance training (18, 42). In agreement with the above, we discovered that total muscle CSA from the five slices increased following training, regardless of the training group allocation. These responses are intriguing considering the plethora of previous studies supporting the efficacy of BFR training to augment skeletal muscle adaptations compared to low-load resistance training alone (1, 28, 35). However, several studies exist in which such adaptations are similar between BFR and unrestricted training groups. Madarame et al (24) and Weatherholt et al (42) both reported increases in muscle CSA with low-load resistance training, independent of BFR. In both studies participants had minimal resistance training experience, which may have increased their responsiveness to the stimuli offered by the control conditions. For individuals new to resistance training, a greater adaptive stimulus may not be reflected in adaptations of a greater magnitude, which explain some of the similarities in CSA responses between groups. The present study included participants from a variety of training backgrounds, with some individuals with limited resistance training experience. Therefore, the combination of exercise loads (30-40% 1RM) and training frequency (3x/week) used in the present study may have provided a considerable stimulus for these individuals, irrespective of the additional stress imposed by the two BFR protocols. Moreover, it may have been that the combination of 30-40% 1RM loads, and the volume of exercise performed each session (2 exercises, 150 repetitions) was sufficient to induce enough peripheral fatigue, even without BFR, to access the highest-threshold motor units in some individuals (43). Indeed, Lixandrão et al. (21) observed that when higher loads are used (e.g. 40% vs 20% 1RM) the influence of cuff pressure (and hence, metabolic perturbation to the exercising muscle) on muscle hypertrophy is diminished. Thus, it seems that the benefit on restricting blood flow during resistance exercise may be exacerbated at lower exercise intensities. In the present study, we began with 30% 1RM loads, and progressively increased these during training. This could explain the lack of notable differences between continuous and intermittent BFR (and unrestricted exercise), which may be more prominent with lower loads (e.g. 20% 1RM)... Therefore, the additional metabolic stress imposed by BFR, specifically the continuous protocol, may not be necessary if loading conditions and volume are adequate, and the stimulus is sufficient for the population. Finally, it should be acknowledged that the degree of hypertrophy in the present study (d=0.03-0.14*)* is less than previous studies with a similar number of training sessions (34). The heterogeneity in participants' training backgrounds and sex may also explain such differences. As observed in Figure 1A, the individual responses suggest some participants responded to training with substantial increases in CSA, while others even showed reductions in CSA. Therefore, it is probable that the group mean responses were impacted by the large variations in CSA adaptations which may have resulted from a heterogeneous sample.

With regard to muscular function, the study by Fitschen et al (12) observed similar increases in muscular strength between all groups, regardless of whether BFR was applied. This aligns with the present study, where the changes in isometric (d=~0.2-0.5) and isotonic strength (d=~0.5) were similar between continuous and intermittent BFR, and CON. Previous studies have reported comparable muscular adaptations between BFR and non-BFR resistance training, however, these primarily involve training until muscular failure (11, 15). It is unclear as to whether training to failure was avoided in the present study, as proximity to failure was not gauged in any group by collecting subjective feedback following each set e.g. repetitions in reserve (RIR). Consequently, it is not known if some individuals were training closer to muscular failure than others, due to the standardised approach of progressive overload which was employed. Once again, this may also be a product of the heterogeneity observed across participants, with some participants achieving robust increases in strength while others displayed minor decrements following training.

The present study did observe a significant pre-post change for the total work completed during a 50-repetition isokinetic endurance task, which may reflect a greater ability of skeletal muscle to buffer against the products of anaerobic metabolism, and delay the onset of fatigue. Once again, the improvement in endurance capacity was independent of training group (group*time interaction $p>0.05$). However, effect sizes tended to favour the BFR groups ($d=0.2-0.3$) compared to CON ($d=0.08$). Improved muscular endurance capacity of skeletal muscle has been reported with continuous (15) and intermittent BFR training (10), and low-load non-restricted training to muscular failure (11). However, the present study is the first to compare these protocols all directly. The lack of tangible differences between groups may have been related to the specificity of the training compared to the isokinetic endurance task, which included 50 consecutive repetitions. Resistance training is typically performed with much higher external loads (>60% 1RM) and lower repetition numbers (<12). Therefore, the training in the present study may have provided a novel stimulus for enhancing local muscular endurance, even in the unrestricted group. However, this may have been enhanced with the application of BFR. A potential mechanism behind these improvements may be the enhanced vascularisation that is reported to occur following resistance training with BFR (36). Such adaptations have been noted to occur rapidly (within two weeks) in response to training (14) and may favour the fatigue-resistant type-I muscle fibres (4). Intramuscular hypoxia and sheer stress, both likely induced by prolonged time under tension during working periods, promote angiogenesis through the HIF-1a/VEGF pathway (14), which ultimately serves to enhance tissue function during low oxygen availability (10). Of interest, the greater degree of hypoxia and sheer stress reportedly imposed by continuous BFR (17, 30) did not elicit a proportional increase in muscular endurance capacity. Therefore, similar to hypertrophy and strength adaptations, a threshold for adaptive stimuli relevant to muscular endurance adaptations may exist.

The influence of BFR on muscular power and RFD qualities is uncertain, and many previous studies have reported a negligible impact (1, 24). The findings of the present study lend support to this theory, as no changes in any variables of jumping performance or explosive strength were observed. It has been proposed that the low-load resistance exercise, particularly with BFR, may preferentially target the slower-contracting type-I muscle fibres (4). Thus, when performed exclusively, low-load BFR may negatively influence the capacity for high-velocity movement, which may in turn explain the lack of changes in muscle power and explosive strength observed in the present study.

In contrast to previous literature (12, 27), we did not find ratings of pain during exercise to be higher with BFR-C compared to BFR-I. Although, both pain and effort perceptions appeared to be greater with BFR-C compared to CON. This suggests that pain and effort is likely elevated with BFR exercise, and these may be exaggerated with a continuous application. Interestingly, perceptual adaptations seem to occur with BFR training, as both pain and effort ratings were reduced following training with BFR-C. This is in alignment with very recent research showing that although pain ratings are initially high with BFR-C, they are reduced following ~16 sessions (40). Thus, the elevated pain and effort perceptions that often occur with BFR-appear to be only temporary and are unlikely to pose a threat to long-term adherence to BFR exercise. Although, in the short-term, unrestricted LL-RT or BFR-I exercise may be preferable for individuals less tolerable to exercise-induced pain and discomfort.

Limitations to the current study must be considered. One of such limitation was the gender heterogeneity of participants included which contributed to the variability in participant responses to training. Such variability is demonstrated by the vastly different effect sizes for CSA in the BFR-I group for males (d=0.69) and females (d=0.03). Secondly, while general dietary advice was given and some nutritional supplementation was provided, diet during the training period was not strictly controlled. Consequently, it is unknown whether a discrepancy in energy balance across participants may have influenced their capacity to support maximal training adaptations. A number of participants displayed reductions in total body fat mass across the study (18 out of 42), which may in fact suggest that total energy consumption may not have been sufficient for these individuals, leading to suboptimal training adaptations. Nonetheless, this study was only the second to directly compare continuous and intermittent BFR protocols in their ability to induce chronic adaptations to low load resistance training, including more specific assessments of hypertrophy and muscular function than the previous one (12).

In conclusion, low-load resistance exercise with continuous and intermittent BFR was as effective as low-load high-volume non-BFR resistance exercise for improving skeletal muscle hypertrophy, strength and endurance qualities in recreationally active males and females. However, it is unknown if these findings extend to other loading conditions that are also frequently used alongside BFR (e.g. 20% 1RM), or for higher-trained individuals, where additional metabolic stress may be required as a product of higher loads (e.g. 30-40% 1RM) and/or in combination with continuous BFR application. All low-load protocols appeared to have a negligible influence on power- and velocity-based qualities in skeletal muscle. It is unknown if higher trained individuals can better tolerate, and may in fact require, the greater metabolic stress of a continuous BFR protocol, to optimize hypertrophy, strength, and endurance adaptations, and requires investigation.

PRACTICAL APPLICATIONS

The results from the present study may be used to inform coaches, trainers and health practitioners on the suitability of different low-load resistance training and BFR protocols. It is well recognised that BFR in combination with low-load resistance exercise can enhance metabolic stress, fatigue and produce robust increases in muscle hypertrophy. However, this may elevate ratings of pain and effort during exercise, particularly when BFR is applied continuously. The data obtained from the present study suggest the additional metabolic stress that is proposed to occur with a continuous BFR protocol does not appear to translate into proportionally greater training adaptations in less-trained individuals. These findings promote the use of both intermittent BFR and low-load resistance training without BFR, as suitable alternative training methods to continuous BFR when training loads of 30-40% 1RM are employed. Such approaches may be practically applicable for those less tolerable to pain and discomfort associated with ischemia and consequently may support adherence to an exercise program.

ACKNOWLEDGEMENTS

The authors would like to thank Bulk Nutrients® for their in-kind provision of nutritional supplements during the study, and the participants for their dedication, time and effort. This research was supported by an Australian Government Research Training Program (RTP) Scholarship. The study was further supported by the Queensland Academy of Sport's Sport Performance Innovation and Knowledge Excellence (SPIKE) unit. The authors declare they have no conflicts of interest. The results of the present study do not constitute endorsement of the product by the authors or the NSCA.

REFERENCES

1. Abe T, Kawamoto K, Yasuda T et al. Eight days KAATSU-resistance training improved sprint but not jump performance in collegiate male track and field athletes. *Int J KAATSU Train Res* 1:19-23, 2005.

2. ACSM. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 41:687-708, 2009.

3. Baechle TR & Earle RW. *Essentials of strength training and conditioning (3.Ed.)*. Champaign, IL: Human Kinetics, 2008.

4. Bjornsen T, Wernbom M, Kirketeig A et al. Type 1 muscle fiber hypertrophy after blood flow-restricted training in powerlifters. *Med Sci Sports Exerc* 51(2):288-298, 2019.

5. Bjornsen T, Wernbom M, Lovstad AT et al. Delayed myonuclear addition, myofiber hypertrophy and increases in strength with high-frequency low-load blood flow restricted training to volitional failure. *J Appl Physiol* 126:578-592, 2019.

6. Brandner C, May A, Clarkson M, Warmington S. Reported side-effects and safety considerations for the use of blood flow restriction during exercise in practice and research. *Tech Orthop* 33(2):114-121, 2018.

7. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Hillsdale (NJ): Lawrence Erlbaum Associates p. 597, 1998.

8. Cook CJ, Kilduff LP, Beaven CM. Improving strength and power in trained athletes with 3 weeks of occlusion training. *Int J Sports Physiol Perform* 9:166-172, 2014.

9. Counts BR, Dankel SJ, Barnett BE et al. Influence of relative blood flow restriction pressure on muscle activation and muscle adaptation. *Muscle Nerve* 53:438-445, 2016.

10. Evans C, Vance S, Brown M. Short-term resistance training with blood flow restriction enhances microvascular filtration capacity of human calf muscles. *J Sports Sci* 28:999-1007, 2010.

11. Fahs CA, Loenneke JP, Thiebaud RS et al. Muscular adaptations to fatiguing exercise with and without blood flow restriction. *Clin Physiol Funct Imaging* 35:167-176, 2015.

12. Fitschen PJ, Kistler BM, Jeong JH et al. Perceptual effects and efficacy of intermittent or continuous blood flow restriction resistance training. *Clin Physiol Funct Imaging* 34:356-363, 2014.

13. Hollander DB, Durand RJ, Trynicki JL et al. RPE, pain, and physiological adjustment to concentric and eccentric contractions. *Med Sci Sports Exerc* 35(6):1017-1025, 2003.

14. Holloway TM, Snijders T, van Kranenburg J, van Loon LJ, Verdijk LB. Temporal responses of angiogenesis and hypertrophy to resistance training in young men. *Med Sci Sports Exerc* 50(1):36-45, 2018.

15. Kacin A, Strazar K. Frequent low-load ischemic resistance exercise to failure enhances muscle oxygen delivery and endurance capacity. *Scand J Med Sci Sports* 21:231-241, 2011.

16. Karabulut M, Abe T, Sato Y, Bemben MG. The effects of low-intensity resistance training with vascular restriction on leg muscle strength in older men. *Eur J Appl Physiol* 108:147-155, 2010.

17. Karabulut M, Leal JA, Garcia SD, Cavazos C, Bemben M. Tissue oxygenation, strength and lactate responses to different blood flow restrictive pressures. *Clin Physiol Funct Imaging* 34:263-269, 2014.

18. Kim SJ, Sherk VD, Bemben MG, Bemben DA. Effects of short term low intensity resistance training with blood flow restriction on bone markers and muscle cross-sectional area in young men. *Int J Ex Sci* 5:136-147, 2012.

19. Kubo K, Komuro T, Ishiguro N et al. Effects of low-load resistance training with vascular occlusion on the mechanical properties of muscle and tendon. *J Appl Biomech* 22:112-119, 2006.

20. Lixandrão ME, Ugrinowitsch C, Berton R et al. Magnitude of muscle strength and mass adaptations between high-load resistance training versus low-load resistance training associated with blood-flow restriction: A systematic review and meta-analysis. *Sports Med* 48:361-378, 2018.

21. Lixandrão ME, Ugrinowitsch C, Laurentino G et al. Effects of exercise intensity and occlusion pressure after 12 weeks of resistance training with blood-flow restriction. *Eur J Appl Physiol* 115:2471-2480, 2015.

22. Loenneke JP, Allen KM, Mouser JG et al. Blood flow restriction in the upper and lower limbs is predicted by limb circumference and systolic blood pressure. *Eur J Appl Physiol* 115:397-405, 2015.

23. Loenneke JP, Wilson JM, Marin PJ, Zourdos MC, Bemben MG. Low intensity blood flow restriction training: A meta-analysis. *Eur J Appl Physiol* 112:1849-1859, 2012.

24. Madarame H, Ochi E, Tomioka Y, Nakazato K, Ishii N. Blood flow restricted training does not improve jump performance in untrained men. *Acta Physiol Hung* 98:465-471, 2011.

25. Manimmanakorn A, Manimmanakorn N, Taylor R et al. Effects of resistance training combined with vascular occlusion or hypoxia on neuromuscular function in athletes. *Eur J Appl Physiol* 113:1767-1774, 2013.

26. Martin-Hernandez J, Marin PJ, Menendez H et al. Muscular adaptations after two different volumes of blood flow-restricted training. *Scand J Med Sci Sports* 23:114-120, 2013.

27. Neto GR, Novaes JS, Salerno VP et al. Acute effects of resistance exercise with continuous and intermittent blood flow restriction on hemodynamic measurements and perceived exertion. *Percept Mot Skills* 124:277-92, 2017.

28. Nielsen JL, Aagard P, Bech RD et al. Proliferation of myogenic stem cells in human skeletal muscle in response to low-load resistance training with blood flow restriction. *J Physiol* 7:4351-4361, 2012.

29. Nielsen JL, Frandsen U, Prokhorova T et al. Delayed effect of blood-flow-restricted resistance training on rapid force capacity. *Med Sci Sports Exerc* 49:1157-1167, 2017.

30. Okita K, Takada S, Morita N et al. Resistance training with interval blood flow restriction effectively enhances intramuscular metabolic stress with less ischemic duration and discomfort. *Appl Physiol Nutr Metab* 19:1-6, 2018.

31. Patterson SD, Hughes L, Warmington S et al. Blood flow restriction exercise position stand: considerations of methodology, application, and safety. *Front Physiol*, 10:533, 2019

32. Pearson SJ, Hussain SR. A review on the mechanisms of blood-flow restriction resistance training-induced muscle hypertrophy. *Sports Med* 45:187-200, 2015.

33. Schoenfeld BJ. *Science and Development of Muscle Hypertrophy*. Champaign, IL: Human Kinetics p. 29-49, 2016.

34. Sieljacks P, Degn R, Hollaender K, Wernbom M, Vissing K. Non-failure blood flow restricted exercise induces similar muscle adaptations and less discomfort than failure protocols. *Scand J Med Sci Sports* 29:336-347, 2019.

35. Slysz J, Stultz J, Burr JF. The efficacy of blood flow restricted exercise: A systematic review & meta-analysis. *J Sci Med Sport* 19:669-675, 2011.

36. Sousa J, Neto GR, Santos HH et al. Effects of strength training with blood flow restriction on torque, muscle activation and local muscular endurance in healthy subjects. *Biol Sport* 34:83-90, 2011.

37. Suga T, Okita K, Morita N et al. Intramuscular metabolism during low-intensity resistance exercise with blood flow restriction. *J Appl Physiol* 106:1119-1124, 2009.

38. Suga T, Okita K, Takada S et al. Effect of multiple set on intramuscular metabolic stress during low-intensity resistance exercise with blood flow restriction. *Eur J Appl Physiol* 112:3915-20, 2012.

39. Takada S, Okita K, Suga T et al. Low-intensity exercise can increase muscle mass and strength proportionally to enhanced metabolic stress under ischemic conditions. *J Appl Physiol* 113:199-205, 2012.

40. Teixeira EL, Painelli VS, Schoenfeld BJ et al. Perceptual and neuromuscular responses adapt similarly between high-load resistance training and low-load resistance training with blood flow restriction. *J Strength Cond Res* published ahead of print, 2020

41. Vechin FC, Libardi CA, Conceicao MS et al. Comparisons between low-intensity resistance training with blood flow restriction and high-intensity resistance training on quadriceps muscle mass and strength in elderly. *J Strength Cond Res* 29:1071-1076, 2015.

42. Weatherholt A, Beekley M, Greer S, Urtel M, Mikesky A. Modified Kaatsu training: adaptations and subject perceptions. *Med Sci Sports Exerc* 45:952-961, 2013.

43. Wernbom M, Aagaard P. Muscle fibre activation and fatigue with low-load blood flow restricted resistance exercise – An integrative physiology review. *Acta Physiol* e13302, 2019.

FIGURES

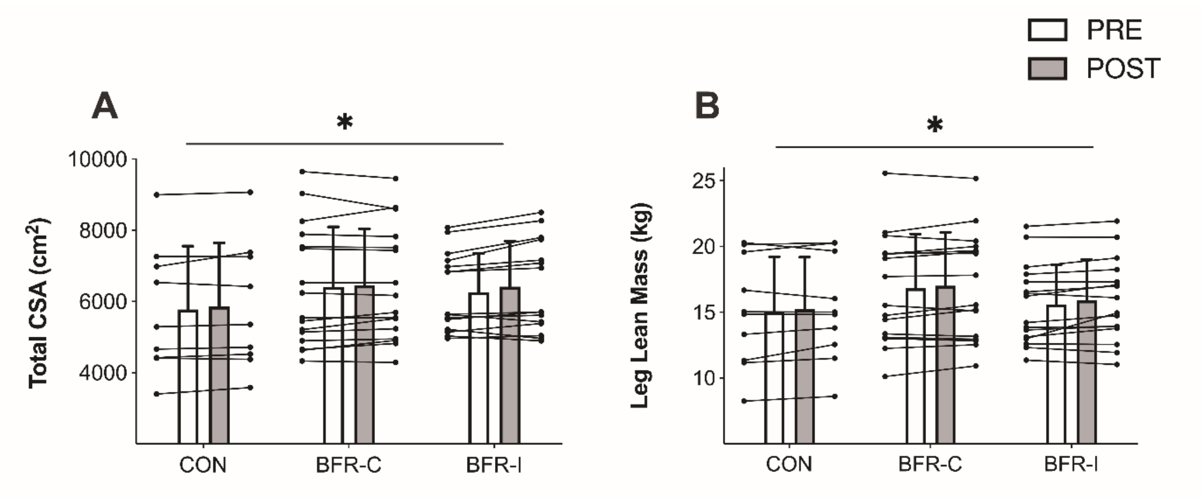

Fig. 1 Training-induced group and individual changes in thigh muscle cross sectional area (CSA) measured by pQCT (A) and lower body lean mass measured by DEXA (B). Total CSA is the combined total area (cm^2) of the five slices that were measured. *Indicates a significant increase from pre- to post-training (p<0.05)

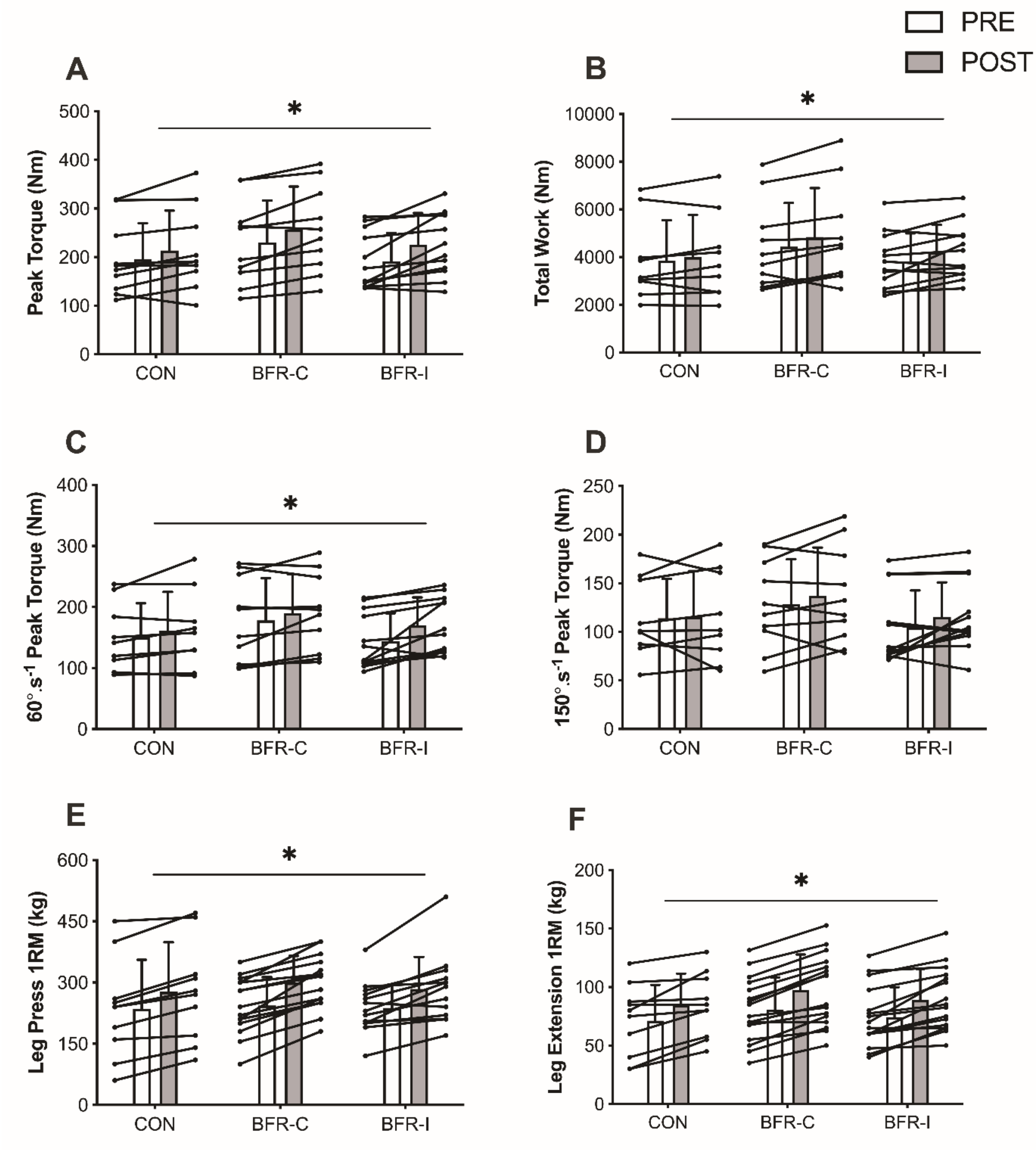

Fig. 2 Training-induced group and individual changes in isometric MVC strength (A) total work during the isokinetic endurance task (B) isokinetic MVC strength during 60°·s^{-1} (C) and 150°·s^{-1} (D) speeds, and leg press (E) and leg extension (F) one-repetition maximum. *Indicates a significant increase from pre- to post-training (*p*<0.05)

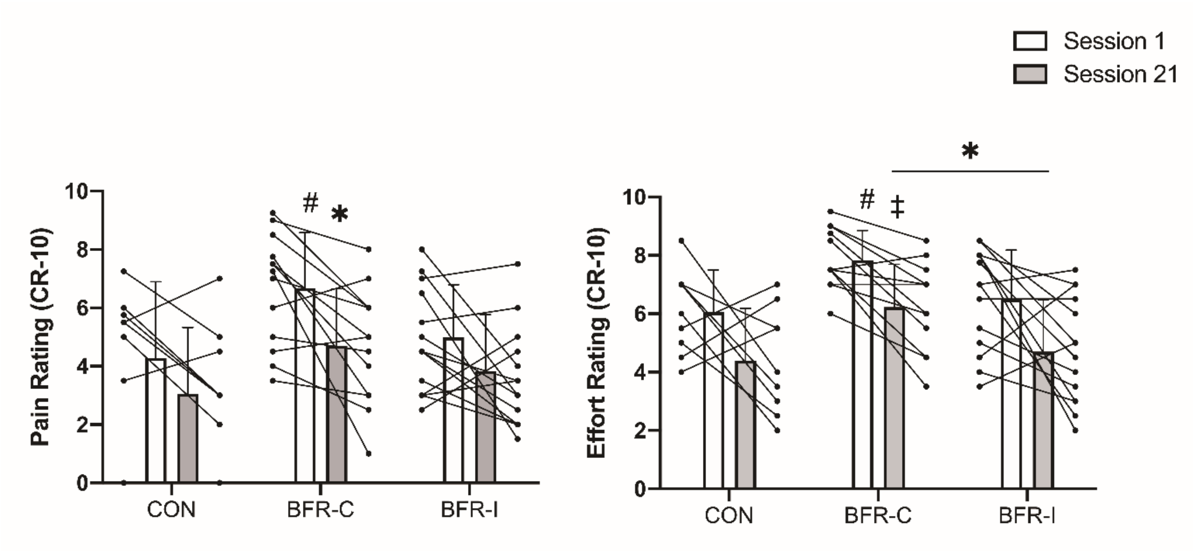

Fig. 3 Training-induced group and individual changes in ratings of pain (A) and effort (B) during the first (session 1) and final session (session 21) of the training block. *Indicates a significant decrease from session 1 to session 21 (p<0.05). #Indicates a significant difference between BFR-C and CON (p<0.05). ‡Indicates a significant difference between BFR-C and all other groups (p<0.05)

TABLES

Table 1 Descriptive characteristics of participants

	CON			BFR-C			BFR-I		
	Total	Male	Female	Total	Male	Female	Total	Male	Female
Participants (n)	10	4	6	16	9	7	16	7	9
Age (years)	24.0 ± 3.0	25.5 ± 1.3	23.0 ± 3.6	23.8 ± 5.4	21.1 ± 2.4	27.3 ± 6.3	25.0 ± 5.8	26.0 ± 7.5	24.2 ± 4.5
Height (m)	1.69 ± 0.1	1.75 ± 0.1	1.65 ± 0.1	1.75 ± 0.1	1.81 ± 0.1	1.67 ± 0.1	1.72 ± 0.1	1.76 ± 0.1	1.69 ± 0.1
Body mass (kg)	78.5 ± 34.0	81.2 ± 9.8	76.6 ± 4.9	71.4 ± 13.5	79.1 ± 10.1	61.4 ± 10.4	69.2 ± 10.9	76.6 ± 10.5	63.5 ± 7.6
Leg press 1RM (kg)	235 ± 121	335 ± 106	168 ± 78	240 ± 69	279 ± 47	191 ± 61	238 ± 57	274 ± 56	209 ± 40
DEXA leg lean mass (kg)	15.1 ± 4.15	19.2 ± 1.69	12.3 ± 2.60	16.8 ± 4.12	19.7 ± 4.05	11.5 ± 4.90	15.6 ± 3.04	18.4 ± 2.03	13.4 ± 1.43
Naturally menstruating	2	N/A	2	4	N/A	4	4	N/A	4
Oral contraceptive use (combined pill)	4	N/A	4	3	N/A	3	5	N/A	5

Data are presented as mean ± SD. No significant differences existed between any groups in any of the variables listed

Table 2 Rate of force development (RFD) values during isometric knee extension, and counter-movement jump (CMJ) variables

	CON				BFR-C				BFR-I			
	Pre	**Post**	**% change**	***d***	**Pre**	**Post**	**% change**	***d***	**Pre**	**Post**	**% change**	***d***
Isometric MVC												
Peak RFD ($N \cdot s^{-1}$)	1321 ± 563	1470 ± 602	13.9	0.26	1705 ± 802	1744 ± 682	13.8	0.05	1161 ± 637	1375 ± 479	33.5	0.38
RFD 0–50 ms ($N \cdot s^{-1}$)	401 ± 164	471 ± 178	19.4	0.41	513 ± 210	564 ± 211	28.9	0.24	373 ± 195	434 ± 172	25.8	0.33
RFD 0–100 ms ($N \cdot s^{-1}$)	617 ± 257	704 ± 287	16.0	0.32	793 ± 380	831 ± 319	23.4	0.11	561 ± 303	655 ± 237	30.0	0.34
RFD 0–250 ms ($N \cdot s^{-1}$)	132 ± 52	136 ± 53	2.8	0.07	111 ± 67	141 ± 55	27.2	0.49	114 ± 39	142 ± 59	24.9	0.57
CMJ												
Peak Power (watts/kg)	36.2 ± 10.2	38.1 ± 7.0	8.4	0.22	45.4 ± 8.6	46.9 ± 9.1	3.4	0.17	39.7 ± 7.7	41.3 ± 7.0	5.0	0.22
Average Power (watts/kg)	17.1 ± 5.2	19.3 ± 4.0	26.3	0.48	22.5 ± 5.5	21.65 ± 6.5	-3.0	-0.14	19.2 ± 4.8	20.8 ± 4.3	8.4	0.35
Peak Velocity ($m \cdot s^{-1}$)	3.4 ± 0.8	3.5 ± 0.7	4.4	0.13	3.5 ± 0.5	3.6 ± 0.6	1.3	0.09	3.4 ± 0.6	3.5 ± 0.5	2.0	0.09
Average Velocity ($m \cdot s^{-1}$)	1.7 ± 0.5	1.9 ± 0.4	7.5	0.30	1.8 ± 0.3	1.8 ± 0.4	-4.2	-0.22	1.7 ± 0.3	1.8 ± 0.3	4.5	0.27
Peak Displacement (cm)	31 ± 9	29 ± 5	-0.4	-0.27	41 ± 11	42 ± 12‡	2.7	0.09	33 ± 10	34 ± 8	6.6	0.11

Mean ± SD, mean percent change and effect sizes (Cohen's d) for RFD and CMJ variables. ‡Indicates a significant difference between CON at post-testing ($p<0.05$).

Supplementary Material 1. Sex-specific percent changes and effect sizes for DEXA and isokinetic strength variables.

	CON				BFR-C				BFR-I			
	Males		**Females**		**Males**		**Females**		**Males**		**Females**	
	% change	***d***	**% change**	***d***	**% change**	***d***	**% change**	***d***	**% change**	***d***	**% change**	***d***
DEXA												
Lower Body Lean Mass	-0.2 ± 1.3%	-0.01 ± 1.34	2.7 ± 2.5%	0.10 ± 0.95	1.5 ± 2.6%	0.09 ± 0.78	1.4 ± 3.1%	0.05 ± 0.88	1.6 ± 2.6%	0.10 ± 0.82	2.1 ± 4.4%	0.12 ± 0.78
Isokinetic Knee Extension												
$60^{\circ}\cdot s^{-1}$	8.6 ± 12.6%	0.34 ± 1.17	4.8 ± 7.7%	0.22 ± 0.95	7.4 ± 16.8%	0.23 ± 0.95	11.9 ± 7.5%	0.53 ± 1.18	11.6 ± 27.8%	1.05 ± 1.22	27.4 ± 30.4%	0.92 ± 0.86
$150^{\circ}\cdot s^{-1}$	7.0 ± 12.9%	0.31 ± 1.17	-2.8 ± 22.4%	-0.24 ± 0.95	5.1 ± 12.1%	0.24 ± 0.95	13.5 ± 27.9%	0.53 ± 1.17	5.2 ± 19.1%	0.41 ± 1.17	23.7 ± 27.5%	0.92 ± 0.90

Mean percent change ± SD and effect sizes (Cohen’s d) ± 90% confidence intervals for DEXA and isokinetic strength variables.