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Effects of low load exercise with and without blood-flow restriction on microvascular oxygenation, muscle excitability and perceived pain

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Abstract

This paper aimed t**o** examine the acute effect of low-load (LL) exercise with blood-flow restriction (LL-BFR) on microvascular oxygenation and muscle excitability of the vastus medialis (VM) and vastus lateralis (VL) muscles during a single bout of unilateral knee extension exercise performed to task failure. Seventeen healthy recreationally resistance-trained males were enrolled in a within-group randomized cross-over study design. Participants performed one set of unilateral knee extensions at 20% of one-repetition maximum (1RM) to task failure, using a LL-BFR or LL free-flow (LL-FF) protocol in a randomized order on separate days. Changes in oxygenation and muscle excitability in VL and VM were assessed using near-infrared spectroscopy (NIRS) and surface electromyography (sEMG), respectively. Pain measures were collected using the visual analog scale (VAS) before and following set completion. Within- and between- protocol comparisons were performed at multiple time points of set completion for each muscle. During LL-BFR, participants performed 43% fewer repetitions and reported feeling more pain compared to LL-FF ($p<0.05$). Normalized to time to task failure, LL-BFR and LL-FF generally demonstrated similar progression in microvascular oxygenation and muscle excitability during exercise to task failure. The present results demonstrate that LL-BFR accelerates time to task failure, compared with LL-FF, resulting in a lower dose of mechanical work to elicit similar levels of oxygenation, blood-pooling, and muscle excitability. LL-BFR may be preferable to LL-FF in clinical settings where high workloads are contraindicated, although increased pain experienced during BFR may limit its application.

Keywords: Exercise, Fatigue, Physiology, Endurance, Biomechanics.

Highlights

Compared to free flow (FF), neuromuscular fatigue mechanisms are accelerated during blood flow restricted (BFR) training. This can be observed as changes in microvascular oxygenation and muscle excitability occurring at a ~43% faster mean rate during BFR compared to FF.

BFR exercise seems to elicit the same level of neuromuscular fatigue as FF training within a shorter timeframe. This reduces total joint load and may be especially helpful in cases where high training volumes may be contraindicated (e.g., recovering from a sports injury or orthopedic surgery).

Introduction

Strength exercise performed with low external loading (LL, ≤50% of one-repetition maximum (1RM)) and partial (< full arterial occlusion) or full (full arterial occlusion) blood flow restriction (BFR) has been shown to be an effective training method promoting gains in neuromuscular function (e.g., maximal muscle strength) and skeletal muscle growth [1-4]. Similar gains in these parameters have been reported between LL-BFR training and conventional high-load resistance training (≥65% 1RM) [1,2], however, these findings are not universal [3].

Notably, previous studies have demonstrated similar gains in muscle growth adaptations regardless of relative exercise load (80 or 30% of 1RM), as long as training is performed to task failure [5]. Similarly, despite shorter time to task failure (i.e., less muscle mechanical work) with LL-BFR compared to LL performed in free-flow (LL-FF) condition, the two training paradigms appear to elicit similar gains in muscle hypertrophy when performed to task failure [6]. The difference in muscle fatigability between LL-BFR and LL-FF conditions is likely mediated by accelerated hypoxia in LL-BFR. This is supported by previous findings showing both single-limb and systemic hypoxia to result in an augmented rate of decline in force-generating capacity [7,8]. In addition, increased muscle excitability with continuous muscle contractions in systemic hypoxia has been observed, suggesting earlier onset of muscular fatigue [9]. Finally, muscle excitability seems to reach the same peak values earlier in response to LL-BFR compared to LL-FF during acute failure-matched exercise protocols [10,11]. Overall, these data suggest that muscular fatigue may be an important determinant of muscle hypertrophy and that gradual muscle fatigue can be accelerated by BFR-mediated microvascular hypoxia. Furthermore, another factor suggested to be involved in LL-BFR exercise-induced myocellular anabolism is the tissue swelling reported with LL-BFR exercise [6,12], which may reflect muscle cell swelling. Muscle swelling has been suggested to be stimulated by blood-pooling induced by partial LL-BFR exercise [6,8,13]. Microvascular hypoxia and localized accumulation of muscle metabolites may occur during both FF and BFR exercise but to greater extent during BFR [14,15]. The increased sensation of pain often reported with BFR exercise [6,16] is likely the result of both localized hypoxia and metabolite accumulation in the exercised musculature [17].

Thus, altogether, it appears important to characterize the level of microvascular oxygenation, muscle excitability, and blood-pooling in response to partial LL-BFR and LL-FF exercise performed to task failure.

However, only a few studies have combined measurements of microvascular oxygenation and muscle excitability, and only one of these studies appears to have used failure-matched protocols [10,18]. Furthermore, previous findings have observed differences in intermuscular knee extensor microvascular hypoxia during submaximal cycling exercise [19], yet the effect of LL-BFR exercise performed to task failure on microvascular tissue oxygenation and/or blood-pooling has primarily been investigated in a single subdivision of the knee extensor muscle group, mostly vastus lateralis (VL) [8,10,14]. Investigating multiple subdivisions of the knee extensor muscle group simultaneously could provide valuable information on potential intermuscular differences in the physiological response with LL-BFR and LL-FF exercise. Potential exercise-induced intermuscular physiological differences may translate to differences in physiological adaptation (i.e., muscle strength) in response to longitudinal training. The VL muscle is the largest, strongest, and most investigated muscle of m. quadriceps. Yet, the less investigated vastus medialis (VM) may play an important role in counterbalancing the laterally directed contractile force of the VL, which is of functional importance for patella tracking and prevention of patellofemoral pain [20b,21]. No study to date has measured excitability and oxygenation of both the VL and VM during exercise to failure.

Therefore, the purpose of the present study was to investigate oxygenation levels, blood-pooling, and muscle excitability during partial LL-BFR, and LL-FF exercise performed to task failure in both the VM and VL muscles. We hypothesized that (a) the two failure-matched exercise regimes would result in similar changes in tissue deoxygenation and muscle excitability, (b) that LL-BFR exercise would result in greater blood-pooling and increased sensation of pain compared to LL-FF and (c) that LL-BFR would reach task failure before LL-FF.

Materials and Methods

Participants

Seventeen healthy recreationally resistance-trained males (cf. table 1) volunteered to participate in the study. Exclusion criteria were (1) resting systolic/diastolic blood pressure ≥140/90 mmHg, (2) adipose tissue thickness ≥2.0 cm at the two sites of surface electromyography (sEMG), and near-infrared spectroscopy (NIRS) measures, and (3) self-reported morbidity contra-indicating strenuous exercise or BFR. All participants received written and oral information about the study procedures and signed informed consent before any experimental

procedures. The study was approved by the National Ethics Committee (S-20150022) and was conducted in accordance with the Declaration of Helsinki.

Experimental Design

Participants visited the laboratory on three occasions. In session one, participants were screened for inclusion. Eligible participants were randomized to use either their dominant or non-dominant leg through all experimental procedures. Finally, during the first session a unilateral knee extension 1RM test was performed (TechnoGym, Italy). This test consisted of 5-min warm-up on a cycle ergometer followed by sets of unilateral knee extensions (8/5/1 repetitions at 50/75/90% of estimated 1RM), after which single repetitions separated by 3-4 min were performed with weight increasing 2.5 to 5 kg at each attempt until the participant was no longer capable of achieving full range of motion (ROM, 0-90º knee extension). The maximal number of attempts needed to reach 1RM was 5 (range:1-5). At the first and second experimental sessions, participants performed the LL-BFR or LL-FF protocols in randomized order. At least 5 days separated session 1 (1-RM test) and the first experimental session. The experimental sessions were placed 3 days (72±2 hours) apart, at similar time of day to account for diurnal variations (±2 hours). Participants were instructed to refrain from caffeine and alcohol ingestion and strenuous physical activity 24 and 48 hours before sessions, respectively.

Exercise protocols

LL-BFR and LL-FF protocols consisted of dynamic unilateral knee extensions performed at 20%-1RM to task failure. All repetitions were performed at a standardized cadence (concentric/eccentric: 1.5/1.5 s ~60 º/s) regulated by a metronome. Repetition frequency and ROM were monitored using inclinometer (DTS-2D-Inclinometer, Noraxon, USA). Task failure was defined as the inability to achieve full ROM or maintain cadence for two subsequent repetitions. Strong standardized verbal encouragement was provided throughout sessions.

During the BFR-session a pneumatic cuff (15.0 cm width) (9-7350-003, Delfi Medical, Canada) was placed proximally at the thigh using an automatic computerized tourniquet system (Zimmer-A.T.S. 750, USA). Fifteen seconds before LL-BFR exercise, the cuff was inflated (100-mmHg) [16,22], and deflated 30-s following task failure.

Measurement procedures

Microvascular oxygenation measurements

Continuous measures of NIRS and sEMG in the VM and VL muscles were obtained throughout sessions. Oxygenated ([O2Hb]), deoxygenated ([HHb]) and total hemoglobin ([cHb]) concentrations were sampled (2Hz) using a two-channel wave NIRS (NIRO-300, Hamamatsu Photonics, Japan).

NIRS optodes were placed on VL and VM muscles in between the EMG electrodes (see specifics below) to allow data sampling from the same region of the muscles. NIRS data were sampled at 1000 Hz, from an underlying 2 Hz hardware sampling rate. A moving (0.1 sec steps) 1.0 sec window was applied to identify the mean amplitude. The lowest mean amplitude values for [O2Hb] during each repetition and the corresponding [HHb] and [cHb] values were used for analysis. NIRS data were expressed as %-difference relative to individual baseline level (30-second interval).

Muscle excitability measurements

sEMG measures were obtained using bipolar surface electrodes (BlueSensor-N, AMBU, Denmark). Electrodes were placed on VL and VM muscles in accordance with seniam.org guidelines, however with a 25 mm inter-electrode distance to allow placement of the NIRS optodes between the EMG electrodes. Optode and electrode placement were outlined on the skin with permanent markers to ensure identical placement between protocols. Careful skin preparation was performed to optimize muscle-to-electrode conduction (<10kΩ). sEMG signals were amplified, band-pass filtered (10-400Hz), and sampled at 1000-Hz. A moving (0.1 steps) root-mean-square filter (window 1.0 sec) was applied. The peak sEMG amplitude (1.0 sec window) within each repetition was obtained for further analysis. sEMG amplitude values were normalized to the highest sEMG amplitude measured during the first repetition of each protocol [10].

Perceived exhaustion and pain

Sensation of pain and rating of perceived exertion (RPE) were assessed 1-min before exercise and immediately upon task failure. RPE was scored 0–10, with 0 indicating “nothing at all” and 10 “very high” degree of

perceived exertion. The pain was scored using a 100-mm VAS, ranging from 0 (no pain) to 100 (worst possible pain).

Statistical Analysis

Initially, a sample size estimation was performed based on the sEMG method. The sample size was based on a 20% difference and standard deviation (SD) (20% of mean). The 20% difference was adapted from Farup et al. [6] showing <20% differences in peak sEMG during acute exercise, and similar adaptations (muscle strength and mass) in response to 6 weeks of training between LL-BFR and LL-FF. With an alpha level of 0.05 and a statistical power of 0.80, a sample size of 17 was deemed sufficient to detect physiological relevant within-participants differences. Before statistical analysis, a timeline expressed as a percentage of elapsed time from the first to the last repetition was used for statistical comparison at multiple time points (0, 20, 40, 60, 80, and 100%) of set completion. I.e., data points were extracted from single repetitions (end timepoints) or extrapolations from two consecutive repetitions (intermediate timepoints). A mixed linear model was used to analyze intermuscular as well as within and between protocol differences with participant-ID defined as a random effect and time and protocol as fixed effects. All within-group time effects were evaluated relative to baseline levels (0 %). Before statistical analysis, model assumptions were verified. Ordinal data sets (RPE, VAS) were assessed using Wilcoxon signed-rank tests. When time x group interactions emerged, effects were estimated by calculations of Cohen's d effect size (ES). All statistical analyses were performed using STATA 15.1 (Stata Corp., USA). The α-level was set at 0.05 for all tests using a two-tailed comparison. Values are presented as means ± (SD).

Results

All 17 participants completed both exercise sessions and no adverse effects showed. The number of repetitions performed was significantly higher ($p=0.001$) with LL-FF (41.3±16.8) than LL-BFR (29.3±6.8), resulting in a higher total mechanical dose (repetitions x load: LL-BFR: 386.6±101.6 kg vs. LL-FF: 556.8±270.2 kg; $p<0.001$).

Microvascular oxygenation

For $\Delta[O_2Hb]$, there was no difference between the protocols in any muscle (Fig. 1A-1B). $\Delta[O_2Hb]$ decreased at all time points in both muscles (VL, VM) and exercise protocols ($P \leq 0.001$). For LL-FF, VL displayed lower $\Delta[O_2Hb]$ values than VM at all time points ($p=0.023$, $p=0.002$, $p=0.001$, $p=0.001$, $p=0.002$ at 20, 40, 60, 80, 100% completion). For LL-BFR, VL showed lower $\Delta[O_2Hb]$ at 40 and 60% completion compared to VM ($p=0.027$, $p=0.035$) (Fig. 1A-1B).

For Δ[HHb] no between-protocol differences were observed in VM (Fig. 1C), while a time effect was present at every time point in both exercise protocols ($p \leq 0.001$). For VL a protocol x time interaction was present at 20, 40 and 60% set completion ($p=0.001$, ES=1.1; $p=0.005$, ES=0.9; $p=0.022$, ES=0.7), with higher Δ[HHb] in LL-FF compared to LL-BFR (Fig. 1D). For LL-FF, VL displayed higher Δ[HHb] than VM at all time points ($p=0.031$, $p= 0.008$, $p=0.011$, $p=0.009$, $p=0.004$ at 20, 40, 60, 80, 100% completion) (Fig. 1C-1D).

For Δ[cHb] no differences were found between protocols for neither VM nor VL (Fig. 1E-1F). In VM, an increase was observed at 20 and 100% completion in the LL-BFR protocol ($p=0.033$, $p=0.006$), whereas increases appeared at 80 and 100% completion ($p=0.003$, $p=0.001$) for LL-FF. In VL, increases were observed at 20% completion for LL-BFR ($p=0.033$) and at 100% completion for LL-FF ($p=0.006$). No intermuscular differences were observed between VM and VL in Δ[cHb] for either protocol (Fig. 1E-1F).

During the 30-s following task failure (with cuff inflated), Δ[cHb] increased in both VL and VM ($p=0.001$, $p=0.016$), $\Delta[O_2Hb]$ increased in both VL and VM ($p=0.001$, $p=0.003$) with LL-BFR, while there was no significant change in Δ[HHb] for either muscle. With LL-FF, $\Delta[O_2Hb]$ increased ($p<0.001$ for VM and VL) and Δ[HHb] decreased ($p=0.002$ for VM and VL). No change was observed for Δ[cHb].

Muscle excitability

In VM, a protocol x time interaction at 100% completion (task failure) was observed (Fig. 2A) showing a higher sEMG amplitude in LL-FF compared to the LL-BFR protocol ($p=0.044$; ES=0.70). No protocol x time interactions were observed for VL (Fig. 2B). There was a time effect at every time point ($p \leq 0.001$) for both exercise protocols in VM and VL. No intermuscular differences in sEMG amplitude were observed (Fig.2A-2B)

Perceived exhaustion and pain

There was no difference between LL-BFR and LL-FF in baseline measures of RPE or pain measures (Pre–pain: LL-BFR/LL-FF: 2.2±3.6/3.0±4.1; Pre-RPE: LL-BFR/LL-FF: 0.4±0.6/0.3±0.4). At task failure, pain measures were significantly higher for LL-BFR (Post-pain: LL-BFR/LL-FF: 57.0±20.3/42.1±20.3 (p=0.039; ES=0.69)), while there was no between-protocol difference for RPE-measures (post-RPE: LL-BFR/LL-FF: 5.2±2.3/4.6±2.4). Pain measures remained higher for LL-BFR after adjusting for baseline pain scores (*Δ*-pain: LL-BFR: 54.9±19.5; LL-FF: 39.9±19.6 (p=0.044; ES=0.75)).

Discussion

The present study is the first to examine microvascular oxygenation and muscle excitability in VM and VL during partial LL-BFR and LL-FF exercise performed to task failure. The main findings of the present study were that; when normalized to time to task failure, i) the LL-BFR and LL-FF protocols yielded similar microvascular oxygenation, ii) the muscle excitability was similar in VL but greater in VM during FF compared to LL-BFR at task failure and iii) during LL-FF participants performed 43% more repetitions before task failure and experienced less pain compared to LL-BFR.

Microvascular oxygenation

Overall, the similarities in normalized microvascular oxygenation ($\Delta[O_2Hb]$, $\Delta[HHb]$) in VL and VM at task failure support the study hypothesis. This suggests the combination of a higher mechanical dose and the occlusive stimuli of constant duty-cycle LL-FF exercise [23] result in similar changes in microvascular oxygenation compared to LL-BFR exercise. The use of external BFR appears to result in an accelerated decrease in peripheral oxygenation ($\Delta[O_2Hb]$). Previous studies support the present data of accelerated local microvascular deoxygenation with partial or full BFR exercise performed to task failure in VL and VM muscles when compared to LL-FF. Yet, at task failure, microvascular oxygenation with LL-BFR and LL-FF have both been reported as being similar and different [8,10], while work-matched protocols (e.g., the 1x30+3x15 repetition protocol) show consistently lower oxygenation during LL-BFR [8, 14].

A previous study reported changes in [O2Hb] and [HHb] of 45 and 40%, respectively, in response to LL (15% 1RM) exercise performed to task failure with full arterial occlusion [10]. Notably, in the present study the mean decrease and increase in [O2Hb] and [HHb], respectively, were somewhat lower (≤20 %) with both protocols. This overall suggests less than full oxygen utilization. Although we can only speculate about the factors leading to task failure in the present study, previous data suggest peripheral muscular factors leads to LL-BFR exercise-evoked muscular fatigue, while central factors seem to play only a negligible role [11]. Thus, the levelling-off of both O2HB and HHB at 20-30 % of set completion in both conditions (Fig 1A and 1B) could suggest limited O2 availability for HB-to-muscle cell diffusion, and consequently generally a reliance on anaerobic metabolism for the remaining condition-specific contractile work. However, the marked difference in total workload completed between the present FF-flow (42 reps) LL-BFR protocols (29 reps) indicates an important physiological discrepancy between the protocols despite great similarities in within-set microvascular oxygenation kinetics. The discrepancy in workload between conditions was paralleled by a difference in perceived pain (BFR: 57 vs. FF: 42). Consequently, these data may reflect a more abundant metabolite accumulation due to BFR, and could, together with the increased pain, mediate the accelerated task failure [24,25].

The only protocol-specific difference in microvascular oxygenation in the present study was a higher initial (i.e., 20-60% of exercise time) level of VL deoxygenation with LL-FF compared to LL-BFR. The initial lower Δ[HHb] in VL is intriguing but may be explained by the higher amount of work performed at any given relative time-point during the FF protocol. However, at 80-100% of exercise time, this effect seems to be equaled out by the effect of BFR. Interestingly, the changes in Δ[HHb] in VL was not replicated in VM, possibly due to intermuscular differences in muscle excitability or degree of BFR [26].

Notably, no difference in Δ[cHb] was observed between the LL-BFR and LL-FF protocols at task failure in contrast to the study hypothesis. Overall, these data suggest a modest level of blood-pooling within the working musculature in the present study compared to the previously reported for studies full arterial BFR. [10]. This is surprising, as it is generally accepted that the use of partial BFR cuff pressure results in full venous occlusion but only reduced arterial inflow, in turn leading to blood-pooling distally to the cuff [4]. This finding indicates that the present LL-BFR exercise protocol elicited high local microvascular pressure and/or contraction-induced increases in intramuscular pressure, resulting in cessation of arterial inflow or enabled venous return despite the application of external cuff-mediated BFR. The importance of muscle contraction in this cascade of events is supported by the present data, showing an increase in [cHB] during the 30-sec rest period after LL-BFR exercise

(cuff pressure maintained). This increase was significant for both muscles, but only during LL-BFR. Previously, similar changes in VM [cHB] have been observed between sets of LL-BFR exercise performed to task failure [8]. Interestingly, these observations could explain the abundant tissue swelling previously observed acutely (0-180 min) in response to LL-BFR exercise [6,12]. High microvascular pressure would likely trigger an increase in microvascular filtration, and in combination with intensive muscular contractions (cf. intra-/extracellular accumulation of metabolites) reduce plasma oncotic pressure altogether resulting in interstitial edema. Such changes likely lead to limited transcapillary diffusion, intracellular accumulation of metabolites, and cellular edema/swelling. BFR-mediated cellular swelling has previously been proposed to represent an independent myocellular anabolic stimulus, as cellular swelling has been shown to elevate and depress myocellular protein synthesis and/or degradation, respectively [13].

Muscle excitability

In the present study, muscle excitability reached the same peak values in VL during LL-FF and LL-BFR, supporting the study hypothesis and previous findings when performed to task failure [6,10,16,27] and in work-matched conditions [18]. Yet, studies have also found higher muscle excitability with BFR exercise when conditions were work-matched [14,28]. However, contrasting the study hypothesis, we are the first to report greater excitability of the VM during LL-FF compared to LL-BFR in a single set of unilateral knee extensor exercise to task failure. This observation may be explained by an increase or inhibition of neural efferent drive with LL-FF and LL-BFR, respectively, and/or protocol-specific differences in m. quadriceps intermuscular load-sharing. Firstly, the higher mechanical dose with LL-FF may have triggered an increase in neural drive (i.e. recruitment of higher threshold motor units (MUs)) to maintain contraction force as initially recruited MUs decrease their contractile force [29]. Secondly, BFR-induced accumulation of metabolites may have triggered pain-dependent or independent neuromotor inhibition mediated through type III/IV muscle afferents [24,25,30]. Lastly, protocol-specific differences in m. quadriceps intermuscular load-sharing may have changed the contractile demands of the VM and therefore neural drive [31].

The difference in muscle excitability between protocols was unexpected. Previous studies have reported similar findings, showing higher excitability in FF compared to BFR during lower extremity exercise performed to failure [16,27]. In these cases, however, this did not occur until the third set [16,27]. Other studies, using a similar protocol have shown no difference between the protocols with exercise performed to task failure [10,32].

In contrast, higher excitability has been observed with BFR exercise when protocols were work-matched [14,28]. It is difficult to elucidate which factors (e.g., methodological, or physiological differences) contribute to these reported differences in muscle excitability between LL-FF and LL-BFR. One candidate may be the applied occlusion pressure, as differences in muscle excitability between BFR and FF seems a more frequent observation in studies applying partial [16,27] compared to full BFR [10,32].

Perceived pain

As hypothesized, LL-BFR participants reported higher perceived pain scores compared to LL-FF. The similar levels of deoxygenation between the protocols conflict with previous studies suggesting BFR-induced hypoxia to be the main exercise-induced stimulator of pain during LL-BFR exercise [17]. The higher pain response (and time to task failure) with LL-BFR, may instead be related to a higher intramuscular accumulation of metabolites due to the use of BFR. A higher accumulation of metabolites and rating of perceived pain may in combination trigger the earlier task failure with BFR exercise, as metabolites/pain-mediated peripheral and central fatigue is well-documented [24,25,30]. Thus, the application of BFR seems to induce a high level of muscular fatigue using less contractile work compared to FF modalities [6,27] making the exercise modality interesting in populations, where lower musculoskeletal peak or total mechanical stress is warranted. However, it comes with the expense of higher perceived pain [6,16], which may limit the appeal of LL-BFR to selected groups of individuals, as the intergroup difference (15 mm) exceeds the specific minimal clinical difference of pain VAS-score (12 mm) previously reported [33]. However, previous findings indicate BFR-related pain may be remedied with prolonged training, as acute pain scores seem to attenuate as more BFR sessions are completed [34,35]. Moreover, recent BFR studies have shown post-exercise analgesic effects [36,37], which may hold value for future clinical application.

Applied Perspectives

Taken together, the results presented in the present study concomitantly indicate that the physiological mechanisms leading to task failure are similar between LL-FF and LL-BFR, but that these mechanisms are accelerated (at a rate of approximately 43%) during LL-BFR leading to earlier task failure in agreement with the

study hypothesis. In an applied perspective, the similar changes in microvascular oxygenation (Δ[O_2Hb], Δ[HHb]) and muscle excitability between protocols indicate that LL-BFR and LL-FF exercise performed to task failure in a training intervention could potentially over time lead to similar physiological adaptations (i.e., gains in muscle strength/mass), as supported by previous data [6]. As the decrease in [O_2Hb] at task failure is only moderate in both LL-BFR and LL-FF, task failure may be related to local accumulation of metabolites rather than oxygen availability. This is interesting as the adaptational gains in muscle force and mass after LL-BFR has been associated with local metabolic stress [38]. Notably, these findings also suggest that work-matched LL-BFR and LL-FF protocols (e.g., with 1x30+3x15 repetition) would result in a superior training response using BFR, which is supported in the literature [10,22,39].

Notably, the potential ability of LL-BFR to provide the same anabolic stimulus with an average or peak mechanical dose compared to LL-FF exercise [1,6], may be beneficial in several applied contexts - particularly to groups for whom high levels of mechanical stress are contraindicated (e.g., postoperative recovery).

Methodological considerations

A potential limitation of the present study was the use of an identical cuff pressure across all individuals (100 mmHg). The absolute pressure is likely to have resulted in full restriction of venous outflow and some variation in arterial inflow during exercise [40]. Little is known about the physiological effect of variations in arterial inflow with BFR exercise, and consequently, we cannot dismiss that potential variability in arterial inflow may have influenced the results to some degree. In addition, some individuals (n=2) showed more substantial sEMG responses relative to the study group in general, however, this was observed consistently across protocols and muscle groups, thus the data were kept for optimizing external validity.

Conclusion

In conclusion, LL-BFR and LL-FF exercise show similar progressive changes in **[**O_2Hb], [HHb], [cHb], and muscle excitability when normalized to time to task failure, suggesting a similar cause of events leading to task failure. However, LL-BFR exercise appears to accelerate the fatiguing processes likely mediated by faster changes in [O_2Hb], [HHb], [cHb], and muscle excitability. Consequently, LL-BFR exercise requires a lower dose of mechanical work than LL-FF, to reach task failure.

The present results may have implications for the therapeutic application of LL-BFR, as an exercise regime enabling neuromuscular improvements with the use of low dose mechanical work at the cost of a higher level of perceived pain. Moreover, the similarities in microvascular oxygenation and muscle excitability between LL-BFR and LL-FF is a novel finding and provides further insight into physiological responses to these modes of exercise. Our findings imply that adjusting for time to task failure when comparing LL-BFR and LL-FF protocols may provide a better base of comparison than volume-matched protocols.

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Conflict of interest

The authors declare no conflict of interest.

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Table 1: Descriptive characteristics of study participants

Age (years)	Height (cm)	BM (kg)	BMI (kg·m^{-2})	SBP (mmHg)	DBP (mmHg)	1RM (kg)
26.2 (2.2)	184.9 (6.5)	88.5 (12.3)	25.8 (2.8)	127.1 (9.8)	74.2 (10.9)	66.2 (11.6)

BM: body mass; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; 1RM: one-repetition maximum in unilateral knee extension exercise. Data are mean (SD)

Figure Legends

Figure 1. Progressive changes in microvascular oxygenation and hemoglobin kinetics from first to the last repetition during blood-flow restriction and free-flow exercise in vastus medialis and vastus lateralis muscles

Mean (SD) changes in Δ[O_2Hb], Δ[HHb], Δ[cHb] measured in vastus medialis (left) and vastus lateralis (right). Square and circle markers denote LL-FF and LL-BFR protocols, respectively. The x-axis shows the amount of relative time elapsed before failure. Measures obtained at 0, 20, 40, 60, 80 and 100% time elapsed were analyzed. # denotes a significant difference between protocols ($p<0.01$). * denotes a significant time effect for LL-FF and LL-BFR ($p<0.01$). † denotes a significant time effect for the BFR protocol. ‡ denotes a significant time effect for the FF protocol ($p<0.05$). [a] denotes a significant difference between VM and VL in the LL-BFR protocol ($p<0.05$). [b] denotes a significant difference between VM and VL in the LL-FF protocol ($p<0.05$).

Figure 2. Progressive changes in muscle excitability from first to the last repetition during blood-flow restriction and free-flow exercise in vastus medialis and vastus lateralis

Mean (SD) changes in sEMG amplitude measured in vastus medialis (left panel) and vastus lateralis (right panel). Square and circle markers denote LL-BFR and LL-FF protocols, respectively. The x-axis shows the normalized time to task failure. Measures obtained at 0, 20, 40, 60, 80 and 100 % time elapsed were analyzed. * denotes a significant time effect ($p<0.01$). # denotes a significant difference between protocols ($p<0.01$).

Figure. 1

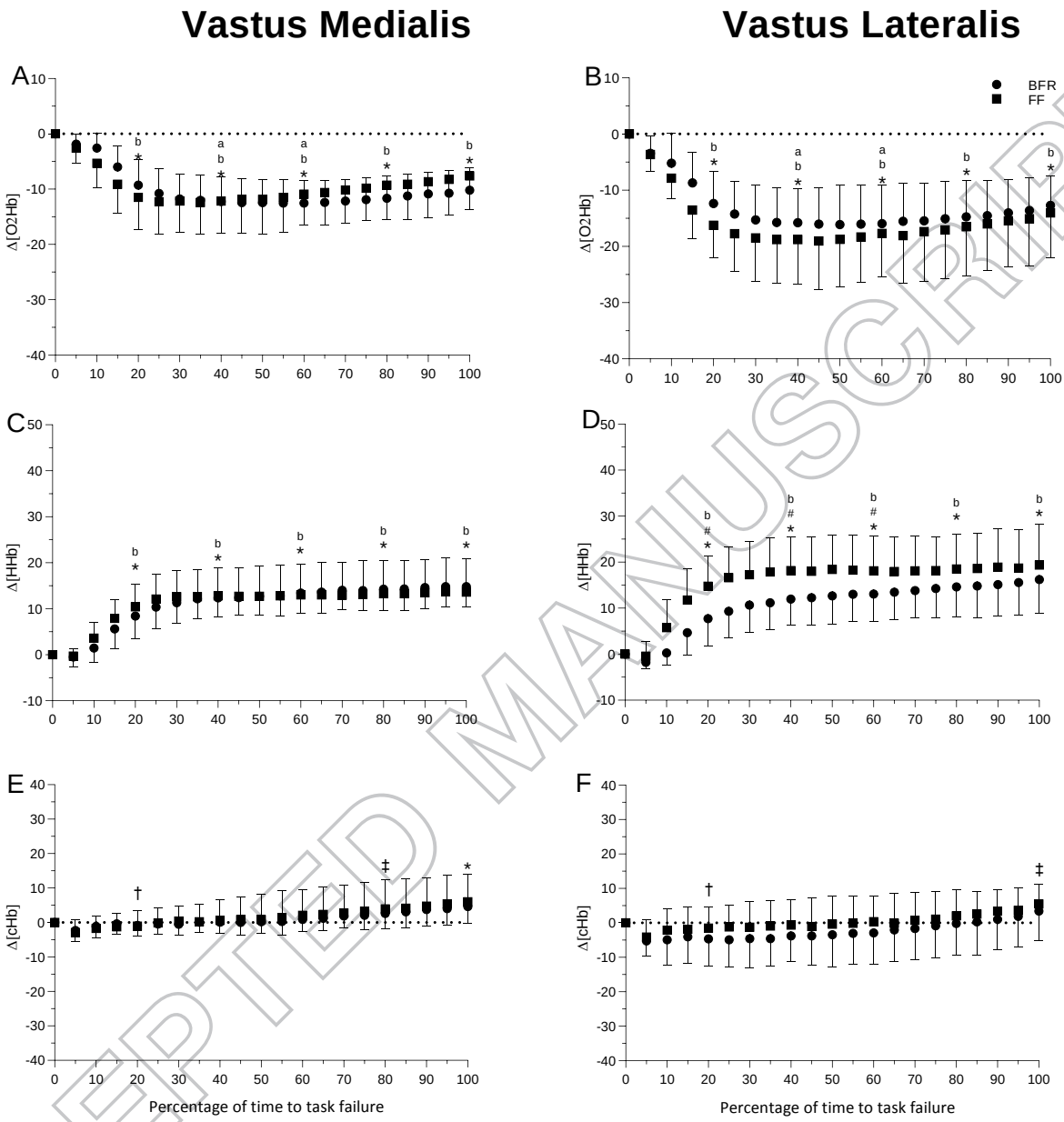

Figure. 2