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Acute Cardiovascular Response to Low-Load Unilateral, Bilateral, and Alternating Resistance Exercise with Blood Flow Restriction in the Lower Body

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ACUTE CARDIOVASCULAR RESPONSE TO LOW-LOAD UNILATERAL, BILATERAL, AND ALTERNATING RESISTANCE EXERCISE WITH BLOOD FLOW RESTRICTION IN THE LOWER BODY

by

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ABSTRACT

Resistance exercise with blood flow restriction (BFR) has been suggested to exaggerate the exercise pressor response over traditional non-BFR exercise. While applying BFR relative to an individual's arterial occlusion pressure (AOP) and exercising at low-loads seems to produce a comparable cardiovascular response to traditional moderate or high-load training, it is beneficial to identify modifications for reducing the cardiovascular response to BFR exercise. PURPOSE: To determine if unilateral (UNI), bilateral (BI), or alternating (ALT) exercise modalities elicit different cardiovascular responses during BFR exercise. METHODS: 18 participants (13 male and 5 female) performed four sets of UNI, BI, and ALT knee-extensions at 30% one-repetition maximum and 40% AOP. Pulse wave analysis was measured before and after exercise. Data were analyzed using Bayesian RMANOVA and presented as mean (SD). RESULTS: Changes in aortic systolic blood pressure, aortic diastolic blood pressure, and aortic mean arterial pressure were greater following ALT. Changes in aortic rate pressure product [ALT = 4873 (2479) mmHg * bpm, UNI = 3243 (1482) mmHg * bpm, BI = 3308 (1449) mmHg * bpm] were also higher following ALT. The volume of work performed was greater in ALT [ALT = 1946 (1787) kg, UNI = 945 (313) kg, BI = 918 (319) kg]. CONCLUSION: Given the greater cardiovascular response following alternating BFR exercise in healthy individuals, those at an increased risk of a cardiovascular event should instead choose unilateral or bilateral BFR exercise until further work is done to determine the degree to which this modality can be tolerated.

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DEDICATION

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LIST OF ABBREVIATIONS

1RM	One-repetition maximum
ACSM	American College of Sports Medicine
ALT	Alternating condition
AIX	Augmentation index
AIX75	Augmentation index corrected for heart rate
AOP	Arterial occlusion pressure
AP	Augmentation pressure
aDBP	Aortic diastolic blood pressure
aMAP	Aortic mean arterial pressure
aSBP	Aortic systolic blood pressure
aRPP	Aortic rate pressure product
bDBP	Brachial diastolic blood pressure
BFR	Blood flow restriction
BI	Bilateral condition
bRPP	Brachial rate pressure product
bSBP	Brachial systolic blood pressure
DBP	Diastolic blood pressure
EMG	Surface electromyography
FH	Forward pressure height
HR	Heart rate
NIRS	Near-infrared Spectroscopy
PAR-Q	Physical Activity Readiness Questionnaire

PWA	Pulse wave analysis
RH	Reflected pressure height
RPE-E	Ratings of perceived exertion
RPE-D	Ratings of perceived discomfort
SBP	Systolic blood pressure
UNI	Unilateral condition
WR	Wave reflection magnitude

CHAPTER I - INTRODUCTION

To increase muscular strength and mass the American College of Sports Medicine (ACSM) recommends using ~60-80% of the person's one repetition maximum (1RM) which is about 8 to 12 repetitions per set (American College of Sports Medicine, 2018). In the United States during 2011, only 29.3% of the population reported meeting muscle-strengthening guidelines set by the U.S Department of Health and Human Services (Centers for Disease Control and Prevention, 2013). This could be because people do not have the ability or desire to meet the exercise-related guidelines set forth by different governing bodies. Researchers continue to investigate alternative and more efficacious means to increase muscle mass and strength in older and at-risk populations.

Increasing muscle mass and strength can be accomplished by exercising with a range of loads until failure, this way a low-load and a high-load exercise produce similar increases in muscle mass and strength by recruiting a similar amount of muscle fibers over a training period (Dankel S. J., et al., 2016; Marcotte, West, & Baar, 2015). For example a high load could be 80% of a person's 1RM and a low load could be 20% of a person's 1RM. Low-load resistance exercise when combined with blood flow restriction (BFR) results in similar increases in muscle mass compared to the ACSM recommendation for resistance exercises at moderate- and high-loads (Loenneke, Wilson, Marin, Zourdos, & Bemben, 2012; Yasuda, et al., 2011), but with less volume (Loenneke, et al., 2012; Jessee, et al., 2017). Muscle mass and strength can also be increased by exercising with a low load to failure, but by combining BFR there is a reduction in the amount of volume needed to reach failure. Typical BFR protocols involve a cuff positioned at the most proximal point of a limb and then increasing the pressure of the cuff until the amount of arterial blood into the limb is reduced, and venous return is occluded creating a hypoxic environment during exercise (Yasuda, et al., 2010). Due to this internal environment around the working muscle failure seems to result in lower loads, which is why lower volumes can be completed yet result in similar increases in muscle size (Jessee, et al., 2018).

With advancements in BFR-related research, a recent systematic review paper came out addressing a hypothetical concern that suggests BFR exercises could exaggerate the exercise pressor reflex, and thus pose a risk for an adverse cardiovascular response in special and even healthy populations (Spranger, Krishnan, Levy, O'Leary, & Smith, 2015). Since Spranger et al., many researchers have investigated the cardiovascular outcomes in response to BFR exercises and found that the cardiovascular response is not different from moderate-load exercise without BFR (Sugawara, Tomoto, & Tanaka, 2015; Broxterman, et al., 2015; Domingos & Polito, 2018; Mouser, et al., 2019; Neto, et al., 2016; Neto, et al., 2016; Kilgas, et al., 2018; Moriggi Jr., et al., 2015). One confounding issue may be the application of BFR given that Spranger et al., reviewed many papers in which the participants were exercising at unknown or suprasystolic cuff pressure and the participants may have had no oxygenated blood for their exercising muscles. Currently, recommendations for BFR protocols have evolved into measuring each person's arterial occlusion pressure (AOP) instead of using one standard pressure applied to all individuals (Jessee M. B., et al., 2016; Mouser, et al., 2017). When the cuff pressures are made relative by measuring AOP and using a percentage of AOP for BFR, then researchers can better control the stimulus to avoid ischemia. Thus, the ability to ensure arterial blood flow, albeit reduced, may be one possible way to reduce the risk of an adverse cardiovascular event due to the exercise pressor reflex outlined by Spranger et al. Manipulating different exercise modalities could be another way to reduce the risk of an adverse cardiovascular event.

Though, there are studies investigating the cardiovascular outcomes of exercising with different muscle groups (Moreira, et al., 2015) and muscle masses (Matos-Santos, Farinatti, Borges, Massaferri, & Monteiro, 2017). In general, these studies found that using a smaller muscle mass, like the unilateral condition, does not elicit a cardiovascular response to the same magnitude of using larger muscle masses like the bilateral or alternating condition. However, there is no literature on the cardiovascular outcomes when combining BFR with unilateral, bilateral, and alternating exercises. As such, the purpose of this study was to quantify and compare the cardiovascular response to different exercise modalities (unilateral, bilateral, and alternating) with a low load when combined with BFR. The results of this study could help identify a potential modification to BFR protocols that would attenuate the risk of a major cardiovascular response.

CHAPTER II - LITERATURE REVIEW

2.1 Blood Flow Restriction Application and the Description of the Stimulus

BFR is typically applied by placing a cuff around the proximal portion of the upper leg or arm and setting the pressure (mmHg) to a percentage of the total pressure that would occlude arterial blood in that limb (known as arterial occlusion or limb occlusion). With a deflated cuff, deoxygenated (venous) blood can flow freely to the heart, and oxygenated (arterial) blood can flow freely into the limb. However, when the pneumatic cuff at the most proximal portion of the limb is inflated to a pressure greater than venous pressure, then venous blood will pool in the limb distal to the pneumatic cuff (Mouser, et al., 2017). As the pressure continues to increase, for example to greater than 60% AOP, then arterial blood flow into the limb is reduced (Mouser, et al., 2017). If the pressure is increased to a point where there is no longer a pulse in the tibial or brachial artery, then, arterial blood has been fully occluded in the limb (100% AOP).

The type, size, pressure, and placement of the cuff should be included in a BFR study so fellow researchers can objectively read and understand the results and conclusions of a BFR study (Rossow, et al., 2012; Mouser, et al., 2017). In addition, these details should be accounted for to properly apply the intended BFR stimulus to the participant. The type of cuff can vary from an inelastic nylon pneumatic cuff to an elastic cuff, which would need a higher pressure to elicit the same occlusion as a pneumatic cuff (Karabulut, McCarron, & Abe, 2011). The width of the cuff is important because a wider cuff will restrict blood flow at a lower pressure than a narrow cuff (Jessee M. B., et al., 2016). Using absolute pressure from previous literature may likely cause different responses for people because of the natural variability amongst individuals, specifically limb circumference and blood pressure (Loenneke, et al., 2015). This is clear when applying the same absolute pressure to an arm and a leg of an individual (Loenneke, et al., 2015). A leg usually has a larger circumference and would need a higher pressure to occlude blood flow, but the arms would need a lower pressure than the legs. Even when comparing individuals with large and small arms the pressure is different due to limb circumference (Jessee M. B., et al., 2016). To illustrate the issue with using an arbitrary pressure a study by Suga et al. used a “moderate pressure” based on 130% of the participants resting systolic blood pressure (SBP) about 147mmHg on average and “high pressure” of 200 mmHg for the arm based off an absolute value in previous literature (2010). In this case, the researchers recorded that metabolic stress in a high-pressure protocol with a low load (20% 1 repetition maximum) was significantly lower when compared to high-load exercise without BFR (Suga, et al., 2010), but these results are indicative of a limb exercising above arterial occlusion pressure (AOP) i.e. ischemic exercise. In addition, the researchers found that there were no significant differences between “moderate pressure” and “high pressure” in intramuscular metabolites and pH with the same load (20% 1RM). While Suga et al. compared what they assumed to be moderate and high pressures, both pressures could have been greater than the participant's arterial occlusion.

To ensure a relative stimulus rather than applying an arbitrary stimulus, BFR should be applied as a percentage of AOP measured for each participant. To illustrate, AOP can be measured when a BFR cuff is placed at the uppermost portion of the limb and slowly inflated while using a Doppler probe (handheld Doppler or Doppler ultrasound) to detect blood flow in the distal portion of the BFR limb (Laurentino G. C., et al., 2018). When the probe no longer detects blood flow, arterial blood is fully (100%) occluded at the set pressure (mmHg) of the cuff. Then, researchers can take a percentage of arterial occlusion, and calculate the relative pressure for BFR resistance exercise depending on the desired level of BFR. Doing so, would also allow researchers to compare the effects of low, moderate, or high BFR protocols. Most BFR studies are seeking to investigate the potential effects of reduced arterial blood flow (Ladlow, et al., 2018; Loenneke, et al., 2015; Lixandrao, et al., 2015; Jessee M. B., et al., 2016; Mouser, et al., 2017; Mattocks, et al., 2017; Laurentino G. C., et al., 2016; Jessee, et al., 2018; Jessee, et al., 2017). Studies using pressures based on arbitrary absolute numbers found in literature (Bunevicius, et al., 2017; Yasuda, et al., 2011) are difficult to interpret because other researchers do not know how much blood flow was reduced for each participant or if it was an ischemic stimulus. The participants with arbitrary absolute values may be exercising under ischemic conditions, or with no change in blood flow, or with completely different amounts of blood flow. By using pressure relative to the participant, researchers can administer similar reductions in blood flow across the population. Without the standardization in protocols with BFR, it is difficult for researchers to fully synthesize and assess the current literature with BFR training (Dankel S. J., Jessee, Abe, & Loenneke, 2015).

2.2 Adaptions seen with Blood Flow Restriction

2.2.1 Blood Flow Restriction Alone and Passive Mobilization

BFR can have positive effects on muscle size and strength when utilized alone or with passive mobilization. When BFR is used alone, it can slow down muscle atrophy when compared to bed rest alone. When compared to passive mobilization used in comatose patients, the addition of BFR can slow the rate of atrophy at a greater rate than passive mobilization alone.

Takarada et al. conducted a two-week investigation on the effects of repeated BFR on participants who recently had anterior cruciate ligament surgery (2000). The control group (n=8) had a pneumatic cuff on their upper thigh, but it was not inflated. An experimental group (n=8) had the pneumatic cuff inflated on their upper thigh twice a day. The protocol was five sets of five minute inflates followed by three minute deflates starting at a pressure of 180 mmHg and then increasing the pressure in increments of 10 mmHg depending on the participant's recovery speed (Takarada, Takazawa, & Ishii, 2000). The experimental group had a cross-sectional area of about 167.5 cm^2 three days after surgery and 156.3 cm^2 after 2 weeks of the BFR protocol. The control group had a cross-sectional area of 161.0 cm^2 three days after the surgery and 137.5 cm^2 after 2 weeks without the BFR protocol. Takarada et al. concluded that when BFR was utilized in the two weeks immediately after surgery, there was less decrease in cross-sectional area as opposed to the control group that received no pressure (2000).

BFR at 80% AOP also delays muscle atrophy in people who are on bedrest when employed with passive mobilization when compared to people who have only passive mobilization (Barbalho, et al., 2018). Barbalho et al. measured the participant's medial thigh circumference, quadriceps thickness with ultrasound, and muscle strength (2018). In this case, the bedrest patients that were in the intervention group (n=20) were not contracting at a percentage of their 1RM, but having their legs manipulated while BFR is administered. The control group (n=20) had their legs passively manipulated without

BFR. BFR with manipulation of the legs slowed down the muscle wasting process when compared to the control group (Barbalho, et al., 2018). In the studies provided by Barbalho et al. and Takarada et al., the effects of BFR were compared with a population that was unable to load their limbs actively. More studies have investigated the impact that BFR can have on exercising participants when compared to participants that are not immobilized.

There seems to be a more pronounced muscular response to BFR for subjects that are immobilized. In a study with recreationally active men, Nyakayiru et al. saw no significant differences in myofibrillar protein synthesis between the resting condition with BFR and without BFR (2019). Nyakayiru et al. then looked to see if there were differences when a low load (20% 1RM) was applied. The researchers saw myofibrillar protein synthesis were greater in low-load with BFR than, low-load (20% 1RM) exercise only. In this case, BFR only does not seem to induce the same environment when compared to exercise or exercise with BFR applied. However, these were recreationally active men. So, if the subjects had been on bedrest like the participants in the study by Barbalho et al., then the results may have been different with the BFR leg in the resting group having a significant difference in myofibrillar protein synthesis. Although, Barbalho et al., was measuring the rate of muscular atrophy and protein synthesis. Thus, further investigations into the myofibrillar protein synthesis response are necessary to determine the mechanism of protein synthesis in clinical populations.

2.2.2 Blood Flow Restriction with Aerobic Exercise

Aerobic exercise, when combined with BFR, has increased muscular strength when compared to aerobic exercise without BFR. A study by Paton et al. found that BFR did not improve the cardiorespiratory system of runners but may have had slight increases in muscle strength (2017). There were two groups, a control group (n=8) and a BFR group (n=8), who underwent eight sessions of aerobic training. The researchers reported non-significant changes in maximal oxygen uptake between groups, but the BFR group had a significant improvement in running economy, which could suggest muscular strengthening (Paton, Addis, & Taylor, 2017). Abe et al. found that a 6-week training program with BFR walking improved isometric and isokinetic muscle strength and leg muscle size in and elderly male population (2010). However, there was not a significant change in estimated aerobic capacity with the BFR walking when compared to a non-exercising control group (Abe, et al., 2010). But, when Abe et al. looked at low-intensity cycling in healthy young me, they saw significant 6.4% increase in aerobic capacity for the BFR group over an 8 week training period when compared to the non-BFR group (2010). The researchers also saw a significant 3.4 - 5.1% increase in muscle cross section area (Abe, et al., 2010). Kim et al. found no significant change between groups in muscle cross sectional area in a study assessing a high-intensity cycle without BFR, low-intensity cycling with BFR, and a non-exercising control group for a 6 week period (2016). But there was a significant increase in leg muscle mass in the low-intensity BFR group from before and after training (Kim, et al., 2016). Since BFR can have these positive benefits in muscular and aerobic capacity, researchers have focused on the cardiovascular response elicited by BFR and aerobic exercise.

Sugawara et al. investigated the aortic systolic blood pressure with and without BFR during walking and compared the results to the participant's baseline (Sugawara, Tomoto, & Tanaka, 2015). The study employed a set BFR pressure of 160 mmHg for all participants. When investigators use absolute BFR pressure for all participants, it is likely that not all participants are getting the same occlusion pressure. As mentioned previously, using relative pressures based on the participants, AOP can help deliver a similar BFR stimulus. Nonetheless, in the study with Sugawara et al., there was a significant increase in aortic systolic blood pressure with walking combined with BFR than walking without BFR (Sugawara, Tomoto, & Tanaka, 2015). Sugawara et al. conclude that walking with BFR causes a hypertensive response because of the reduction in stroke volume and large increases in heart rate to maintain cardiac output. One reason for the significant hypertensive response could be that the participants had different or a greater BFR stimulus than the investigators intended. In the study, Sugawara et al. did not report the size or type of cuff that was used for the BFR protocol, and this can vary the stimulus when using absolute pressures.

In a study conducted by Renzi et al., the researchers looked at the effect of BFR with walking in a healthy population (n=17). All participants did a BFR walking condition and a control walking condition without BFR about 7 days apart. In the exercise the participants did five sets of 2-minute walking at a pace of 2 miles an hour with 1 minute of rest between sets for three weeks (Renzi, Tanaka, & Sugawara, 2010). The researchers found that a low intensity walk with BFR needs a greater cardiovascular response and decreases vascular endothelial function (2010). The researchers looked at flow-mediated vasodilation and saw no change in the control group, but a significant decrease in the BFR group (Renzi, Tanaka, & Sugawara, 2010). There was also a greater blood pressure response in the BFR group, and Renzi et al. concluded this was due to an increase in total peripheral resistance from the BFR cuffs on the legs (2010). In addition, the double product, also known as rate pressure product, reached about a 90% increase from baseline in the BFR group, but the control group only saw about a 30% increase from baseline. Renzi et al. used arbitrary absolute pressures for the BFR condition and increased the cuff pressure until 160 mmHg for the exercise.

Sugawara et al. and Renzi et al. illustrate the potential dangers of using BFR with exercise, but there is some research that combining a low relative BFR pressure with low-load exercise produces a similar cardiovascular response to moderate- or high-load exercise.

2.2.3 Blood Flow Restriction with Resistance Exercise

Different combinations of resistance training load and BFR pressures lead to muscle hypertrophy (Ladlow, et al., 2018). Dankel et al. concluded in a literature review, that muscle size increased in areas proximal and distal to the BFR cuff placement as participants exercised at a low load of 20-30% 1RM (Dankel S. J., Jessee, Abe, & Loenneke, 2015). However, Lixandrao et al. concluded that if a person can perform high-load resistance training, then it would be more efficient than low-load training with BFR (Lixandrao, et al., 2015). In this study participants exercised at either 20% or 40% of their 1RM with either 40% or 80% of AOP and each of the four conditions was compared to exercise at 80% 1RM without BFR. Lixandrao et al. suggested that the AOP percentage was not the most crucial factor in the therapy, but the exercise load had a primary impact. However, Lixandrao et al. had participants perform two sets of the exercise with 15 repetitions and increasing to three sets of exercise toward the end of the twenty-four-week training program (2015). In this case, is a limitation that the participants exercising with 80% of their 1RM has greater load on their muscles than participants that were exercising 20% of their 1RM. The 80% 1RM likely induced fatigue and stimulated more of the overall muscle to grow while stopping prior to fatiguing the muscle with 20% does not fully stimulate all the muscle fibers. In addition, Lixandrao et al. did not report the average total work volume of participants for each condition (2015).

Yasuda et al. came to a similar conclusion and found that significant increases in muscle strength and size occurred in the training protocols that combined high-load resistance training once a week with low-load BFR training twice a week (Yasuda, et al., 2011). In this study, the high-load group exercised at 75% 1RM without BFR and the low-load group exercised at 30% 1RM with a BFR set at 100 mmHg and increasing over the course of the training period. Yasuda et al. found that the greatest increases in muscular strength and size occurred when low-load BFR resistance exercise was combined with high-load resistance exercise. However, Yasuda et al. did not control for relative pressure of the person and did not exercise the participants until volitional failure (2011). As mentioned before, BFR pressures should be relative to the cuff and the person by finding the point of total occlusion and taking a percentage of that pressure. But, exercising until volitional failure is also a very important aspect of standardizing muscle hypertrophy. Instead of using arbitrary exercise sets and repetitions, exercising until voluntary failure helps to truly compare the exercise stimulus across varying loads. With BFR, failure may be reached sooner in low-load exercises than without BFR or with similar loads, but varying AOP percentages. When BFR pressure is based on a percentage of the participants AOP, then groups under a low BFR stimulus would have a relative pressure that gives them that low BFR stimulus. In addition, the participants could reach failure in a similar amount of time than they would if absolute pressures were used. The purpose of exercising to volitional failure is that we can access the ability of the stimulus to elicit an effect of adaption.

By combining BFR with low-load resistance exercises, people can increase muscular strength and size even though they are not exercising at the ACSM guidelines (Loenneke, Wilson, Marin, Zourdos, & Bemben, 2012). This is beneficial for populations that may not have the ability to exercise at high-loads of 60-80% of their 1RM. Nyakayiru et al. saw a significant increase in biomarkers for myofibrillar protein synthesis in twelve recreationally active young men under single-leg low-load BFR conditions (Nyakayiru, et al., 2019). The participants were divided into two groups, one was the resting condition group, and the other was the low-load group (20% 1RM) (Nyakayiru, et al., 2019). The study was a within-subject design, and the low-load group had one leg randomly assigned to two five-minute cycles under BFR, and the opposite leg was considered the control measure without BFR (Nyakayiru, et al., 2019). In the participants that were under low-load conditions, over the five hour period, the low-load leg with BFR had a significantly higher amount of myofibrillar protein synthesis when compared to the leg with only low-load resistance exercise (Nyakayiru, et al., 2019).

In BFR application alone and with passive mobilization there was a delay in muscle atrophy, but when a person can exercise with a low-load to failure, they can increase their muscular strength and size (Loenneke, Wilson, Marin, Zourdos, &

Bemben, 2012). Thus, BFR can be used as a transitioning period for injured, immobile, or elderly populations, and the safety of BFR protocols should be thoroughly understood before recommendations can be made for these specific populations (Loenneke, Wilson, Marin, Zourdos, & Bemben, 2012).

2.3 Cardiovascular Response and Concerns

The circulatory system has a variety of functions: hormone transport, immune support, clotting factors, transporting oxygen, etc. It is a closed system, and changes in one side of the heart will affect the blood flowing to the other side. Oxygenated blood flows from the heart to the needed muscles and organs. Then, deoxygenated blood flows from the organs to the heart, to the lungs, and back to the heart for the cycle to continue. In a healthy individual, this system operates very efficiently (Smith & Fernhall, 2011). However, in unhealthy individuals, heart disease can make simple tasks difficult and difficult tasks challenging. This is because a heart that does not receive enough blood, eject enough blood, or eject blood with enough pressure could increase your chance for heart attack, stroke, poor circulation, blood clots, etc. ACSM reports that acute myocardial infarctions and sudden cardiac death are associated with vigorous exercise (American College of Sports Medicine, 2018).

As mentioned before, there are some concerns about how BFR might affect the cardiovascular system by enhancing the exercise pressor reflex in response to the deoxygenated tissue distal from the BFR cuff and a reduced return of blood flow (Spranger, Krishnan, Levy, O'Leary, & Smith, 2015). The most concerning of those issues include the possibility of myocardial infarction (MI or heart attack). While BFR does provide a way to exercise at a low load while still inducing muscle hypertrophy, the participant's cardiovascular responses should be moderated because BFR does artificially decrease the amount of blood returning to the heart. When the muscle signals a need for more oxygen, the central nervous system responds by withdrawing parasympathetic activation and increasing sympathetic activation (Smith & Fernhall, 2011). As this occurs, the body tries to send more blood to the deoxygenated tissue by causing an increase in heart rate, and this increases the workload of the heart and the heart requires more oxygen for the myocardium (Smith & Fernhall, 2011).

In many cases, Spranger et al. reviewed studies with participants likely at full arterial occlusion and receiving no oxygenated blood to the muscle (Jessee M. B., Buckner, Mouser, Mattocks, & Loenneke, 2016). However, these values were based on previous absolute pressures in literature like in the case of Yasuda et al. and Sugawara et al. (2011; 2015). Yasuda et al. based their study in 2011 off a previous study in 2008, where pressures from 100 mmHg to 160 mmHg were used for all participants (2011; 2008). A study by Shimizu et al. inflated the pneumatic cuff to the systolic blood pressure in the femoral artery of the participant (2016), which could cut off blood flow since SBP is the highest BP in the arteries. With these studies of varying absolute pressures, it may not be an accurate assumption that all BFR exercise could be dangerous. Cuff size and pressure should be relative to the participant to maximize safety in BFR exercises because if the pressure is not relative, we cannot ensure they were not under arterial occlusion (Kilgas, et al., 2018; Neto, et al., 2016; Mouser, et al., 2017). When BFR is based off an absolute value in literature, then the investigator is unable to quantify the participant's arterial blood flow making the study difficult to replicate or the researchers are not creating their desired stimulus for the study. Fully occluding arterial blood increases blood pressure and load on the heart (Spranger, Krishnan, Levy, O'Leary, & Smith, 2015). However, partial arterial occlusion can be applied to ensure the participants are receiving some arterial blood flow during the BFR exercise, which would put less load on the heart.

Unpublished results from our lab, Credeur et al., looked at the cardiovascular response to unilateral handgrip exercise with and without BFR under a moderate-load (60% maximum voluntary contraction) and with BFR under a low-load (40% maximum voluntary contraction) for five minutes. Measurements were compared to baseline and a time control condition when BFR was applied without exercise. Blood flow was reduced on average by about 71% and assessed by Doppler-ultrasound. The moderate-load condition when combined with a BFR stimulus that is reducing blood flow by 71% on average, there is a reduced central pressor response to exercise. Heart rate for the low-load BFR condition did not have a significant difference when compared to time control. Credeur et al, did not see any changes in wave reflection magnitude or augmentation index from the baseline condition.

Spitz et al. assessed the impact of cuff width on perceived discomfort with a relative pressure (40% AOP) BFR arm exercise (Spitz, et al., 2019). Spitz et al. used a discomfort scale with values from 0 to 100 and read the Steele et al. ratings of perceived discomfort. The researchers had three different experiments. The first (n=96), involved 4 sets of biceps curls to failure with the same relative pressure for a narrow (5 cm) and a wide cuff (12 cm). The researchers saw that participants had less discomfort with the narrow cuff (40.6 men and 38.0 women) than the wide cuff (45.9 men and 39.2 women) inflated to the same relative pressure during the exercise (Spitz, et al., 2019). The other two experiments concluded that if a wide cuff was inflated based on a relative pressure found with a narrow cuff, participants had a higher discomfort and there was no difference in discomfort between the wide and narrow cuff at rest when set to a relative pressure (Spitz, et al., 2019).

2.3.1 Quantifying the Cardiovascular Response

Different methods to maximize BFR exercise safety include using tools to get accurate and precise measurements for different individuals. Comparing arterial occlusion before and after exercise can be used as a surrogate measure to quantify the cardiovascular response (Jessee, et al., 2018). When exercising with low- (30% 1RM) and moderate-loads (50% 1RM) adding BFR causes an increase in arterial occlusion pressure (Jessee, et al., 2018). But there are other direct measures that give a holistic view of the cardiovascular response to BFR resistance exercises like central and peripheral blood pressure, heart rate, and oxygen saturation (Neto, et al., 2016; Neto, et al., 2016; Kilgas, et al., 2018; Mouser, et al., 2019; Rossow, et al., 2012; Nitzsche, et al., 2016; Kacin & Strazar, 2011; Matos-Santos, Farinatti, Borges, Massaferri, & Monteiro, 2017; Ganesan, et al., 2015).

Even though there may be many different variables to quantify a cardiovascular response, many BFR studies include oxygen saturation (tissue saturation) collected from either a finger oximeter (Broxterman, et al., 2015) or a near-infrared spectroscopy (NIRS) device (Cayot, Lauver, Silette, & Scheuermann, 2014; Ganesan, et al., 2015). NIRS is a reliable sensor that captures the relative changes in concentrations of oxygenated, deoxygenated, and total hemoglobin by emitting wavelengths of 760-850 nm at the skin contact point (Ganesan, et al., 2015). The NIRS device can show changes in tissue oxygenation over time for different BFR protocols without an invasive procedure.

Heart rate is a cardiovascular variable that is easy to track throughout an exercise condition. When blood pressure is also measured, then the rate pressure product (double product) can be determined (Neto, et al., 2016; Matos-Santos, Farinatti, Borges, Massaferri, & Monteiro, 2017; Rossow, et al., 2012). Devices like a SphygmoCor, are automatic blood pressure measuring devices and include other cardiovascular information like mean arterial pressure, peripheral and central blood pressures, augmentation pressures, and augmentation indexes (Rossow, et al., 2012). By knowing the SBP and DBP of the participant, the researcher can estimate mean arterial pressure. For example, if the load on the heart is high, then the mean arterial pressure will also be high. If the mean arterial pressure is high, then the baroreflex will signal for a change to accommodate the high pressure. Since BFR reduces the amount of deoxygenated blood returning to the heart, then there is a lower stroke volume, and the heart will beat faster to maintain cardiac output. As the workload on the heart increases then it would be more likely for a person to have a myocardial infarction. The augmentation index and augmentation pressure are measures of arterial stiffness. Augmentation pressure is then found by subtracting the pressure inflection point from the maximum SBP (Credeur, et al., 2018). Then, augmentation index is expressed as a percent of pulse pressure (Credeur, et al., 2018). When arteries are less elastic, the mean arterial pressure does not dampen and could cause damage to other blood vessels in the circulatory system (Smith & Fernhall, 2011).

Ratings of perceived effort (RPE-E) is a good indicator of the participant's effort during exercise and can help understand the difficulty of the exercise for the participant (Steele, Fisher, McKinnon, & McKinnon, 2017). Ratings of perceived discomfort (RPE-D) should indicate the participant's discomfort during the exercise and should not include the participant's effort during the exercise (Steele, Fisher, McKinnon, & McKinnon, 2017). These scales can also help to predict adherence or tolerance to the protocol being performed. If the participant does not have a good understanding between the two measurements, then the participant may provide inaccurate results, or if different scales are used between studies, then the results may not be comparable (Steele, Fisher, McKinnon, & McKinnon, 2017).

Steele et al. suggests using vivid scales to clearly instruct the participant of the differences between effort and discomfort (2017). While using the 6-20 Borg scale for RPE and the CR10+ scale for discomfort Jessee et al. and Mattocks et al. found participants had greater discomfort using higher BFR pressures with increasing loads during exercise (Dankel S. J., et al., 2018; Jessee, et al., 2017). In one study, participants who had a higher BFR pressure also had a higher ratings of perceived exertion (Mattocks, et al., 2017), but Jessee et al. saw no difference across conditions with a ratings of perceived exertion or perceived discomfort even though both investigators reported using the same scales. This discrepancy could be because Jessee et al. looked at the effects of compound exercise movements where the primary movers are not under BFR. In addition, Mattocks et al. performed unilateral elbow flexion exercises, and Jessee et al. performed bilateral exercise with the bench press.

2.4 The Possibilities of Blood Flow Restriction Combined with Unilateral, Bilateral, and Alternating Exercises

There have been many investigations into the cardiovascular response of BFR, but the cardiovascular response can also be affected by the amount of muscle mass utilized during exercise. When exercising bilaterally, a participant is activating more muscles at the same time, and the demand for oxygen for these tissues is increased. The cardiovascular system responds by vasodilating vessels to exercising muscles and vasoconstricting vessels that are not absolutely necessary during exercise (Smith & Fernhall, 2011).

Current literature seems to have conflicting results about the cardiovascular response when comparing bilateral and unilateral exercises (Saeterbakken & Fimland, 2012). Moreira et al. assessed the cardiovascular response in fifteen healthy male subjects by three different types of exercises (bicep curls, knee extensions, and barbell rows) for each set of exercise. The subjects performed unilateral, bilateral, and alternating exercise conditions for each body segment to see the cardiovascular difference between modalities. When looking at unilateral, bilateral, and alternating resistance training exercises in the upper and lower body, Moreira et al. concluded that the bilateral upper body had a higher cardiovascular response than the other exercises bilaterally (2015). Moreira et al., discuss that the structure of the vascular tree increases the cardiovascular demand of the bilateral upper body exercise because there is greater resistance to blood flow (2015). In addition, the bilateral exercise had a greater cardiovascular response when compared to unilateral exercise in the same body segment (Moreira, et al., 2015). A possible limitation to this study is that participants did not exercise to failure; instead, they performed three sets of ten repetitions for each exercise.

Matos-Santos et al. reported a significant increase in blood pressure, heart rate, cardiac output, and rate pressure product in bilateral compared to unilateral knee-extensions. One limitation of the study is that participants did four sets of twelve repetitions for both exercises. So, Matos-Santos et al. did not have the participants exercise until volitional failure. Two things are suggested from these studies. First, that the amount of muscle mass contracting can affect the cardiac response (i.e., higher blood pressure, heart rate, and rate pressure product) (Matos-Santos, Farinatti, Borges, Massaferri, & Monteiro, 2017; Moreira, et al., 2015). Second, the upper limbs have a greater resistance to blood flow than the lower limbs and have greater cardiovascular response (Matos-Santos, Farinatti, Borges, Massaferri, & Monteiro, 2017). By manipulating the amount of active tissue or exercise modality (unilateral, bilateral, or alternating), researchers may be able to attenuate the cardiovascular response to exercise. This could mean that there are different ways that researchers can minimize a heightened cardiovascular response during BFR exercise, by applying different relative pressures, exercising with different loads, and possibly manipulating the exercise modality. To the best of our knowledge, there is no research currently investigating the cardiovascular response of BFR resistance exercise with different modalities (unilateral, bilateral, alternating).

CHAPTER III - METHODOLOGY

3.1 Participants

The participants in this study were recruited if they were 18-35 years old. We recruited twenty-three volunteers with 13 males and 5 females. The participants were recruited from email, classroom announcements, and word of mouth. Participants were excluded from participation if they took medication that would influence blood pressure or heart rate, or had any orthopedic issues prohibiting resistance exercise in the lower body. Also, participants were excluded if they met two of the following risk factors for thromboembolism: currently using birth control, diagnosis of Crohn's disease, previous fracture of hip, pelvis or femur, major surgery within the last 6 months, varicose veins, family or personal history of pulmonary embolism or thromboembolism, or a BMI >30 (Motykie et al., 2000).

3.2 Experimental Design

The first visit the participants filled out the exclusion criteria (Figure 5.11), informed consent, and a PAR-Q. If the participants were eligible and willing to participate, then their height and weight was recorded. Then, the participants performed a 1RM test. During the 1RM test, Participants were familiarized with two separate scales to measure ratings of perceived effort (RPE-E) and perceived discomfort (RPE-D). Then, the participants were familiarized with each exercise modality by performing five repetitions of each condition to a metronome with a deflated cuff on their left upper leg.

Subsequent visits (at least 2 days and not more than 10 apart) included one of three randomly ordered experimental protocols. Participants performed a protocol under

BFR using either unilateral, bilateral, or alternating left and right limb exercises (Moreira, et al., 2015). AOP was measured for each limb before the exercise protocol for each visit. RPE-E and RPE-D were taken before, between sets, and immediately after exercise. RPE-E was taken immediately after each set, and RPE-D was taken 20 seconds after each set. Pulse wave analysis (PWA) was measured two times before and once immediately after the exercise condition. Exercises were performed under 40% AOP and at 30% of the participant's averaged bilateral 1RM. The participant was asked to do four sets of exercise to volitional failure with 30 seconds of rest between set (Jessee, et al., 2018). Then, the BFR cuff was deflated and removed. Each visit lasted about forty-five minutes but not longer than one hour.

3.2.1 Informed Consent

The participant was welcomed into the lab and given the exclusion criteria (Figure 6.9). Then, the investigator described the entire study to the participant, this includes but is not limited to the purpose, procedures, risks and discomforts, benefits, confidentiality of the participant, early withdraw from the study, and predicted date the study would be finished. The participant was also informed to avoid alcohol, nicotine, and exercise 24 hours prior to the study and avoid caffeine 8 hours prior to each visit. The participant was able to ask for further information prior to providing verbal and written consent. After consent was obtained, the participant filled out a Physical Activity Readiness Questionnaire (PAR-Q [2019+]) to ensure they were not at an increased risk of a cardiovascular event. If the participant was at an increased risk for a cardiovascular event, then they were excluded from the study. If they were eligible to participate then height and body mass measures were taken.

3.2.2 Height and Body Mass

Participants height and body mass were measured using standard equipment. Height was measured in centimeters and mass was measured in kilograms. The participants body mass index was then calculated.

3.2.3 One Repetition Maximum (1RM)

Participants were seated in an isolateral leg extension machine, which is illustrated in Figure 5.9 with the model number in Figure 6.8 (Hammer Strength®, Model IL-LE). Then, they warmed-up by completing no more than 10 unloaded knee extensions for each leg. The participant was asked to undergo a full range of motion for each repetition attempt, which is extending the knee about 90 degrees until stopped at the safety bar on the machine. When the participant was ready, a lighter weight that the participant was confident in lifting was added to the bar and increased with each successful knee extension attempt. If the participant was unsuccessful, then the load was lowered in smaller increments until the 1RM was determined. There were 60 seconds between each leg attempt, and the starting leg was randomized. Investigators tried to determine the participants 1RM in less than approximately 5 attempts per leg. If the 1RM was different between legs, then they were averaged together for the participants average bilateral 1RM. Each exercise was performed at 30% of the participants averaged bilateral 1RM.

3.2.4 Arterial Occlusion Pressure (AOP)

A 10cm wide, pneumatic nylon cuff (Hokanson®, SC10D) was placed on the proximal portion of each upper leg while the participant was standing (Figure 6.5). Then, the participant was asked to sit in the knee-extension machine. RPE-E, RPE-D, and PWA were assessed while the participant rested in the machine. Then, an Ultrasonic Pocket Doppler probe (Edan, SD3 Vascular) was used to detect the pulse in the posterior tibial artery. To determine the participant's AOP, the cuff pressure was slowly increased (Hokanson®, E20-Rapid Cuff Inflator) from 50 mmHg until a pulse was no longer audible and this pressure was recorded to the nearest mmHg. AOP of each exercising leg was measured prior to each condition. Each cuff was inflated to 40% of the respective AOP in each leg before the exercise condition began. If the pressure exceeded 300 mmHg, then 40% of 300mmHg was used due to limitation of equipment being unable to inflate the cuff any further.

3.3 Exercise Conditions

3.3.1 Bilateral Exercise

The participant had a nylon pneumatic cuff placed at the proximal portion of the upper left and right thigh. Then, the previously averaged 1RM from the first lab visit was used for the bilateral exercise. Both legs synchronously extended to the pre-set safety bar and returned, completing a full 90-degree motion. The participant continued to exercise until volitional failure, or until they were unable to maintain a 2-second cadence (1 second concentric, 1 second eccentric), or if one leg was unable to keep pace with the cadence. If the participant missed the safety bar or was off beat for more than two consecutive attempts per leg, then the investigator ended the set.

3.3.2 Unilateral Exercise

During the unilateral exercise, the participant had a nylon pneumatic cuff placed at the proximal portion of both legs, but only one cuff was inflated and attached at a time. The investigator randomized which leg the participant used for exercise first, and the opposing limb remained relaxed while the exercising leg extended to the pre-set safety bar and returned, completing a full 90-degree motion. The participant continued until volitional failure, or until they were unable to maintain a 2-second cadence (1 second concentric, 1 second eccentric) for four sets. If the participant was offbeat or missed the safety bar for more than 2 consecutive attempts, then the investigator ended the set. Cuffs were undone if not exercising and had to be secured before starting the exercise

Once four sets were completed on the first leg, then the investigators deflated and unattached the Velcro of the cuff. Then, the investigators attached the Velcro and inflated the cuff of the rested leg, and the participants were asked to begin the same protocol on the opposite limb while the first exercised leg rested.

3.3.3 Alternating Exercise

During the alternating exercise, the participant had a nylon pneumatic cuff placed at the proximal portion of both legs. The investigator randomized which leg was first for exercise, and the opposing limb extended to the pre-set safety bar when the original leg returned to a 90-degree angle. The participant continued to alternate until volitional failure, or until they were unable to maintain a 2-second cadence (1 second concentric, 1 second eccentric) for two consecutive attempts per leg.

3.4 Variables

3.4.1 Systolic (SBP) and Diastolic Blood Pressure (DBP), Pulse Wave Analysis (PWA)

PWA, SBP, and DBP were measured twice with an automatic blood pressure cuff (SphygmoCor XCEL, AtCor Medical) prior to exercise and once immediately after exercise. The two PWA measurements taken at baseline were averaged together. An example of the SphygmoCor can be seen in Figure 6.1. The participant remained seated in the knee-extension machine, and a cuff was placed on the proximal portion of the upper left arm. Figure 6.2 illustrates the placement of the SphygmoCor, and Figure 6.3 illustrates the information needed about the participant prior to measurement. Figure 6.4 is a visual of the SphygmoCor XCEL system on a cart that is rolled closer to the participant as they are seated in the leg extension machine. The participant was informed that the cuff would inflate a total of four times, and the investigator began the SphygmoCor measurement (took up to 3 minutes for one measurement). The cuff inflated the first time to measure brachial SBP and brachial DBP and then inflated to sub-systolic blood pressure to analyze the brachial pressure waveform.

3.4.2 Rate Pressure Product (RPP)

RPP (sometimes referred to as double product) is a measure of cardiovascular stress and was determined by taking the product of SBP and HR data from the PWA measures before and immediately after exercise. The investigators calculated aortic RPP (aRPP) and brachial RPP (bRPP) by using the aortic SBP and the brachial SBP measurements.

3.4.3 Ratings of perceived effort (RPE-E) and perceived discomfort (RPE-D)

RPE-E and RPE-D were measured with two different scales, with a range of 0 to 10, which have been validated previously (Steele, Fisher, McKinnon, & McKinnon, 2017). The participant was familiarized with the different scales on the first visit and prior to the protocol on subsequent visits. The participant was asked before and immediately after the exercise to describe how hard they feel they were working during the exercise condition based on the RPE-E scale (Figure 6.6). The participant was asked 20 after the exercise condition to describe how much discomfort they felt currently based on the RPE-D scale (Figure 6.7). The participant pointed to or said the number on the appropriate scale that accurately represents either their RPE-E or RPE-D.

3.4.4 The Volume of Load Lifted

The total number of repetitions completed were recorded by the investigator and multiplied by the load to quantify the volume of load lifted by the participant for each condition (Jessee, et al., 2018).

3.5 Data Analysis

Body mass index was measured for all participants by dividing the participants weight in kilograms by their height (converted to meters) squared. Cardiovascular measures were collected and analyzed with 17 participants. aRPP was calculated by multiplying aSBP by HR. bRPP was calculated by multiplying bSBP by HR. Volume was calculated by multiplying the number of repetitions for each condition by the amount of weight the participant moved. The unilateral condition left, and right leg results were averaged together. All data presented as mean (SD) unless noted otherwise. AIX%75 was analyzed with 15 participants because the instrument was unable to provide us with this data for 2 participants. In addition, one of the participant's did not have their waveform assessed. Participants were excluded from analysis if they did not have the variables for all three conditions.

3.6 Statistical Analysis

A Bayesian one-way ANOVA was performed to compare volume and the change in cardiovascular measures from PWA across conditions. Bayesian repeated measures ANOVA was conducted for RPE-E, RPE-D, and volume. Cardiovascular variables were assessed based on differences from the averaged PWA measure before the start of the exercise condition minus the PWA measure after the exercise condition. In Figure 3.1, Wagenmaker et al. illustrates a way to interpret the bayes factors. If the bayes factor (BF) was greater than 3, then there would be moderate evidence for the alternative hypothesis (Wagenmakers, et al., 2018). If the BF was less than .333, then there would be moderate evidence for the null hypothesis (Wagenmakers, et al., 2018). BF values between .333 and 3 are anecdotal evidence, and more data would be necessary to see if the evidence supports one hypothesis over another (Wagenmakers, et al., 2018). In addition, if there was an interaction, then post-hoc comparisons were used to investigate simple effects. If there was no evidence for a significant interaction, then main effects of condition and time were investigated (JASP 0.9.2.0).

Table 1 A descriptive and approximate classification scheme for the interpretation of Bayes factors BF_{10} (Lee & Wagenmakers 2013; adjusted from Jeffreys 1961)

Bayes factor	Evidence category
> 100	Extreme evidence for $\mathcal{H}_1$
30 - 100	Very strong evidence for $\mathcal{H}_1$
10 - 30	Strong evidence for $\mathcal{H}_1$
3 - 10	Moderate evidence for $\mathcal{H}_1$
1 - 3	Anecdotal evidence for $\mathcal{H}_1$
1	No evidence
1/3 - 1	Anecdotal evidence for $\mathcal{H}_0$
1/10 - 1/3	Moderate evidence for $\mathcal{H}_0$
1/30 - 1/10	Strong evidence for $\mathcal{H}_0$
1/100 - 1/30	Very strong evidence for $\mathcal{H}_0$
$< 1/100$	Extreme evidence for $\mathcal{H}_0$

Figure 3.1 Classification Scheme from Wagenmakers et al. 2018

This image illustrates how to interpret the bayes factor when comparing the null and alternative hypothesis (Wagenmakers, et al., 2018).

CHAPTER IV – RESULTS

4.1 Cardiovascular measures

A table of all mean values for cardiovascular variables at each time point can be found in Table 4.1.

	Unilateral			*Bilateral*			*Alternating*		
	Before 1	Before 2	After	Before 1	Before 2	After	Before 1	Before 2	After
bSBP (mmHg)	132.2 (13.4)	125.9 (11.0)	149.7 (15.9)	132.1 (14.6)	127.1 (12.9)	152.3 (14.7)	129.7 (11.5)	126.7 (10.0)	157.0 (12.2)
bDBP (mmHg)	78.8 (10.6)	78.8 (8.9)	84.9 (12.4)	79.5 (7.1)	77.3 (6.9)	85.4 (10.5)	77.2 (9.9)	74.9 (7.8)	86.9 (11.9)
aSBP (mmHg)	114.8 (11.0)	111.0 (9.8)	125.5 (12.4)	115.2 (11.0)	111.6 (9.9)	127.7 (11.7)	112.8 (9.0)	109.1 (8.0)	131.8 (10.3)
aDBP (mmHg)	80.1 (11.0)	79.9 (8.7)	86.8 (12.4)	80.4 (7.3)	78.3 (6.9)	87.5 (10.6)	77.8 (10.1)	76.3 (7.3)	89.7 (12.2)
aPP (mmHg)	34.7 (10.0)	31.1 (7.3)	38.7 (7.5)	34.8 (7.6)	33.3 (8.7)	40.2 (8.4)	34.9 (9.7)	32.8 (5.0)	42.1 (8.2)
aMAP (mmHg)	93.9 (10.8)	92.8 (8.9)	104.1 (12.8)	95.6 (9.2)	92.3 (7.3)	106.1 (11.3)	92.2 (9.2)	89.4 (7.7)	108.9 (12.9)
HR (bpm)	70.0 (12.4)	70.2 (11.6)	87.9 (13.0)	72.4 (9.0)	70.1 (8.7)	89.4 (12.7)	69.8 (11.6)	69.6 (10.5)	94.1 (19.9)
*aRPP (bpm*mmHg)*	9261.3 (1868.9)	8829.4 (1509.4)	11079.1 (2150.8)	9606.7 (1780.6)	8885.8 (1282.7)	11435.3 (2002.1)	9040.7 (1599.4)	8794.7 (1312.4)	12506.6 (3229.9)
*bRPP (bpm*mmHg)*	8045.7 (1605.4)	7789.6 (1369.2)	13204.3 (2573.6)	8370.8 (1431.7)	7800.6 (1040.9)	13621.7 (2348.6)	7877.2 (1429.2)	7583.7 (1189.7)	14878.7 (3801.3)
AP (mmHg)	2.5 (6.0)	2.2 (5.2)	-0.9 (6.9)	3.6 (5.8)	3.8 (6.7)	1.3 (6.9)	3.4 (5.6)	1.4 (4.1)	0.4 (8.2)
AIX (%)	4.8 (15.1)	4.4 (15.2)	-2.6 (17.0)	9.1 (14.2)	9.5 (15.5)	1.7 (17.5)	7.8 (15.2)	3.3 (12.4)	-0.5 (20.7)
AIX75 (%)	2.3 (14.9)	2.1 (15.2)	3.7 (17.0)	7.8 (14.9)	7.2 (16.8)	8.6 (16.8)	5.2 (17.2)	0.7 (14.9)	7.4 (18.0)
WR (%)	47.1 (6.6)	47.2 (6.3)	41.4 (7.7)	48.2 (6.5)	48.8 (8.4)	43.2 (6.2)	47.1 (7.0)	46.3 (8.9)	42.1 (6.9)
FH (mmHg)	29.4 (6.2)	25.8 (5.1)	35.7 (7.4)	29.6 (6.2)	28.2 (7.2)	36.6 (6.7)	30.0 (7.3)	28.6 (5.1)	37.4 (6.0)
RH (mmHg)	14.1 (4.3)	12.4 (3.5)	14.4 (2.6)	14.2 (3.6)	14.2 (6.3)	15.8 (3.8)	14.2 (4.3)	13.1 (2.2)	15.9 (3.9)

Table 4.1 Average Changes in Cardiovascular Variables

The values are expressed as the first measurement before exercise (Before 1), the second measurement before exercise (Before 2), and the measurement immediately after exercise (After). The standard deviations are in parenthesis next to each measurement. bSBP = brachial systolic blood pressure; bDBP = brachial diastolic blood pressure; aSBP = aortic systolic blood pressure; bSBP = brachial systolic blood pressure; aPP = aortic pulse pressure; aMAP = aortic mean arterial pressure; HR = heart rate; aRPP = aortic rate pressure product; bRPP = brachial rate pressure product; AP = augmentation pressure; AIX% = augmentation index; AIX75% = augmentation index when corrected for heart rate; WR = wave reflection magnitude; FH = forward pressure height; RH = reflected pressure height.

There was anecdotal evidence ($BF_{10} = 1.838$) that the changes in bSBP were different between conditions (Figure 4.1). Follow-up comparisons showed changes in ALT were greater than UNI [28 (10) vs. 20 (12) mmHg; $BF_{10} = 7.086$], but not different from BI [28 (10) vs. 22 (9) mmHg; $BF_{10} = 0.680$]. The changes in UNI were not different from BI [20 (12) vs. 22 (9) mmHg; $BF_{10} = 0.294$].

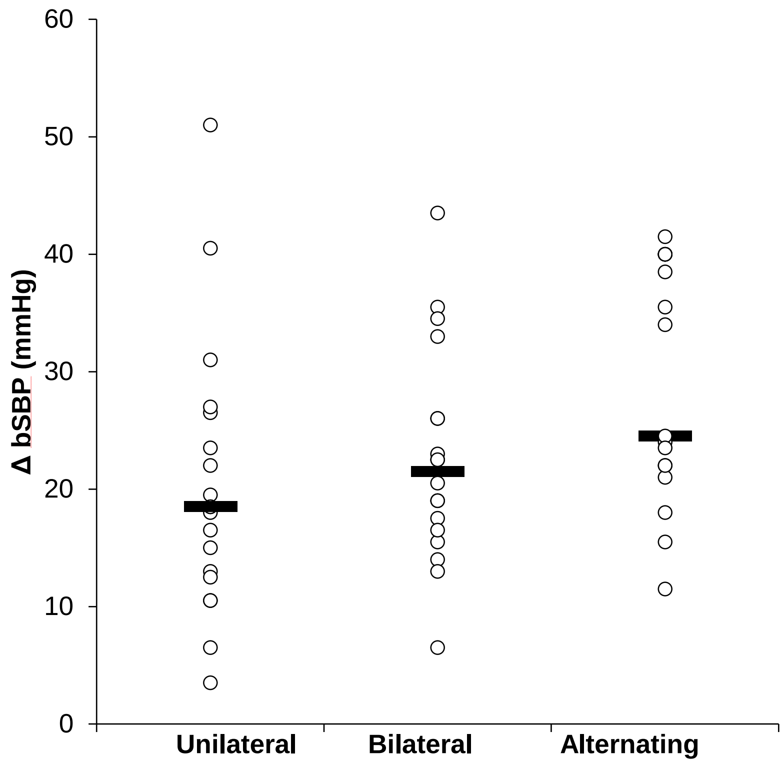

Figure 4.1 Changes in Brachial Systolic Blood Pressure

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was anecdotal evidence ($BF_{10} = 1.114$) that changes in bDBP were different between conditions (Figure 4.2). Follow-up comparisons showed changes in ALT were greater than UNI [11 (8) vs. 6 (11) mmHg; $BF_{10} = 2.009$] and were greater than BI [11 (8) vs. 7 (8) mmHg; BF_{10} = 1.338]. The changes in UNI were not different from BI [6 (11) vs. 7 (8) mmHg; BF_{10} = 0.272].

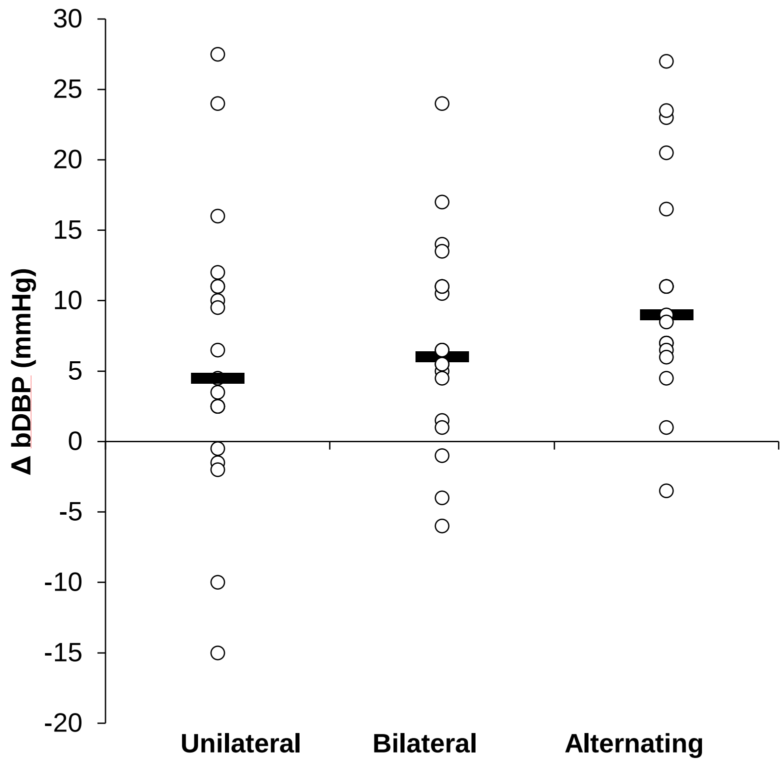

Figure 4.2 Changes in Brachial Diastolic Blood Pressure

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was strong evidence (BF_{10} = 17.949) that changes in aSBP were different between conditions (Figure 4.3). Follow-up comparisons show changes in ALT were greater than UNI [21 (9) vs. 13 (11) mmHg; BF_{10} = 151.605) and were greater than BI [21 (9) vs. 14 (8) mmHg; BF_{10} = 2.640]. The changes in UNI were not different from BI [13 (11) vs. 14 (8) mmHg; BF_{10} = 0.304].

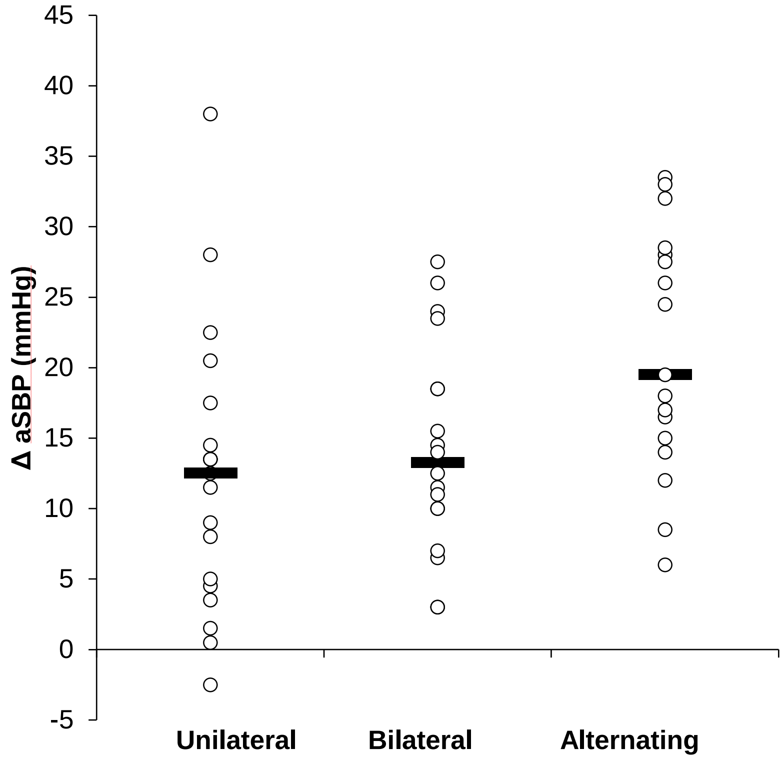

Figure 4.3 Changes in Aortic Systolic Blood Pressure

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was moderate evidence (BF_{10} = 3.214) that changes in aDBP were different between conditions (Figure 4.4). Follow-up comparisons show changes in ALT were greater than UNI [12 (8) vs. 7 (11) mmHg; BF_{10} = 5.452] and were greater than BI [12 (8) vs. 8 (8) mmHg; BF_{10} = 3.732]. Changes in UNI were not different from BI [7 (11) vs. 8 (8) mmHg; BF_{10} = 0.292].

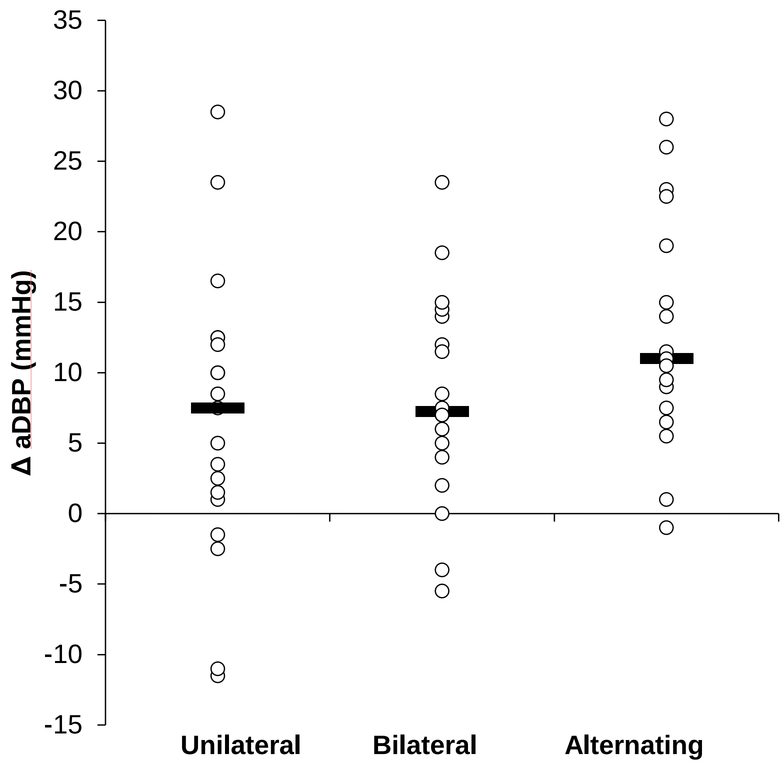

Figure 4.4 Changes in Aortic Diastolic Blood Pressure

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was strong evidence (BF_{10} = 27.005) that changes in aMAP were different between conditions (Figure 4.5). Follow-up comparisons show changes in ALT were greater than UNI [18 (9) vs. 11 (10) mmHg; BF_{10} = 49.973] and were greater than BI [18 (9) vs. 12 (7) mmHg; BF_{10} = 9.211). The changes in UNI were not different from BI [11 (10) vs. 12 (7) mmHg; BF_{10} = 0.309].

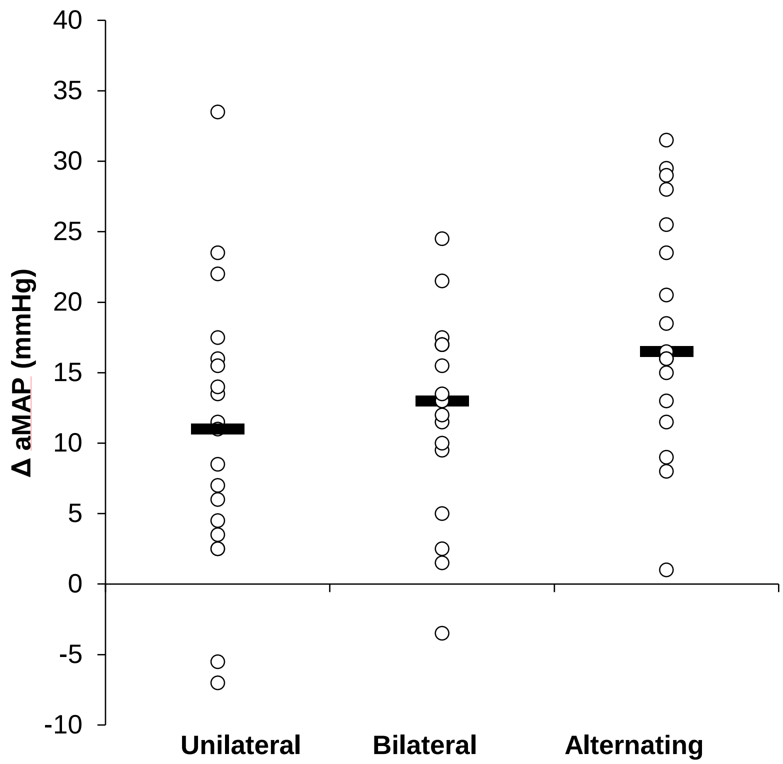

Figure 4.5 Changes in Aortic Mean Arterial Pressure

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was moderate evidence (BF_{10} = 3.956) that changes in HR were different between conditions (Figure 4.6). Follow-up comparisons show changes in ALT were greater than UNI [25 (15) bpm vs. 19 (8) bpm; BF_{10} = 1.306] and were greater than BI [25 (15) bpm vs. 18 (11) bpm; BF_{10} = 9.372]. The changes in UNI were not different from BI [19 (8) bpm vs. 18 (11) bpm; BF_{10} = 0.262].

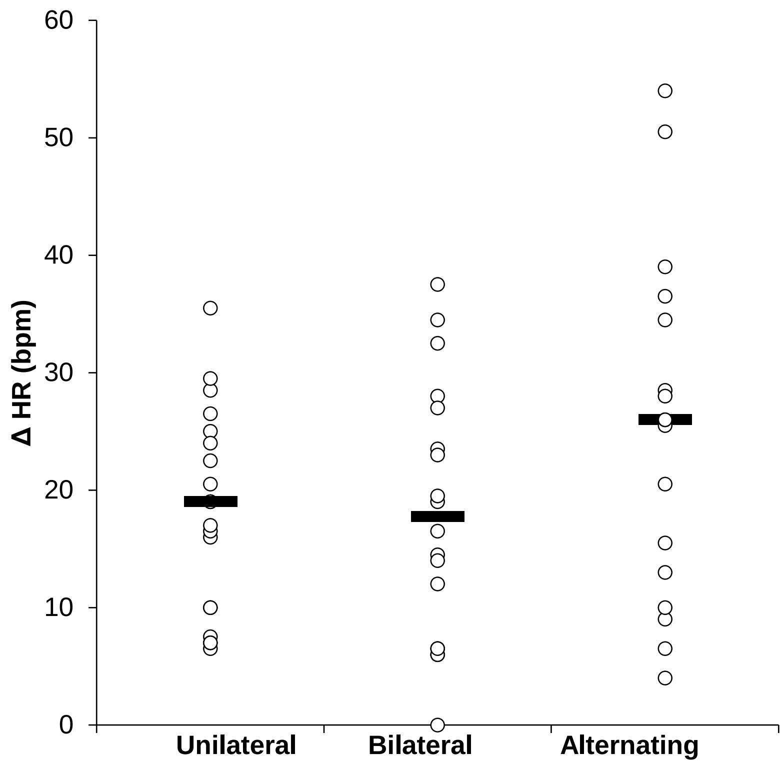

Figure 4.6 Changes in Heart Rate

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was strong evidence (BF_{10} = 14.378) that changes in bRPP were different between conditions (Figure 4.7). Follow-up comparisons show changes in ALT were greater than UNI [6060 (2915) vs. 4270 (1809) mmHg * bpm; BF_{10} = 3.538] and were greater than BI [6060 (2915) vs. 4328 (1673) mmHg * bpm; BF_{10} = 11.180]. The changes in UNI were not different from BI [4270 (1809) vs. 4328 (1673) mmHg * bpm; BF_{10} = 0.148].

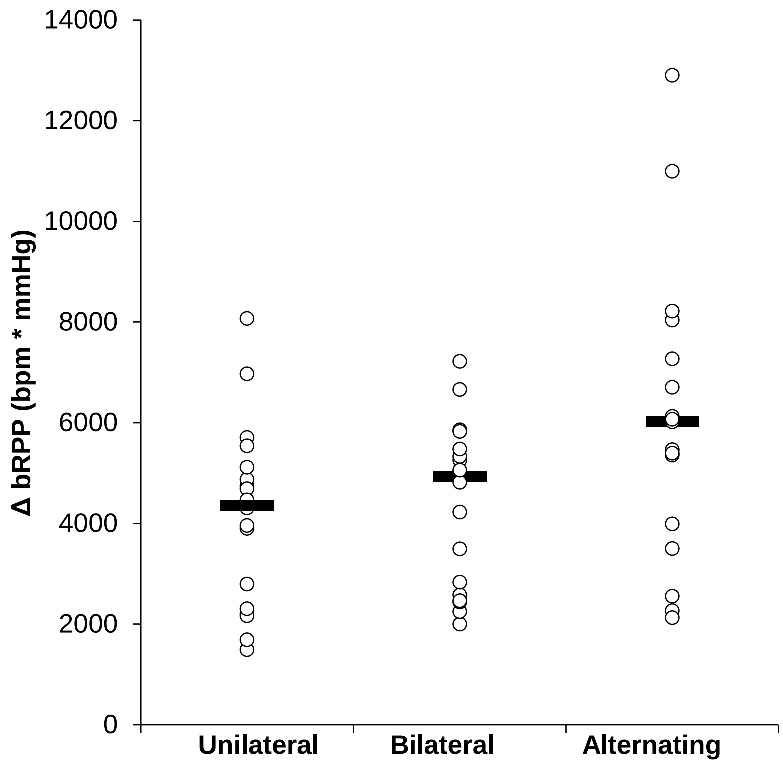

Figure 4.7 Changes in Brachial Rate Pressure Product

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was very strong evidence (BF_{10} = 41.682) that changes in aRPP were different between conditions (Figure 4.8). Follow-up comparisons show changes in ALT were greater than UNI [4873 (2479) vs. 3243 (1482) mmHg * bpm; BF_{10} = 6.625] and greater than BI [4873 (2470) vs. 3308 (1449) mmHg * bpm; BF_{10} = 22.785]. The changes in UNI were not different from BI [3243 (1482) vs. 3308 (1449) mmHg * bpm; BF_{10} = 0.253].

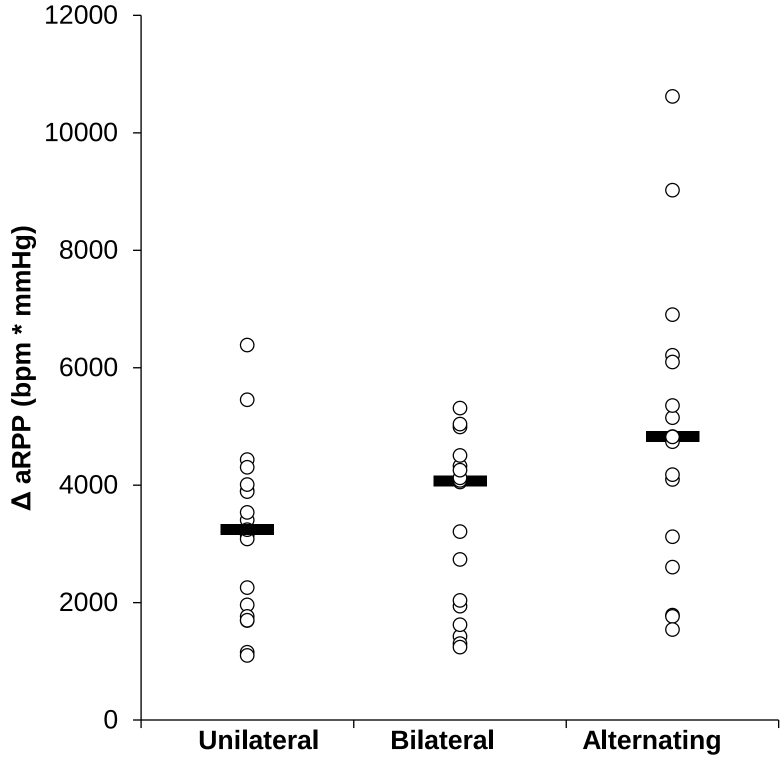

Figure 4.8 Changes in Aortic Rate Pressure Product

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was moderate evidence (BF_{10} = 0.274) that changes in pulse pressure were not different across UNI [6.0 (5.9) mmHg], BI [6.2 (7.4) mmHg], and ALT [8.3 (5.6) mmHg] conditions (Figure 4.9).

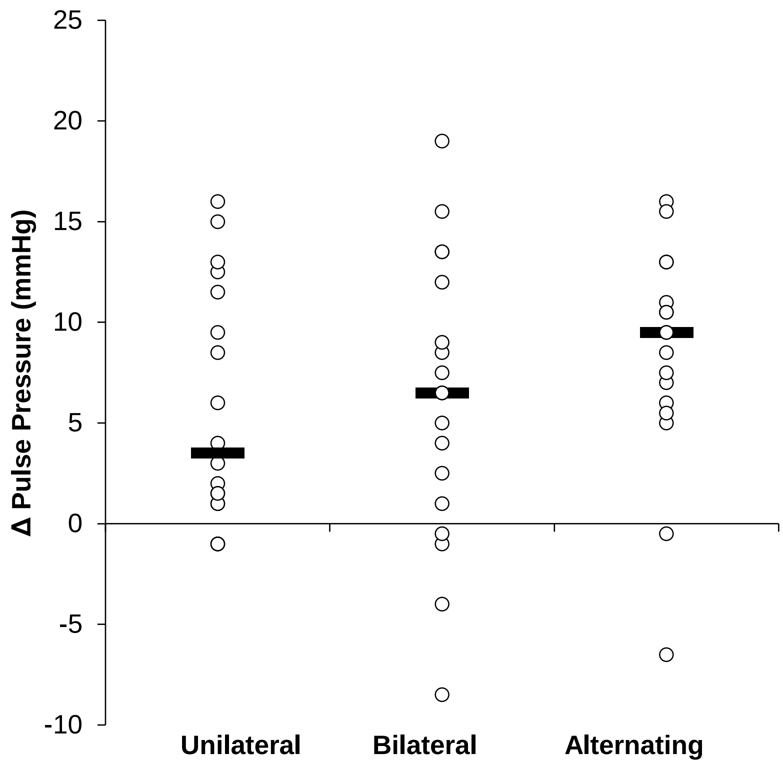

Figure 4.9 Changes in Pulse Pressure

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was moderate evidence ($BF_{10} = 0.202$) that changes in augmentation pressure were not different across UNI [-3.3 (5.2) mmHg], BI [-2.4 (5.9) mmHg], and ALT [-1.8 (6.5) mmHg] conditions (Figure 4.10).

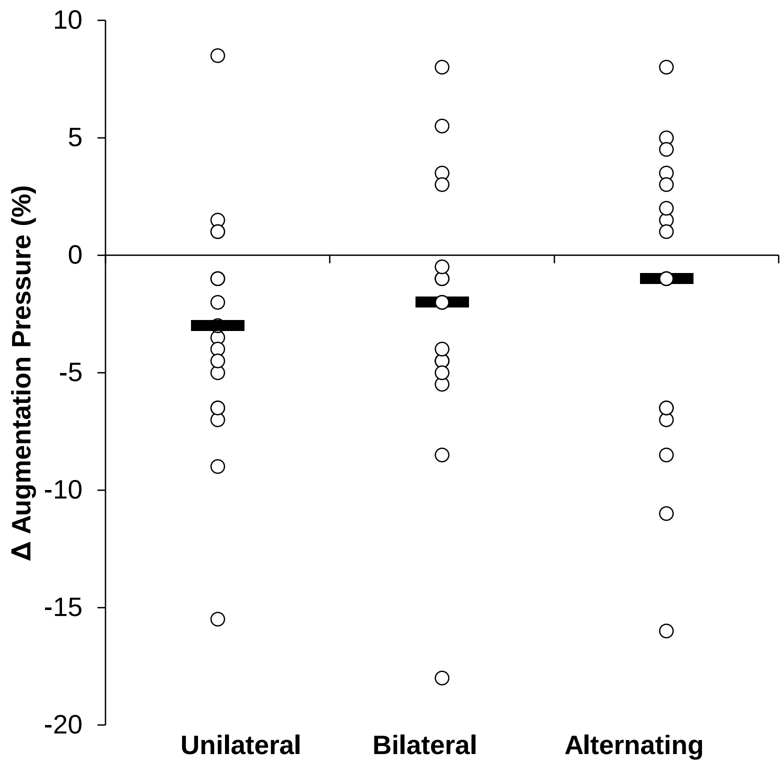

Figure 4.10 Changes in Augmentation Pressure

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was moderate evidence (BF_{10} = 0.162) that changes in augmentation index (%) were not different across UNI [-7.1 (12.8)], BI [-7.7 (11.7)], and ALT [-5.7 (16.5)] conditions (Figure 4.11).

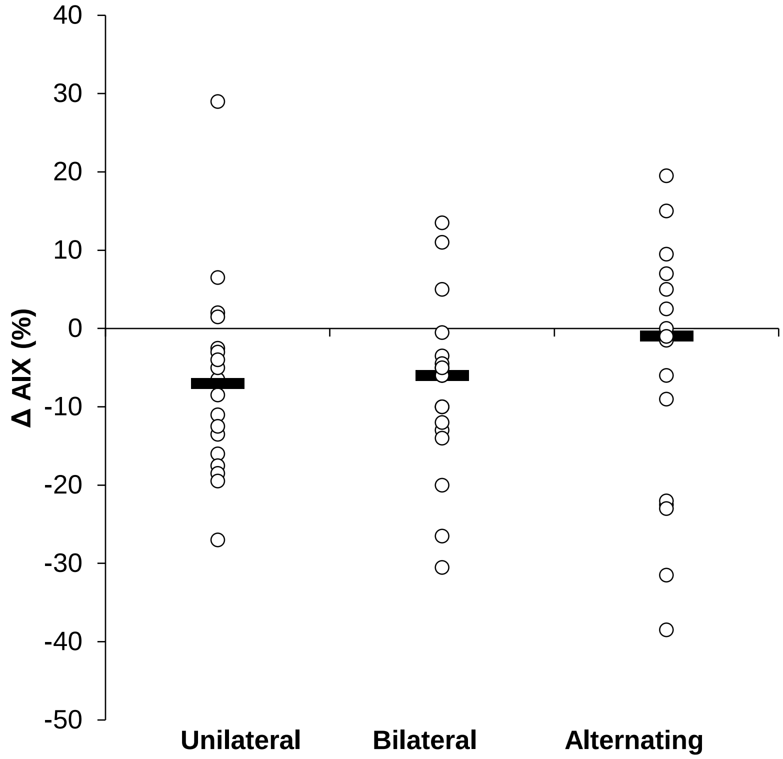

Figure 4.11 Changes in Augmentation Index

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was anecdotal evidence (BF_{10} = 1.354) that changes in augmentation index (%) when corrected for heart rate were different between conditions (Figure 4.12). Follow-up comparisons show that changes in ALT is greater than UNI [7.20 (13.7) vs. 0.10 (8.9); BF_{10} = 2.252], but not different from BI [7.20 (13.7) vs. 0.47 (8.6); BF_{10} = 0.905]. The changes in UNI were not different from BI [0.10 (8.9) vs. 0.47 (8.6); BF_{10} = .264].

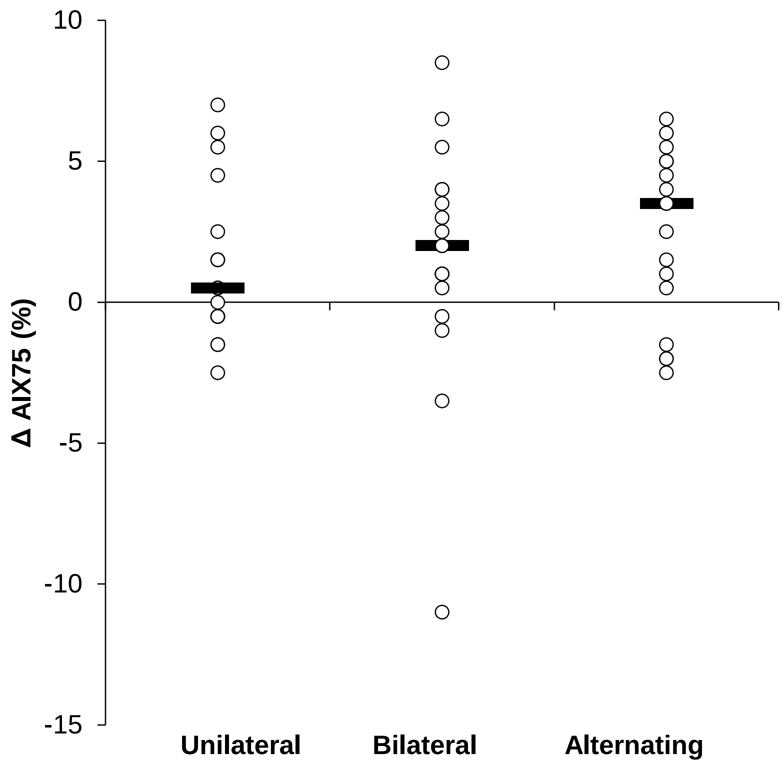

Figure 4.12 Changes of Augmentation Index when Corrected for Heart Rate

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was moderate evidence (BF_{10} = 0.172) that changes in wave reflection magnitude were not different across UNI [-5.5 (8.7) %], BI [-4.7 (7.2) %], and ALT [-4.3 (6.9) %] conditions (Figure 4.13).

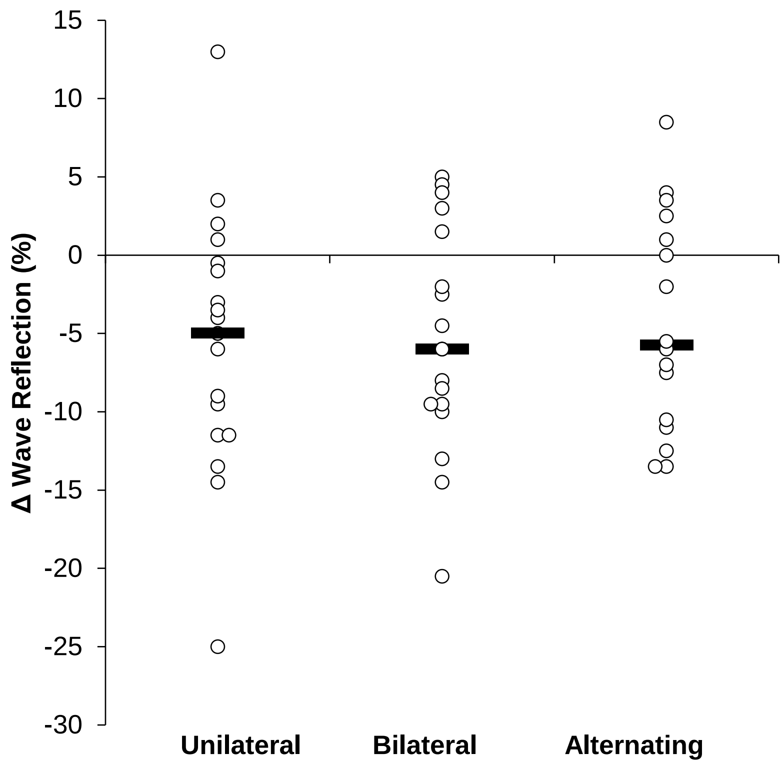

Figure 4.13 Changes in Wave Reflection Magnitude

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was moderate evidence (BF_{10} = 0.154) that changes in the forward wave height component were not different across UNI [8.6 (6.8) mmHg], BI [8.3 (6.2) mmHg], and ALT [8.4 (4.4) mmHg] conditions (Figure 4.14).

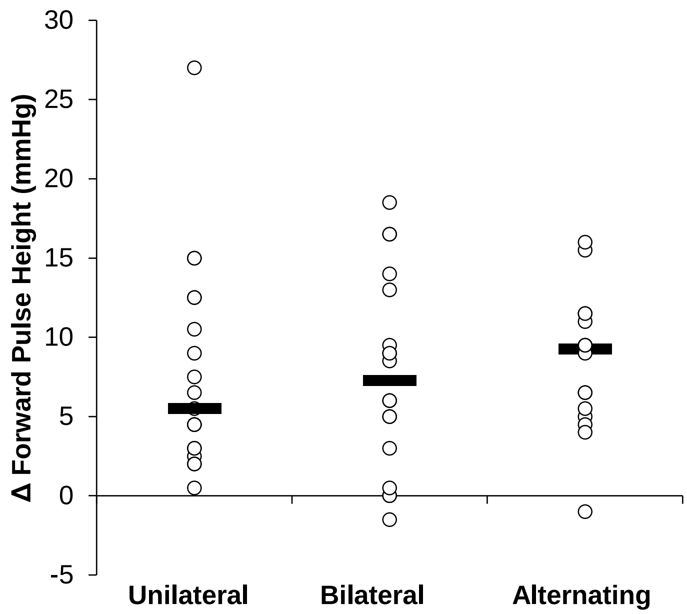

Figure 4.14 Changes in Forward Pulse Height

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

There was moderate evidence (BF_{10} = 0.274) that changes in the reflected wave height component were not different across UNI [1.5 (2.8) mmHg], BI [2.4 (3.0) mmHg], and ALT [2.5 (3.1) mmHg] conditions (Figure 4.15).

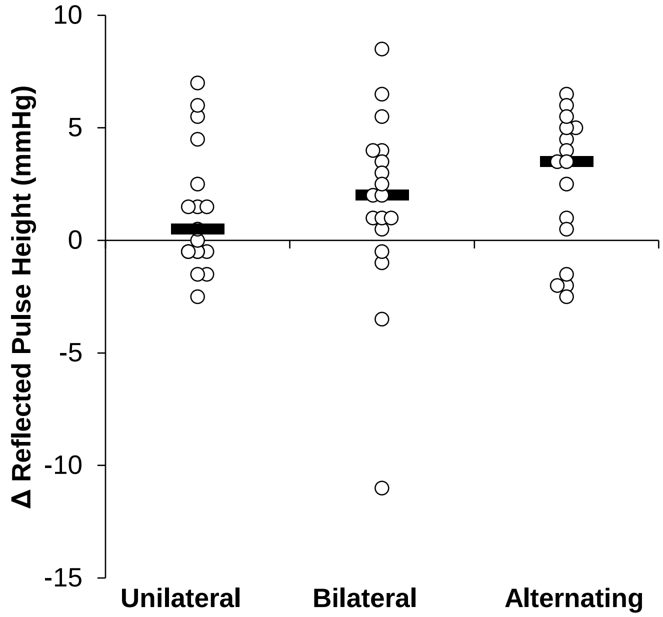

Figure 4.15 Changes in Reflected Pulse Height

Open circles indicate individual changes in brachial systolic blood pressure from before and after each condition. Black lines indication median values of the group change.

4.2 Ratings of perceived discomfort and ratings of perceived effort

There is very strong evidence ($BF_{10} = 0.074$) that RPE-D did not change differently over time across conditions. When analyzing main effects, there is extreme evidence ($BF_{10} = 4.144e +69$) for a main effect of time and extreme evidence for a main effect of condition ($BF_{10} = 1389.871$). Post hoc comparisons between conditions show that ALT was greater than UNI ($BF_{10} = 4584.549$) and BI ($BF_{10} = 471028.653$), while UNI and BI conditions were not different ($BF_{10} = 0.127$). Post hoc comparisons for main effect of time can be seen in Table 4.2. Averaged values for each time point can be seen in Table 4.3.

		Prior Odds	Posterior Odds	BF $_{10, U}$	error %
BEFORE	SET 1	0.320	1.178e +19	3.686e +19	1.119e -23
	SET 2	0.320	1.037e +21	3.245e +21	2.226e -24
	SET 3	0.320	3.906e +21	1.223e +22	6.263e -26
	SET 4	0.320	1.590e +22	4.975e +22	1.367e -25
SET 1	SET 2	0.320	2198.890	6882.113	1.734e -11
	SET 3	0.320	10084.523	31562.670	1.267e -11
	SET 4	0.320	4.242e +7	1.328e +8	2.851e -14
SET 2	SET 3	0.320	2.204	6.899	6.083e -7
	SET 4	0.320	41832.585	130928.167	4.288e -8
SET 3	SET 4	0.320	4.566	14.291	3.232e -7

Table 4.2 RPE-D Post Hoc Comparisons of Time

The posterior odds have been corrected for multiple testing by fixing to 0.5 the prior probability that the null hypothesis holds across all comparisons (Westfall, Johnson, & Utts, 1997). Individual comparisons are based on the default t-test with a Cauchy (0, r =1/sqrt(2)) prior. The "U" in the Bayes factor denotes that it is uncorrected.

RPE-D	Before	Set 1	Set 2	Set 3	Set 4
Unilateral	0.1 (0.2)	4.3 (2.0)	4.8 (2.0)	5.1 (2.0)	5.4 (2.1)
Bilateral	0.1 (0.2)	3.8 (1.6)	4.9 (1.9)	5.1 (2.1)	5.6 (2.1)
Alternating	0.0 (0.1)	4.9 (1.8)	5.8 (1.9)	6.2 (1.7)	6.5 (1.8)

Table 4.3 RPE-D Averaged Values for Each Time Point

The scores were recorded before exercise (Before), 20 seconds after each set of exercise denoted by Set 1, Set 2, and Set 3, and immediately after completion of the exercise (Set 4). The scores are recorded as a mean (SD).

There is very strong evidence (BF_{10} = 0.013) the RPE-E did not change differently over time across conditions. When examining main effects, there is extreme evidence (BF_{10} = 1.133e +125) that there is a main effect of time, but not a main effect of condition (BF_{10} = 0.104). Post hoc comparisons for time can be seen in Table 4.4. Averaged values for each time point can be seen in Table 4.5.

		Prior Odds	Posterior Odds	$BF_{10, U}$	error %
BEFORE	SET 1	0.320	8.697e +26	2.722e +27	1.854e -30
	SET 2	0.320	6.506e +34	2.036e +35	6.486e -38
	SET 3	0.320	1.894e +38	5.928e +38	3.255e -41
	SET 4	0.320	1.317e +41	4.122e +41	1.921e -44
SET 1	SET 2	0.320	102.688	321.394	8.711e -9
	SET 3	0.320	73.580	230.292	1.376e -8
	SET 4	0.320	1597.753	5000.668	5.196e -11
SET 2	SET 3	0.320	0.493	1.542	1.586e -6
	SET 4	0.320	391.657	1225.813	1.095e -9
SET 3	SET 4	0.320	139.976	438.099	5.592e -9

Table 4.4 RPE-E Post Hoc Comparisons of Time

The posterior odds have been corrected for multiple testing by fixing to 0.5 the prior probability that the null hypothesis holds across all comparisons (Westfall, Johnson, & Utts, 1997). Individual comparisons are based on the default t-test with a Cauchy (0, r =1/sqrt(2)) prior. The "U" in the Bayes factor denotes that it is uncorrected.

RPE-E	Before	Set 1	Set 2	Set 3	Set 4
Unilateral	0.0 (0.0)	7.7 (2.1)	8.4 (1.6)	8.6 (1.3)	9.0 (1.2)
Bilateral	0.0 (0.0)	7.3 (2.5)	8.2 (1.7)	8.4 (1.5)	8.9 (1.1)
Alternating	0.0 (0.0)	7.9 (1.7)	8.4 (1.5)	8.7 (1.4)	8.9 (1.5)

Table 4.5 RPE-E Averaged Values for Each Time Point

The scores were recorded before exercise (Before), and immediately after each set of exercise denoted by Set 1, Set 2, Set 3 and Set 4. The scores are recorded as a mean (SD).

4.3 Volume of Load Lifted

There was strong evidence (BF_{10} = 26.945) that changes in volume of work performed were different between conditions (Graph 16). Follow up comparisons show that ALT was greater than UNI [1946 (1787) kg vs. 945 (313) kg; BF_{10} = 3.355] and greater than BI [1946 (1787) kg vs. 918 (319) kg; BF_{10} = 4.310]. UNI and BI were not different between conditions [945 (313) kg vs. 918 (319) kg; BF_{10} = 0.282].

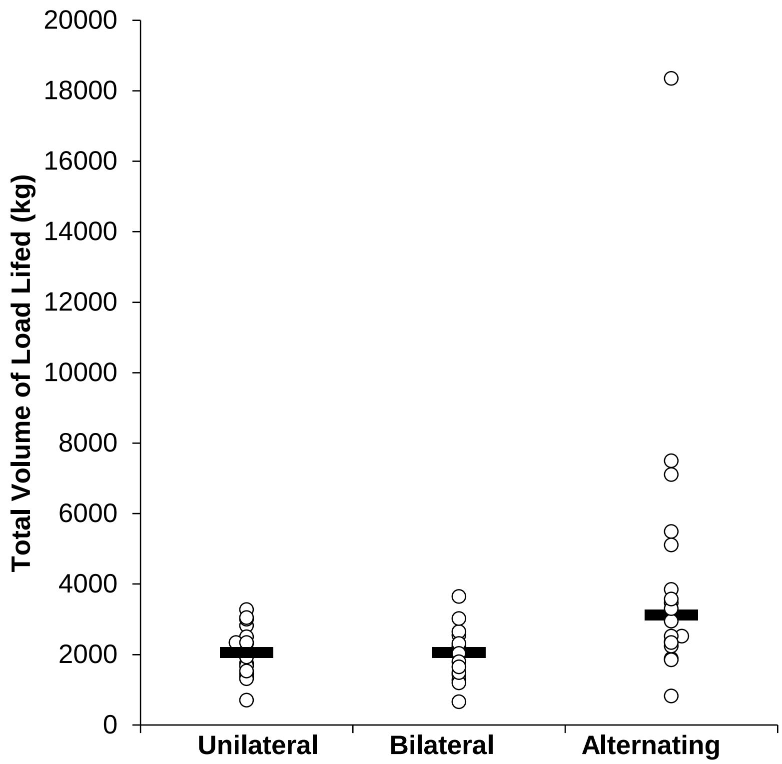

Figure 4.16 Averaged Total Volume of Load Lifted

Black filled circles represent the average score for all participants in that condition and the errors bars are standard deviations.

Correlations were looked at for each variable measured in each condition. For ALT there was moderate evidence for a positive correlation between volume and augmentation index (Pearson's r = .558; BF_{10} = 3.657), augmentation index when corrected for heart rate (Pearson's r = .671; BF_{10} = 9.727), and wave reflection (Pearson's r = .629; BF_{10} = 7.074) as seen in Graph 17. There was moderate evidence (Pearson's r = .522; BF_{10} = 3.293) for a positive correlation between volume and bSBP in UNI.

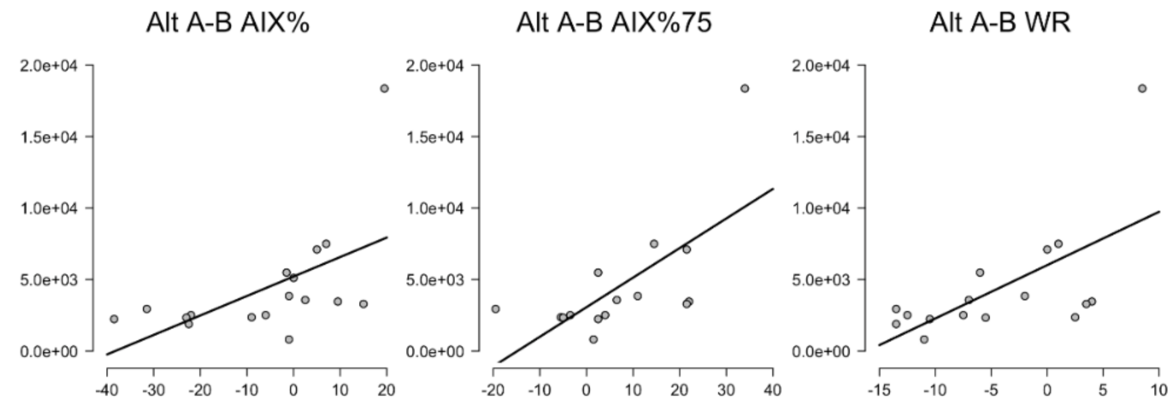

Figure 4.17 Differences in Augmentation Index, Augmentation Index Corrected for Heart Rate, and Wave Reflection

Open circles represent each participant score in the alternating condition when compared to total volume of load lifted. Alt = alternating; A-B = difference between before and after exercise; AIX% = augmentation index; AIX%75 = augmentation index when corrected for heart rate; WR = wave reflection.

CHAPTER V – DISCUSSION

5.1 Central hemodynamics with unilateral, bilateral, and alternating exercise

Populations at a disadvantage to exercise to their fully capacity could benefit from using BFR exercise. In addition, some of these populations at an increased cardiovascular risk may benefit from exercises that have a lower cardiovascular response. In this study, we looked at how different modalities of low-load knee extensions with BFR affected central and peripheral hemodynamics. When exercise occurs without blood flow restriction, there is localized muscle swelling in the exercising muscles and an accumulation of metabolites. Muscle metaboreceptors sense the accumulation of metabolites, send a signal up the afferent nerves to the brainstem, and the cardiovascular center responds by altering blood pressure, heart rate, and local and peripheral vasculature. When BFR is applied this can increase the build-up of metabolites in the muscle inducing a greater cardiovascular response than traditional exercise without BFR.

Previous studies have indicated that the cardiovascular response with BFR exercise is comparable to traditional moderate- and high-load training if blood flow is not occluded. Neto et al. looked at high-load exercise, low-load exercise, and low-load exercise with BFR (2016). The researchers saw no difference in double product or heart rate across conditions, but a significant increase from rest (Neto, et al., 2016). In addition, they looked are ratings of perceived exertion and found that there was a greater rating of perceived exertion in the legs in the low-load BFR condition when compared to a high-load (Neto, et al., 2016). Jessee et al. compared AOP from before and immediately after upper body exercise and found that if pressure applied or load was increased, then a greater AOP was necessary. AOP was a way for the researchers to immediately measure the participants cardiovascular response after the completion of exercise. In our study, we looked at central and peripheral cardiovascular measures using a SphygmoCor device. This allowed us to have a more reliable method for estimating cardiovascular risk. We tried to see if using a different exercise modality would elicit a different cardiovascular response.

In most central hemodynamic measurements, when there was evidence for differences between conditions there was usually evidence that the alternating form of exercise produced the greatest change from before exercise to immediately after. We also saw that there was usually evidence to support that there was no difference between the unilateral and bilateral conditions. When we looked at the amount of volume that each participant had for each exercise condition, there was evidence that participants had the greatest amount of volume during the alternating condition. RPE-D was not different between conditions over time, but the alternating condition had the greatest amount of perceived discomfort when compared to unilateral and bilateral exercise.

With the experimental design of this study, participants exercised to a metronome at 60 beats per minute. They were instructed to lift on a beat, and lower on a beat. For the unilateral and bilateral exercise conditions the exercising leg(s) did not have rest between repetitions. However, in the alternating exercise condition there was a 2 second rest for each leg because the participants were asked to raise and lower the randomized leg first on each beat, and then do the same thing for the opposite leg. This amount of time between legs could attribute for the greater volume of work performed by the participant in the alternating condition when compared to the unilateral or bilateral condition. The greater amount of volume could also contribute to the higher change in central cardiovascular measure like augmentation index, augmentation index corrected for heart rate, and wave reflection magnitude. We saw positive correlations for these values, so as volume increased, so did changes in augmentation index, augmentation index corrected for heart rate, and wave reflection magnitude.

In some of the central hemodynamic measure, like wave reflection magnitude, pulse pressure, augmentation pressure, and augmentation index there was evidence (moderate or anecdotal) that there were no changes from before to after exercise across conditions. However, this could be because the device used did not capture the wave form as quickly after the alternating condition, due to a greater cardiovascular response, as it did for the unilateral or bilateral condition because the device was designed to take resting measurements. The SpyghmoCor first takes an initial blood pressure, then inflates to a sub systolic pressure to estimate aortic cardiovascular measures. In some cases, it would take up to three minutes before the wave form was captured. This could give the cardiovascular system time to recover toward baseline values. Even 1-2 minutes after exercise has shown a significant decrease in heart rate (Javorka, Zila, Balharek, & Javorka, 2002). The device did not compute the augmentation index when corrected for heart rate for three participants that completed the alternating condition.

Three participants became dizzy, nauseous, or lightheaded immediately following or during the alternating condition. One participant was stopped before volitional failure because their last two sets of exercise were over 100 repetitions and we did not want to risk the possibility of rhabdomyolysis. These details are important to consider, because we were using healthy participants for this study. Based on previous studies without blood flow restriction, we did not expect the alternating condition to elicit a greater cardiovascular response than bilateral exercise or bilateral and unilateral exercise to not have significantly different results.

5.2 Results from previous studies without BFR

Matos-Santos et al. examined the cardiovascular response between unilateral and bilateral exercise. One of the biggest differences when compared to our study is that we had participants exercise both legs in the unilateral condition. In addition, participants in our study had 30 seconds of rest between sets, as common with BFR protocols, and were asked to exercise with 30% of their 1RM until they could no longer keep going. Matos-Santos et al. also used photoplethysmography with a Finometer to measure SBP, DBP, HR, RPP, SV, and CO before, after, and throughout the exercise conditions, but the device we used was unable to assess the cardiovascular response throughout exercise. However, we were able to get data on central hemodynamic instead of just brachial blood pressure measurements. In our study, only anecdotal evidence was found for changes in bSBP and bDBP when compared to the unilateral condition. We used the Bayesian inference for our statistical analysis so that we could compare the alternative (differences between conditions) hypothesis to the null (no differences between conditions) hypothesis. Where Matos-Santos et al. saw a significant difference between unilateral and bilateral exercise, we saw evidence that there was no difference between unilateral and bilateral exercise in post hoc comparisons. The differences in our results could be from several factors, but a very important factor is that we had the participants exercise both legs (randomized leg first for four sets and then the opposing leg for four sets) in the unilateral condition instead of just one. Matos-Santos did not report the volume of load lifted in the unilateral and bilateral condition, but since the participants were using 70% of their 12 repetition maximum for each set, with a standardized number of sets, then it can be assumed that participants had about half of the volume of work in the unilateral condition when compared to the bilateral condition. In our study, there was evidence to support no differences between bilateral and unilateral exercise in volume of work performed, but the unilateral had the greatest volume of load lifted with a greater cardiovascular response in many variables.

Moreira et al. conducted a study to examine HR, SBP, DBP, and RPP with different exercise modalities using 80% of their 10-repetition maximum for 3 sets of 10 repetitions. Participants used a knee extension machine, barbell rows, and bicep curls with unilateral, bilateral, and exercising conditions (performed 9 different exercises). The results from the knee extension machine showed no significant difference in HR, SBP, DBP, or RPP for the unilateral condition. Moreira et al. saw that the cardiovascular stress increased with additional sets of exercise. This is like what we saw as the participants had a greater RPE-E and RPE-D with additional sets of exercise. Moreira et al. investigated whether there was a different cardiovascular response depending on the muscle group used and the different exercise modalities. Moreira et al. also concluded that the bilateral exercise demanded a significantly greater cardiovascular response than unilateral or alternating exercise conditions. Again, this is different from the results that we found in our study.

We found that there was not a significant difference between unilateral and bilateral exercise. In addition, there was a greater cardiovascular response in the alternating condition when compared to unilateral and bilateral conditions. However, Moreira et al. also did not go into detail about their methods for conducting unilateral, bilateral, or alternating methods. Moreira et al. also did not report the volume of load lifted for each participant for each condition. This makes it more difficult to compare our current study with their results. However, since the researchers did not mention averaging together the unilateral condition, it seems that the participants only performed exercises on one leg for the unilateral condition. And, if participants were only performing 3 sets of 10 repetitions on one leg, then they may have been able to perform more repetition when compared to someone exercising both legs for the same exercise protocol.

In a study by Costa et al. they compared the use of bilateral and unilateral exercise by total volume of load lifted, blood lactate, and ratings of perceived exertion (2015). Costa et al. did not have a significant difference in the volume of load lifted between unilateral and bilateral conditions, which is like our study. The exercise protocol was similar with participants exercising to volitional failure for 3 sets with 2 minutes of rest between each set. In the unilateral exercise condition, one leg exercised entirely and then the participant switched legs. Costa et al. did not find a significant difference between unilateral and bilateral conditions, but there was a main effect of time where each set and five minutes after exercise was significantly different from before exercise. Costa et al. did not look at cardiovascular measures but saw that blood lactate is not different with unilateral and bilateral conditions of exercise. Similarly, we found that cardiovascular measures were not different between unilateral and bilateral conditions. In addition, Costa et al. found that as the sets increased there was an increase in ratings of perceived exertion. This is similar to what we found with our study with similar exercise protocol, but BFR added. These conclusions make sense because blood lactate is a marker of muscular fatigue and our methodology for unilateral and bilateral conditions both had participants exercise to fatigue. In addition, we saw that between unilateral and bilateral conditions total volume of load lifted was not different. This leads us to believe that when the volume of load lifted is not different with blood flow restricted exercise, then the cardiovascular response is not different because it is not engaging the exercise pressor response differently.

CHAPTER VI – CONCLUSION

Our study investigates the cardiovascular response to different exercise modalities with BFR and a low load. There was evidence to support the changes in cardiovascular measures, volume of load lifted, ratings of perceived effort, and ratings of perceived discomfort, were not different between the unilateral and bilateral conditions. In addition, we saw that the alternating exercise condition has the greatest cardiovascular response when compared to unilateral and bilateral exercise if there was evidence for a difference between conditions. In addition, the alternating condition had a greater volume of load lifted when compared to either the bilateral or unilateral condition. Whether or not the alternating condition at a low load combined with BFR should be avoided for people at an increased risk of a cardiovascular event warrants further research on the volume of load lifted during the condition.

APPENDIX A - Lab Equipment and Data Collection

Figure 6.1 SphygmoCor XCEL

This is the SphygmoCor XCEL device that was used to measure pulse wave analysis in participants.

Figure 6.2 SphygmoCor XCEL Example Set Up

This is an example of the SphygmoCor XCEL device on the arm of another person to measure pulse wave analysis.

Figure 6.3 SphygmoCor XCEL Participant Data

This is an example of the information needed prior to conducting pulse wave analysis. We input gender and date of birth. Other information was coded based on the participants experimental identification code.

Figure 6.4 SphygmoCor XCEL Lab Set-Up

This image represents our experimental set up with the SphygmoCor XCEL. We had the device on the cart pictured above and rolled to the left side of the participant.

Figure 6.5 Hokanson®10cm Cuff E20 Rapid Cuff Inflator

The Hokanson device was used to measure arterial occlusion pressure and reduce participants blood flow during the experiment.

HOW HARD DO YOU THINK
YOU'RE WORKING?

0	NO EXERTION
1	EXTREMELY EASY
2	
3	EASY
4	
5	SOMEWHAT HARD
6	
7	HARD
8	
9	VERY HARD
10	MAXIMAL EFFORT

Figure 6.6 Ratings of Percieved Effort (RPE-E)

This is the scale was used to quantify the participants ratings of percieved effort during exercise (Steele, Fisher, McKinnon, & McKinnon, 2017).

HOW MUCH DISCOMFORT
DO YOU FEEL?

0	NO DISCOMFORT
1	MINOR DISCOMFORT
2	
3	MILD DISCOMFORT
4	
5	MODERATE DISCOMFORT
6	
7	SEVERE DISCOMFORT
8	
9	VERY SEVERE DISCOMFORT
10	MAXIMAL DISCOMFORT

Figure 6.7 Perceived Discomfort (RPE-D)

This figure was used to quantify how much discomfort the participant felt (Steele, Fisher, McKinnon, & McKinnon, 2017).

Figure 6.8 Hammer Strength IL-LE

This is the machine used for the exercise protocol of this study.

Exclusionary Criteria Checklist	Yes	No
Are you less than 18 years old?		
Are you more than 35 years old?		
Do you have an orthopedic injury that would prevent resistance exercise in the lower body?		
Do you take medication that would influence heart rate or blood pressure?		
Have you exercised in the last 24 hours?		
Have you consumed alcohol within the last 24 hours?		
Do you regularly use nicotine products?		

Risk Factors for Thromboembolism

Do you take birth control pills?		
Have you had major surgery within the last six months?		
Have you been diagnosed with Crohn's or Inflammatory Bowel Disease?		
Have you had a past fracture of the hip, pelvis, or femur?		
Have you been diagnosed with varicose veins?		
Do you have a personal/family history of deep vein thrombosis?		
Do you have a personal/family history of pulmonary embolism?		
Do you have a body mass index of > 30? (we can calculate it)		

Restrictions

Are you able/willing to avoid caffeine 8 hours prior to a condition?		
Are you able/willing avoid exercise 24 hours prior to a condition?		
Are you able/willing to avoid alcohol 24 hours prior to a condition?		

Figure 6.9 Exclusion Criteria Checklist

This is the exclusion criteria checklist that was presented when participants came into the lab for the first time.

APPENDIX B – IRB Approval Letter

IRB-19-211 - Initial: Sacco Committee Letter - Expedited and Full

irb@usm.edu

Tue 5/14/2019 2:23 PM

To: Daphney Stanford <Daphney.Stanford@usm.edu>; Joonsun Park <Joonsun.Park@usm.edu>; Matthew Jessee <Matthew.Jessee@usm.edu>; Raymond Jones <Raymond.Jones@usm.edu>; Sue Fayard <Sue.Fayard@usm.edu>; Michaela Donohue <Michaela.Donohue@usm.edu>;

Office *of* Research Integrity

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NOTICE OF INSTITUTIONAL REVIEW BOARD ACTION

The project below has been reviewed by The University of Southern Mississippi Institutional Review Board in accordance with Federal Drug Administration regulations (21 CFR 26, 111), Department of Health and Human Services regulations (45 CFR Part 46), and University Policy to ensure:

- The risks to subjects are minimized and reasonable in relation to the anticipated benefits.
- The selection of subjects is equitable.
- Informed consent is adequate and appropriately documented.
- Where appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of the subjects.
- Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of all data.
- Appropriate additional safeguards have been included to protect vulnerable subjects.
- Any unanticipated, serious, or continuing problems encountered involving risks to subjects must be reported immediately. Problems should be reported to ORI via the incident template on Cayuse IRB.
- The period of approval is twelve months. An application for renewal must be submitted for projects exceeding twelve months.

PROTOCOL NUMBER: IRB-19-211
PROJECT TITLE: The cardiovascular and muscular responses to different exercise modalities with blood flow restriction.
SCHOOL/PROGRAM: School of Kinesiology
RESEARCHER(S): Daphney Stanford, Joonsun Park, Raymond Jones, Matthew Jessee,

IRB COMMITTEE ACTION: Approved
CATEGORY: Expedited

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

PERIOD OF APPROVAL: May 13, 2019 to May 12, 2020

Donald Sacco, Ph.D.
Institutional Review Board Chairperson

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