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ORIGINAL ARTICLE

Limb blood flow and tissue perfusion during exercise with blood flow restriction

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Abstract

Introduction Exercise with blood flow restriction (BFR) is emerging as an effective modality for improving muscular function in clinical and athletic populations. Selection of cuff pressure is critical because it should maximize metabolic stress without completely occluding blood flow or compromising user safety. It is unknown how cuff pressures determined at rest influence blood flow hemodynamics during exercise.

Purpose We evaluated changes in blood flow and tissue perfusion before, during, and after exercise with BFR.

Methods Ten males performed rhythmic handgrip exercise (30 contractions, 30% MVC) at 0%, 60%, 80%, 100%, and 120% of limb occlusion pressure (LOP). Brachial artery blood flow and tissue saturation were assessed using Doppler ultrasound and near-infrared spectroscopy, respectively.

Results At rest blood flow generally decreased with increased pressure (0% > 60% ≈ 80% > 100% ≈ 120% LOP). During 60% and 80% LOP conditions, blood flow increased during exercise from rest and decreased after exercise (all $P < 0.05$). Compared to 0% LOP, relative blood flow at 60% and 80% LOP decreased by 22–47% at rest, 22–48% during exercise, and 52–71% after exercise (all $P < 0.05$). Increased LOP decreased tissue saturation during exercise with BFR ($P < 0.05$). Heart rate, mean arterial pressure, and cardiac output did not differ across LOP.

Conclusion At pressures below LOP the cardiovascular system overcame the external pressure and increased blood flow to exercising muscles. Relative reductions in blood flow at rest were similar to those during exercise. Thus, the relative occlusion measured at rest approximated the degree of occlusion during exercise. Moderate cuff pressures increased metabolic stress without completely occluding blood flow.

Keywords Vascular occlusion · Kaatsu · Resistance exercise · Handgrip exercise · Arterial blood flow · Functional near inferred spectroscopy

Abbreviations

BFR	Blood flow restriction
LOP	Limb occlusion pressure
RM	Repetition maximum

Introduction

Resistance exercise is widely recommended to restore function following injury, maintain health across the lifespan, and improve athletic performance. In general, performing resistance exercise at 65–70% of one repetition maximum (RM) 2–3 times per week for 8 weeks is sufficient to increase muscle size and strength (Garber et al. 2011). This type of exercise, however, is not always possible because high training loads are often contraindicated or impossible for some populations (e.g., older adults, individuals with orthopedic

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limitations). Alternatively, implementation of resistance exercise with blood flow restriction (BFR) is emerging as an effective option to build muscle and improve strength in healthy, clinical, and athletic populations (Scott et al. 2015). This exercise modality involves the use of mechanical compression of the limb to occlude blood flow, usually with a pressurized cuff or tourniquet, used in combination with much lower loads than traditional resistance training (e.g., 20% vs. 70% of 1 RM) (Scott et al. 2015). The main advantage of exercise with BFR is that increases in muscle size and strength are elicited at low training loads which is clinically relevant when high loads are contraindicated (for a review see Hughes et al. 2017).

To date, there are no standardized recommendations for the proper application of cuff pressure during exercise with BFR. Theoretically, cuff pressure should be set high enough to prevent the return of venous blood flow, but low enough to maintain some level of arterial blood flow (Scott et al. 2015). Cuff pressure should also maximize metabolic stress (Cayot et al. 2016; Takada et al. 2012) without completely occluding arterial blood flow and inducing excessive discomfort. Several previous investigators have measured blood flow at rest with BFR (Iida et al. 2005; Hunt et al. 2016; Mouser et al. 2017a, b). Specifically, brachial and femoral artery blood flow decreases linearly with increasing cuff pressure between 80 and 120 and 100–250 mm Hg, respectively (Iida et al. 2005; Hunt et al. 2016). When cuff pressure is set relative to individual limb occlusion pressure (LOP), a non-linear decrease occurs with minimal changes in blood flow from 50 to 90% of LOP (Mouser et al. 2017a, b). However, it is unclear if the cuff-induced changes in blood flow measured *at rest* translates to similar hemodynamic changes *during exercise*. Several factors including increase in blood pressure, activation of the skeletal muscle pump, and change in limb position (Sieljacks et al. 2018; Hughes et al. 2018) during exercise may reduce the effectiveness of the cuff at restricting blood flow. Previous investigators have used near-infrared spectroscopy to quantify tissue oxygenation during exercise with BFR (Cayot et al. 2016; Corvino et al. 2017; Lauver et al. 2017), which has provided indirect insight into the level of blood flow and metabolic stress associated with BFR cuff pressures. To our knowledge, there are no reports documenting changes in blood flow and tissue perfusion during exercise with BFR.

Understanding the extent to which cuff pressure alters blood flow and tissue perfusion during exercise with BFR would have important implications for exercise prescription and training. Most notably, high cuff pressures that completely occlude arterial blood flow could cause harmful side effects including adverse cardiovascular responses, blood clotting, and muscle/nerve damage (Manini and Clark 2009). Accordingly, the purpose of this study was to evaluate changes in arterial blood flow and tissue perfusion before, during, and after rhythmic handgrip exercise with BFR across a range of cuff pressures. We hypothesized that BFR-induced reductions in arterial blood flow during exercise would be less than those reductions during rest. We also hypothesized that application of moderate pressure, based on LOP, would elicit considerable metabolic stress (as quantified by reductions in tissue saturation index and increases in deoxygenated hemoglobin concentration) without completely occluding arterial blood flow.

Methods

Participants

Ten active men between 18 and 44 yrs volunteered to participate in this study (demographic and anthropometric characteristics reported in Table 1). All participants self-reported that they performed physical activity at a moderate intensity at least 150 min/week, which is consistent with the American College of Sports Medicine guidelines (Garber et al. 2011). However, participants did not perform exercise with BFR on a regular basis. Participants were excluded from the study if they used nicotine products, had diabetes, or had any cardiopulmonary disorders. Following the initial screening, participants were informed of the purpose of the study, the risks involved, and gave informed written consent. This study was approved by the Institutional Review Boards at Michigan Technological University and Kent State University. Finally, given the effect size calculated from partial eta squared (0.823), an alpha level of 0.05, and a sample of 10 participants, the statistical power was calculated to be 0.99.

Table 1 Participant demographic and anthropometric characteristics ($n = 10$)

Variable	Value
Age (years)	27 ± 4
Body mass (kg)	82 ± 14
Height (m)	1.77 ± 0.1
Body mass index (kg m^{-2})	26 ± 3
Systolic blood pressure (mmHg)	118 ± 5
Diastolic blood pressure (mmHg)	75 ± 7
Triceps Skinfold (mm)	10 ± 3
Biceps Skinfold (mm)	5 ± 1
Upper arm circumference (cm)	32 ± 3
Upper arm muscle area (cm^2)[a]	59 ± 13

Values are reported as mean ± SD

[a]Estimated bone-free arm muscle area

Study design and overview

In this investigation, we used a single-group repeated measures design. Participants performed rhythmic handgrip exercise across a range of cuff pressure conditions (0%, 60%, 80%, 100%, and 120% of LOP). Our primary outcome variable was brachial artery blood flow and secondary outcome variables included tissue saturation index and deoxyhemoglobin concentration. These variables were selected because level of blood flow restriction and metabolic stress are factors that likely contribute to the robust increases in muscle size and strength with BFR exercise training (Corvino et al. 2017; Yanagisawa and Sanomura 2017). Primary and secondary variables were assessed before, during, and after exercise. With this experimental design, we aimed to determine the extent to which cuff pressure alters blood flow and tissue perfusion during exercise with BFR.

Participants reported to the laboratory in a resting condition, not having consumed alcohol or participated in vigorous exercise in the previous 24 h. Participants were asked to lay supine on an examination table for 10 min prior to testing and remained in this position for the duration of the experimental protocol. Resting heart rate, mean arterial pressure, and cardiac output were monitored to ensure normal physiological ranges. Resting brachial artery blood flow was monitored for 1 min and then LOP was determined. Relative pressures of 0%, 60%, 80%, 100%, and 120% of LOP were calculated and the order of pressures was randomized. Participants rested for 5 min for physiological values to return to baseline. Participants then performed rhythmic handgrip contractions at each pressure condition, with 5 min of rest between conditions. All testing was performed in a controlled thermoneutral environment (25 °C).

Rhythmic handgrip exercise

Prior to exercise participants performed three maximal voluntary contractions (MVC) using a handgrip dynamometer (ADInstruments, Colorado Springs, CO, USA). Handgrip forces were recorded using a data acquisition system (Powerlab 16, ADInstruments, Colorado Springs, CO, USA). The highest MVC was identified and 30% of the participant's MVC force was calculated and used as the exercise intensity. The cuff was inflated to the desired pressure and was maintained throughout that pressure condition. Pre-exercise brachial artery blood flow was measured for 30 s with the cuff inflated. Participants then performed 30 handgrip contractions. Participants were instructed to perform one contraction every 2 s while exercise blood flow was recorded. A metronome was used to help participants match the desired contraction frequency. Force tracings were streamed onto a monitor so that the participants had visual feedback of the force they produced, which enabled them to more accurately reach the target intensity. The cuff remained inflated for 30 s after exercise to determine if the various cuff pressures had a similar impact on post-exercise blood flow as they did pre-exercise. After the cuff pressure was released, the participant was given 5 min of rest before the next cuff pressure condition.

Blood flow calculation

Blood velocity (V_{mean}) and vessel diameter (V_d) were measured with a Logic 7 ultrasound system (General Electric Medical Systems, Milwaukee, WI) equipped with a linear array transducer operating at an imaging frequency of 12 MHz and Doppler frequency of 5 MHz. Doppler pulse wave spectrum and ultrasound images were continuously recorded throughout the pre-exercise, exercise, post-exercise period. Vessel diameters were determined by averaging the perpendicular distance between the superficial and deep walls of the brachial artery at three nonconsecutive *R* waves during the last 15 s of the pre-exercise time period. Measurements of V_{mean} were obtained with the probe positioned to maintain an insonation angle of $\leq 60°$. Mean blood velocity was averaged across 15 s intervals throughout the protocol. Importantly, blood velocity data obtained during exercise using Doppler ultrasound are reliable (Nyberg et al. 2018) which is notable given the complex nature of blood velocity during dynamic muscle contractions. Using pre-exercise mean blood velocity and arterial diameter, blood flow was calculated as blood flow $= V_{mean} \times \pi \times (V_d/2)^2 \times 60$. Blood flow was averaged over each time period, 30 s pre-exercise, 60 s exercise, and 30 s post-exercise within each cuff pressure. Peak blood flow was determined as the 15 s intervals with the highest blood flow. Relative blood flow was determined by normalizing blood flow at 60%, 80%, 100%, and 120% LOP to the 0% LOP condition within each time period.

Limb occlusion pressure

A 10 cm wide nylon pneumatic cuff (Hokanson, Belleview, WA, USA) was wrapped around the right arm at the most proximal location and pressurized with a rapid cuff inflator (Hokanson, Belleview, WA, USA). The ultrasound probe was positioned distal to the cuff and proximal to the cubital fossa. Limb occlusion pressure was determined by inflating the cuff to 75 mmHg, and slowly increasing the pressure until brachial blood velocity reached zero based on the absence of the Doppler spectrum. The minimum pressure required to completely occlude arterial blood flow was recorded as the LOP. Finally, previous authors (Bezerra de Morais et al. 2016) have reported that upper-arm limb occlusion pressure data obtained using Doppler ultrasound are reliable.

Tissue perfusion

A near-infrared spectroscopy (NIRS) system was used to measure tissue oxygen saturation (Oxymon MKIII; Artinis Medical Systems, Einsteinweg, Netherlands). The NIRS sensor was placed on the right forearm approximately 1/3 of the distance from the medial epicondyle of the humerus to the styloid process of the radius and adhered with double-sided tape. The sensor site was prepared by shaving hair, abrading the skin with sandpaper, and removing any oils or contaminants using an alcohol swab prior to sensor placement. Data were recorded at 10 Hz. The concentration of total hemoglobin (THB), oxyhemoglobin (OHB) and deoxyhemoglobin (HHB) was recorded. Tissue saturation index (TSI) was calculated by TSI (%) = (OHB/THB) × 100 and averaged over each time period. Changes in deoxyhemoglobin were calculated by assessing the difference between the average value in the last 15 s of each time period and the baseline values prior to cuff inflation. It is important to note that tissue saturation index and deoxyhemoglobin data obtained during handgrip exercise using NIRS are reliable (Celie et al. 2012).

Central variables

Beat-by-beat mean arterial pressure and cardiac output were measured with a Nexfin HD Monitor (Edwards LifeSciences, Irvine CA, USA). Heart rate was determined with the use of a three-lead ECG running through a BioAmp acquisition box (ADInstruments, Colorado Springs, CO, USA). The finger cuff electrode was placed over the middle phalanx of the left, non-exercising hand. These data were also continuously streamed into the power lab 16 and analyzed with Lab chart 8. Each dependent variable was averaged over 15 s throughout each pressure condition.

Forearm muscle activity

Forearm muscle activity was assessed using surface electromyography (EMG). Electrodes were placed on the right forearm approximately 1/3 of the distance from the medial epicondyle of the humerus to the styloid process of the radius as recommended by Davis (1959). Disposable self-adhesive electrodes were placed on the muscle in line with the fiber direction. The electrode-site placement was prepared in the same manner as the NIRS sensor. EMG data were recorded at 4000 Hz and acquired on the data acquisition system described above and analyzed using commercially available software (Lab Chart 8 Pro, ADInstruments, Colorado Springs, CO, USA). The raw EMG signal was band-pass filtered (10–450 Hz) and rectified. Afterward, a root mean squared integration was performed. Integrated software (Peak Analysis, Lab Chart 8 Pro, AD Instruments, Colorado Springs, CO, USA) was used to calculate the mean area under the curve for the first and last 10 contractions for each condition.

Statistical analysis

To test the hypothesis that BFR-induced reductions in arterial blood flow during exercise would be less than those reductions during rest, we used a two-way repeated measures analysis of variance (ANOVA) procedure to evaluate the effects of time (pre-exercise, exercise, post-exercise) and pressure (0%, 60%, 80%, 100%, and 120% of LOP) on the primary outcome variable brachial artery blood flow. Note that, changes in both absolute and relative blood flow were assessed. Additionally, to test the hypothesis that application of moderate cuff pressure would elicit considerable metabolic stress, we used separate two-way repeated measures (ANOVA) procedures to evaluate the effects of time and pressure on secondary outcome variables of tissue saturation index and deoxyhemoglobin concentration. Repeated measures ANOVA procedures were also used to assess changes in select cardiovascular response variables (heart rate, mean arterial pressure, cardiac output). When the assumption of sphericity was violated a Greenhouse-Geisser correction was used. If there were any significant main effects or interactions identified then subsequent post-hoc tests (Fisher's least significant difference) were used to explore where differences occurred. Paired samples t-tests were used to assess differences in forearm muscle activation for all cuff pressure conditions. Partial eta squared (η_p^2) values were calculated as a measure of effect sizes with $\eta_p^2 \geq 0.01$ indicating small, ≥ 0.059 medium, and ≥ 0.138 large effects, respectively (Cohen 1988). Statistical procedures were performed using IBM SPSS 24 (Chicago, IL, USA). Data are reported as mean ± standard deviation and alpha was set to 0.05.

Results

Limb occlusion and cuff pressure

Mean limb occlusion pressure was 130 ± 12 mmHg. Cuff pressures for the 60%, 80%, 100%, and 120% LOP conditions corresponded to 81 ± 11, 108 ± 15, 135 ± 19, and 162 ± 23 mmHg, respectively.

Blood flow

Absolute blood flow kinetics are illustrated in Fig. 1a for descriptive purposes. The repeated measures ANOVA procedures revealed significant main effects of pressure ($P < 0.01$, $\eta_p^2 = 0.839$) and time ($P < 0.01$, $\eta_p^2 = 0.823$), as well

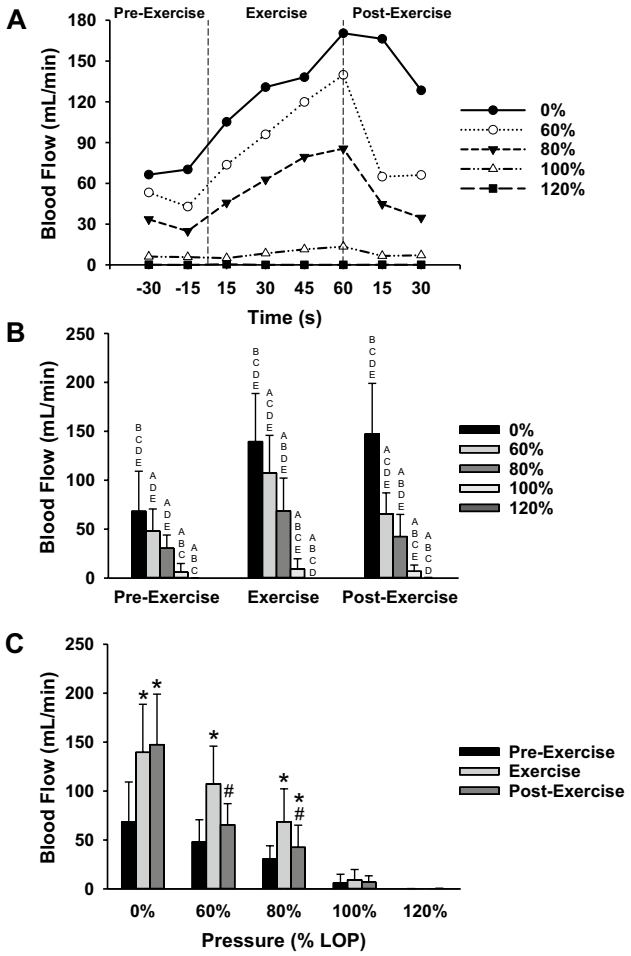

Fig. 1 Time course of alterations in absolute brachial artery blood flow across different cuff pressures (**a**). Brachial artery blood flow measured during pre-exercise, exercise, and post-exercise with the cuff inflated (**b**). Blood flow different from 0%, 60%, 80%, 100%, and 120% ($P < 0.05$) are indicated by A, B, C, D, and E, respectively. Brachial artery blood flow measured at each cuff pressure for pre-exercise, exercise, and post-exercise (**c**). Blood flow different than pre-exercise and exercise ($P < 0.05$) are indicated by * and #, respectively. Data are reported as mean in panel **a** and mean ± SD in panel **b** and **c**. Note that, blood flow measured at 120% LOP was minimal

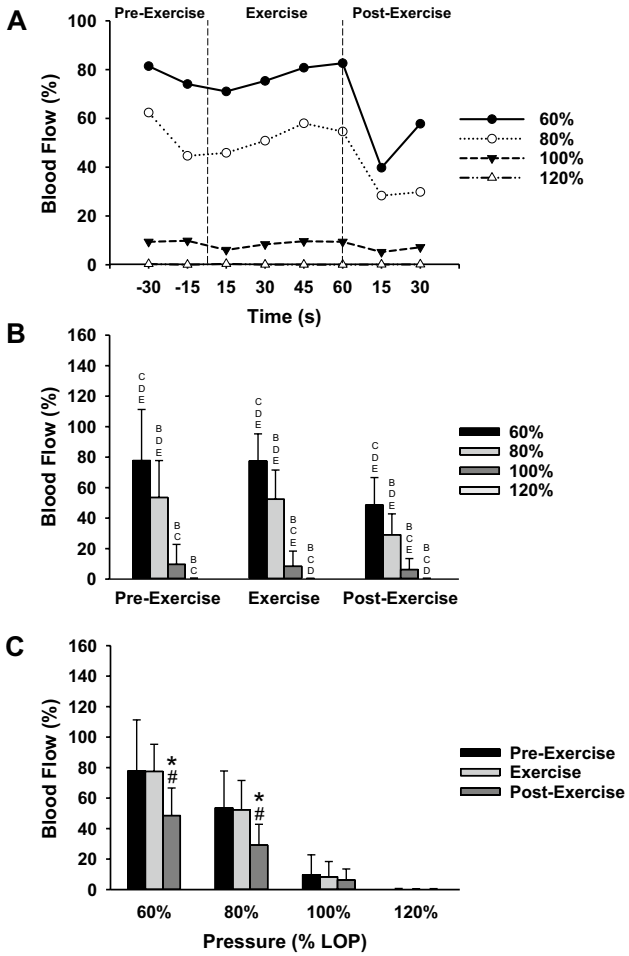

Fig. 2 Time course of alterations in relative brachial artery blood flow across different cuff pressures (**a**). Brachial artery blood flow measured during pre-exercise, exercise, and post-exercise with the cuff inflated (**b**). Relative blood flow different from 60%, 80%, 100%, and 120% ($P < 0.05$) are indicated by B, C, D, and E, respectively. Brachial artery blood flow measured at each cuff pressure for pre-exercise, exercise, and post-exercise (**c**). Blood flow different than pre-exercise and exercise ($P < 0.05$) are indicated by * and #, respectively. Data are as reported mean in panel **a** and mean ± SD in panel **b** and **c**. Note that, blood flow measured at 120% LOP was minimal

as a pressure × time interaction ($P < 0.01$, $\eta_p^2 = 0.725$). At rest prior to exercise, blood flow generally decreased with increased cuff pressure: 0% > 60% ≈ 80% > 100% ≈ 120% (Fig. 1b). During exercise, blood flow decreased with increased cuff pressure: 0% > 60% > 80% > 100% > 120% (Fig. 1b). The pressure–blood flow relationships during exercise were also maintained after exercise (Fig. 1b). For the 0%, 60%, and 80% LOP conditions, blood flow increased from rest during exercise (all $P < 0.05$, Fig. 1c). Blood flow decreased after exercise for the 60% and 80% LOP conditions (all $P < 0.05$, Fig. 1c). For the 100% and 120% LOP conditions, blood flow did not differ before, during, or after exercise. Note that, pressure–blood flow relationships for peak blood flow followed the same patterns as those for mean blood flow.

Relative blood flow kinetics are illustrated in Fig. 2a for descriptive purposes. The repeated measures ANOVA procedures revealed significant main effects of pressure ($P < 0.01$, $\eta_p^2 = 0.927$) and time ($P < 0.01$, $\eta_p^2 = 0.564$), as well as a pressure × time interaction ($P < 0.01$, $\eta_p^2 = 0.339$). The relative reductions in blood flow before exercise did not differ from those during exercise (Fig. 2b). Specifically, blood flow in the 60% LOP condition was reduced by 22 ± 3% before exercise and remained reduced by 22 ± 2% during

exercise (Fig. 2c). Similarly, blood flow in the 80% LOP condition was reduced by 47 ± 2% and 48 ± 2% before and during exercise, respectively (Fig. 2c). After exercise blood flow for both the 60% and 80% LOP conditions was reduced even further (52 ± 2% and 71 ± 1%, respectively, both $P < 0.05$, Fig. 2c). In the 100% and 120% LOP condition there were no differences in relative blood flow.

Tissue perfusion

Changes in tissue saturation index are illustrated in Fig. 3a for descriptive purposes. The repeated measures ANOVA procedures revealed significant main effects of pressure ($P < 0.01$, $\eta_p^2 = 0.682$) and time ($P < 0.01$, $\eta_p^2 = 0.782$), as well as a pressure × time interaction ($P < 0.01$, $\eta_p^2 = 0.588$). At rest prior to exercise, there were no differences in tissue saturation index with increased pressure. There were trends for the 60%, 100%, and 120% LOP conditions to be lower than 0% LOP condition ($P = 0.08$, $P = 0.06$, $P = 0.07$, respectively). During exercise, tissue saturation index generally decreased with increased pressure: 0% > 60% ≈ 80% > 100% ≈ 120% (Fig. 3b). After exercise, all pressure conditions were different (all $P < 0.05$) except for 80% and 100% (0% > 60% > 80% ≈ 100% > 120%, Fig. 3b). For the 0% condition, tissue saturation index decreased only after exercise ($P = 0.04$, Fig. 3c). For the 60%, 80%, 100, and 120% LOP conditions, tissue saturation index decreased from rest during exercise and decreased further after exercise (all $P < 0.05$, Fig. 3c).

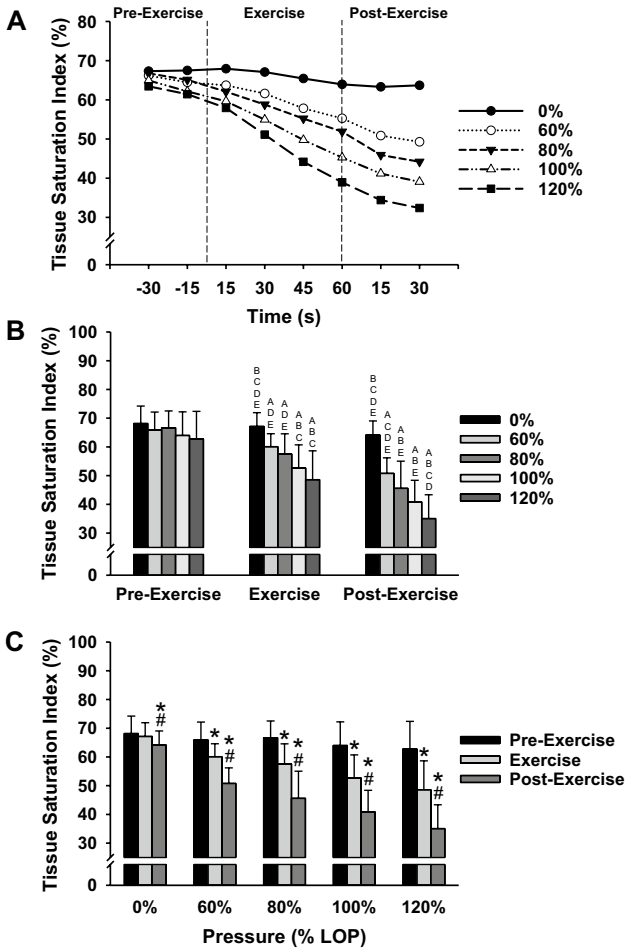

Fig. 3 Time course of alterations in tissue saturation index across different cuff pressures (**a**). Tissue saturation index measured during pre-exercise, exercise, and post-exercise with the cuff inflated (**b**). Tissue saturation index different from 0%, 60%, 80%, 100%, and 120% ($P < 0.05$) are indicated by A, B, C, D, and E, respectively. Tissue saturation index measured at each cuff pressure for pre-exercise, exercise, and post-exercise (**c**). Tissue saturation index different than pre-exercise and exercise ($P < 0.05$) are indicated by * and #, respectively. Data are as reported mean in panel **a** and mean ± SD in panel **b** and **c**

Changes in deoxyhemoglobin are illustrated in Fig. 4a for descriptive purposes. The repeated measures ANOVA revealed significant main effects of pressure ($P < 0.01$, $\eta_p^2 = 0.812$) and time ($P < 0.01$, $\eta_p^2 = 0.916$), as well as a pressure × time interaction ($P < 0.01$, $\eta_p^2 = 0.796$). At rest prior to exercise, deoxyhemoglobin increased with the initial increase in pressure but did not increase at pressures higher than 60% LOP: 0% < 60% ≈ 80% ≈ 100% ≈ 120% (Fig. 4b). During exercise, deoxyhemoglobin increased with the initial increases in pressure but did not increase at pressures higher than 80% LOP: 0% < 60% < 80% ≈ 100% ≈ 120% (Fig. 4b). The pressure-deoxyhemoglobin relationships during exercise were generally maintained after exercise. For the 0% condition, deoxyhemoglobin increased from rest during exercise and remained elevated after exercise (both $P < 0.05$, Fig. 4c). For the 60%, 80%, 100, and 120% LOP conditions, deoxyhemoglobin increased from rest during exercise and increased further after exercise (all $P < 0.05$, Fig. 4c).

Central variables

For cardiac output and heart rate there were no significant main effects for time ($P = 0.54$, $\eta_p^2 = 0.081$, $P = 0.22$, $\eta_p^2 = 0.145$, respectively) or pressure ($P = 0.8$, $\eta_p^2 = 0.279$, $P = 0.22$, $\eta_p^2 = 0.156$, respectively) or pressure × time interactions ($P = 0.07$, $\eta_p^2 = 0.219$, $P = 0.54$, $\eta_p^2 = 0.077$, respectively). For mean arterial pressure there was a significant effect of time ($P < 0.01$, $\eta_p^2 = 0.625$), but not for cuff pressure ($P = 0.59$, $\eta_p^2 = 0.058$) or the cuff pressure × time interaction ($P = 0.14$, $\eta_p^2 = 0.151$). Mean arterial pressure increased during exercise in all LOP conditions (all $P < 0.05$), but only decreased post-exercise in 0% and 60% LOP conditions (both $P < 0.05$; Fig. 5).

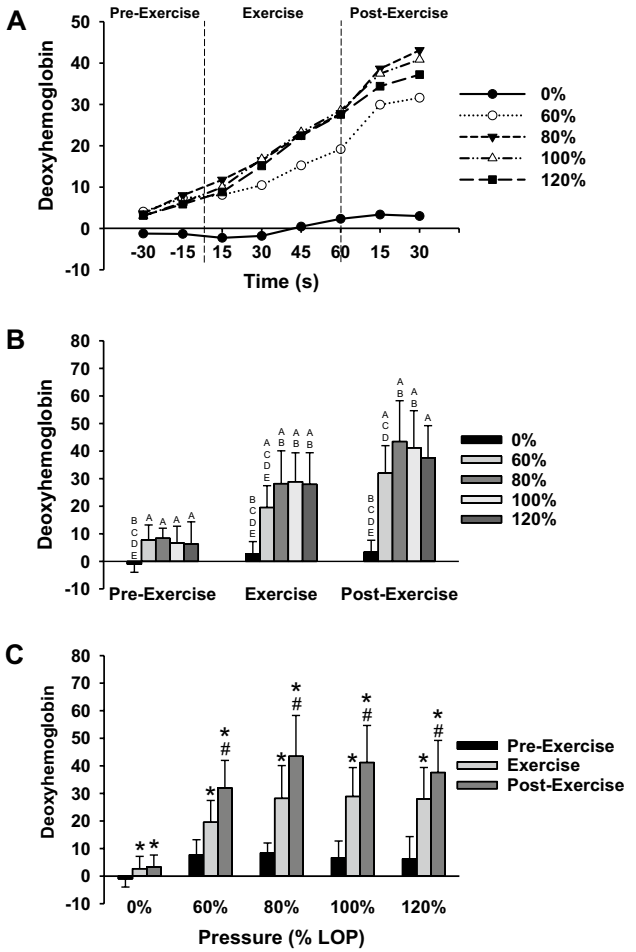

Fig. 4 Time course of alterations in concentration of deoxyhemoglobin across different cuff pressures (**a**). Concentration of deoxyhemoglobin measured during pre-exercise, exercise, and post-exercise with the cuff inflated (**b**). Concentration of deoxyhemoglobin different from 0%, 60%, 80%, 100%, and 120% ($P < 0.05$) are indicated by A, B, C, D, and E, respectively. Concentration of deoxyhemoglobin measured at each cuff pressure for pre-exercise, exercise, and post-exercise (**c**). Concentration of deoxyhemoglobin different than pre-exercise and exercise ($P < 0.05$) are indicated by * and #, respectively. Data are as reported mean in panel **a** and mean ± SD in panel **b** and **c**

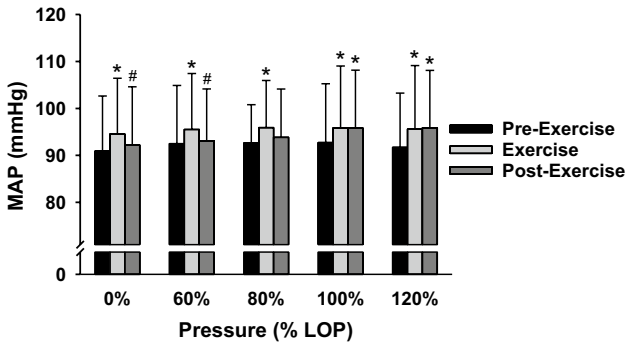

Fig. 5 Alterations in mean arterial pressure (MAP). Mean arterial pressure different than pre-exercise and exercise ($P < 0.05$) are indicated by * and #, respectively. Data are reported as mean ± SD

Forearm muscle activity

Forearm EMG activity for the first 10 to last 10 contractions did not differ for any pressure condition (all $P > 0.05$).

Discussion

The purpose of this study was to evaluate changes in arterial blood flow and tissue perfusion before, during, and after rhythmic handgrip exercise with BFR across a range of occlusion pressures. The key findings were that: (1) at pressures below LOP the cardiovascular system was able to overcome the external pressure and increase blood flow to the working muscles during exercise, (2) relative reductions in blood flow at rest were similar to those during exercise, and (3) cuff pressures of 60 and 80% LOP reduced tissue saturation index and increased deoxyhemoglobin concentrations, which is consistent with an increase in metabolic stress and metabolite accumulation (Ganesan et al. 2015; Gobbo et al. 2011), without completely occluding arterial blood flow. Taken together, these findings provide novel insight into hemodynamic changes during exercise with BFR and have important implications. Specifically, the relative level of blood flow occlusion measured at rest may approximate the degree of occlusion during exercise and application of moderate cuff pressure seems to offer an appropriate BFR occlusion stimulus for small muscle mass exercise.

Assessment of blood flow during exercise

To the best of our knowledge, we are the first group to report alterations in blood flow before, during, and after exercise with BFR. Previous research has focused on examinations of blood flow at rest (Iida et al. 2005; Hunt et al. 2016; Mouser et al. 2017a, b) and immediately after exercise (Downs et al. 2014; Takano et al. 2005) with BFR. However, measurement of blood flow during exercise is very difficult as the motion of the exercising limb may influence the artery being examined and consequently give rise to motion artifacts (Downs et al. 2014). To circumvent this limitation, we implemented BFR during rhythmic handgrip exercise; an exercise modality that is often used to measure blood flow to exercising muscles and assess peripheral vascular health (Kamiya et al. 2001; Pyke et al. 2008; Taylor et al. 1989). Our brachial artery blood flow data at rest and during exercise without occlusion (0% LOP) are consistent with previously reported data on blood flow during handgrip exercise (Green et al. 2005; Shoemaker et al. 1997). Thus, we are confident that our assessment of blood flow during handgrip exercise

yielded reliable results and that changes in blood flow with BFR were due to the occlusion pressure.

Alterations in blood flow

Prior to exercise, there were no significant differences in blood flow between the 60% and 80% and the 100% and 120% LOP conditions. These data are in agreement with that of Mouser and colleagues (2017a, b) who demonstrated that under relative occlusion pressure, the reduction in blood flow does not linearly decrease with increasing pressure; as they reported similar blood flow values between 50–90% of LOP. This non-linear decrease in blood flow is unique to relative pressures as previous reports indicate a linear decrease in blood flow with absolute increases in cuff pressures above 80 mmHg (Hunt et al. 2016). These differences are likely due to individual differences in LOP and variations in absolute and relative cuff pressures. For example, an absolute pressure of 140 mmHg would range from approximately 80–105% LOP for the participants in this study, which would completely occlude blood flow in the majority of participants (7 of 10). According to a recent questionnaire on the use of exercise with BFR, only 12% of practitioners are currently basing cuff pressure on LOP when implementing exercise with BFR (Patterson and Brandner 2017). These findings re-enforce the need to individualize pressures before performing exercise with BFR to ensure user safety and facilitate consistent training adaptations.

During exercise, blood flow increased in the 0%, 60%, and 80% LOP conditions from rest. Thus, at pressures below LOP the cardiovascular system increased blood flow to the working muscles even despite the mechanical compression. However, blood flow was minimal (< 10 ml/min) during the 100% and 120% LOP conditions. At these pressures, the cardiovascular system cannot overcome the external pressure. Moreover, while the absolute blood flow increased during exercise with the lower cuff pressures the relative reduction in blood flow due to the applied pressure at rest was, for the most part, maintained during exercise. Specifically, at 60% LOP blood flow was reduced by ~ 20% at rest as well as during exercise. Likewise, at 80% LOP blood flow was reduced by ~ 45% at rest and during exercise. This finding is important as these two pressures are often reported in the literature and shed light on previous speculations that cuff pressure would have to be increased during exercise to maintain the same level of blood flow restriction (Hunt et al. 2016).

In the 0% LOP control condition blood flow remained elevated following exercise; however, this hyperemic response was blunted by the cuff across all cuff pressures. Post-exercise absolute blood flow decreased in the 60% and 80% LOP conditions from the exercise values. This is in contrast to the work by Downs and colleagues (2014) as these authors speculated that post-exercise blood flow would be similar to blood flow during exercise due to the low loads used, or higher, due to post-exercise reactive hyperemia. Although the 60% and 80% LOP conditions did reduce blood flow during exercise by ~ 20% and ~ 45% compared to the 0% control condition, the post-exercise reductions during these two conditions were much greater. Specifically, post-exercise blood flow was reduced by ~ 50% and ~ 70% during the 60% and 80% LOP conditions, respectively. These results may be explained by the skeletal muscle pump, which during exercise would increase venous return and allow for greater arterial blood flow. Following exercise, the absence of the skeletal muscle pump's assistance with venous return would augment venous pooling and venous pressure thus reducing the pressure gradient needed to achieve post-exercise hyperemia. If the goal of exercise with BFR is to maintain the relative reduction in blood flow, then cuff pressure should be held constant before and during exercise and reduced between sets. Alternatively, if the goal is to keep the reduction in absolute blood flow constant, then the cuff pressure set at rest should be increased during and after exercise, but to a greater extent during exercise. A long-term training intervention is required to elucidate the best strategy for restricting blood flow during exercise with BFR.

Tissue perfusion

Results indicated that increased pressure reduced tissue saturation index. This relationship is similar to blood flow, which seems logical as blood flow and tissue perfusion are highly correlated (Boushel et al. 2000; Habazettl et al. 2010). There were, however, no differences in deoxyhemoglobin in the 80%, 100%, and 120% LOP conditions. Although not measured in this study, this could be because pressures above 80% LOP completely occlude venous blood flow, and therefore there was no deoxyhemoglobin clearance from the muscle in these conditions. Ganesan and colleagues (Ganesan et al. 2015) proposed that BFR-induced hypertrophy is due to localized hypoxia and metabolite accumulation. With this in mind, our data suggest that cuff pressures above 60% LOP do cause tissue hypoxia and increase metabolite accumulation. Moreover, the finding that pressures greater than 80% LOP do not increase deoxyhemoglobin suggests that these higher pressures may not be entirely necessary. Higher pressures would likely increase discomfort and risk for adverse cardiovascular responses (Spranger et al. 2015) without increasing metabolite accumulation. Based on the above results, cuff pressures between 60–80% LOP seem appropriate for increasing metabolic stress and metabolite accumulation without completely occluding blood flow and compromising individual safety.

In all pressure conditions above 0% LOP, tissue saturation index continued to decrease post-exercise. These results are consistent with previous reports on tissue saturation index following knee extension exercise with BFR (Downs et al.

2014; Ganesan et al. 2015). Suga and colleagues (2012) reported that metabolic stress and metabolite accumulation induced from multiple sets of BFR exercise is similar to that of high-intensity exercise, only if the cuff pressure is maintained during the rest period. If the goal of exercise with BFR is to create a hypoxic environment within the muscle and to increase the accumulation of metabolites to a similar level of high-intensity exercise, then the cuff pressure should be maintained between sets. Such a strategy would limit post-exercise hyperemia and consequently decrease tissue saturation index and increase metabolite build-up.

Mean arterial pressure

There were no differences in mean arterial pressure across different cuff pressures. This may be due to the small muscle mass used or the type of exercise used. It is possible that there would be a change in mean arterial pressure across pressures during dynamic exercise with larger muscle masses. Mean arterial pressure increased from before exercise to exercise in all conditions, and returned to pre-exercise levels within the post-exercise time period in the 0% and 60% LOP condition and nearly returned for the 80% LOP condition. However, in the 100% and 120% LOP conditions mean arterial pressure remained elevated during the post-exercise time period. These results are in agreement with Shoemaker and colleagues (Shoemaker et al. 2007) who demonstrated that mean arterial pressure remained elevated with post-exercise circulatory occlusion following handgrip exercise. These differences can be explained by the muscle metaboreflex which is activated due to the accumulation of metabolites, and or the reduction in oxygen delivery (Kaufman and Hayes 2002), both of which were found to be elevated at higher pressures (80%, 100%, 120% LOP). Thus, these pressures would have more fully activated this reflex, causing mean arterial pressure to remain elevated post-exercise (Spranger et al. 2015). It is important to note that this reflex is exaggerated in disease states in which perfusion to the muscle is impaired including hypertension, heart failure, and peripheral artery disease (Spranger et al. 2015). Therefore, caution should be taken before using BFR exercise in these populations, including using lower occlusion pressures (e.g., < 60% LOP), and normalizing the restrictive stimulus to the individual.

Implications

Exercise with BFR is gaining popularity among practitioners in clinical and applied sport training settings (Patterson and Brandner 2017). However, more care is needed to ensure that current practice matches the research to ensure the safety of this exercise modality (Patterson and Brandner 2017). With this in mind, our findings have implications for researchers, clinicians, coaches, and athletes. Specifically, researchers who use exercise with BFR may be able to better standardize their BFR stimulus before exercise without needing to measure blood flow during exercise, which is difficult. These results benefit clinicians by demonstrating that moderate cuff pressures (≤ 80% LOP) do not occlude blood flow during small muscle mass exercise with BFR. Because deoxyhemoglobin concentration was the same at pressures above 80% LOP, higher cuff pressures may be unnecessary. Moreover, the use of higher cuff pressures could cause MAP to remain elevated during the rest period which would be contraindicated for populations that have an exacerbated blood pressure response to exercise. Finally, coaches and athletes including exercise with BFR in training programs may need to consider that individual LOP differs, which affects the stimulus for BFR-induced improvements in muscle size and strength. It is recommended that practitioners base the cuff pressure on LOP if possible (Scott et al. 2015). Accordingly, careful standardization of BFR stimulus during rest may facilitate more consistent training adaptations during exercise.

Limitations

We implemented BFR during rhythmic handgrip exercise, an exercise modality that is often used to measure blood flow to exercising muscles. This allowed us to measure blood flow during exercise with BFR for the first time. Handgrip exercise is, however, not without its limitations. Our findings relating to the hemodynamics of BFR with handgrip exercise are limited by the type of muscle contraction (quasi-isometric) and small muscle mass engaged. Thus, these findings may not be entirely transferrable to more dynamic exercises with BFR involving a larger muscle mass. More common exercises used in conjunction with BFR such as knee extension, bench press, and elbow flexion, would likely increase acute cardiovascular responses (i.e., heart rate, mean arterial pressure, cardiac output) to a much greater extent than that measured in this study. Thus, relative reductions in blood flow from various occlusion pressures are likely specific to the limb and exercise involved. Also, we did not measure vessel diameter during exercise, which may have impacted our blood flow data. However, if diameter did change during exercise, it is far more likely to increase rather than decrease; resulting in an underestimation of blood flow. Considering that the purpose of this exercise modality was to restrict, but not completely occlude arterial blood flow, this would result in conservative estimates for an overall effect. It is also important to note that we indirectly quantified metabolic stress by changes in tissue saturation index and deoxyhemoglobin concentration as opposed to a more direct assessment. Therefore, our interpretation of metabolic stress associated with BFR is limited to an indirect estimation.

We acknowledge that multiple sets are commonly used during exercise with BFR (e.g., 30 reps × 3 sets) (Patterson and Brandner 2017). There was no change in forearm EMG activity for the first ten to last ten contractions suggesting that one set of handgrip exercise did not cause fatigue in the forearm muscles. These results are likely due to the light intensity (30% MVC) utilized. Exercise with BFR involving larger muscle masses over multiple sets would likely increase EMG activity. Therefore, further investigation into the mechanisms of blood flow during exercise with BFR utilizing dynamic exercise, with multiple sets, in larger muscle groups is warranted. Lastly, we should note that these data were collected in a supine position, which is not the same position for most upper-body exercises that are performed seated or standing. This reiterates the need for future research exploring exercise with BFR during varying dynamic exercise.

Summary

During exercise with BFR, blood flow to the working muscles increased even despite the external pressure. Relative reductions in blood flow prior to exercise were generally maintained during exercise with BFR. Occlusion pressures ranging from 60 to 80% LOP provided considerable metabolic stress while still maintaining partial arterial blood flow, thus lowering relative risk of adverse cardiovascular responses to exercise with BFR, including prolonged increases in MAP during recovery. Overall, these findings provide novel insight into hemodynamic changes during exercise with BFR and serve as an important step for creating better BFR exercise guidelines.

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