International Journal of EXERCISE SCIENCE

Original Research

Cardiovascular Responses During Light-intensity Aerobic Exercise with Varying Levels of Limb Occlusion Pressures

WILLIAM R. VANWYE‡[1], ALYSSA M. WEATHERHOLT‡[2], LEE J. WINCHESTER‡[3], JOHNNY G. OWENS‡[4], and MICAH SPEARS†[5]

[1]School of Physical Therapy, Florida Southern College, Lakeland, FL, USA; [2]Department of Kinesiology and Sport, University of Southern Indiana, Evansville, IN, USA; [3]Department of Kinesiology, University of Alabama, Tuscaloosa, AL, USA; [4]Owens Recovery Science, San Antonio, TX, USA; [5]Department of Physical Therapy, Western Kentucky University, Bowling Green, KY, USA

†Denotes graduate student author, ‡Denotes professional author

ABSTRACT

International Journal of Exercise Science 16(2): 676-687, 2023. The study aimed to assess cardiovascular responses to low-intensity aerobic exercise with varying levels of limb occlusion pressures (LOP) in a healthy population of men and women 30 to 60 years. The study was a single-session repeated measures design. Thirty individuals completed the study. All subjects participated in a single bout of low-intensity cycling (30-39% HRR) with bilateral lower extremity (LE) BFR for four 5-minute stages [0% (No BFR), 40%, 60%, and 80% LOP] with a 2-minute active rest between stages (BFR pressure released). The subjects' systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), oxygen saturation (SpO_2), and ratings of perceived exertion (RPE) were measured at rest, peak, immediately post, post-15 minutes, and post-30 minutes. Peak SBP (no BFR 160.7 ±19.1 mmHg; 40% LOP 173.6 ± 18.7 mmHg; 60 % LOP; 182.5 ± 21.1 mmHg; 80% LOP 193.5± 23.3 mmHg ; $p<0.001$; $\eta_P^2=.747$), DBP (no BFR 74.9 ± 8.5 mmHg; 40% LOP (83.0 ± 9.0 mmHg;60 % LOP 90.4 ± 8.7 mmHg; 80% LOP 97.7 ± 9.5 mmHg ;$p<0.001$; $\eta_P^2=.924$), MAP (no BFR 103.5 ± 10.1 mmHg; 40% LOP 113.2 ± 10.5 mmHg; 60% LOP 121.1 ± 11.7 mmHg; 80% LOP 129.7 ± 12.9 mmHg; $p<0.001$; $\eta_P^2=.960$), and RPE (No BFR 10.0 ± 2.0; 40 % LOP 11.5 ± 2.3; 60% LOP 13.2 ± 2.6; 80% LOP 14.5 ± 3.; $p<0.001$; $\eta_P^2=.826$) were significantly higher with each progressing stage. The results indicate that low-intensity cycling with bilateral LE BFR for each LOP stage resulted in elevated SBP, DBP, MAP, and RPE despite maintaining a fixed HR.

KEY WORDS: Cycling, cardiovascular, endurance, blood pressure, exercise pressure reflex, electrocardiogram

INTRODUCTION

Blood flow restriction (BFR) exercise is a well-established method for improving muscular strength and hypertrophy (22). Interestingly, these improvements are achieved by combining

BFR with low-intensity exercise. This combination is advantageous when working with older adults or clinical populations that cannot tolerate moderate to high-intensity exercise (12,18). BFR exercise involves applying a tourniquet-style cuff on the proximal aspect of a limb. The cuff is manually or pneumatically tightened to a pressure that occludes venous outflow with partial restriction of arterial inflow. The cuff remains inflated throughout the exercise session.

Additionally, light-intensity aerobic exercise with BFR has demonstrated improved benefits in aerobic capacity, as well as muscular strength and hypertrophy, compared to low-intensity exercise without BFR (9). Thus, this is an additional intervention for improving aerobic and muscular fitness in clinical populations. Furthermore, with training and proper procedures, BFR exercise is safe (25). However, a potential concern of combining aerobic exercise and BFR is the possibility of an intensified exercise pressor reflex (EPR) (7,34).

Blood pressure is regulated by neural and endocrine mechanisms to ensure adequate blood flow to vital organs. One neural mechanism that enhances blood flow to the skeletal muscle and maintains arterial pressure during exercise is the EPR (10,31). Seminal work by Alam & Smirk established that this reflex is engaged due to muscle ischemia during exercise (1,2). However, it is suggested that the mechanical stimuli imposed on active skeletal muscle also play a critical role in EPR engagement (16). The EPR can be subdivided into two functional components: the metaboreflex and mechanoreflex (6). The metaboreflex responds to chemical or metabolic stimuli (e.g., lactic acid, bradykinin, arachidonic acid, ATP, H+ ions) via group IV afferent neurons.

In contrast, the mechanoreflex responds to mechanical stimuli such as pressure or stretch via group III afferent neurons (15,30). Initiation of the group IV afferent metaboreflex has a 5-30 second firing quiescence (16) and appears to be regulated by acid-sensing ion channels 1 and 3 (ASIC 1/3) (4), bradykinin B2 (20), and transient receptor potential vanilloid 1 (TRPV1) receptor (33). This cell signaling suggests that the alterations to local pH, inflammation, and temperature play critical roles in the metabolic arm of the exercise pressor reflex.

Conversely, the group III afferent mechanoreflex engages in mechanical tension development (16). It is suggested that mechanical deformation of the sarcolemma stimulates mechanically-sensitive cation channels (5), such as the Piezo 1 and 2 channels (29), which elicit this reflex. Interestingly, control of the mechanical and metabolic divisions of the exercise pressor reflex does not appear to be independently regulated by group III and group IV afferents, respectively (27). For example, the metabolites produced by contracting skeletal muscle appear to enhance the sensitivity of the group III afferents (27). Thus, there is speculation that using BFR during exercise could lead to EPR-mediated cardiovascular complications due to an excessive increase in blood pressure (34). Spranger and colleagues cautioned that BFR exercise could be especially concerning for individuals with cardiovascular risk factors, such as hypertension, and for individuals with known cardiovascular disease (CVD), such as heart failure or peripheral arterial disease, considering that these individuals are predisposed to a dangerous exaggerated EPR reflex. As a result, a better understanding of the impact of aerobic exercise with BFR would

be prudent prior to widespread clinical application (7,34). The study aimed to assess cardiovascular responses to low-intensity aerobic exercise with varying levels of limb occlusion pressures (LOP) in a healthy population of men and women 30 to 60 years of age. We hypothesized that the participants would have increased systolic blood pressure (SBP), diastolic blood pressure (DBP), and ratings of perceived exertion (RPE) with increasing LOP. Also, we hypothesized minimal to no change in oxygen saturation (SpO2) and that no arrhythmias would be observed.

METHODS

The study design was a single session between participants' comparison with a same repeated measures design. All participants rested in a chair for 5 minutes during the single session before completing the intervention. The intervention consisted of cycling for 4 stages at 30-39% of the subject's heart rate reserve (HRR). Each stage was 5 minutes long with a 2- minute active rest between stages (BFR pressure released). Stage 1 was without BFR, Stage 2 was with BFR at 40% LOP, Stage 3 was with BFR at 60% LOP, and Stage 4 was with BFR at 80% LOP. After the 4 stages, the participants rested for 30 minutes. The measurements assessed were SBP, DBP, heart rate (HR), electrocardiogram (ECG), SpO2, and RPE at baseline, at the end of each stage, immediately post, post-15 minutes and post-30 minutes (See Figure 1).

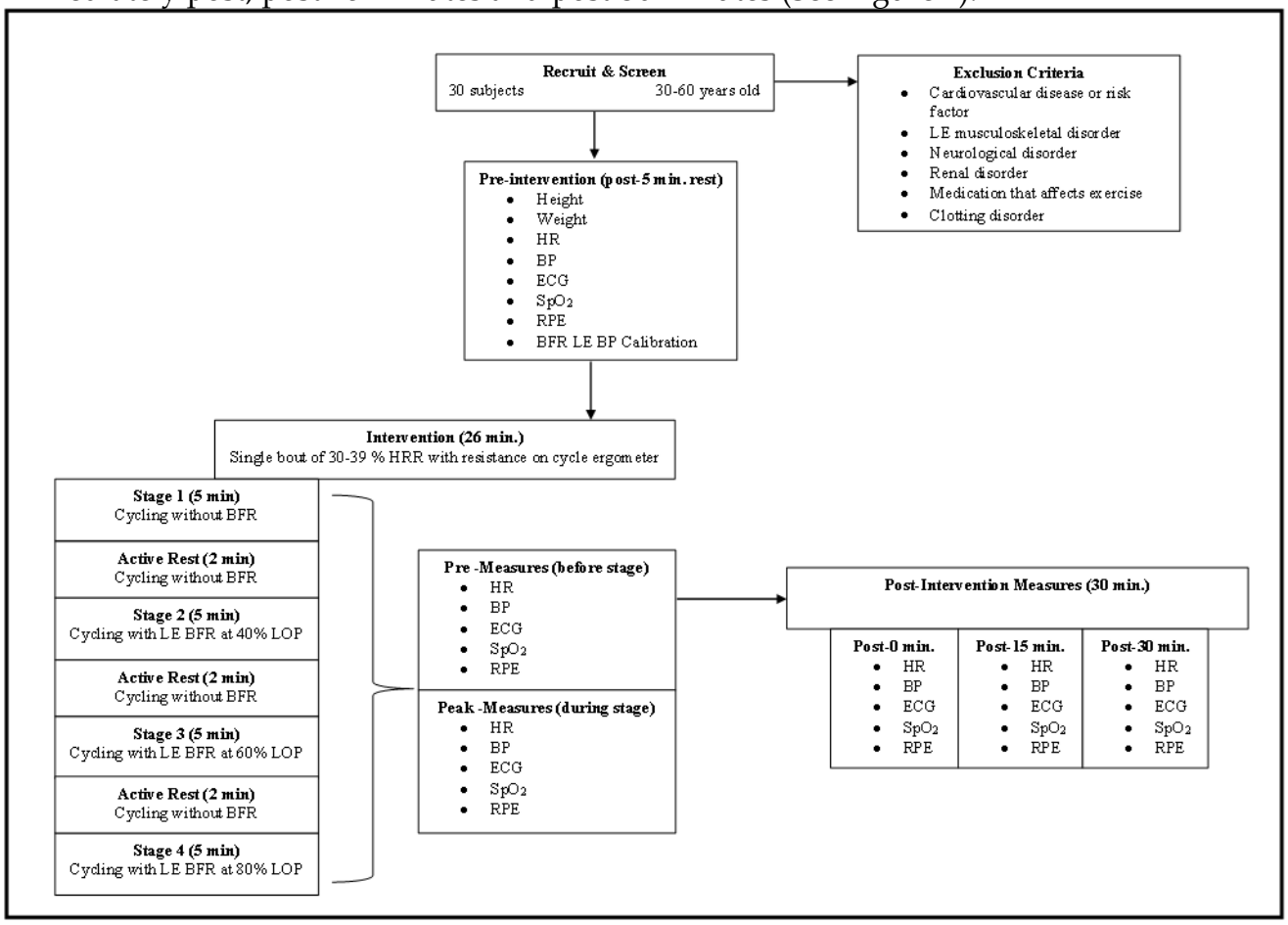

Figure 1. Schematic of the experimental study design.

Participants

Thirty apparently healthy males (n = 16) and females (n = 14) completed the study and were analyzed. The mean age was 39.3 ± 7.7 years, height 173.3 ± 8.6 cm, body mass 81.0 ± 16.2 kg, and Body Mass Index (BMI) 26.8 ± 4.0 kg/m^2. The Western Kentucky University's Institutional Review Board approved this study to protect human participants. This research was carried out entirely under the ethical standards of the International Journal of Exercise Science (24).

Participants were excluded from the study if they had known cardiovascular, metabolic, or renal disease or signs or symptoms of CVD. Additional exclusion criteria included reporting any known neurological disorder, LE musculoskeletal disorder affecting gait, clotting disorder, or current medication use that would affect blood pressure response. No specific training status was required for this study. The inclusion and exclusion criteria were selected to 1) match the age range with those typically seen in individuals who are at moderate to high risk for or who have known CVD, allowing for future comparisons, and 2) establish the effects of BFR personalized tourniquet system on the cardiovascular system for individuals who are apparently healthy or low risk prior to clinical populations such as individuals with known CVD.

Protocol

Initially, the participants underwent a phone screen to determine inclusion in the study. If they met the inclusion and exclusion criteria after the phone screen, they were scheduled for a time to participate in the study. All participants reported to the laboratory for one visit. All measurements were performed in a quiet, temperature-controlled room (22–24°C) after at least 4 hours of fasting and caffeine abstinence, as well as no vigorous exercise within the previous 24 hours. After providing informed consent, the participants filled out a health history questionnaire for CVD risk factors, and a physical therapist performed a systems review. After confirming they did not meet exclusion criteria, height (to the nearest 0.1 cm) and weight (to the nearest 0.1 kg) were measured using a mechanical scale with an attached telescoping height rod (Detecto model 439 Eye, Webb City, MO). Body mass index (BMI) was calculated (kg/m^2). Resting SBP and DBP, HR, ECG, SpO_2, and RPE were taken. HR and ECG were assessed via a 12 Lead ECG (ECG 12 Lead Switch Box (Dual Bio Amps), ADInstruments MLA0115; Dual Bio Amp FE135, ADInstruments; PowerLab 8/35 and LabChart Pro, ADInstruments, Colorado Springs, CO). Predicted HRmax was calculated utilizing the Tanaka formula {208 - (.7*age)} (21). Heart rate reserve (HRR) was calculated as follows: (predicted HRmax - HRresting) x (30-39%) + (HRresting) (21). SpO_2 was measured using a pulse oximeter (Nellcor™ Portable SpO2 Patient Monitoring System, PM10N, Medtronic, Minneapolis, MN) with the sensor attached to the subject's index finger. Brachial blood pressure was measured via a non-invasive beat-to-beat blood measure instrument via finger arterial pressure (ML282-SM, ADInstruments, Colorado Springs, CO). RPE, a beneficial measure of internal workload, was used to determine how hard the participant perceived the exercise. RPE was measured via the 6-20 Borg scale, with 6 indicating no exertion and 20 indicating maximal exertion (21).

The participants had their bilateral LE fitted for the appropriate cuff associated with the BFR personalized tourniquet system (Delfi Medical Innovations PTS for BFR, Vancouver, BC V6H 1C3, Canada). The investigator positioned the cuff on the proximal portion of the thigh, in the groin area, distal to the gluteal fold and close to the torso medially and anteriorly. Delfi describes the unit as a personalized tourniquet system due to the LOP technology embedded within the unit, which can accurately assess LOP, allowing adjustment specifically for the individual (23). After calibration, the unit had a default setting of BFR to 80% of the patient's LOP. The investigator altered the settings to the desired percentage for the intervention session.

Then, the subject pedaled on a recumbent bike at 50 RPMs (Precor Assurance Series 615, Precore, Woodinville, WA) while the investigator progressively adjusted the bike's resistance to reach and maintain the subject's HRR of 30-39% for 5 minutes to collect the intervention measurements, which served as stage 1 of the protocol. 5-20 minutes is the recommended time for BFR aerobic exercise (25). The 30-39% HRR range was selected as it corresponds to low-intensity aerobic exercise, which is the recommended intensity for BFR aerobic exercise (21,25). There were 4 stages lasting 5 minutes per stage: 1) cycling without BFR, 2) cycling with bilateral lower extremity (LE) BFR at 40% LOP, 3) cycling with bilateral LE BFR at 60% LOP, and 4) cycling with bilateral LE BFR at 80% LOP. Cadence was adjusted for each stage to maintain 30-39% HRR for 5 minutes to measure HR, ECG, SpO_2, BP, and RPE. The BFR cuffs were deflated between stages for 2 minutes while the participant continued cycling at 50 RPMs. (i.e., active rest). The participant continued the active rest until their perceived exertion (via the RPE 6-20 Borg scale) was ≤11/20 (fairly light intensity), but for at least 2 minutes prior to progressing to the next stage. A 2-minute deflation period was chosen based on prior research suggesting that the acute responses to BFR last for less than 2 minutes post-deflation (13,28). Post-intervention measurements included HR, ECG, SpO_2, SBP, DBP, and RPE. These measurements were taken immediately post, post +15 minutes, and post +30 minutes. All SBP and DBP measurements were used to calculate Mean Arterial Pressure (MAP). MAP was calculated using the following formula: MAP = [(2 x DBP) + SBP] / 3 (8).

Statistical Analysis

The significance level was set at 0.05, and analyses were performed with IBM SPSS Statistics (v24; SPSS Inc., Armonk, NY). The descriptive statistics for the participants are presented as means ± SD. A one-way repeated measures ANOVA with a Bonferroni adjustment was used for each measure to compare the responses at each time point. A prior experimental power analysis was conducted with G*POWER 3.1.9.7 (Universitat Kiel, Germany), which determined that 28 participants included in this study had a power of .99, with an effect size of 0.25, and an $\alpha = 0.05$. The magnitude of the change between means was determined by partial eta squared (η_P^2). A η_P^2 value of 0.14 represents a large effect, 0.06 represents a medium effect, and 0.01 represents a small effect (19).

RESULTS

Resting Measures: Resting baseline HR (68.1 ± 7.6 bpm) was significantly different compared to resting measures of BFR at 40% LOP (72.9 ± 8.9 bpm; p=0.009), at 60 % LOP (75.2 ± 7.3 bpm; p <.001), and at 80% LOP (75.7 ± 8.2 bpm; p <.001; η_P^2=.669). Resting baseline SBP (121.8 ±12.2 mmHg) was significantly different compared to resting measures of BFR at 40% LOP (134.4 ± 11.1 mmHg; p<0.001), at 60 % LOP (133.8 ± 11.8 mmHg; p <.001), and at 80% LOP (135.8± 11.5 mmHg; p <.001; η_P^2=.665). Resting baseline DBP (67.9 ± 6.9 mmHg) was significantly different compared to resting measures of BFR at 40% LOP (72.0 ± 7.2 mmHg; p=0.011), at 60 % LOP (72.3 ± 7.6 mmHg; p =.035), and at 80% LOP (72.5 ± 8.6 mmHg; p =0.019; η_P^2=.334). Resting baseline RPE (6 ± 0.0) was significantly different compared to resting measures of BFR at 40% LOP (6.8 ± 1.1; p=0.002), at 60 % LOP (6.8 ± 1.3; p =.018), and at 80% LOP (6.9 ± 1.4; p =0.011; η_P^2=.406). However, there were no significant differences in resting SpO_2 at those stages (p=0.26-0.17; Figure 2). No dysrhythmias were observed.

Peak Measures: Peak SBP (160.7 ±19.1 mmHg) during the first stage (no BFR) was significantly different compared to peak measures of BFR at 40% LOP (173.6 ± 18.7 mmHg; p<0.001), at 60 % LOP (182.5 ± 21.1 mmHg; p<0.001), and at 80% LOP (193.5± 23.3 mmHg; p<0.001), as well as between each BFR stage (p<0.001; η_P^2=.747). Peak DBP (74.9 ± 8.5 mmHg) during the first stage (no BFR) was significantly different compared to peak measures of BFR at 40% LOP (83.0 ± 9.0 mmHg; p<0.001), at 60 % LOP (90.4 ± 8.7 mmHg; p<0.001), and at 80% LOP (97.7 ± 9.5 mmHg; p<0.001), as well as between each BFR stage (p<0.001; η_P^2=.924). Although peak HR was the same during each 5-minute stage (i.e., HRR 30-39%; all p >0.05), RPE was significantly higher at each stage: 0% LOP (10.0 ± 2.0), 40 % LOP (11.5 ± 2.3), 60% LOP (13.2 ± 2.6), and 80% LOP (14.5 ± 3.1) (p<0.001; η_P^2=.826; Figure 2). No significant differences were found in peak SpO_2 between each stage (all p >0.05). No dysrhythmias were observed.

Post Measures: Resting HR (68.1 ± 7.6 bpm) measures were significantly lower than immediately post (95.3 ± 6.7 bpm) and post-15-minutes (73.6 ± 8.1), with post-15-minutes being significantly lower than immediately post (p<0.001; η_P^2=.964). Resting SBP (121.8 ± 12.2 mmHg), post-15 min. (122.8 ± 12.6 mmHg), and post-30 min. (116.4 ± 8.5 mmHg) were significantly lower (160.6 ± 21.0 mmHg, p<0.001; η_P^2=.882). Resting DBP (67.9 ± 6.9 mmHg) measures compared to immediately post (74.9 ± 10.6 mmHg) and post-30 minutes (73.3 ± 6.4 mmHg) were significantly lower (p<0.05; η_P^2=.639). Resting RPE (6.0 ± 0.0) measures were significantly lower compared to immediately post (7.8 ± 2.0, η_P^2=.456; p<0.001). (Figure 2). No significant differences between resting SpO_2 and all post-measurement time points (all p >0.05) were found. No dysrhythmias were observed.

Mean Arterial Pressure: Resting MAP (90.3 ± 6.4 mmHg) was significantly lower than 0% LOP (103.5 ± 10.1 mmHg), 40% LOP (113.2 ± 10.5 mmHg), 60% LOP (121.1 ± 11.7 mmHg), 80% LOP (129.7 ± 12.9 mmHg), and immediately post-exercise (103.5 ± 12.5 mmHg; p<0.001; η_P^2=.960). 80 % LOP MAP (129.7 ± 12.9 mmHg) was significantly higher than resting MAP (90.3 ± 6.4 mmHg), 0% LOP (103.5 ± 10.1 mmHg), 40% LOP (113.2 ± 10.5 mmHg), 60% LOP (121.1 ± 11.7 mmHg),

immediately post (103.5 ± 12.5 mmHg), post-15 minutes (86.4 ± 8.6 mmHg), and post-30 minutes (87.7±6.2; p<0.001; η_P^2=.960) (Figure 3). No differences in MAP were detected between resting, post-15 minutes, and post-30 minutes exercise (p>0.05).

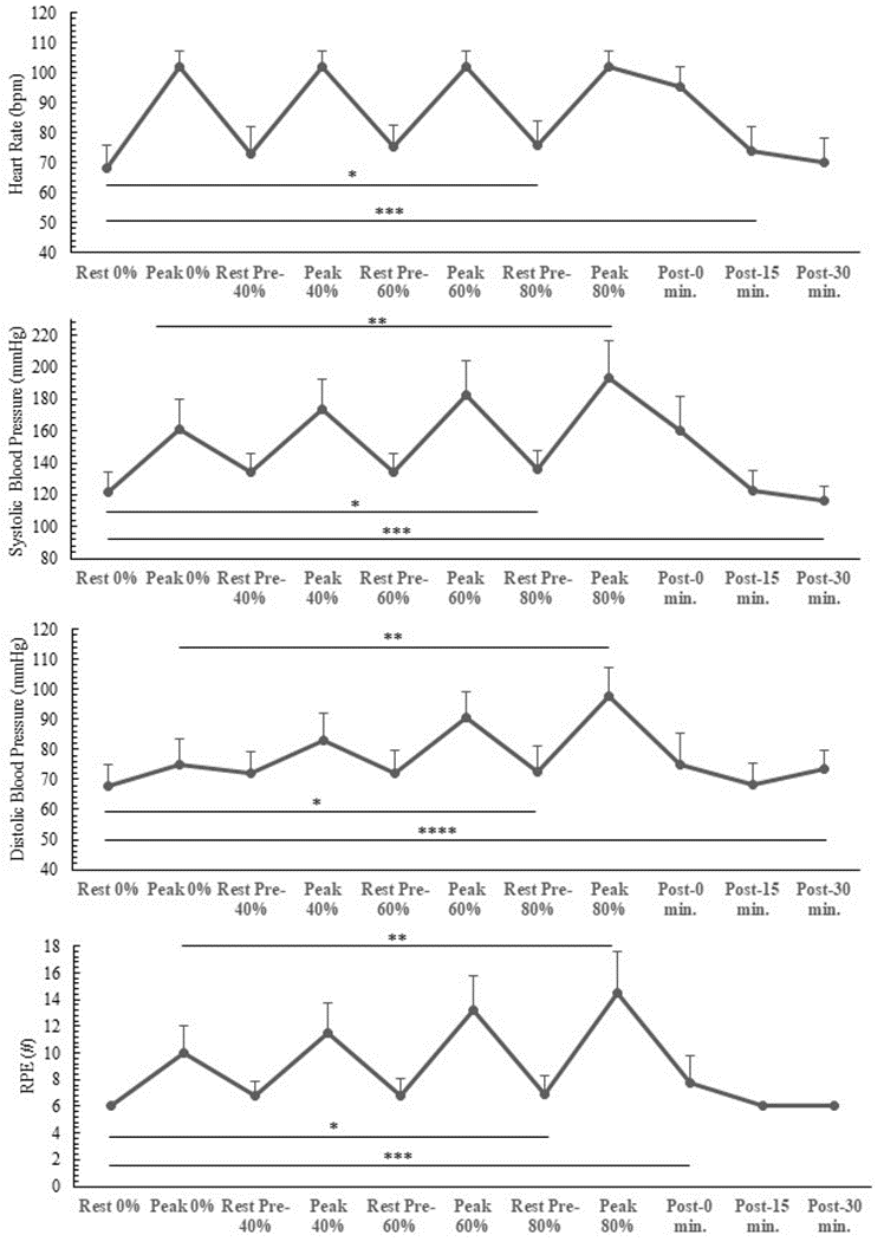

Figure 2. Mean resting, peak, and post measures of HR, SBP, DBP, and RPE and comparisons at each LE BFR LOP. *Indicates significant differences from resting 0% LOP to each LOP (p<0.05). **indicates significant differences from peak 0% to each LE BFR LOP (p<0.05). ***indicates significant differences from rest 0% to post measures (p<0.05). ****indicates significantly lower at rest 0%, post-15 min., post-30 min. measures compared to immediately post measure (p<0.05).

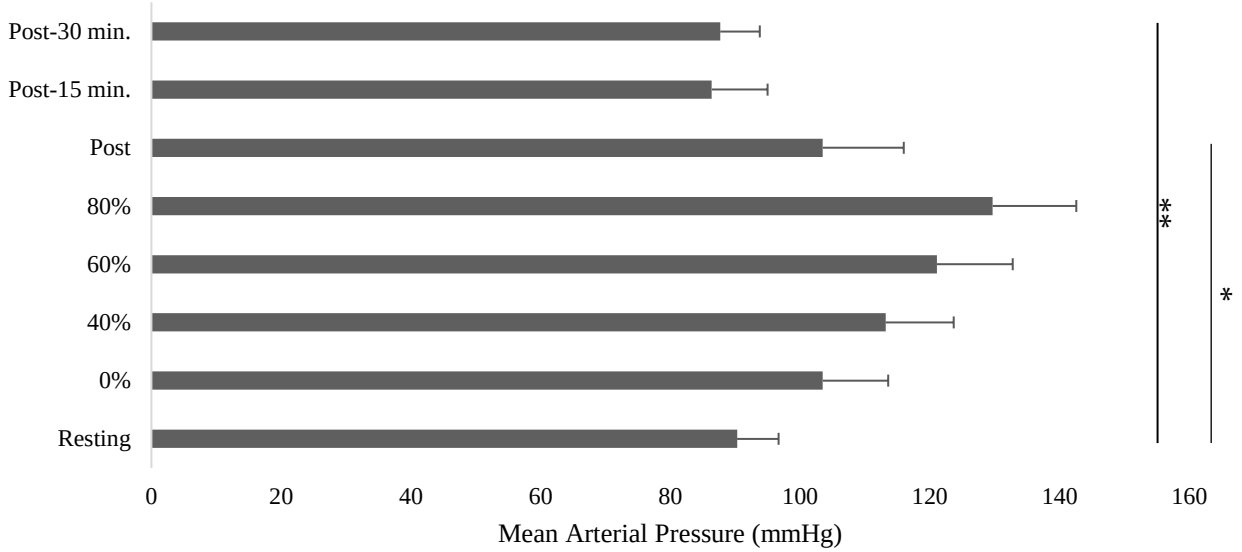

Figure 3. Mean scores and comparisons of MAP at each stage point. *indicates significant differences from resting to each time point ($p<0.05$). **indicates significant differences from 80% LOP to each stage point ($p<0.05$).

DISCUSSION

The primary purpose of this study was to assess cardiovascular responses to low-intensity LE cycling with and without bilateral BFR in a healthy population of men and women 30 to 60 years of age. The present study indicated that although the subject's HRR was maintained at 30-39% for each stage, low-intensity aerobic exercise with BFR resulted in higher SBP, DBP, MAP, and RPE compared to aerobic exercise without BFR. In addition, SBP, DBP, MAP, and RPE each increased with increasing LOP. SpO_2 and ECG were unchanged.

Regarding SBP, Karabulut and Garcia found similar results to our study (14). The authors observed the cardiovascular function of adult participants who were sedentary and obese (i.e., BMI ≥30 kg m^{-2}). The participants cycled with and without bilateral LE BFR while SBP was manually assessed via an aneroid sphygmomanometer at three-minute intervals during the exercise session. The authors found SBP to be significantly higher during BFR cycling when compared to cycling without BFR. Thomas et al. also observed SBP to be significantly higher during BFR cycling when compared to cycling without BFR (36). The authors monitored the cardiovascular function of 18 healthy adult men while they cycled with and without bilateral LE BFR for three separate sessions, including a low-intensity interval session with BFR and low-intensity and high-intensity interval sessions without BFR. They recorded SBP manually via an aneroid sphygmomanometer during each two-minute interval and found SBP was significantly higher during the low-intensity interval session with BFR than in the low-intensity interval session without BFR. However, SBP was significantly higher during the high-intensity interval sessions without BFR compared to the low-intensity interval session with BFR.

The DBP response in our study is consistent with Thomas et al. who observed that DBP was

significantly higher during BFR cycling when compared to cycling without BFR. Also, the authors noted that the elevated DBP resulted in a significantly higher MAP compared to the high-intensity interval LE cycling without BFR (36). MAP is a measure of tissue perfusion, which is typically 70-110 mmHg at rest, while a minimum of 60 mmHg is necessary to perfuse vital organs (11). Normally SBP increases during exercise, yet MAP is relatively stable because DBP is normally unchanged or decreases slightly. Although the typical range for MAP at rest is well established, what is less clear is the safe upper limit for MAP during exercise. Utilizing the ACSM BP guidelines for an exercise test, the upper limit for MAP would be 160 mmHg (21). Our peak MAP results of 129.7 (± 12.9 mmHg) were consistent with Thomas et al. who observed a peak MAP of 124.2 (±2.3 mmHg) during low-intensity LE cycling with BFR compared to a peak MAP of 113.9 (±2 mmHg) during high-intensity interval LE cycling without BFR (36).

RPE increased with each increase in LOP despite our participants maintaining an HRR of 30-39% for each stage. Our results were consistent with Kilgas et al., who had participants perform low-intensity (40% VO2peak) cycling with BFR at 60 and 80% LOP (17). The authors found that increased LOP resulted in higher RPE, even with intensity unchanged. Their results and ours are consistent with a systematic review and meta-analysis that found higher RPE levels with increasing BFR cuff pressures (9). Although it was not measured in this study, the higher perceptions of exertion during BFR were likely related to the mechanical stimuli and accumulation of intramuscular metabolites caused by blood flow restriction (32).

A strength of this study is that it adds to the literature on BFR and aerobic exercise, particularly the hemodynamic responses observed during exercise due to incremental BFR LOP in the lower extremities. To our knowledge, this is the first study to assess cardiovascular responses to low-intensity aerobic exercise with BFR using an incremental LOP design. These findings may assist in determining an appropriate LOP for clinical populations engaging in BFR aerobic exercise. Our study differs from previous research in that we maintained workload via the subject's HRR at 30-39%. Maintaining a fixed HRR allows for observation of hemodynamic responses and perceptual effort to BFR while autonomic stimulation of the heart is fairly constant.

In contrast, other research studies examining the effects of BFR on cardiovascular responses have implemented protocols requiring participants to exercise at a maintained VO2peak, external workload, or utilizing different exercise modalities (14,26,35,36). However, despite these protocol discrepancies, our results were similar to the findings from these previous investigations. Nevertheless, our data show that hemodynamic responses such as SBP, DBP, and MAP still increase with BFR exercise even when HR is stable.

This study has some limitations. First, these results can only be applied to healthy men and women 30 to 60 years of age. Additionally, the stages of cycling with and without BFR were not in a randomized order, which limits the certainty that observed changes were the result of changes in pressure rather than time. Therefore, potential cardiovascular responses could be different if the protocol was randomized at different stages. However, our findings suggesting elevated physiological responses to increased LOP are in agreement with that of other research

which demonstrates greater muscle oxygen saturation decrements and hormone release with higher LOP, suggesting that our findings were not likely due to a time effect (3,37). Nevertheless, future research studies focused on BFR will include randomized ordering of conditions. Other cardiovascular variables that could have been useful to support our data include blood lactate and oxygen consumption (VO_2). Therefore, future investigations need to include different study designs with different populations.

This research highlights the impact of BFR LOP on hemodynamics during low-intensity aerobic exercise, which is important to ensure safety for individuals with CVD or CVD risk factors. Data from this investigation indicate that low-intensity cycling with bilateral LE BFR at each LOP resulted in elevations in SBP, DPB, MAP, and RPE despite maintaining a fixed HRR. Although increased SBP is normal with increasing workloads, DBP should decrease or remain unchanged. Therefore, LE cycling with bilateral LE BFR at increasing LOP resulted in an abnormal DBP response. However, the response did not warrant termination of exercise per ACSM guidelines, suggesting that the added BFR-induced EPR may be largely benign. Future research investigating whether BFR enhances the EPR during higher exercise intensities is warranted to determine the safety limits of BFR utility. If clinicians and exercise professionals are concerned with the possibility of an adverse cardiovascular event during low-intensity cycling with BFR, lower relative cuff inflation pressures are recommended to minimize the added EPR while potentially enhancing exercise adaptations.

ACKNOWLEDGEMENTS

We want to like to thank all participants who volunteered for this study.

REFERENCES

1. Alam M, Smirk FH. Observations in man upon a blood pressure raising reflex arising from the voluntary muscles. J Physiol 89(4):372-383, 1937.

2. Alam M, Smirk FH. Observations in man on a pulse-accelerating reflex from the voluntary muscles of the legs. J Physiol 92(2):167-177, 1938.

3. Bartolomei S, Montesanto P, Lanzoni IM, Gatta G, Cortesi M, Fantozzi S. A comparison between high and low cuff pressures on muscle oxygen saturation and recovery responses following blood-flow restriction resistance exercise. Sensors 22(23):9138, 2022.

4. Campos MO, Mansur DE, Mattos JD, et al. Acid-sensing ion channels blockade attenuates pressor and sympathetic responses to skeletal muscle metaboreflex activation in humans. J Appl Physiol Bethesda Md 1985 127(5):1491-1501, 2019.

5. Copp SW, Kim JS, Ruiz-Velasco V, Kaufman MP. The mechano-gated channel inhibitor GsMTx4 reduces the exercise pressor reflex in decerebrate rats. J Physiol 594(3):641-655, 2016.

6. Crisafulli A, Marongiu E, Ogoh S. Cardiovascular reflexes activity and their interaction during exercise. BioMed Res Int 394183, 2015.

7. Cristina-Oliveira M, Meireles K, Spranger MD, O'Leary DS, Roschel H, Peçanha T. Clinical safety of blood flow-restricted training? A comprehensive review of altered muscle metaboreflex in cardiovascular disease during ischemic exercise. Am J Physiol Heart Circ Physiol 318(1):H90-H109, 2020.

8. DeMers D, Wachs D. Physiology, mean arterial pressure. In: StatPearls. StatPearls Publishing; 2022. Accessed August 26, 2022. http://www.ncbi.nlm.nih.gov/books/NBK538226/

9. Formiga MF, Fay R, Hutchinson S, et al. Effect of aerobic exercise training with and without blood flow restriction on aerobic capacity in healthy young adults: a systematic review with meta-analysis. Int J Sports Phys Ther 15(2):175-187, 2020.

10. Grotle AK, Macefield VG, Farquhar WB, O'Leary DS, Stone AJ. Recent advances in exercise pressor reflex function in health and disease. Auton Neurosci Basic Clin 228:102698, 2020.

11. Hillegass EA. Essentials of cardiopulmonary physical therapy. 5th ed. St. Louis: Elsevier/Saunders; 2022.

12. Hughes L, Paton B, Rosenblatt B, Gissane C, Patterson SD. Blood flow restriction training in clinical musculoskeletal rehabilitation: a systematic review and meta-analysis. Br J Sports Med 51(13):1003-1011, 2017.

13. Husmann F, Mittlmeier T, Bruhn S, Zschorlich V, Behrens M. Impact of blood flow restriction exercise on muscle fatigue development and recovery. Med Sci Sports Exerc 50(3):436-446, 2018.

14. Karabulut M, Garcia SD. Hemodynamic responses and energy expenditure during blood flow restriction exercise in obese population. Clin Physiol Funct Imaging. 37(1):1-7, 2017.

15. Kaufman MP, Longhurst JC, Rybicki KJ, Wallach JH, Mitchell JH. Effects of static muscular contraction on impulse activity of groups III and IV afferents in cats. J Appl Physiol 55(1 Pt 1):105-112, 1983.

16. Kaufman MP. The exercise pressor reflex in animals. Exp Physiol 97(1):51-58, 2012.

17. Kilgas MA, Yoon T, McDaniel J, Phillips KC, Elmer SJ. Physiological responses to acute cycling with blood flow restriction. Front Physiol 13:800155, 2022.

18. Labata-Lezaun N, Llurda-Almuzara L, González-Rueda V, et al. Effectiveness of blood flow restriction training on muscle strength and physical performance in older adults: a systematic review and meta-analysis. Arch Phys Med Rehabil 103(9):1848-1857, 2022.

19. Lakens, D. (2013). Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. Front. Psychol 4:863, 2013.

20. Leal AK, Stone AJ, Yamauchi K, McCord JL, Kaufman MP. Blockade of B2 receptors attenuates the responses of group III afferents to static contraction. Neurosci Lett 555:231-236, 2013.

21. Liguori G, Feito Y, Fountaine C, Roy BA. ACSM's guidelines for exercise testing and prescription. 11th ed. Philadelphia: Wolters Kluwer; 2022.

22. Loenneke JP, Wilson JM, Marín PJ, Zourdos MC, Bemben MG. Low intensity blood flow restriction training: a meta-analysis. Eur J Appl Physiol 112(5):1849-1859, 2012.

23. Masri BA, Day B, Younger ASE, Jeyasurya J. Technique for measuring limb occlusion pressure that facilitates personalized tourniquet systems: a randomized trial. J Med Biol Eng 36(5):644-650, 2016.

24. Navalta J, Stone W, Lyons S. Ethical issues relating to scientific discovery in exercise science. Int J Exerc Sci 12(1), 2019.

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

26. Renzi CP, Tanaka H, Sugawara J. Effects of leg blood flow restriction during walking on cardiovascular function. Med Sci Sports Exerc 42(4):726-732, 2010.

27. Rotto DM, Kaufman MP. Effect of metabolic products of muscular contraction on discharge of group III and IV afferents. J Appl Physiol Bethesda Md 1985 64(6):2306-2313, 1988.

28. Saffold K, Hornikel B, MacDonald H, Aguiar E, Wind S, Winchester1 L. Acute decrements in performance and recovery of the distal musculature with automated blood flow occlusion in the proximal limb. J Exerc Physiol Online 26(1):40-52, 2023.

29. Sanderson BC, Rollins KS, Hopkins TD, et al. GsMTx4 reduces the reflex pressor response during dynamic hindlimb skeletal muscle stretch in decerebrate rats. Physiol Rep 7(1):e13974, 2019.

30. Secher NH, Amann M. Human investigations into the exercise pressor reflex. Exp Physiol 97(1):59-69, 2012.

31. Sheriff DD, Rowell LB, Scher AM. Is rapid rise in vascular conductance at onset of dynamic exercise due to muscle pump? Am J Physiol 265(4 Pt 2):H1227-1234, 1993.

32. Silva JCG, Domingos-Gomes JR, Freitas EDS, et al. Physiological and perceptual responses to aerobic exercise with and without blood flow restriction. J Strength Cond Res 35(9):2479-2485, 2021.

33. Smith SA, Leal AK, Williams MA, Murphy MN, Mitchell JH, Garry MG. The TRPv1 receptor is a mediator of the exercise pressor reflex in rats. J Physiol 588(Pt 7):1179-1189, 2010.

34. Spranger MD, Krishnan AC, Levy PD, O'Leary DS, Smith SA. Blood flow restriction training and the exercise pressor reflex: a call for concern. Am J Physiol Heart Circ Physiol 309(9):H1440-1452, 2015.

35. Sugawara J, Tomoto T, Tanaka H. Impact of leg blood flow restriction during walking on central arterial hemodynamics. Am J Physiol Regul Integr Comp Physiol 309(7):R732-739, 2015.

36. Thomas HJ, Scott BR, Peiffer JJ. Acute physiological responses to low-intensity blood flow restriction cycling. J Sci Med Sport 21(9):969-974, 2018.

37. Yinghao L, Jing Y, Yongqi W, et al. Effects of a blood flow restriction exercise under different pressures on testosterone, growth hormone, and insulin-like growth factor levels. J Int Med Res 49(9):3000605211039564, 2021.