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The Blood Flow and Perceptual Response To Lower Body Resistance Training With and Without Blood Flow Restriction

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THE BLOOD FLOW AND PERCEPTUAL RESPONSE TO LOWER BODY RESISTANCE TRAINING WITH AND WITHOUT BLOOD FLOW RESTRICTION

A Dissertation

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by

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ABSTRACT

The muscular response to low-load resistance exercise in combination with blood flow restriction (BFR) is well studied but less was known about the cardiovascular response. It is also unknown what impact resistance exercise at 15% 1RM with or without BFR would have on the acute and chronic cardiovascular adaptations and how that compares to high load resistance exercise. Examining the perceptual responses across a training program is also important as this may dictate overall compliance to an exercise protocol. The purpose of this study was to determine the acute and chronic cardiovascular changes following very low-load (15% 1RM) resistance exercise with or without BFR and how it compares to high load (70% 1RM) resistance exercise.

Acute: An interaction occurred for systolic blood pressure. 15/0 [Pre-Post Δ: 19 (10) mmHg], 15/40 [Pre-Post Δ: 16 (12) mmHg], and 70/0 [Pre-Post Δ: 18 (12) mmHg] were higher compared to 15/80 [Pre-Post Δ: 5 (10) mmHg] post exercise. All conditions increased similarly from pre-post [overall average change of 3 (6) mmHg] for diastolic blood pressure and heart rate [overall average change 15 (10) bpm]. Only 15/0 [Pre-Post Δ: 4.5 (-1.4, 8.2) $ml \cdot min^{-1}$] and 15/40 [Pre-Post Δ: 2.7 (0.29, 6.6) $ml \cdot min^{-1}$] increased blood flow.

Chronic: There was an interaction for calf blood flow. 15/80 [0.613 (0.232, 0.995) ml per 100 ml^{-1} min^{-1}] and 70/0 [0.544 (0.162, 0.926) ml per 100 ml^{-1} min^{-1}] increased following 8 weeks of training. Further, 15/80 [7.9 (3.4, 12.3) flow $*10^2$ mmHg] and 70/0 [7.2 (2.7, 11.7)] increased calf vascular conductance. Calf venous compliance did not change. An interaction occurred for RPE. Condition 15/40 [-1.4 (-2.3, -0.431)] decreased from Visit 1-16. There was an interaction for discomfort where 15/80 [-0.479 (-1.3, 0.304)] did not observe any changes over time while all other conditions decreased. The current findings suggest that lifting a very low-load with a high pressure attenuated blood flow acutely, but long term produced similar adaptations compared to high load exercise; albeit with greater discomfort. Very low-load exercise with and without moderate BFR increased blood flow acutely but did not produce long term changes in the cardiovascular measurements.

DEDICATION

I want to dedicate this work to Tim and Jackie Mattocks for their support and encouragement throughout this dissertation.

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CHAPTER I: INTRODUCTION

Blood flow restriction is a method where an individual applies pneumatic cuffs at the most proximal portion of the limbs (i.e., upper thighs and upper arms) while performing low load resistance exercise (20-30% 1RM), low intensity aerobic exercise (~45% VO_{2max}), or even in the absence of exercise (1–3) in an effort to elicit favorable muscle adaptations. It has previously been observed that blood flow restriction combined with a low load can induce similar muscle growth as traditional high-load resistance training (2). In addition, blood flow restriction combined with low-intensity aerobic exercise such as walking or cycling have observed increases in muscle size and strength, although not to the degree seen with resistance training (1, 4). In general, the standard protocol for blood flow restriction is one set of 30 repetitions followed by three sets of 15 repetitions (5). When exercise is performed to failure with or without blood flow restriction, there is a similar increase in muscular size compared to traditional high load resistance training (6–8)

It is suggested that when applying the restriction pressure for blood flow restriction exercise, the pressure should account for the individual's limb circumference and the width of the cuff used (9, 10). Previous studies have applied an arbitrary pressure to individuals which may lead to an exaggerated cardiovascular response (11). A method to avoid applying an arbitrary pressure to all individuals is to measure the resting arterial occlusion pressure (lowest pressure at which blood flow is cut off) and apply a percentage of that. Ingram et al. (12) investigated arterial occlusion pressure at different time points throughout the day and found that arterial occlusion pressure differed depending on the time of day. This suggests that researchers applying a relative restriction pressure based on arterial occlusion pressure should measure each training visit rather than applying a pressure based on one measurement time point. Counts et al. (13) examined two different restriction pressures, a high restriction pressure (90% arterial occlusion pressure) and a moderate restriction pressure (40% arterial occlusion pressure). The authors observed a similar muscular response between both restriction pressures. Based on the aforementioned study, a higher restriction pressure provided no further benefit in the muscular adaptation compared to the moderate restriction pressure. However, Lixandrão et al. (14) suggested that a higher restriction pressure may be beneficial for muscle size when utilizing loads less than 30% 1RM (i.e. 20% 1RM), but it remains unknown if even lower loads can be effectively used for blood flow restriction exercise. Our lab has recently investigated the acute muscular response to three different resistance exercise loads (10,15%, 20% 1RM) combined with blood flow restriction while utilizing either 40% or 80% arterial occlusion pressure. We observed that the application of blood flow restriction with very low loads (10-15% 1RM) provided an acute muscle swelling response which was largely comparable to that observed with a load of 20% 1RM which is normally used within the blood flow restriction literature (Unpublished observations). Additionally, the decrement in torque immediately post exercise was greater when a very low load (10-15% 1RM) was combined with higher levels of blood flow restriction. This acute change in muscle swelling and torque provide potential insight into muscle adaptation as these acute changes are often associated with long term muscle growth (15, 16). Based on these results, it would seem that a load as low as 10% 1RM in combination with higher levels of blood flow restriction may be efficacious for long term adaptations in skeletal muscle. However, it is unknown what the cardiovascular response was during this study and what the chronic adaptations to the cardiovascular system are.

Exercise induced hyperemia often characterizes the muscle vasodilatory capacity which is regulated through a variety of factors (e.g. nitric oxide, prostaglandins, K^+-stimulated vascular hyperpolarization). Additionally, the sympathetic nervous system is the primary regulator of peripheral vascular resistance in skeletal muscle (17). During dynamic muscular contractions, an increase in skeletal muscle blood flow is due to the vasodilatory response (18). When observing the cardiovascular exercise response to resistance exercise in the lower body, there is a greater increase in blood pressure compared to the upper body which is due to a larger muscle mass involved which causes compression across a greater portion of the vasculature network (19). In general, the brachial and/or femoral artery are used to measure blood flow which is estimated from blood velocity by knowing the vessel diameter (20). An increase in blood flow causes an increase in shear stress which triggers the stimulation of angiogenesis which results in the formation of new capillaries (21). The increase in capillaries can improve oxygen diffusion into the muscle and the removal of metabolites from the muscle (21). When comparing blood flow responses to exercise there may be some differences between aerobic and resistance exercise. Recently, Spence et al. (22) observed that resistance training increased resting brachial and peak artery diameter, but not femoral artery diameter. The resistance exercises were mainly focused on the upper body but did incorporate some lower body resistance exercises as well. However, the resistance exercises that did involve the legs were not enough to elicit an increase in femoral artery diameter (22). It may be possible that additional lower body resistance exercises are needed to observe an increase in femoral artery diameter. In contrast, lower body aerobic endurance exercise increased resting femoral and peak artery diameter but not the brachial artery. These results suggest that the type of exercise can impact the blood flow response and/or be volume dependent.

Muscle adaptation to blood flow restriction exercise has been well documented; however, considerably less is known on the cardiovascular response to this type of exercise. When investigating the blood flow response to blood flow restriction in the lower body, previous studies (23, 24) have observed a decrease in blood flow at the superficial femoral artery; however, these studies applied the same pressure to each individual and it is unsure what the blood flow response would be if the authors had applied a relative restriction pressure.

Pilot work in our laboratory suggests that there are different blood flow responses midway through exercising (measurement was taken at rest in between sets) and following unilateral elbow flexion exercise at different pressures (i.e. 0% arterial occlusion pressure, 40% arterial occlusion pressure and 80% arterial occlusion pressure). During the rest period between set 2 and 3 of exercise, 80% arterial occlusion pressure suppressed the exercise-induced increase in blood flow compared to 0% and 40% arterial occlusion pressure. One minute following cuff deflation, there were no differences in blood flow in any conditions for the males but were for the females. However, this previous work has only examined this in the upper body and it is unknown what the blood flow response is in the lower body to different relative blood flow restriction pressures. Further investigation on this blood flow response in the lower body while also comparing it to traditional high load resistance exercise will provide further knowledge on this mode of exercise.

Other cardiovascular measurements examined within the blood flow restriction literature include calf vascular conductance and calf venous compliance. Following an acute bout of low load resistance exercise combined with blood flow restriction, calf vascular conductance did not increase compared to traditional high load resistance exercise. This may be due to blood flow restriction not having an impact on local arteriole vasodilation compared to traditional high load resistance exercise (25). However, when looking at calf vascular conductance following 6 weeks of resistance training, there was an increase in calf vascular conductance which may be due to be due to repeatedly stimulating angiogenesis which may have caused capillary growth.

Venous compliance has been shown to increase following 6 weeks of walking (26); however, this was not observed following resistance exercise (27). These conflicting results may be due to the modality of exercise. Iida et al (26) involved walking which directly involves the calf muscle while Fahs et al. (27) performed knee extension exercise which does not directly involve the calf muscle.

Another important factor to consider when resistance exercising with blood flow restriction is the perceptual responses associated with its use (ratings of perceived exertion (RPE) and discomfort). This may be important for individuals exercising with blood flow restriction as high RPE and discomfort ratings may cause the individual not to perform this type of exercise. When applying a similar restriction pressure, a wider cuff induced greater pain and perceived effort compared to a narrow cuff which may be due to greater restriction of blood flow (28). Moreover, when the cuff size is similar between conditions but different restriction pressures are applied, the higher restriction pressure often induces a greater perceptual response compared to a low to moderate restriction pressure (13, 29).

Due to the limited research investigating resistance exercise using very low loads (<20% 1RM) combined with blood flow restriction or alone, the hemodynamic response to this type of exercise in the lower body is largely unknown. The application of blood flow may be beneficial for individuals who are relatively weak such as individuals following ACL surgery, the elderly, and possibly astronauts following space flight. Although exercising to failure without blood flow restriction results in favorable muscular adaptations (8), there is likely a point where the load is too low for this method to be efficacious as it does not create a high enough pressure within the muscle to reach fatigue. Therefore, the application of blood flow restriction may be needed in order to see favorable adaptations at very low relative loads. Examining the acute and chronic differences in the hemodynamic response between different resistance training protocols will also provide a better understanding on the hemodynamic response to different forms of resistance exercise.

Purpose

To determine the acute changes in blood pressure and blood flow following resistance exercise with and without different levels of blood flow restriction while using a very low load (15% 1RM) and traditional high load (70% 1RM). In addition, we wanted to determine the chronic changes of calf vascular conductance, calf venous compliance, and perceptual responses (RPE and discomfort) following 8 weeks of very low load resistance exercise with and without different levels of blood flow restriction and see how that compares with traditional high load resistance exercise.

Research Questions

1. Were the acute changes in blood pressure and blood flow similar between conditions using 15% 1RM with or without blood flow restriction and traditional high load resistance exercise (70% 1RM)?

2. What was the effect of resistance training using a very low load (15% 1RM) with or without blood flow restriction on calf vascular conductance and calf venous compliance and how did this compare with traditional high load resistance training (70% 1RM)?

3. What were the perceptual responses (RPE and discomfort) to resistance training at a very low load (15% 1RM) with or without blood flow restriction and how did it compare to traditional high load (70% 1RM) resistance exercise?

Hypotheses

1. It was hypothesized that blood pressure would be greatest following traditional high load resistance exercise compared to other exercise conditions. Further, blood pressure would be greater at a restriction pressure of 80% arterial occlusion pressure compared to a restriction pressure of 40% arterial occlusion pressure. Resistance exercise at very low loads without blood flow restriction would have the lowest blood pressure change.

2. It was hypothesized that participants performing very low load resistance exercise with blood flow restriction (40% and 80% AOP) would have similar post-exercise blood flow values compared to low load resistance exercise without blood flow restriction and traditional high load resistance exercise.

3. It was hypothesized that calf vascular conductance would increase in all conditions following 8 weeks of resistance training.

4. It was hypothesized that calf venous compliance would not change in any of the conditions but would remain similar to their respective baseline values following 8 weeks of resistance training.

5. It was hypothesized that RPE and discomfort ratings would be greatest for traditional high load training compared to very low load resistance training alone or combined with blood flow restriction. Also, a restriction pressure of 80% arterial occlusion pressure would produce a greater RPE and discomfort rating compared to a restriction pressure of 40% arterial occlusion pressure.

Significance of Study

The literature on the blood flow response in the lower body to resistance exercise with or without blood flow restriction is limited. Studies that have examined the blood flow response in the lower body have mainly utilized arbitrary pressures which is a methodological limitation and have examined the blood flow response using loads between 20%-30% 1RM. When lifting a load at 30% 1RM to volitional failure, it has been observed that there is an increase in muscle size and strength similar to high load resistance exercise (8, 30). A load of 30% 1RM seems to be heavy enough to induce failure through reductions in blood flow by increasing the intramuscular pressure (31). However, it is unknown if a load <20% 1RM can create a high enough intramuscular pressure by contraction induced reductions in blood flow to induce muscular failure. Applying blood flow restriction can cause blood flow to be artificially reduced which may help create an environment necessary to induce fatigue when exercising with a load <20% 1RM. Furthermore, it is unknown what impact exercising at 15% 1RM will have on the blood flow response in the lower body. Using loads at 15% 1RM combined with or without blood flow restriction may be beneficial for individuals who are coming off ACL surgery, athletes, the elderly, and possibly astronauts following space flight. This study determined the blood flow and perceptual responses while using very low loads alone or combined with blood flow restriction and how it compared to traditional high load resistance exercise.

Assumptions

1. Participants would give maximal effort for all resistance exercise protocols.
2. Participants would comply with directions prior to testing.
3. Participants would maintain their current level of physical activity and diet.
4. Ultrasound was used to measure blood flow velocity.

Delimitations

1. The findings of this study were only applicable to men and women between the ages of 18-35 years.
2. The participants were willing volunteers and do not represent a true random sample.

Limitations

1. Due to the nature of our study design, the resistance exercise protocol was performed unilaterally and not bilaterally.
2. Previous blood flow restriction studies have measured blood flow at the superficial femoral artery; however, due to equipment availability and cuff width, blood flow would be measured at the posterior tibial artery.

3. The width of the cuff was 10 cm and the blood flow and perceptual responses may differ with different size cuffs

Operational Definitions

1. Arterial occlusion pressure (AOP) - The lowest pressure at which blood flow at the posterior tibial artery is no longer present

2. Rating of Perceived Exertion (RPE) – A rating on how hard and strenuous the exercise feels to the participants on a scale of 6-20.

3. Rating of Discomfort – A rating from 0-10+ on how uncomfortable the exercise is based on their previous worst discomfort.

4. Blood flow velocity – A measurement of change in blood pressure and vessel resistance

5. Pulse wave ultrasound – A measurement made by B-mode ultrasound to determine blood velocity

6. Calf vascular conductance – A measurement of resistance vessel blood of the arterioles and capillaries

7. Calf venous compliance – A measurement of elastic properties of the veins

CHAPTER II: LITERATURE REVIEW

Blood Flow Regulation

When an individual begins to exercise, blood flow and shear stress increase in the active region to meet the increase in metabolic demands (32). The sympathetic nervous system plays a role in regulating cardiovascular factors in which an increase in activity results in an elevated cardiac output and peripheral vasoconstriction (17). An increase in sympathetic activity can be due to a direct effect of the central command, sensory inputs via group III and IV nerve fibers from active skeletal muscles, and the baroreceptors which can reset their operational thresholds or set points (33). An increase in blood flow in the active skeletal muscle is regulated by local vasodilatory mechanisms along with an increase in arterial pressure and cardiac output (34). It has been demonstrated that as intensity is increased there is an increase in blood velocity and blood flow (35, 36). It has also been suggested that the initial increase in blood flow from muscular contractions is mainly due to muscle-mechanical factors (phase one) followed by vasodilation (second phase) (36, 37). This transition from the first phase to the second phase causes the arterial blood pressure to drop momentarily and then increase again (36). Given the suggestion that there is no delay between phases, the increase in arterial inflow is likely caused by the redistribution of blood flow from other vascular beds (38). Nonetheless, blood flow becomes stable within 30-150 seconds of work depending on intensity (i.e. higher intensity requires a longer time to plateau) (20, 36).

When an individual begins to perform lower limb exercise (e.g. cycling), blood flow to the upper limbs decreases but later increases as exercise continues (39, 40). For example, Green et al. (40) had individuals perform 15 minutes of lower limb cycling and measured blood flow in the brachial artery. The authors found that mean blood flow decreased in the initial work stage but gradually increased as the workload increased. It is suggested that the initial decrease in brachial blood flow when performing lower limb exercise is due to blocking nitric oxide synthase (41).

A Doppler ultrasound is a device generally used to determine muscle blood flow (20, 36, 42). The vessel diameter has to be known to estimate blood flow from blood velocity. Previous studies have utilized Doppler ultrasound to determine femoral and brachial artery inflow in forearm and knee-extensor muscles (36, 41). Other tools to measure cardiovascular function include vascular conductance and venous compliance. When using vascular conductance, Anton et al. (43) found that limb blood flow and vascular conductance increased following 13 weeks of resistance training which may be due to a decrease in vasoconstriction activity. This may be important as a reduction in basal limb blood flow is associated with the development of the metabolic syndrome (44). Venous compliance is a determinant of the venous pooling during orthostatic stress in which a high compliance outcome represents less tolerance to orthostatic stress and a low compliance outcome represents a decrease in the elastin-to-collagen ratio of the venous wall (45, 46). Previous studies have shown that endurance exercise improves venous compliance which may be important to prevent orthostatic intolerance (46, 47). This increase in venous compliance may increase tonic nitric oxide and/or reduce sympathetic α-adrenergic vasomotor tone. Although increasing compliance may be a positive benefit, it may also lead to greater incidence of orthostatic intolerance if veins become too compliant (47). Therefore, it seems likely that venous compliance is on a continuum and that there is some range to be in. The majority of the data on venous compliance is related to endurance exercise and little is known on the effects of resistance exercise. Since the goal of blood flow restriction is to occlude venous return, venous compliance might be negatively affected by blood flow restriction due to the pooling of blood in the venous system. By comparing different resistance exercise protocols, this may provide a better understanding of the changes in the vascular structure and function following different forms of resistance exercise.

Blood Flow Mechanisms

Upon skeletal muscle contraction, arterial blood inflow may be blocked or retrograded followed by an increase in blood flow due to refilling of the vascular bed (36). In general, mechanical and vasodilatory factors play a role in the elevated blood flow during dynamic contractions (37, 42). One proposed mechanical mechanism is the venous emptying produced by muscle contraction. A decrease in venous pressure through venous emptying would stimulate blood flow from the arteries into the reduced venous sections (37). Moreover, it seems that contraction intensity (workload) rather than frequency is primarily contributing to the initial increase in blood flow (48).

Local vasodilatory responses are another proposed mechanism that contributes to the initial increase in blood flow. Some vasodilator pathways that are thought to contribute to this response include K^+-stimulated vascular hyperpolarization, nitric oxide, vasodilating prostaglandin, endothelium-derived hyperpolarizing factor, and possibly ATP (18, 49). For instance, Crecelius et al.(18) observed that if K^+ -mediated vascular hyperpolarization, nitric oxide, and vasodilating prostaglandin synthesis were inhibited, peak and total vasodilatory responses were significantly reduced. When examining blood flow through Doppler ultrasound, Tschakovsky et al. (50) observed that following one forearm contraction, blood flow increased over three cardiac cycles.

When transitioning to steady-state blood flow, vasodilator accumulation, shear-induced vasodilation, and red blood cell deoxygenation are all mechanisms that may be contributing to this transition (42). Conversely, it seems that there are conflicting results on whether the initial increase in blood flow is induced mechanically or by local vasodilatory factors. It could be that both mechanisms are occurring together and acting synergistically to increase blood flow (50).

Vascular Adaptation

Determining the vascular adaptations to exercise are important to consider as individuals who have hypertension or type 2 diabetes mellitus have impaired endothelial function and regulation of vascular tone (51). Hambrecht et al. (52) investigated the effects of exercise on endothelial function in the left internal mammary artery of patients with coronary artery disease. The patients performed three 10 minute bouts on the row and bicycle ergometer throughout the day for 4 weeks. The authors found that phosphorylation at the endothelial nitric oxide synthase (eNOS) Ser^{1177} site significantly increased and that exercise activates eNOS through a shear stress-induced/Akt-dependent increase which leads to an improvement in endothelial function (52).

Resistance vessels are arterioles that respond to muscular contractions which can affect the blood flow response. When investigating the impact of resistance exercise on resistance vessels, Maiorana et al. (53) examined individuals with type 2 diabetes and found that 8 weeks of total body resistance exercise performed three times a week in the lower body improved endothelial function (how well the endothelium releases nitric oxide). Endothelial function was determined by flow-mediated dilation (FMD) which measures the vessel dilation in response to nitric oxide. Moreover, Beck et al. (54) observed that both resistance training and endurance training enhanced resistance vessel endothelial function in pre-hypertensive individuals possibly by upregulating nitric oxide signaling. Based on these studies, it seems that exercise improves endothelial function in individuals with already impaired function. However, the impact of resistance exercise on endothelial function in healthy adults is less clear. A previous study found that aerobic plus resistance exercise did not improve vascular function (ability to produce nitric oxide) in healthy adults which may indicate that endothelial function was unaltered (55). The authors suggest that healthy individuals may not be able to further increase the vasodilatory system from exercise but individuals who have endothelial dysfunction can (56).

Resistance training may also have an effect on arterial compliance which represents the elastic properties of the arteries. A decrease in arterial compliance has been associated with an increase in blood pressure, heart disease, and reduced baroreflex sensitivity (57). A previous study (58) examined healthy individuals and observed that resistance exercise decreased arterial compliance (increased artery stiffness). However, in contrast to the previous finding, other research studies (59, 60) have found that healthy individuals who resistance train can increase arterial compliance and may prevent a decrease in limb blood flow by reducing vasoconstriction activity. Due to conflicting results on the impact of resistance exercise on vascular function, it may be that exercise intensity or modality may be playing a role.

What is Blood Flow Restriction?

In 1966, during a Buddhist ceremony, Yoshiaki Sato’s leg became numb while kneeling on the floor. He noticed swelling and discomfort in his calf area comparable to performing strenuous calf-raise exercises (61). This event inspired him to develop a method of training termed KAATSU. It is said that Sato created devices using bicycle tubing where he experimented with optimal positioning of the device on the limb as well as the pressure in order to reduce blood flow to the active muscle. After vast amounts of trial and error, KAATSU training was generalized for public use in 1983 (61). Moreover, Sato went on to develop pressurized cuffs with pressure sensors (KAATSU Master/Mini) allowing the individual to regulate the restriction pressure. Given that KAATSU is the name of a company, the technique is more commonly known as blood flow restriction. This method of exercise has gained a lot of attention as an alternative technique that can promote muscle hypertrophy while utilizing low loads (20-30% 1RM) and reducing mechanical stress to the joints. In addition, blood flow restriction has been utilized successfully in the rehabilitation setting (3) and improving sports performance in athletes (62).

Safety of Blood Flow Restriction

One question of blood flow restriction exercise is the overall safety of this type of training. A common concern with blood flow restriction exercise is the theoretical risk of developing a blood clot. Clark et al. (63) compared high load resistance exercise to low load blood flow restriction exercise and observed that both conditions enhanced fibrinolytic activity (breakdown of blood clots). This has also been observed in individuals with ischemic heart disease (64). It has been suggested that vascular compression alone can stimulate fibrinolytic activity (65) without increasing the coagulation system and that resistance exercise in general can increase fibrinolytic activity (66). Therefore, the increase in fibrinolytic activity may be due to resistance exercise, the application of blood flow restriction, or both. Another concern with blood flow restriction exercise is muscle damage. A study by Wernbom et al. (67) examined if low load resistance exercise with or without blood flow restriction resulted in muscle damage. In this study, the blood flow restriction condition performed five sets of exercise to volitional failure while the free flow limb performed the same number of sets and repetitions. The authors observed that blood flow restriction exercise resulted in a prolonged reduction in maximal voluntary contraction compared to the free flow limb which they suggest was due to muscle damage (67). Using a similar study design by Wernbom et al. (67), Loenneke et al. (68) did not observe prolonged decrements in torque and observed that torque returned to baseline within 24 hours. Furthermore, Thiebaud et al. (69) examined concentric and eccentric exercise with blood flow restriction in the upper body and observed that all markers of exercise induced muscle damage (e.g. torque, arm circumference, range of motion, etc.) returned back to baseline within one day which suggests that exercise induced muscle damage may not be occurring to a large degree with this type of exercise. Overall, when blood flow restriction is performed appropriately, it can be a safe and effective alternative to traditional high load resistance exercise (70).

Application of Blood Flow Restriction

An assortment of devices utilizing an elastic pneumatic cuff (62), nylon pneumatic cuff (9), elastic wraps (71) or even standard blood pressure cuffs (72) have been applied within the literature to restrict blood flow during exercise. In addition, a variety of cuff widths (3cm – 18cm) have been applied throughout the literature (14, 73, 74). In a research setting, inflatable pneumatic cuffs are used during blood flow restriction exercise which is regulated by a pressure device (e.g. Hokanson). It is important to consider the individual’s limb circumference and width of the cuff being used when applying a restriction pressure to the individual (10). A previous study showed that a wide cuff (13.5cm) induced a greater cardiovascular response (e.g., blood pressure and heart rate) compared to a narrow cuff (5cm) when inflated to a similar restriction pressure (28). Loenneke et al. (74) examined different factors (i.e. limb circumference, blood pressure, and limb composition) that should be accounted for when applying a restrictive pressure to the lower body. The authors found that thigh circumference, regardless of thigh composition, explained the most unique variance in arterial occlusion pressure. Crenshaw et al. (75) examined four different cuff widths (4.5 cm, 8 cm, 12 cm, and 18 cm) on eliminating blood flow to the lower body and established that a wider cuff (18 cm) occluded blood flow at a lower restriction pressure compared to a narrow cuff (4.5 cm). This has recently been supported in the blood flow restriction literature by Loenneke et al. (74) who found that a wider cuff requires less inflation to reach arterial occlusion. Additionally, this has been observed in the upper body (9).

Previous blood flow restriction studies have applied the same restrictive pressure to each individual which may be considered a potential safety concern as it could lead to an exaggerated cardiovascular response (11, 76). For example, setting the same restriction pressure to all individuals may restrict blood flow to a greater extent in some individuals and may cause some individuals to be under complete arterial occlusion (no arterial inflow). Therefore, when applying inflation pressure to the cuff, it should be individualized to the limb to which it is being applied. The aim of blood flow restriction is to reduce arterial inflow and occlude venous return causing venous pooling around the working muscle. A method that is often applied within the literature is to set the restrictive pressure based on brachial systolic blood pressure (130% SBP). However, previous findings suggest that the restrictive pressure in the lower body be based on thigh circumference and width of the cuff used for exercise rather than brachial systolic blood pressure

(SBP) as this explains little unique variance in arterial occlusion (74, 77). One proposed method to make the restriction pressure relative to the individual is to the take resting arterial occlusion pressure of the limb (pressure to cut off blood flow momentarily) and apply a percentage of that pressure. For example, commonly applied relative pressures for blood flow restriction include 40% and 80% of resting arterial occlusion pressure (2, 13). Since the equipment used to measure resting arterial occlusion has a maximum capacity of 300 mmHg (E20 Rapid Cuff Inflator, Hokanson), a narrow cuff may not completely restrict blood flow in individuals who have larger limbs. Therefore, if applying a narrow cuff to the lower body, using a percentage based on estimated arterial occlusion determined from thigh circumference may be more pragmatic (78, 79). In theory, by applying a percentage of the resting arterial occlusion pressure to each individual, this method will ensure that all individuals will receive a similar stimulus and lessen the chance of an adverse cardiovascular event (11).

Blood Flow Restriction Perceptual Responses

The perceptual responses (RPE and discomfort) to blood flow restriction exercise are often compared to unrestricted resistance exercise (80, 81, 82, 83, 84,85) or to different cuff widths (28, 86). Previous research has shown RPE and discomfort to be greater with blood flow restriction resistance exercise compared to unrestricted resistance exercise despite completing less work (80, 82, 83, 85). For example, Loenneke et al. (82) performed low load resistance exercise with or without blood flow restriction in the lower body and observed that RPE and discomfort were rated greater compared in the blood flow restriction condition compared to unrestricted exercise. When examining the perceptual responses between different cuff widths, Rossow et al. (28) found that a wider cuff (13.5cm) induced a greater RPE and pain rating compared to a narrow cuff (5cm) despite performing less work in the knee extension exercise which may be due to greater vascular restriction.

A recent study compared the perceptual ratings of blood flow restriction to traditional high load training in untrained individuals (84). The authors examined the time course of RPE and pain response over six training sessions and observed that the ratings were highest during the first session but gradually decreased over time. Interestingly, the traditional high load exercise triggered a greater RPE in all sessions compared to blood flow restriction exercise. In contrast, blood flow restriction caused a greater pain rating, however, this response was attenuated with continued use (84). One methodological limitation in the aforementioned study is that the authors applied an arbitrary pressure which may have inflated the perceptual response to exercise. When the restriction pressure was made relative to the individual (50% AOP), blood flow restriction exercise still caused a greater discomfort rating initially compared to traditional high load exercise but decreased over time and was similar to traditional high load exercise (81).

The perceptual responses to blood flow restriction across different levels of restriction has been observed in the upper body (13, 29, 87) while there is limited data in the lower body (83). Loenneke et al. (83) observed that individuals who performed knee extension using 20% 1RM gave a greater RPE rating when the restriction pressure was increased from 40% to 50% arterial occlusion pressure. However, this was not observed with 30% 1RM which suggests that the restriction pressure being applied may modify RPE and discomfort ratings when lifting at 20% 1RM.

Blood Flow Restriction Resistance Exercise Cardiovascular Response

The practice of blood flow restriction is normally used to increase muscular strength and size while the cardiovascular response is less considered. Examining the short-term and long-term cardiovascular responses to blood flow restriction exercise should be investigated as this method of training can elevate the sympathetic nervous system and increase the chance of a cardiovascular related event in healthy and diseased individuals (11). For instance, Takano et al. (24) reported a greater heart rate and blood pressure response to knee extension exercise with blood flow restriction compared to a repetition matched control without blood flow restriction. In addition, stroke volume decreased in the blood flow restriction condition which is explained by the decrease in venous return (24). This observed elevated heart rate and blood pressure response to blood flow restriction resistance exercise is also supported by Rossow et al. (28). The elevated cardiovascular response could be due to the combination of external mechanical compression from the cuff and muscular compression (the muscle contraction itself) of the vascular tree which may augment the exercise-induce pressor response (28). A methodological limitation of the aforementioned studies is that the authors applied a restriction pressure of 130% bSBP which may have exacerbated the response. However, heart rate and blood pressure returns back to baseline within 5 minutes post exercise (28). Interestingly, a recent study observed that heart rate was the highest following traditional high load and low load resistance exercise compared to low load resistance exercise with blood flow restriction (88). Despite blood flow restriction having a lower heart rate, it did have greater blood pressure values and a decrease in stroke volume which agrees with previous studies (24, 28)

Investigating the blood flow response to low load resistance exercise with blood flow restriction in the lower body is limited. Takano et al. (24) and Iida et al. (23) examined the blood flow response to blood flow restriction at the superficial femoral artery. Takano et al.(24)

measured blood flow before and after the application of blood flow restriction and before releasing the pressure after exercise. This study found that blood flow decreased after the cuffs were inflated and remained below resting blood flow values after exercise (before cuff deflation). Furthermore, Iida et al. (23) showed that as the restriction pressure increases, blood flow decreases proportionally. Recently, Downs et al. (88) examined the blood flow response to four different exercise conditions going to volitional failure; low load resistance exercise, high load resistance exercise, low load resistance exercise with blood flow restriction with a high restriction pressure, and low load resistance exercise with blood flow restriction with a low restriction pressure. At rest, they observed that the higher restriction pressure condition decreased blood flow below resting values to a greater extent than the lower restriction pressure condition which is agreement with previous studies (23, 24). During exercise, the higher restriction pressure attenuated the exercise-induced increase in blood flow where blood flow did not reach to resting values while all other conditions observed an increase above resting values (88).

Basal limb blood flow and vascular conductance are measurements associated with cardiovascular health (44). It has been reported that limb blood flow and vascular conductance both decrease with age potentially due to an increase in sympathetic vasoconstrictor nerve activity (44). However, traditional high load and low load resistance exercise has been shown to increase basal femoral blood flow and vascular conductance (43, 89). Another important marker for cardiovascular health is limb venous compliance. Orthostatic stress causes blood to shift from the thoracic region to the lower body which can reduce central blood flow and cardiac preload and can elevate heart rate and sympathetic nerve activity (47). Reducing the responses from orthostatic stress can be accomplished by preventing the fluid shift into the legs, thus suggesting that limb compliance is important in determining the degree of stress to the cardiovascular system (47).

A previous acute study examined vascular conductance to three different resistance exercise protocols; low load resistance exercise with blood flow restriction, low load resistance exercise without blood flow restriction, and traditional high load resistance exercise (25). The authors found that traditional high load resistance exercise increased calf vascular conductance compared to blood flow restriction resistance exercise. The increase in vascular conductance may be due to a greater change in local arteriole vasodilation which can be explained by mechanically induced vasodilation or flow-mediated mechanisms (25). The continuous contracting and relaxing of the skeletal muscle creates a “muscle pump” which causes potassium ions, adenosine, and nitric oxide to be released from the muscle to the arterioles (90). Additionally, membrane hyperpolarization and calcium efflux may also be responsible for an increase in blood flow (91). The lack of increase in vascular conductance from the blood flow restriction condition may be due a decline in flow mediated vasodilation mechanisms. In addition, it may be that the workload or force of contraction caused lower levels of mechanical vessel distortion which may result in a lower blood flow response compared to high load resistance exercise. Moreover, the same research group further investigated the chronic (~6 weeks) vascular effects (vascular conductance) following low load blood flow restriction, moderate load, and high load resistance exercise (92). The authors found that low load blood flow restriction was able to increase vascular conductance and calf blood flow which suggests that there was an increase in arteriole numbers and/or capillaries in parallel and that this type of training does not appear to have harmful effects on the vascular system (92). The increase in capillaries can be stimulated by shear stress, passive stretch of the tissues, and/or metabolic changes (21). It is also possible that vascular endothelial growth factor (VEGF) played a role as VEGF may promote angiogenesis which can respond to mechanical and/or metabolic changes (24). The muscle contraction can stimulate capillary growth through sprouting angiogenesis while shear stress stimulates growth by longitudinal splitting of existing capillaries (21). Furthermore, a hypoxic like environment can prompt HIF1-α expression which is a transcription factor for VEGF expression (21).

When examining the vascular adaptations following 6 weeks of resistance exercise to volitional failure, blood flow restriction did not increase calf vascular conductance or venous compliance. However, the free flow limb was able to increase calf vascular conductance which could be due to a local mechanism (e.g. nitric oxide bioavailability) (27). Since the free flow limb had greater total training volume compared to the blood flow restriction condition, it is possible that the greater number of contractions and relaxations of the skeletal muscle may have impacted vasodilation factors (i.e. nitric oxide) and thus resulted in greater blood flow (90). Blood flow restriction did not increase calf venous compliance as the authors hypothesized; however, a previous study (26) did observe an increase in calf venous compliance following six weeks of walking with blood flow restriction. This lack of increase in calf venous compliance could be due to the lack of number of training sessions, the duration under blood flow restriction, and/or the type of exercise (knee extension versus walking) (27). Further investigation of blood flow restriction exercise on limb venous compliance from resistance exercise is needed.

Blood flow restriction exercise can be a substitute to traditional high load resistance exercise as it uses low loads and reduces mechanical stress to the joints. In general, blood flow restriction elevates heart rate and blood pressure to a greater degree during exercise compared to unrestricted resistance exercise, however, these responses return to baseline within 5 minutes.

Due to the implications of blood flow restriction exercise, it is important to gain a better understanding of the cardiovascular system to this type of exercise.

CHAPTER III: METHODOLOGY

Experimental Design #1 (Acute)

Ninety-one participants visited the Kevser Ermin Applied Physiology Laboratory on two separate occasions. During the first visit, participants filled out an informed consent and after confirming that they did not meet any exclusion criteria, height and body mass was measured using a standard stadiometer and an electronic scale. Next, the participant performed a one-repetition maximum (1RM) for the knee extension exercise in one leg (randomized). Upon completion of 1RM testing, a 10 minute seated rest period was provided. Following this rest period, resting blood flow of the exercising limb was taken at the posterior tibial artery. After the resting blood flow measurement, blood pressure was taken. If the participant was randomly selected to a blood flow restriction condition, arterial occlusion pressure was determined in the exercising limb (randomized) after the blood pressure measurement. To illustrate, participants had a 10 cm nylon cuff placed at the top of their thigh. The pressure was increased until there was a cessation of blood flow to the distal portion of the limb as detected by a Doppler probe. The cuff was then deflated. The participant then performed one of four conditions. The participant exercised with or without cuffs inflated and the load was randomly assigned as either 15% or 70% of the individual's 1RM. When using a load of 15% 1RM, the exercise protocol consisted of 4 sets to volitional failure/90 repetitions (whichever came first) with 30 second rest periods. The high load exercise (70% 1RM) condition consisted of 4 sets to failure with 90 second rest periods. For blood flow restriction, a restriction pressure of 40% or 80% of resting arterial occlusion pressure was applied while exercising at 15% 1RM for 4 sets to volitional failure/90 repetitions (whichever came first) with 30 second rest periods. Following the final set of exercise blood pressure and blood flow was measured.

Inclusion Criteria

1. Male and Female
2. Anyone between the ages of 18-35 years
3. No orthopedic issues preventing strength testing or exercise
4. Individuals who did not use any tobacco related products (cigarettes, cigars, chew/snuff, etc.)
5. Individuals who were not on hypertensive medication
6. Individuals who were not obese based on a Body Mass Index of ≤ 29.9 kg/m^2

Exclusion Criteria

1. Outside the age range of 18-35 years
2. Currently using a tobacco related product (cigarettes, cigars, chew/snuff, etc.)
3. Classified as obese based on a Body Mass Index of ≥ 30 kg/m^2
4. Individuals who were on hypertensive medication
5. Having more than one risk factor for thromboembolisms (Motykie et al.(93))
    a. Diagnosed Crohn's or Inflammatory Bowel Disease
    b. Past fracture of a hip, pelvis, or femur
    c. Major surgery within the past 6 months
    d. Varicose veins
    e. Family history of deep vein thrombosis or pulmonary embolism

Standing Height and Body Mass

Height was measured to the nearest 0.5 cm using a stadiometer with participant's head in a horizontal position, shoulders back, and heels together (60°). Body mass was measured using an electronic scale to the nearest 0.1 kg with participants wearing minimal clothing such as a t-shirt and shorts.

Brachial Blood Pressure

Participants had 10 minutes of seated rest in a quiet room. Brachial blood pressure was determined using an automated blood pressure machine (Omron #HEM-907XL) using an appropriately sized cuff. Blood pressure was taken before and after exercise.

One Repetition Maximum (1RM)

The heaviest weight that can be lifted one time with good form was record as the individual's 1RM. The participants performed a 1RM for one leg. First, the seat was adjusted accordingly for each participant. The participants were instructed to have their arms crossed over the chest to ensure strict form and to avoid extra movement. In addition, a seat belt was crossed over the waist and pulled securely. A pre-set bar was used to determine full knee extension and only those attempts that touched the pre-set bar was counted. Participants warmed up with a relative low load estimated at 30% 1RM. Following this brief warm-up, the load was adjusted to an estimated 1RM and the first attempt was made. The first attempt was estimated off of how the individual's warm-up looked to the investigators and how the warm-up felt to the participant. As participants got closer to their 1RM, the load was either increased or decreased in 1.25 kg increments until a 1RM was obtained (usually within 5 attempts). A period of 90 seconds of rest was given between each attempt.

Blood Velocity Measurements

The participant's leg was supported by a bench with the knee slightly bent but relaxed. After the application of transmission gel, a wide-band linear array ultrasound probe (Logiq e, L4-12t, GE Company, Fairfield, CT) was placed over the posterior tibial artery. B-mode ultrasound (10 MHz) was employed to determine the location of the posterior tibial artery. The probe was adjusted so that the entire lumen of the posterior tibial artery was insonated with an insonation angle of ≤60° for each measurement. Resting blood flow and posterior tibial artery diameter was recorded and calculated immediately prior to exercise over five consecutive cardiac cycles using on-screen manufacturer-provided software (General Electric Company, Fairfield, CT). Measurements were taken immediately before exercise and one minute post exercise.

Arterial Occlusion Pressure

Arterial occlusion was measured only in the blood flow restriction condition. While participants were seated, we applied a 10 cm nylon blood pressure cuff to the upper most portion of the participant's thigh. The lowest pressure at which blood flow at the posterior tibial artery was no longer present was determined using a Doppler hand-held probe (MD6 Doppler Probe, Hokanson, Bellevue, WA, USA). Pressure was regulated by the E20 Rapid Cuff Inflator (Hokanson, Bellevue, WA) and was inflated to 50 mmHg before being progressively increased by 1 mmHg increments until a pulse was no longer detected.

Resistance Exercise Protocol

Participants were randomly assigned to one of four conditions: 1) 15% 1RM, no blood flow restriction, 2) 15% 1RM, 40% arterial occlusion pressure, 3) 15% 1RM, 80% arterial occlusion pressure, and 4) 70% 1RM, no blood flow restriction. The exercise protocols were comparing exercise load and different levels of blood flow restriction. Participants performed 4 sets of volitional failure/90 repetitions with 30 second rest periods in-between sets. The high-load condition (70% 1RM) performed 4 sets to failure with 90 second rest period in-between sets. A pre-set bar for knee extension was used to determine full range of motion and only those attempts that touched the bar was counted as a repetition. If the participant missed reaching the bar twice in a row, the set was terminated.

Blood Flow Restriction

A 10 cm wide nylon cuff (Hokanson, Inc.) was placed at the most proximal portion of the participant's thigh. The cuff was inflated to either 40% or 80% of the participant's resting arterial occlusion pressure. The cuff remained inflated throughout the duration of exercise and upon completion of the exercise was deflated and removed.

Metronome

A metronome was used to ensure that the participants performed 1 second concentric muscle action and 1 second eccentric muscle action during the unilateral knee extension exercise.

Statistical Analyses

Using the SPSS 23.0 statistical software package (SPSS Inc., Chicago, IL), a repeated measures ANOVA on time was performed with a between subject factor of group to determine whether the changes in variables (e.g. heart rate and blood pressure) differ by group. If there was no interaction, main effects were examined. If there was an interaction, simple effects were examined. A paired samples t-test was used to determine differences across time within each condition (Pre vs. Post) and a one-way ANOVA determined differences across conditions within each time point (Pre and Post). For blood flow, a Shapiro-Wilk test determined that the data was not normally distributed. Therefore, non-parametric tests were performed. A Wilcoxon related samples nonparametric tests were used to determine where the difference occurred. All data are presented as means and standard deviation (SD) except for blood flow which are presented as 50th, (25th – 75th percentile). Statistical significance for all tests was set at an alpha level of 0.05.

Experimental Design # 2 (Chronic)

Forty-six participants were recruited for the current study. Six individuals were unable to complete the study due to personal reasons; therefore, their data was excluded from all analyses. Therefore, 40 participants completed the protocol. Participants visited the Kevser Ermin Applied Physiology Laboratory on twenty two separate occasions; three pre-testing visits, 16 training visits (two training sessions per week), and three post-testing visits. During the first visit, participants filled out an informed consent form. After confirming that they did not meet any exclusion criteria, height and body mass was measured using a standard stadiometer and an electronic scale. For visit 2, brachial blood pressure, resting calf blood flow, and venous compliance was measured. Additionally, familiarization with lower body strength tests were performed. The participant then had each leg randomly assigned to one of four possible unilateral resistance exercise conditions: 1) 15% 1RM, no blood flow restriction, 2) 15% 1RM, 40% arterial occlusion pressure, 3) 15% 1RM, 80% arterial occlusion pressure, and 4) 70% 1RM, no blood flow restriction. During visits 4-19, the participant exercised each leg twice a week with at least 48 hours in-between training visits to the beat of a metronome with 1 second for the concentric portion and 1 second for the eccentric portion of the lift. Arterial occlusion pressure was determined before exercise. Ratings of perceived exertion and discomfort were taken before (pre) and after each set of exercise. The first post-testing visit was performed 48-72 hours after the final training session at the same time of day as pre-visit 1. The second post-testing visit was at the same time of day as pre-visit 2 with at least one day apart after the first post-testing visit. The third post-testing visit was at the same of day as pre-visit 3 with at least one day apart after the second post-testing visit.

Inclusion Criteria

1. Male and Female

2. Between the ages of 18-35 years

3. Untrained individuals who have not performed resistance exercise in the past 6 months or more

5. No orthopedic issues preventing strength testing or exercise

6. Individuals who have not used any tobacco related products (cigarettes, cigars, chew/snuff, etc.)

7. Individuals who are not on hypertensive medication

8. Individuals who are not obese based on a Body Mass Index of $\leq$ 29.9 kg/m^2

Exclusion Criteria

1. Outside the age range of 18-35 years

2. Resistance trained

3. Currently using a tobacco related product (cigarettes, cigars, chew/snuff, etc.)

4. Classified as obese based on a Body Mass Index of ≥ 30 kg/m^2

5. Individuals who are on hypertensive medication

5. Having more than one risk factor for thromboembolisms (Motykie et al.(93)

a. Diagnosed Crohn's or Inflammatory Bowel Disease

b. Past fracture of a hip, pelvis, or femur

c. Major surgery within the past 6 months

d. Varicose veins

e. Family history of deep vein thrombosis or pulmonary embolism

Standing Height and Body Mass

Height was measured to the nearest 0.5 cm using a stadiometer with participant's head in a horizontal position, shoulders back, and heels together (60°). Body mass was measured using an electronic scale to the nearest 0.1 kg with participants wearing minimal clothing such as a t-shirt, shorts, and shoes off.

Brachial Blood Pressure

Participants had 10 minutes of supine rest in a quiet room. Brachial blood pressure was taken by an automated blood pressure machine (Omron #HEM-907XL) using an appropriately sized cuff. Blood pressure was taken twice and the value was averaged. If the measurements were not within 5 mmHg, a third measurement was taken and the closest two were averaged.

One Repetition Maximum (1RM)

The heaviest weight that can be lifted one time with good form was record as the individual's 1RM. The participants performed a 1RM for each leg. First, the seat was adjusted accordingly for each participant. The participants were instructed to have their arms crossed over the chest to ensure strict form and to avoid extra movement. In addition, a seat belt was crossed over the waist and pulled securely. A pre-set bar was used to determine full knee extension and only those attempts that touched the pre-set bar was counted. Participants warmed up with a relative low load estimated at 30% 1RM. Following this brief warm-up, the load was adjusted to an estimated 1RM and the first attempt was made. The first attempt was estimated off of how the individual's warm-up looked to the investigators and how the warm-up felt to the participant. As participants got closer to their 1RM, the load was either increased or decreased in 1.25 kg increments until a 1RM was obtained (usually within 5 attempts). A period of 90 seconds of rest was given between each attempt.

Arterial Occlusion Pressure

Arterial occlusion was measured only in the blood flow restriction condition. While participants were seated, we applied a 10 cm nylon blood pressure cuff to the upper most portion of the participant's thigh. The lowest pressure at which blood flow at the posterior tibial artery was no longer present was determined using a Doppler hand-held probe (MD6 Doppler Probe, Hokanson, Bellevue, WA, USA). Pressure was regulated by the E20 Rapid Cuff Inflator (Hokanson, Bellevue, WA) and was inflated to 50 mmHg before being progressively increased by 1 mmHg increments until a pulse was no longer detected.

Resistance Training Protocol

Each leg was randomly assigned to one of four conditions: 1) 15% 1RM, no blood flow restriction, 2) 15% 1RM, 40% arterial occlusion pressure, 3) 15% 1RM, 80% arterial occlusion pressure, and 4) 70% 1RM, no blood flow restriction. The exercise protocols were comparing exercise load and different levels of blood flow restriction. For conditions that utilized 15% 1RM, participants performed 4 sets to volitional failure/90 repetitions with 30 second rest periods in-between sets. The high load condition (70% 1RM) performed 4 sets to failure with 90 second rest period in-between sets. This resistance training protocol was progressively ramped up. During week 1, participants performed 1 set on visit 1 while the subsequent visit (visit 2) participants performed 2 sets. Participants then performed 3 sets during week 2. During week 3, participants performed 4 sets and this was continued throughout the rest of the training period. A pre-set bar for knee extension was used to determine full range of motion and only those attempts that touched the bar were counted as a repetition. If the participant missed reaching the bar twice in a row, the set was terminated.

Metronome

A metronome was used to ensure that the participants performed 1 second concentric muscle action and 1 second eccentric muscle action during the unilateral knee extension exercise.

Ratings of Perceived Exertion (RPE)

Ratings of perceived exertion were taken before the start of exercise and immediately following each set using the standard Borg 6-20 scale as previously described (79). Participants were explained in depth how to rate their RPE and to ensure they understood the scale being used. Participants were told, “We want you to rate your perception of exertion, that is, how heavy and strenuous the exercise feels to you. The perception of exertion depends mainly on the strain and fatigue in your muscles. We want you to use this scale from 6-20, where 6 means ‘no exertion at all' and 20 means 'maximal exertion'; any questions?" Participants confirmed that they fully understood how to rate RPE prior to actual testing. RPE was taken immediately after sets 1, 2, 3 and 4.

Ratings of Discomfort

A rating of discomfort was taken prior to the start of exercise and following each set using the Borg Discomfort scale (CR-10+) as described previously (79). For example, participants will be asked, "What are your worst experiences of discomfort? 'Maximum discomfort (rating of 10)' is your main point of reference; it is anchored by your previously experienced worst discomfort. The worst discomfort that you have ever experienced, the 'Maximum discomfort' may not be the highest possible level of discomfort. There may be a level of discomfort that is still stronger than your 10; if this is the case, you will say 11 or 12. If the discomfort is much stronger, for example, 1.5 times 'Maximum Discomfort' you will say 15; any questions?" Participants confirmed that they fully understood how to rate discomfort prior to actual testing. Ratings of discomfort were taken before exercise, as well as 20 seconds after sets 1, 2, 3, and immediately after set 4. Discomfort was taken 20 seconds after each set because participants in previous blood flow restriction studies anecdotally noted greater discomfort later in the rest periods.

Blood Flow Restriction

A 10 cm wide nylon cuff (Hokanson, Inc.) was placed at the most proximal portion of the participant's thigh. The cuff was inflated to either 40% or 80% of the participant's resting arterial occlusion pressure. The cuff remained inflated throughout the duration of exercise and upon completion of the exercise was deflated and removed.

Calf Vascular Conductance

Calf blood flow was measured using venous occlusion strain-gauge plethysmography (EC5; Hokanson, Bellevue, WA, USA) on both legs following 10 minutes supine rest. An appropriate sized (2 cm less than greatest circumference of the calf) mercury-filled strain gauge was placed around the calf at the area with the greatest circumference and blood pressure cuffs were placed on the ankle (5cm wide) and the thigh (10 cm wide) while the leg was slightly elevated above heart level to prevent venous pooling between measurements. The ankle cuff was inflated to a pressure of 250 mmHg one minute prior to blood flow measurements, remaining inflated for the duration of blood flow assessment in order to temporarily occlude blood flow to the foot. The thigh cuff was inflated to a pressure of 50 mmHg during each blood flow measurement. The average of five 15s plethysmographic cycles were used for determining calf blood flow (ml per 100 ml $tissue^{-1}min^{-1}$). Using the procedures of Fahs et al.(27), calf blood flow was normalized to flow per unit of mean arterial pressure to calculate calf vascular conductance using the equation: Calf Vascular Conductance = (Calf Blood Flow / Mean Arterial Pressure) x 1000. Upon completion of the first leg, a 5 minute rest period was given and the same procedure was conducted on the opposite leg.

Calf Venous Compliance

Calf venous compliance was measured using a strain-gauge plethysmography (EC5; Hokanson, Bellevue, WA, USA) on both legs following 10 additional minutes of supine rest. An appropriate sized strain gauge (2 cm smaller than the maximum circumference of the calf) was placed around the calf at the greatest circumference while connected to the plethysmograph (EC6 Strain Gauge Plethysmograph, D.E. Hokanson Inc., Bellevue, WA). A venous collecting blood pressure cuff was placed on the thigh (4-5 cm above the patella; 10 cm wide). The cuff was inflated to 20 mmHg for 45 seconds followed by subsequent cuff inflation pressures of 20, 40, 60, and 80 mmHg. The inflation pressures were sustained for 1, 2, 3, and 4 minutes while a 1 minute period was allotted between inflations for restoration to baseline measurement. Venous volume variation (VVV; ml/100 ml) was recorded by the plethysmograph in the Noninvasive Vascular Program (D.E. Hokanson Inc., Bellevue, WA). Venous volume variation is the greatest change in the calf at each cuff pressure. A pressure-volume curve was created to plot venous volume variation across the different cuff pressures. Using the procedures of Fahs et al.(27), calf venous compliance was calculated from the slope of the pressure-volume curve. After each cuff inflation, maximum venous outflow (MVO: ml/100 ml/min) was calculated as the slope of the line tangent to the curve 0.5 seconds after cuff release and was also recorded in the program. Upon completion of the first leg, a 5 minute rest period was given and the same procedure was conducted on the opposite leg.

Statistical Analyses

Using the SPSS 23.0 statistical software package (SPSS Inc., Chicago, IL), a mixed model accounting for participant and condition was performed to determine differences in calf blood flow, calf vascular conductance, maximum venous outflow, calf venous compliance, and perceptual responses (RPE and discomfort). An unstructured or compound symmetry model was chosen based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. If there is no interaction, main effects were examined. If there was an interaction, simple effects were examined. A one-way repeated measures ANOVA was performed to determine if arterial occlusion pressure was different over time (Visit 1, Visit 9, and Visit 16) within each pressure. A paired t-test was performed to determine if AOP was different between conditions at each time point. All data will be presented as mean and 95% confidence interval. Statistical significance for all tests will be set at an alpha level of 0.05.

CHAPTER IV: RESULTS

Experimental Design # 1 (Acute)

Participant Characteristics

A total of 91 individuals (males=46; [mean (SD) Age 23.1 (3.6) yrs; Height: 178.6 (8.3) cm; Body mass: 80.0 (10.1) kg; BMI: 25.1 (2.3); 1RM: 40 (8.2) kg]) (females=45; [mean (SD) Age: 20.8 (2.0) yrs; Height: 165.7 (6.2) cm; Body mass: 62.4 (8) kg; BMI: 22.7 (2.6); 1RM: 24.1 (4) kg]) completed the protocol. Participants were excluded if they had more than one risk factor for thromboembolism which included the following: obesity (BMI ≥ 30 kg/m^2); diagnosed Crohn's disease; a past fracture of the hip, pelvis or femur; major surgery within the last 6 months; varicose veins; a family or personal history of deep vein thrombosis or pulmonary embolism. Also, participants who were not between the ages of 18-35, currently using tobacco products or hypertensive medication were excluded. All participants were instructed to refrain from: 1) eating 2 hours prior; 2) consuming caffeine 8 hours prior; 3) consuming alcohol 24 hours prior; and 4) vigorous physical activity 24 hours prior to the visit. Participant characteristics can be found in Table 1

Table 1. Participant Characteristics. All values presented as means (SD)

	15/0 (n=22)	15/40 (n=23)	15/80 (n=22)	70/0 (n=24)
Age (yrs)	21.1 (2.9)	21.9 (2.4)	23.5 (4.3)	21.3 (2.3)
Height (cm)	174.1 (10)	171.6 (8.5)	172.1 (12.2)	171.1 (8.1)
Weight (kg)	69.9 (11.8)	71.9 (11.4)	73.7 (15)	69.9 (12.8)
BMI (kg/m^2)	22.9 (2.1)	24.3 (2.7)	24.7 (2.9)	23.7 (2.8)
1RM (kg)	32.2 (10.3)	32.6 (10.4)	33.05 (11.2)	30.8 (9.7)
AOP (mmHg)		197 (28)	195 (33)	
Applied pressure (mmHg)		78 (11)	155 (26)	
Set 1	79 (19)	73 (18)	50 (19)	12 (3)
Set 2	34 (19)	24 (20)	14 (15)	7 (2)
Set 3	26 (16)	16 (10)	6 (4)	7 (2)
Set 4	26 (17)	15 (10)	4 (4)	6 (2)

BMI=body mass index; 1RM=one-repetition maximum; AOP=arterial occlusion pressure

Blood Pressure (Acute)

A repeated measures ANOVA was performed with a between subject factor of group to determine differences in blood pressure between groups. There was a statistically significant interaction for systolic blood pressure ($p<.001$) (Figure 1). A post-hoc one-way ANOVA revealed that there were no differences between groups at pre ($p=.719$); however, there were differences at post ($p=.003$). The 15/0 [140 (14) mmHg; Pre-Post Δ: 19 (10) mmHg] and 15/40 [134 (16) mmHg; Pre-Post Δ: 16 (12) mmHg] conditions were significantly different compared to the 15/80 condition [123 (14) mmHg; Pre-Post Δ: 5 (10) mmHg]. In addition, the 15/80 condition was significantly different compared to the 70/0 [136 (16) mmHg; Pre-Post Δ: 18 (12) mmHg] condition (Table 2). There were no statistically significant differences between the 15/0 condition compared to the 15/40 condition ($p=.180$) and 70/0 condition ($p=.436$). In addition, there were no statistically significant differences between the 15/40 condition and 70/0 condition ($p=.552$). All conditions increased from pre-post [overall average change of 15 (12) mmHg ($p<.001$)] (Figure 1).

A repeated measures ANOVA was performed with a between subject factor of group to determine differences in blood pressure between groups. For diastolic blood pressure, there was no interaction ($p=.199$) but there was a main effect of time ($p<.001$) (Figure 2). All conditions increased from pre-post [overall average change of 3 (6) mmHg ($p<.001$)]. The change in diastolic pressure from pre-post for each condition is the following: 15/0 [Pre-Post Δ: 5 (4) mmHg], 15/40 [Pre-Post Δ: 3 (9) mmHg], 15/80 [Pre-Post Δ: 1 (7) mmHg], 70/0 [Pre-Post Δ: 2 (4) mmHg] (Table 3).

Table 2. Systolic blood pressure (mmHg). Values presented as means (SD)

Condition †	Pre	Post	Pre-Post Δ
15/0	120 (10)	140 (14)^{a*}	19 (10)
15/40	118 (9)	134 (16)^{a*}	16 (12)
15/80	118 (12)	123 (14)^{b*}	5 (10)
70/0	118 (8)	136 (16)^{a*}	18 (12)

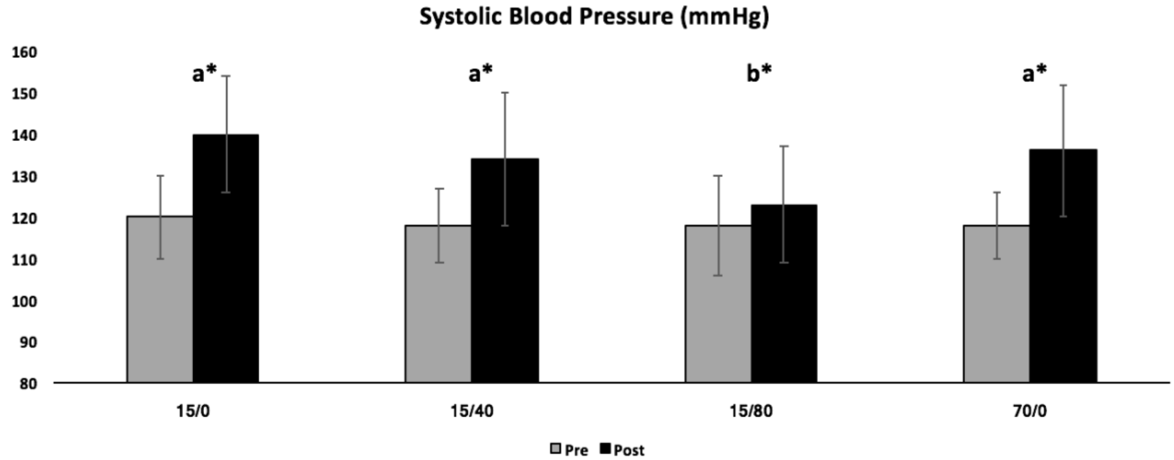
If conditions contain at least one of the same letter, they are not significantly different from each other. * denotes simple effect. † denotes an interaction

Table 3. Diastolic blood pressure (mmHg). Values presented as means (SD)

Condition	Pre	Post	Pre-Post Δ
15/0	72 (7)	78 (6)$^{\#}$	5 (4)
15/40	74 (7)	78 (12)$^{\#}$	3 (9)
15/80	72 (8)	73 (7)$^{\#}$	1 (7)
70/0	72 (6)	74 (6)$^{\#}$	2 (4)

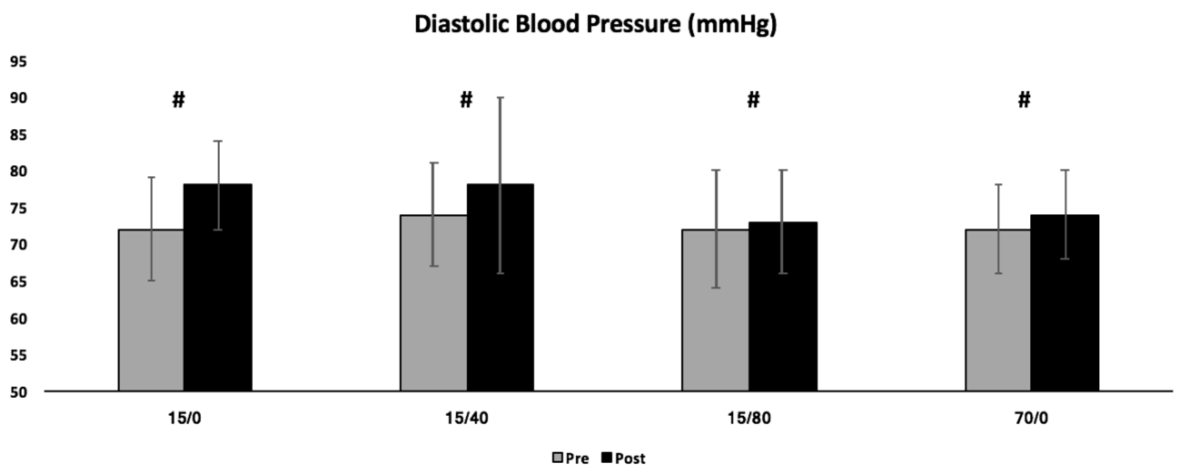
# denotes main effect of time.

Figure 1. Systolic Blood Pressure (mmHg) Pre-Post. Values presented as means (SD)



If conditions contain at least one of the same letter, they are not significantly different from each other. * denotes simple effect.

Figure 2. Diastolic Blood Pressure (mmHg) Pre-Post. Values presented as means (SD)



# denotes main effect of time

Heart Rate (Acute)

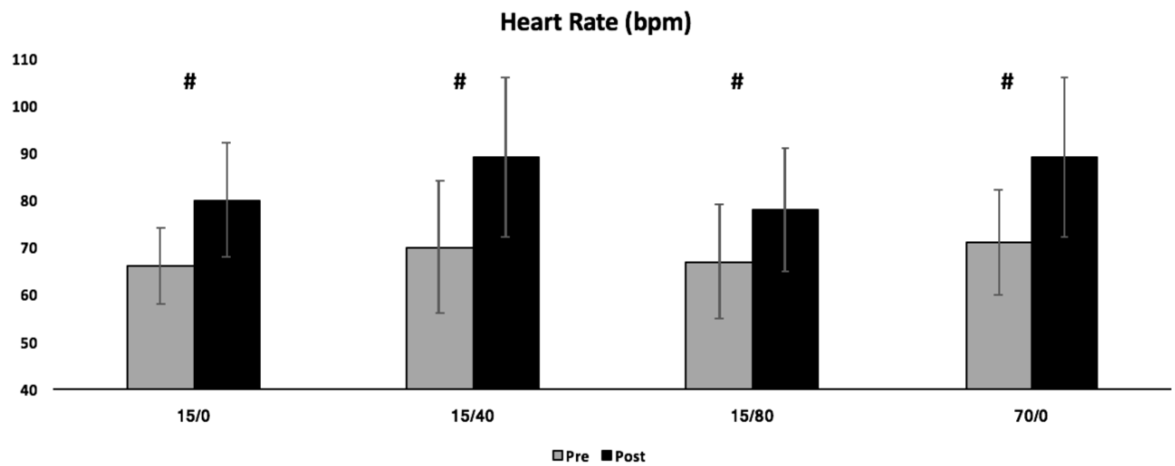
For heart rate, there was no interaction (p=.063) but there was a main effect of time (p<.001). All conditions increased pre-post [overall average change 15 (10) bpm (p<.001)] (Figure 3). The pre-post change for each condition is displayed in Table 4.

Table 4. Heart rate values (bpm). Values presented as means (SD)

Condition	Pre	Post	Pre-Post Δ
15/0	66 (8)	80 (12)#	14 (8)
15/40	70 (14)	89 (17)#	18 (10)
15/80	67 (12)	78 (13)#	11 (7)
70/0	71 (11)	89 (17)#	17 (11)

# denotes main effect of time

Figure 3. Heart rate (bpm) Pre-Post. Values presented as means (SD)



# denotes main effect of time

Blood Flow (Acute)

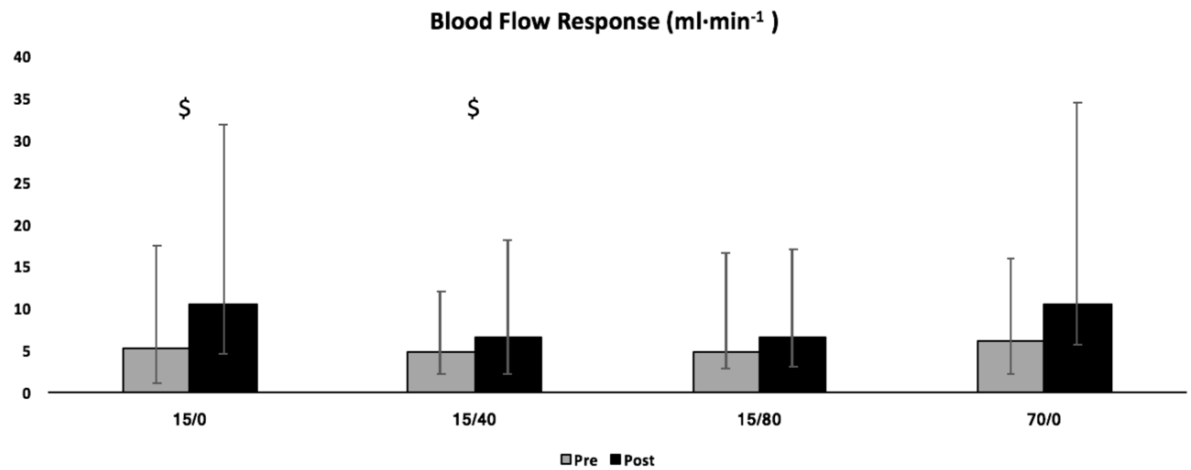
A Shapiro-Wilk test determined that the data was not normally distributed. Therefore, non-parametric tests were performed. A Kruskal-Wallis H test showed that there was no statistically significant difference in blood flow between groups at pre [H(3) = 3.377, p=.337] or at post [H(3) = 4.437, p=.218]. A Wilcoxon signed rank test revealed that condition 15/0 (Z=-2.416, p=.016) and condition 15/40 (Z=-2.981, p=.003) increased blood flow over time (Figure 4). Conditions 15/80 (Z=-.146, p=.884) and 70/0 (Z=-1.343, p=.179) did not observe a statistically significant change in blood flow (Table 5). Figure 5 displays the change scores of the blood flow response for each condition. Values are presented as median (25th -75th percentile). There was no interaction (p=.550) or main effect of time (p=.515) for diameter (Table 6).

Table 5. Blood flow values (ml·min^{-1}). Values presented as median (25th-75th)

Condition	Pre	Post	Pre-Post Δ
15/0	5.3 (4.2, 12.2)	10.4 (5.8, 21.4)$	4.5 (-1.4, 8.2)
15/40	4.7 (2.6, 7.2)	6.5 (4.4, 11.5)$	2.7 (0.29, 6.6)
15/80	4.9 (2.0, 11.6)	6.6 (3.5, 10.4)	-0.18 (-2.7, 2.2)
70/0	6.1 (3.9, 9.9)	10.4 (4.7, 24.0)	1.2 (-1.7, 5.5)

$ denotes pre-post differences

Figure 4. Blood flow values (ml·min^{-1}) Pre-Post. Values presented as median (25th-75th)



$ denotes pre-post differences

Figure 5. Change scores of blood flow (ml·min^{-1}). Values presented as median (25th-75th)

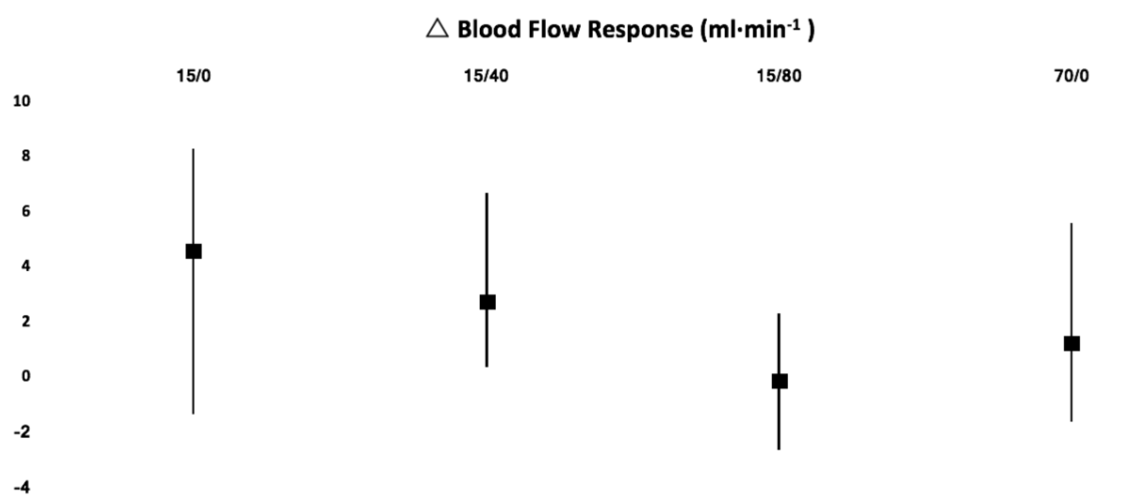


Table 6. Diameter values (cm). Values presented as means (SD)

Condition	Pre	Post
15/0	.18 (.03)	.18 (.04)
15/40	.18 (.04)	.19 (.04)
15/80	.19 (.07)	.19 (.06)
70/0	.19 (.04)	.19 (.03)

Experimental Design # 2 (Chronic)

Participant Characteristics

A total of 40 individuals (males=20; [mean (95% CI) Age 21.8 (20.5, 23) yrs; Height: 178.3 (175, 181) cm; Body mass: 75.8 (71.2, 80.3) kg; BMI: 23.8 (22.6, 25.1)]) (females=20; [mean (95% CI) Age: 21.2 (20.2, 22.2) yrs; Height: 164.8 (162.2, 167.4) cm; Body mass: 61 (57.3, 64.6) kg; BMI: 22.2 (20.9, 23.6)]) completed the protocol. Participants were excluded if they had more than one risk factor for thromboembolism which included the following: obesity (BMI ≥ 30 kg/m^2); diagnosed Crohn's disease; a past fracture of the hip, pelvis or femur; major surgery within the last 6 months; varicose veins; a family or personal history of deep vein thrombosis or pulmonary embolism. Also, participants who were not between the ages of 18-35, currently using tobacco products or hypertensive medication were excluded. All participants were instructed to refrain from: 1) eating 2 hours prior; 2) consuming caffeine 8 hours prior; 3) consuming alcohol 24 hours prior; and 4) vigorous physical activity 24 hours prior to their pre and post visits. Participant characteristics can be found in Table 7. Average exercise volume per session can be found in Table 8 where exercise volume was calculated as the number of repetitions completed multiplied by the load being lifted (i.e. repetitions x load). It was then averaged over the two training sessions for each week. Additionally, average repetitions per session can be found in Table 9 where weekly repetitions were calculated as the sum of repetitions completed each training visit and then averaged over the two training sessions for each week.

Table 7. Participant Characteristics. Values presented as means (95% CI)

	Male (n=20)	Female (n=20)
Age	21.8 (20.5, 23)	21.2 (20.2, 22.2)
Height (cm)	178.3 (175, 181)	164.8 (162.2, 167.4)
Body Mass (kg)	75.8 (71.2, 80.3)	61 (57.3, 64.6)
BMI (kg/m^2)	23.8 (22.6, 25.1)	22.2 (20.9, 23.6)

Table 8. Average Exercise Volume per session. Values presented as means (95% CI)

Condition	Week1	Week2	Week3	Week4
15/0	398 (340, 456)	537 (447, 628)	639 (525, 754)	674 (549, 800)
15/40	321(247, 396)	436 (345, 528)	482 (385, 581)	528 (416,641)
15/80	244 (194,296)	306 (244,370)	321(250, 392)	343 (260, 426)
70/0	331(281, 382)	576 (486, 66.7)	701(606, 797)	759 (659, 860)
	Week 5	Week 6	Week 7	Week 8
15/0	733 (603, 863)	733 (596, 870)	747 (614, 880)	768 (632, 905)
15/40	558 (448, 668)	552 (441, 663)	590 (473, 706)	629 (482, 776)
15/80	354 (270, 439)	356 (275, 439)	382 (284, 481)	383 (284, 482)
70/0	766 (663, 870)	803 (701, 906)	800 (700, 901)	805 (701, 800)

Table 9. Average Repetitions per session. Values presented as means (95% CI)

Condition	Week1	Week2	Week3	Week4
15/0	89 (78, 99)	120 (101, 138)	144 (117, 172)	152 (123, 182)
15/40	72 (60, 83)	97 (84, 111)	109 (92, 126)	119 (100, 138)
15/80	53 (47, 58)	66 (58, 75)	69 (60, 77)	74 (62, 86)
70/0	16 (14, 17)	28 (25, 30)	34 (31, 37)	37 (34, 40)
	Week 5	Week 6	Week 7	Week 8
15/0	166 (135, 197)	166 (133, 198)	170 (137, 203)	176 (141, 210)
15/40	128 (106, 151)	128 (103, 154)	137 (111, 162)	142 (116, 169)
15/80	76 (64, 88)	78 (66, 90)	82 (68, 97)	83 (68, 98)
70/0	37 (35, 40)	40 (36, 43)	39 (36, 43)	40 (36, 44)

Figure 6. Average Exercise Volume per session. Values presented as means

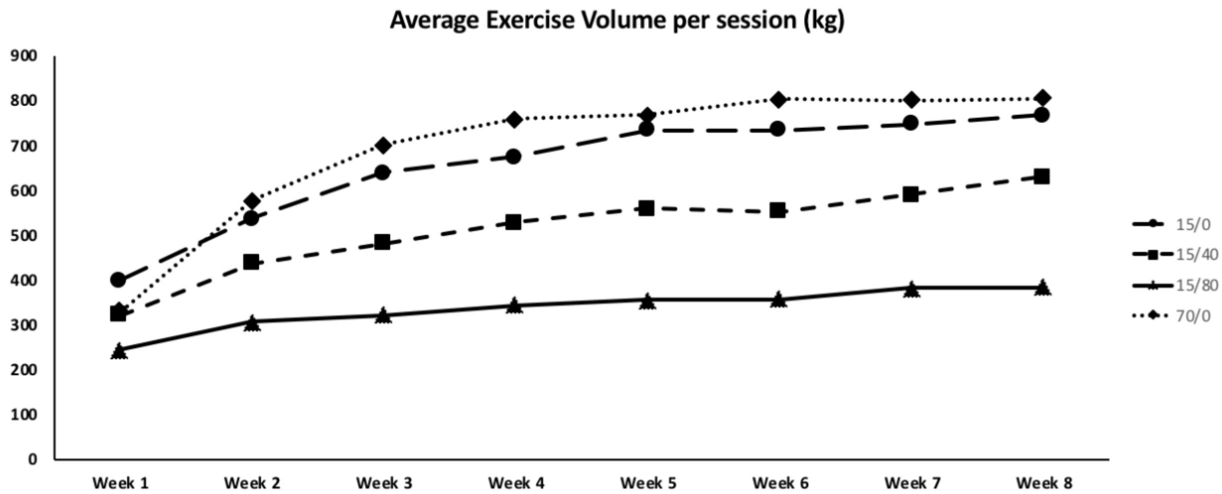
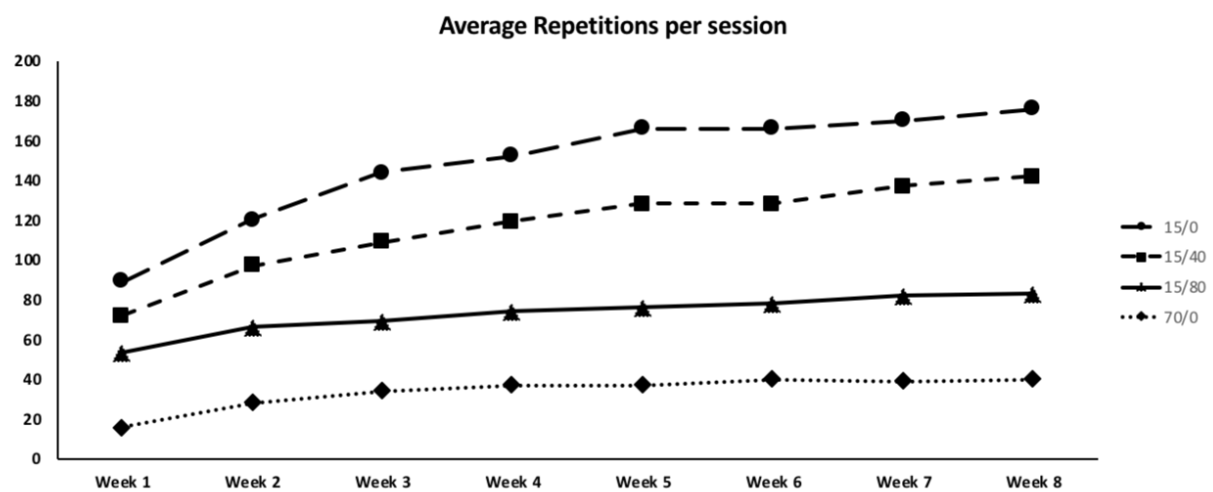


Figure 7. Average Weekly Repetitions per session. Values presented as means



Calf Blood Flow

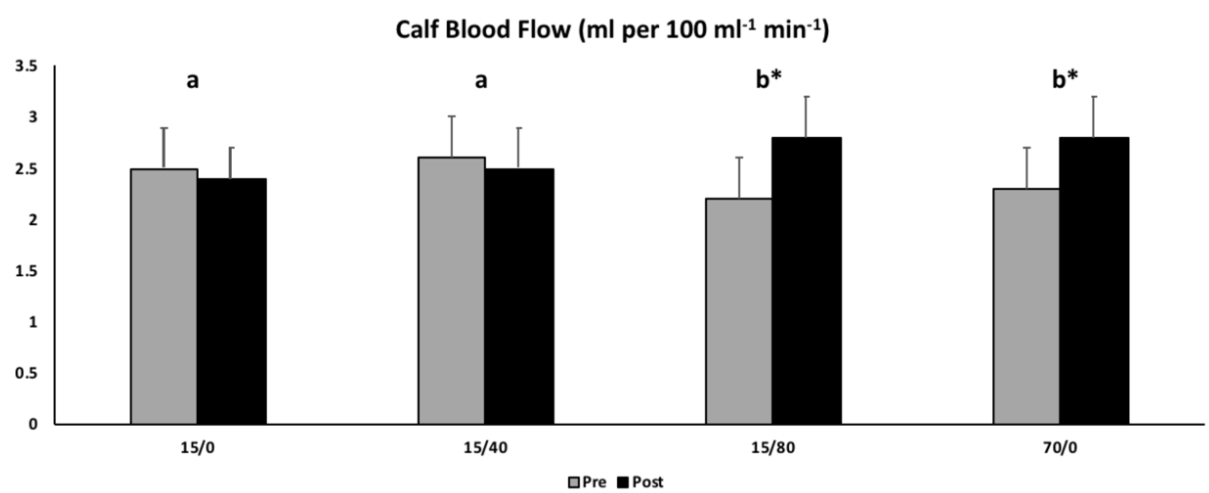
A mixed model accounting for participant and condition was performed to determine differences in calf blood flow. The compound symmetry model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. There was a statistically significant interaction for calf blood flow ($p=.006$). There were statistical significant differences between condition 70/0 compared to 15/0 [mean difference: 0.68 (0.14, 1.2) ml/min (p=.013)] and 15/40 [mean difference: 0.65 (0.09, 1.2) ml/min (p=.022)]. However, there were no differences between conditions 70/0 and 15/80 [mean difference: -0.07 (-0.61, 0.47) ml/min (p=.799)]. Condition 15/0 was not statistically different to condition 15/40 [mean difference: -0.04 (-0.59, 0.51) ml/min (p=.898)] but was different compared to condition 15/80 [mean difference: -0.75 (-1.3, -0.21) ml/min (p=.007)]. Moreover, there were differences between condition 15/40 and 15/80 [mean: -0.72 (-1.3, -0.16) ml/min (p=.012)] (Table 10). Conditions 15/80 and 70/0 were the only conditions that increased blood flow pre-post (Table 10). Figure 8 displays the pre-post change for each condition.

Table 10. Calf Blood Flow (ml per 100 ml^{-1} min^{-1}). Values presented as means (95% CI)

Condition †	Pre	Post	Pre-Post Δ
15/0	2.5 (2.1, 2.9)	2.4 (2.0, 2.7)	-0.140 (-0.241, 0.522)[a]
15/40	2.6 (2.2, 3.0)	2.5 (2.1, 2.9)	-0.104 (-0.507, 0.298)[a]
15/80	2.2 (1.8, 2.6)	2.8 (2.5, 3.2)	0.613 (0.232, 0.995)[b*]
70/0	2.3 (1.9, 2.7)	2.8 (2.4, 3.2)	0.544 (0.162, 0.926)[b*]

† denotes an interaction. * denotes differences pre-post. If conditions contain at least one of the same letter, they are not significantly different from each other.

Figure 8. Calf Blood Flow (ml per 100 ml^{-1} min^{-1}). Values presented as means (95% CI)



* denotes differences pre-post. If conditions contain at least one of the same letter, they are not significantly different from each other.

Calf Vascular Conductance

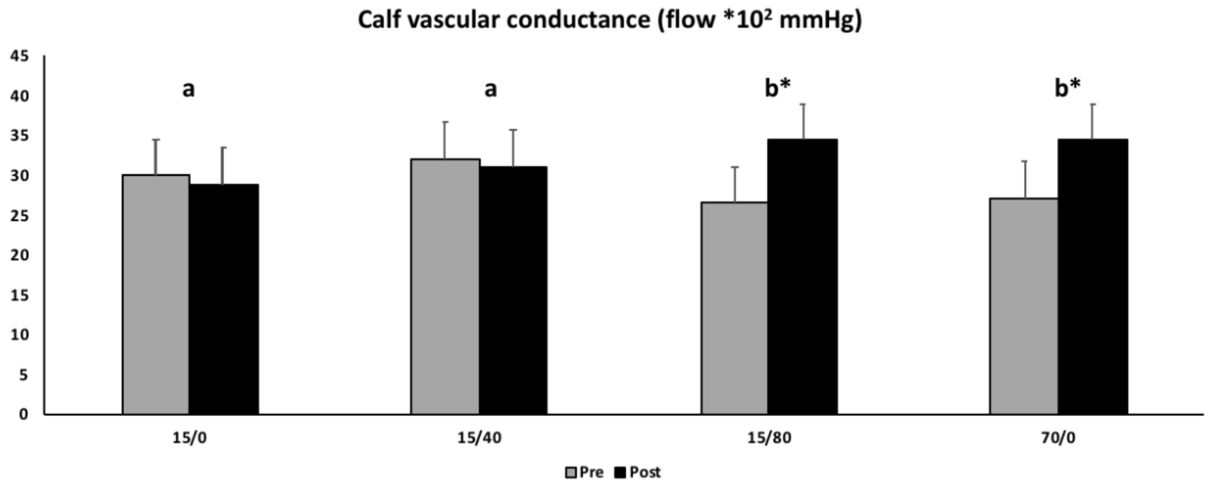
A mixed model accounting for participant and condition was performed to determine differences in calf vascular conductance. The compound symmetry model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. There was a statistically significant interaction for calf vascular conductance (p=.004) (Table 11). Condition 70/0 was different compared to condition 15/0 [mean difference: 8.4 (2.1, 14.8) flow $*10^2$ mmHg (p=.010)] and 15/40 [mean difference: 8.1 (1.5, 14.6) flow $*10^2$ mmHg (p=.016)] but not 15/80 [mean difference: -0.66 (-7.0, 5.7) flow $*10^2$ mmHg (p=.838)]. There were no differences between conditions 15/0 and 15/40 [mean difference: -0.35 (-6.9, 6.2) flow $*10^2$ mmHg (p=.915)]; however, there were differences between 15/0 and 15/80 [mean difference: -9.1 (-15.4, -2.7) flow $*10^2$ mmHg (p=.005)]. There were differences between conditions 15/40 and 15/80 [mean difference: -8.7 (-15.2, -2.2) flow $*10^2$ mmHg (p=.009)]. Only conditions 15/80 and 70/0 increased from pre-post (Table 11). Figure 9 displays the pre-post changes for each condition.

Table 11. Calf vascular conductance (flow $*10^2$ mmHg). Values presented as means (95% CI)

Condition †	Pre	Post	Pre-Post Δ
15/0	30.0 (25.5, 34.6)	28.8 (24.3, 33.4)	-1.2 (-5.7, 3.3)^{a}
15/40	31.9 (27.2, 36.6)	31.0 (26.3, 35.7)	-0.864 (-5.6, 3.9)^{a}
15/80	26.6 (22.0, 31.1)	34.4 (29.9, 39.0)	7.9 (3.4, 12.3)^{b*}
70/0	27.2 (22.7, 31.8)	34.4 (29.9, 39.0)	7.2 (2.7, 11.7)^{b*}

† denotes an interaction. * denotes differences pre-post. If conditions contain at least one of the same letter, they are not significantly different from each other.

Figure 9. Calf vascular conductance (flow $*10^2$ mmHg). Values presented as means (95% CI)



* denotes differences pre-post. If conditions contain at least one of the same letter, they are not significantly different from each other.

Maximum Venous Outflow (MVO)

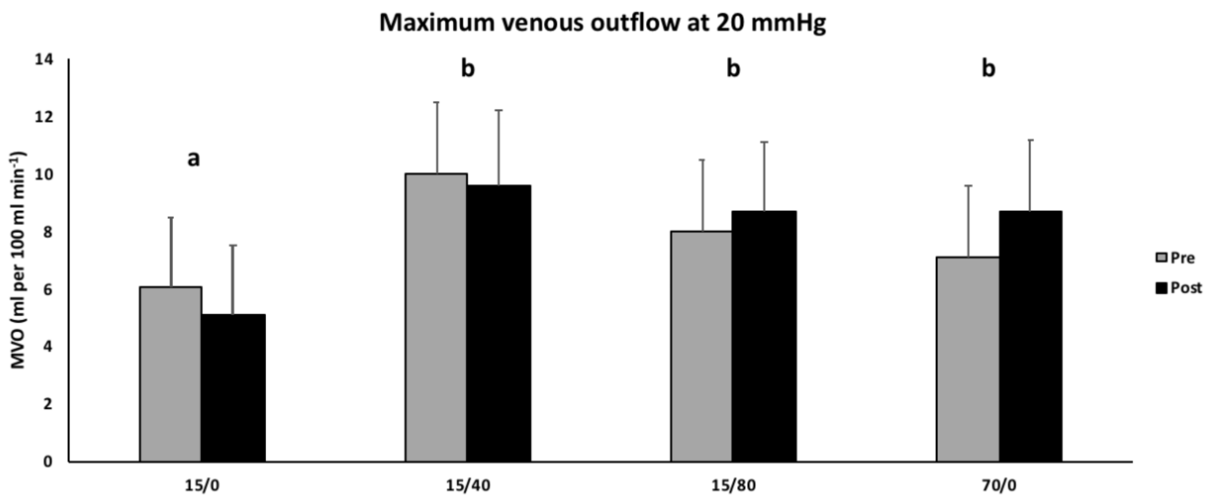
A mixed model accounting for participant and condition was performed to determine differences in maximum venous outflow at 20 mmHg. The compound symmetry model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. There was no interaction (p=.618) or main effect of time (p=.749). However, there was a main effect of condition (p=.007) (Table 12). Condition 15/0 was different compared to 15/40 [mean difference: -4.2 (-6.6, -1.8) (ml per 100 ml min^{-1})], 15/80 [mean difference: -2.8 (-5.1, -0.418) (ml per 100 ml min^{-1})] and 70/0 [mean difference: - 2.3 (-4.7, 0.004) (ml per 100 ml min^{-1})] (Table 12).

Table 12. MVO at 20 mmHg. Values presented as means (ml per 100 ml min^{-1}) (95% CI)

Condition ¶	Pre	Post	Pre-Post Δ
15/0[a]	6.1 (3.6, 8.5)	5.1 (2.7, 7.5)	-0.975 (-3.9, 1.9)
15/40[b]	10.0 (7.4, 12.5)	9.6 (7.1, 12.2)	-0.350 (-3.4, 2.7)
15/80[b]	8.0 (5.6, 10.5)	8.7 (6.3, 11.1)	0.670 (-2.2 ,3.6)
70/0[b]	7.1 (4.7, 9.6)	8.7 (6.3,11.2)	1.6 (-1.3, 4.5)

¶ denotes main effect of condition. If conditions contain at least one of the same letter, they are not significantly different from each other.

Figure 10. MVO at 20 mmHg. Values presented as means (ml per 100 ml min^{-1}) (95% CI)



If conditions contain at least one of the same letter, they are not significantly different from each other.

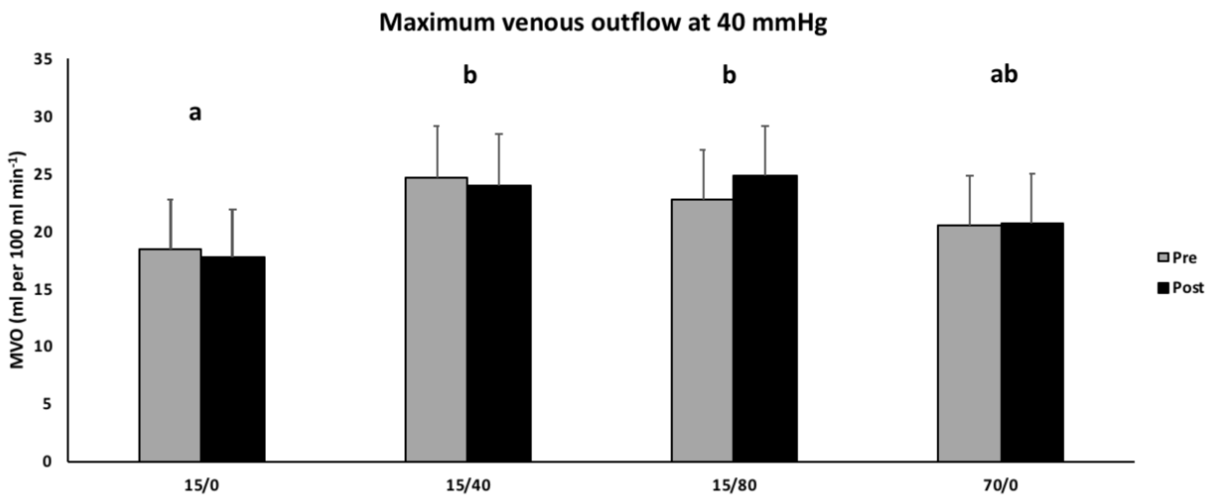
A mixed model accounting for participant and condition was performed to determine differences in maximum venous outflow at 40 mmHg. The compound symmetry model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. There was no interaction (p=.839) or main effect of time (p=.864). However, there was a main effect of condition (p=.007) (Table 13). Condition 15/0 was different compared to 15/40 [mean difference: -6.3 (-10.4, -2.3) (ml per 100 ml min^{-1})] and 15/80 [mean difference: -5.8 (-9.8, -1.8) (ml per 100 ml min^{-1})]. There were no differences between 15/0 and 70/0 [mean difference: -2.5 (-6.6, -1.4) (ml per 100 ml min^{-1})] (Table 13).

Table 13. MVO at 40 mmHg. Values presented as means (ml per 100 ml min^{-1}) (95% CI)

Condition ¶	Pre	Post	Pre-Post Δ
15/0[a]	18.4 (14.1, 22.7)	17.7 (13.4, 22.0)	-0.690 (-5.6, 4.2)
15/40[b]	24.7 (20.2, 29.2)	24.0 (19.5, 28.5)	-0.750 (-5.9, 4.4)
15/80[b]	22.8 (18.5, 27.1)	24.9 (20.6, 29.2)	2.1 (-2.8, 6.9)
70/0[ab]	20.5 (16.2, 24.8)	20.7 (16.4, 25.0)	0.230 (-4.6, 5.1)

¶ denotes main effect of condition. If conditions contain at least one of the same letter, they are not significantly different from each other.

Figure 11. MVO at 40 mmHg. Values presented as means (ml per 100 ml min^{-1}) (95% CI)



If conditions contain at least one of the same letter, they are not significantly different from each other.

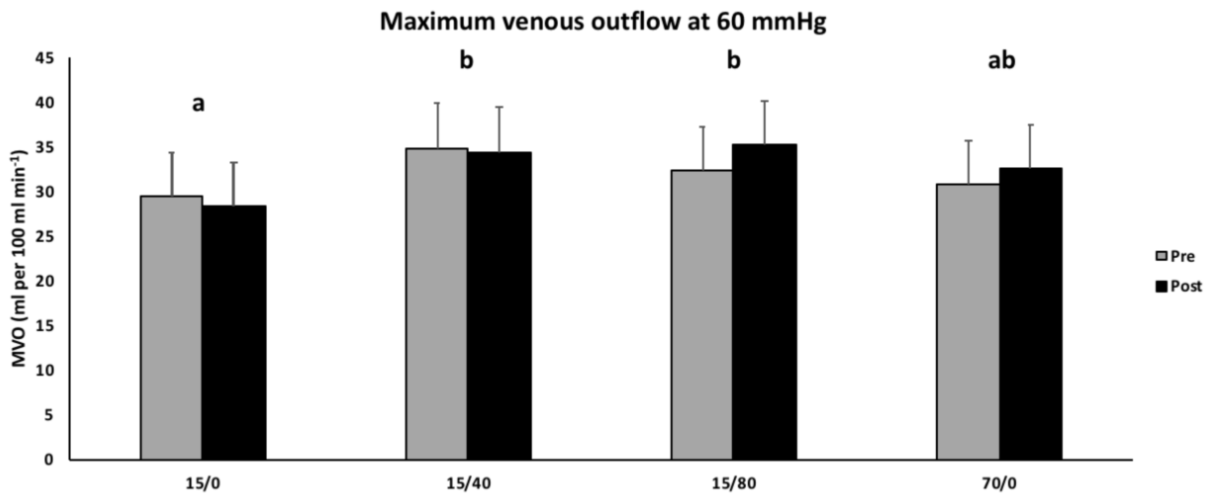
A mixed model accounting for participant and condition was performed to determine differences in maximum venous outflow at 60 mmHg. The compound symmetry model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. There was no interaction (p=.673) or main effect of time (p=.551). However, there was a main effect of condition (p=.048) (Table 14). Condition 15/0 was different compared to 15/40 [mean difference: -5.6 (-10.0, -1.3) (ml per 100 ml min^{-1})] and 15/80 [mean difference: -4.8 (-9.2, -0.591) (ml per 100 ml min^{-1})]. There were no differences between conditions 15/0 and 70/0 [mean difference: -2.7 (-7.0, 1.5) (ml per 100 ml min^{-1})] (Table 14).

Table 14. MVO at 60 mmHg. Values presented as means (ml per 100 ml min^{-1}) (95% CI)

Condition ¶	Pre	Post	Pre-Post Δ
15/0[a]	29.5 (24.6, 34.5)	28.4 (23.4, 33.3)	-1.2 (-6.3, 3.9)
15/40[b]	34.8 (29.7, 39.9)	34.4 (29.3, 39.5)	-0.339 (-5.7, 5.0)
15/80[b]	32.4 (27.5, 37.3)	35.3 (30.3, 40.2)	2.8 (-2.3, 8.0)
70/0[ab]	30.8 (25.9, 35.7)	32.6 (27.7, 37.5)	1.8 (-3.3, 6.9)

¶ denotes main effect of condition. If conditions contain at least one of the same letter, they are not significantly different from each other.

Figure 12. MVO at 60 mmHg. Values presented as means (ml per 100 ml min^{-1}) (95% CI)



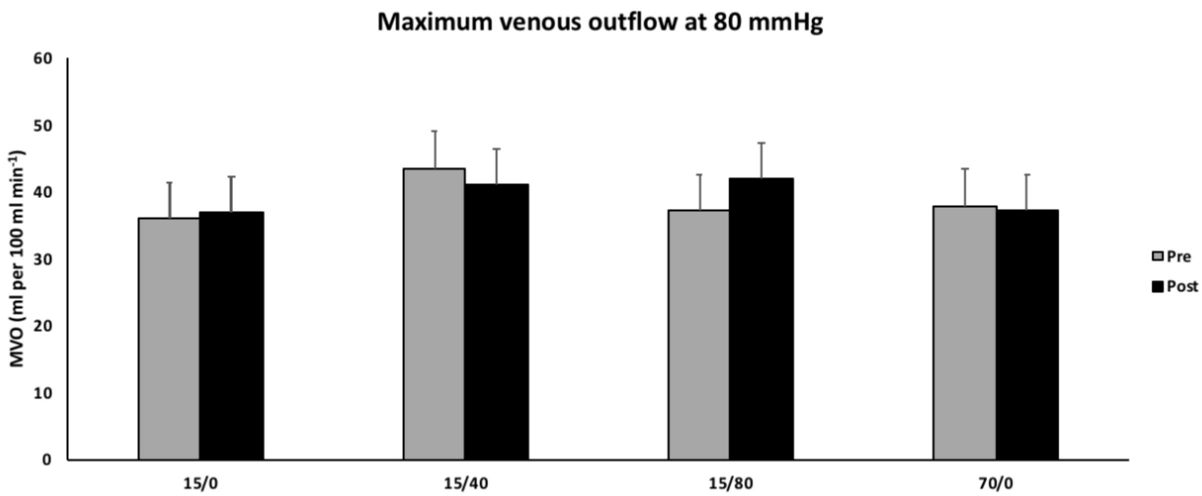
If conditions contain at least one of the same letter, they are not significantly different from each other.

A mixed model accounting for participant and condition was performed to determine differences in maximum venous outflow at 80 mmHg. The compound symmetry model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. There was no interaction (p=.304), no main effect of time (p=.664), and no main effect of condition (p=.096). There was no statistical difference for any outcomes for maximum venous outflow at 80 mmHg (Table 15).

Table 15. MVO at 80 mmHg. Values presented as means (ml per 100 ml min^{-1}) (95% CI)

Condition	Pre	Post	Pre-Post Δ
15/0	36.1 (30.8, 41.4)	36.9 (31.5, 42.2)	0.755 (-4.8, 6.3)
15/40	43.4 (37.9, 49.0)	41.0 (35.5, 46.6)	-2.4 (-8.3, 3.5)
15/80	37.2 (31.8, 42.5)	42.1 (36.8, 47.5)	5.0 (-0.629, 10.6)
70/0	38.0 (32.7, 43.4)	37.2 (31.9, 42.6)	-0.790 (-6.4, 4.8)

Figure 13. MVO at 80 mmHg. Values presented as means (95% CI)



Venous Compliance

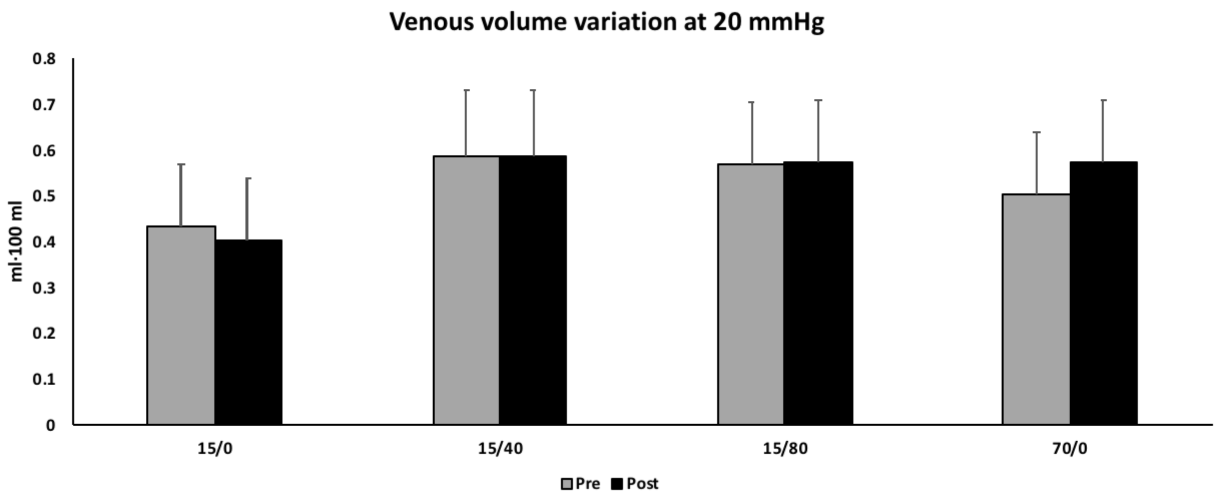
Venous volume variation (VVV) (ml·100 ml $tissue^{-1}$) was calculated as the maximal volume change in the calf at each respective pressure (20, 40, 60, and 80 mmHg) which was able to create a pressure-volume curve. Calf venous compliance (ml/100 ml/mmHg) was calculated as the slope of the pressure-volume curve (27).

A mixed model accounting for participant and condition was performed to determine differences in VVV at 20 mmHg. The compound symmetry model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. There was no interaction (p=.848), no main effect of time (p=.816), and no main effect of condition (p=.066). There was no statistical difference for any outcomes for VVV at 20 mmHg (Table 16).

Table 16. VVV at 20 mmHg. Values presented as means (ml·100 ml) (95% CI)

Condition	Pre	Post	Pre-Post Δ
15/0	0.439 (0.303, 0.575)	0.404 (0.268, 0.540)	-0.035 (-0.132, 0.202)
15/40	0.588 (0.445, 0.730)	0.588 (0.445, 0.730)	0.000 (-0.176, 0.176)
15/80	0.569 (0.433, 0.706)	0.574 (0.438, 0.711)	0.005 (-0.162, 0.172)
70/0	0.503 (0.367, 0.639)	0.573 (0.437, 0.709)	0.070 (-0.097, 0.237)

Figure 14. VVV at 20 mmHg. Values presented as means (ml·100 ml) (95% CI)

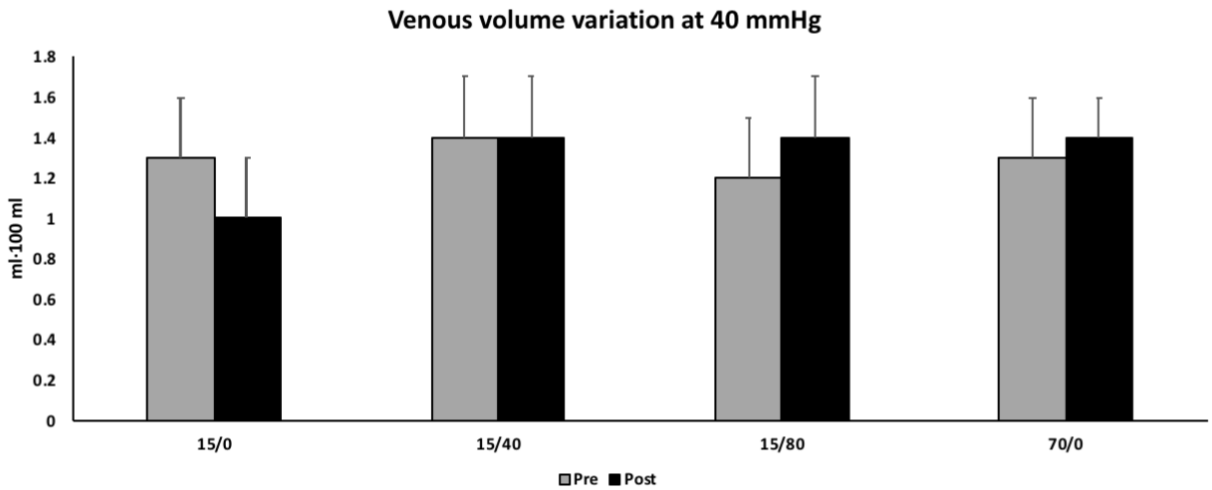


A mixed model accounting for participant and condition was performed to determine differences in VVV at 40 mmHg. The compound symmetry model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. There was no interaction (p=.131), no main effect of time (p=.850), and no main effect of condition (p=.340). There was no statistical difference for any outcomes for VVV at 40 mmHg (Table 17).

Table 17. VVV at 40 mmHg. Values presented as means (ml·100 ml) (95% CI)

Condition	Pre	Post	Pre-Post Δ
15/0	1.3 (1.1, 1.6)	1.0 (.748, 1.3)	-0.320 (-0.641, 0.001)
15/40	1.4 (1.1, 1.7)	1.4 (1.1, 1.7)	-0.022 (-0.360, 0.316)
15/80	1.2 (0.968, 1.5)	1.4 (1.2, 1.7)	0.210 (-0.111, 0.531)
70/0	1.3 (1.0, 1.6)	1.4 (1.1, 1.6)	0.070 (-0.251, 0.391)

Figure 15. VVV at 40 mmHg. Values presented as means (ml·100 ml) (95% CI)



A mixed model accounting for participant and condition was performed to determine differences in VVV at 60 mmHg. The compound symmetry model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values.

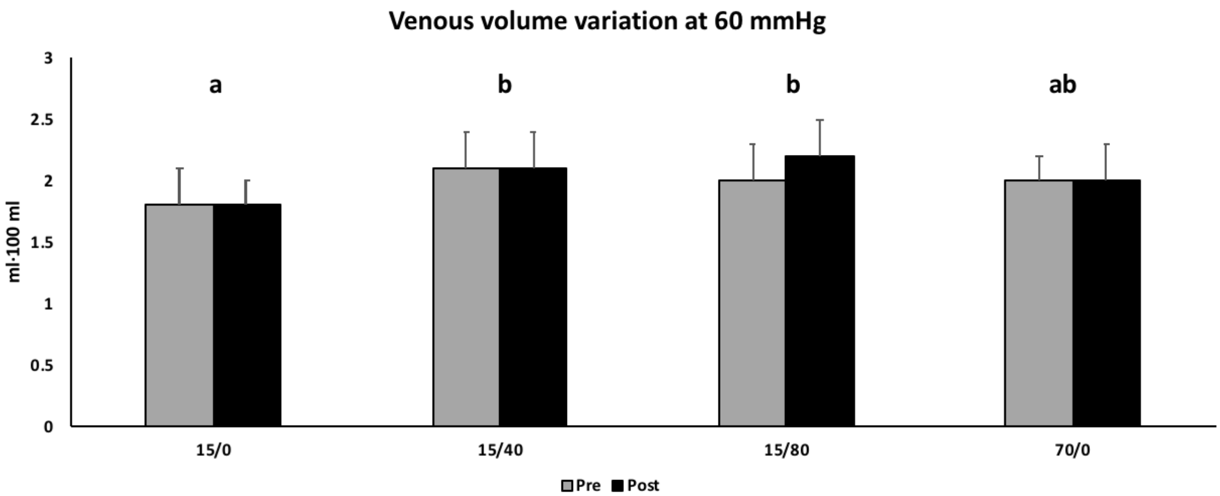
There was no interaction (p=.616) or main effect of time (p=.559). However, there was a main effect of condition (p=.035). Condition 15/0 was lower than 15/40 [mean difference: -0.298 (-0.530, -0.066) mmHg] and 15/80 [mean difference: -0.301 (-0.532, -0.071) mmHg]. There were no differences between conditions 15/0 and 70/0 [mean difference: -0.203 (-0.430, 0.025) mmHg] (Table 18).

Table 18. VVV at 60 mmHg. Values presented as means (ml·100 ml) (95% CI)

Condition ¶	Pre	Post	Pre-Post Δ
15/0[a]	1.8 (1.6, 2.1)	1.8 (1.5, 2.0)	-0.065 (-0.338, 0.208)
15/40[b]	2.1 (1.8, 2.4)	2.1 (1.8, 2.4)	-0.017 (-0.304, 0.271)
15/80[b]	2.0 (1.7, 2.3)	2.2 (1.9, 2.5)	0.180 (-0.093, 0.453)
70/0[ab]	2.0 (1.7, 2.2)	2.0 (1.8, 2.3)	0.065 (-0.208, 0.338)

¶ denotes main effect of condition. If conditions contain at least one of the same letter, they are not significantly different from each other.

Figure 16. VVV at 60 mmHg. Values presented as means (ml·100 ml) (95% CI)

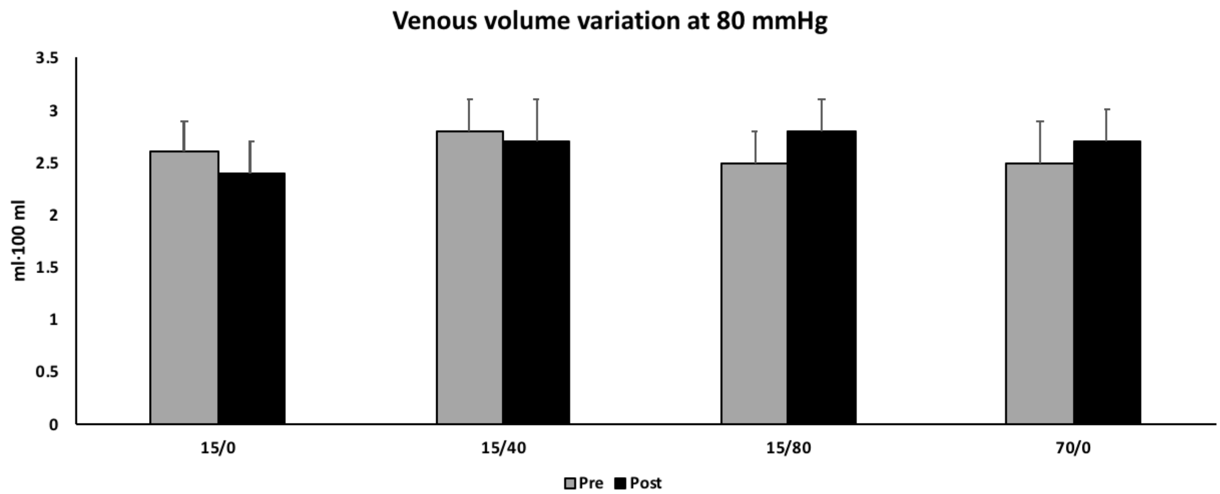


A mixed model accounting for participant and condition was performed to determine differences in VVV at 80 mmHg. The compound symmetry model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. There was no interaction (p=.161), no main effect of time (.277), and no main effect of condition (p=.224). There was no statistical difference for any outcomes for VVV at 80 mmHg (Table 19).

Table 19. VVV at 80 mmHg. Values presented as means (ml·100 ml) (95% CI)

Condition	Pre	Post	Pre-Post Δ
15/0	2.6 (2.3, 2.9)	2.4 (2.1, 2.7)	-0.125 (-0.426, 0.176)
15/40	2.8 (2.5, 3.1)	2.7 (2.4, 3.1)	-0.033 (-0.351, 0.284)
15/80	2.5 (2.2, 2.8)	2.8 (2.5, 3.1)	0.325 (0.024, 0.626)
70/0	2.5 (2.2, 2.9)	2.7 (2.4, 3.0)	0.170 (-0.131, 0.471)

Figure 17. VVV at 80 mmHg. Values presented as means (ml·100 ml) (95% CI)

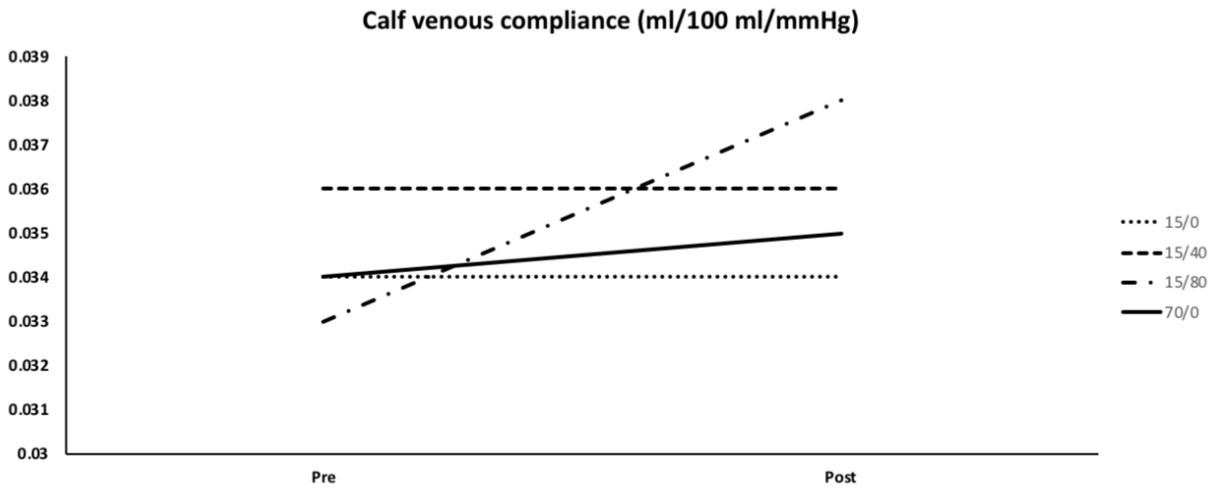


A mixed model accounting for participant and condition was performed to determine differences in pressure-volume curve between conditions. The compound symmetry model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. There was no interaction (p=.335), no main effect of time (p=.204), and no main effect of condition (p=.684) (Table 20). Figure 18 displays the pressure-volume curve for each condition.

Table 20. Calf venous compliance (ml/100 ml/mmHg). Values presented as means (95% CI)

Condition	Pre	Post	Pre-Post Δ
15/0	0.034 (0.030, 0.038)	0.034 (0.030, 0.038)	0.000 (-0.004, 0.004)
15/40	0.036 (0.032, 0.041)	0.036 (0.032, 0.040)	0.000 (-0.005, 0.004)
15/80	0.033 (0.029, 0.037)	0.038 (0.034, 0.042)	0.005 (0.000, 0.009)
70/0	0.034 (0.030, 0.038)	0.035 (0.031, 0.039)	0.001 (-0.003, 0.006)

Figure 18. Calf venous compliance pre-post values (ml/100 ml/mmHg).



Ratings of Perceived Exertion (RPE)

A mixed model account for participant and condition was performed to determine differences in ratings of perceived exertion (RPE). The unstructured model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. There was a statistically significant interaction for RPE (p=.002).

From Visit 1 – Visit 9, condition 70/0 was not different to condition 15/0 [mean difference: 0.686 (-0.202, 1.6)]. However, condition 70/0 was different to 15/40 [mean difference: -1.0 (-1.9, -0.093)] and 15/80 [mean difference: -0.972 (-1.9, -0.083)]. Condition 15/0 was different to 15/40 [mean difference: -1.7 (-2.6, -0.817)] and 15/80 [mean difference: -1.7 (-2.6, -0.764)]. There were no differences between conditions 15/40 and 15/80 [mean difference: 0.043 (-0.868, 0.954)].

From Visit 9 – Visit 16, condition 70/0 was not different to condition 15/0 [mean difference: 0.490 (-0.270, 1.3)], 15/40 [mean difference: 0.419 (-0.372, 1.2)], and 15/80 [mean difference: -0.081 (-0.855, 0.694). Condition 15/0 was not different to condition 15/40 [mean difference: -0.071 (-0.832, 0.691) and 15/80 [mean difference: -0.571 (-1.3, 0.198)]. There were no differences between conditions 15/40 and 15/80 [mean difference: -0.500 (-1.3, 0.290)].

From Visit 1 – Visit 16, condition 70/0 was not different to condition 15/0 [mean difference: -0.196 (-1.4, 0.979)] and 15/80 [mean difference: 0.891 (-0.290, 2.1)]. However, there were differences between 70/0 and 15/40 [mean difference: 1.4 (0.227, 2.6)]. Condition 15/0 was different to condition 15/40 [mean difference: 1.6 (0.458, 2.8)] but not 15/80 [mean difference: 1.1 (-0.090, 2.3)]. Furthermore, 15/40 was not different to 15/80 [mean difference: -0.543 (-1.7, 0.654).

Table 22 displays the changes over time where conditions 15/0 and 70/0 did not observed significant changes in RPE while 15/40, and 15/80 observed a significant decrease from Visit 1 – Visit 9. Moreover, conditions 15/0, 15/80, and 70/0 did not observe a significant change from Visit 1 – Visit 16. Condition 15/40 did observe a significant decrease in RPE across time. Figure 19 displays the RPE rating for each condition for each visit.

Table 21. RPE. Values presented as means (95% CI)

Condition †	Visit 1	Visit 9	Visit 16
15/0	14.1 (13.2, 15.0)	14.8 (13.8, 15.8)	14.3 (13.3, 15.4)
15/40	15.7 (14.7, 16.6)	14.6 (13.7, 15.7)	14.3 (13.2, 15.3)
15/80	15.9 (15.0, 16.9)	15.0 (14.0, 16.0)	15.1 (14.1, 16.1)
70/0	15.0 (14.0, 15.9)	15.0 (14.0, 16.0)	15.0 (14.0, 16.1)

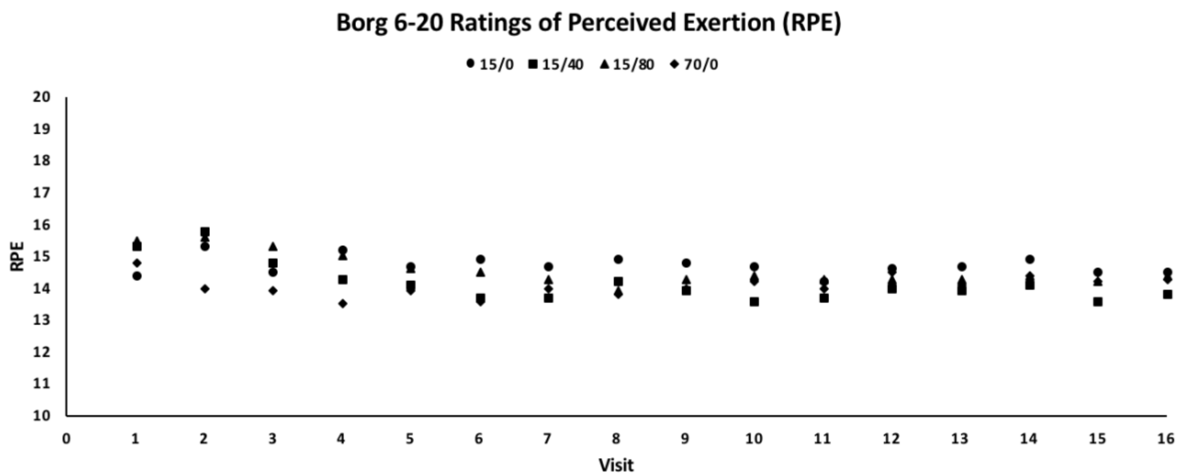
† denotes an interaction.

Table 22. RPE change scores. Values presented as means (95% CI)

Condition †	Visit 1-9 Δ	Visit 9-16 Δ	Visit 1-16 Δ
15/0	0.717 (-0.062, 1.5)[a]	-0.463 (-1.0, 0.114)	0.255 (-0.664, 1.2)[a]
15/40	-0.984 (-1.8, -0.182)[b‡]	-0.392 (-1.0, 0.220)	-1.4 (-2.3, -0.431)[bc‡]
15/80	-0.941 (-1.7, -0.150)[a‡]	0.108 (-0.500, 0.716)	-0.832 (-1.8, 0.104)[ac]
70/0	0.031 (-0.761, 0.823)[a]	0.027 (-0.574, 0.629)	0.059 (-0.884, 1.0)[a]

† denotes an interaction. If conditions contain at least one of the same letter, they are not significantly different from each other. ‡ significant change across visits

Figure 19. Ratings of Perceived Exertion (RPE) across time.



Discomfort

A mixed model account for participant and condition was performed to determine differences in discomfort. The unstructured model was chosen for analysis based on Schwarz's Bayesian Criterion (BIC) and Akaike's Information Criterion (AIC) values. There was a statistically significant interaction for discomfort (p=.012).

From Visit 1 – Visit 9, condition 70/0 was different to conditions 15/0 [mean difference: 0.872 (0.180, 1.6)] and 15/80 [mean difference: 1.4 (0.719, 2.1)] but not to condition 15/40 [mean difference: 0.513 (-0.212, 1.2)]. Condition 15/0 was not different to conditions 15/40 [mean difference: -0.359 (-1.0, 0.331)] and 15/80 [mean difference: 0.536 (-0.163, 1.2)]. Condition 15/40 was different compared to 15/80 [mean difference: 0.895 (0.179, 1.6)]

When comparing from Visit 9 – 16, condition 70/0 was not different to 15/0 [mean difference: 0.075 (-0.481, 0.632)], 15/40 [mean difference: 0.119 (-0.457, 0.696)], and 15/80 [mean difference: 0.048 (-0.518, 0.614)]. Furthermore, condition 15/0 was not different compared to 15/40 [mean difference: 0.044 (-0.510, 0.597)] and 15/80 [mean difference: -0.027

(-0.587, 0.533)]. There were no differences between conditions 15/40 and 15/80 [mean difference: -0.071 (-0.643, 0.501)].

From Visit 1 – Visit 16, the 70/0 condition was not different to conditions 15/0 [mean difference –0.796 (-1.6, 0.052) and 15/40 [mean difference: -0.394 (-1.3, 0.494)]. Additionally, there were differences between condition 70/0 and 15/80 [mean difference: -1.4 (-2.2, -0.507)]. Condition 15/0 was not different compared to 15/40 [mean difference: 0.402 (-0.443, 1.2)] and 15/80 [mean difference: -0.563 (-1.4, 0.295)]. When comparing between conditions 15/40 and 15/80, there were differences between conditions from Visit 1 – Visit 16 [mean difference: -0.965 (-1.8, -0.086)]

Table 24 displays the changes over time where conditions 15/0, 15/40, and 70/0 observed a significant decrease in discomfort from Visit 1 – Visit 9 while condition 15/80 did not. Moreover, conditions 15/0, 15/40, and 70/0 observed a significant decrease from Visit 1 – Visit 16. Condition 15/80 did not observe any significant changes across visits. Figure 20 displays the discomfort rating for each condition for each visit.

Table 23. Discomfort. Values presented as means (95% CI)

Condition †	Visit 1	Visit 9	Visit 16
15/0	3.6 (2.7, 4.5)	2.6 (1.9, 3.4)	2.6 (1.9, 3.3)
15/40	4.8 (3.9, 5.8)	3.5 (2.7, 4.2)	3.4 (2.7, 4.1)
15/80	5.1 (4.2, 6.0)	4.7 (3.9, 5.4)	4.6 (3.9, 5.4)
70/0	4.2 (3.3, 5.1)	2.3 (1.6, 3.1)	2.3 (1.6, 3.1)

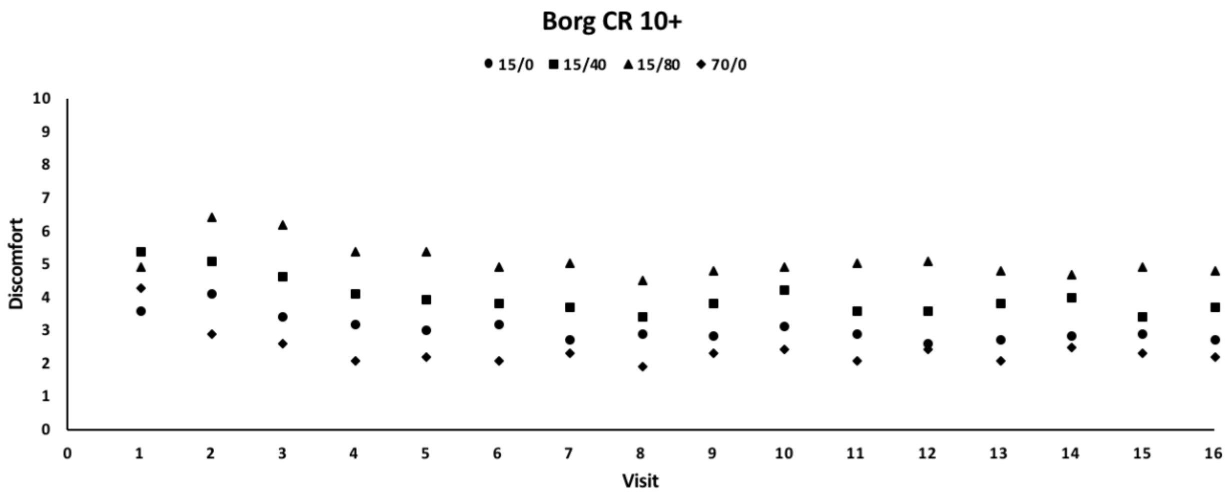
† denotes interaction.

Table 24. Discomfort change scores. Values presented as means (95% CI)

Condition †	Visit 1-9 Δ	Visit 9-16 Δ	Visit 1-16 Δ
15/0	-1.0 (-1.7, -0.346)^{acd‡}	-0.042 (-0.456, 0.372)	-1.0 (-1.8, -0.278)^{abc‡}
15/40	-1.4 (-2.0, -0.682)^{bc‡}	-0.086 (-0.519, 0.347)	-1.4 (-2.2, -0.651)^{ab‡}
15/80	-0.464 (-1.1, 0.201)^{ad}	-0.015 (-0.447, 0.416)	-0.479 (-1.3, 0.304)^{bc}
70/0	-1.9 (-2.5, -1.2)^{b‡}	0.033 (-0.399, 0.466)	-1.8 (-2.6, -1.1)^{a‡}

† denotes interaction. If conditions contain at least one of the same letter, they are not significantly different from each other. ‡ significant change across visits

Figure 20. Discomfort rating (Borg CR 10+) across time



Arterial Occlusion Pressure

A one-way repeated measures ANOVA was performed to determine if arterial occlusion pressure (AOP) was different over time (Visit 1, Visit 9, and Visit 16) within each pressure. There were no differences in AOP over time for either the 15/40 condition (p=.423) or the 15/80 condition (p=.305). Table 25 displays the change score of arterial occlusion pressure over time. Figure 21 displays the change in AOP from Visit 1 to 16. Additionally, Figure 22 displays the means of AOP at Visit 1, 9, and 16.

Table 25. AOP change scores (mmHg). Values presented as means (95% CI)

Condition	Visit 1- 9Δ	Visit 9-16Δ	Visit 1-16Δ
15/40	3 (-8, 15)	4 (-10, 19)	8 (-4, 20)
15/80	0 (-10, 11)	7 (-5, 20)	8 (-4, 20)

Table 26. AOP (mmHg). Values presented as means (95% CI)

Condition	Visit 1	Visit 9	Visit 16
15/40	190 (180, 200)	193 (182, 205)	198 (185, 212)
15/80	189 (180, 199)	189 (178, 201)	197 (184, 211)

Figure 21. AOP (mmHg) change scores Visit 1-16. Values presented as mean (95% CI)

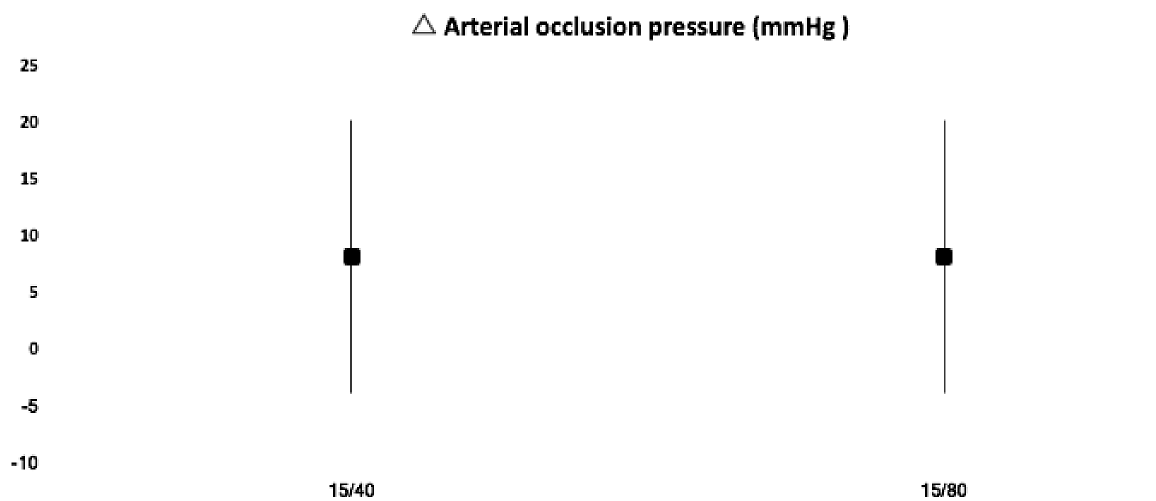
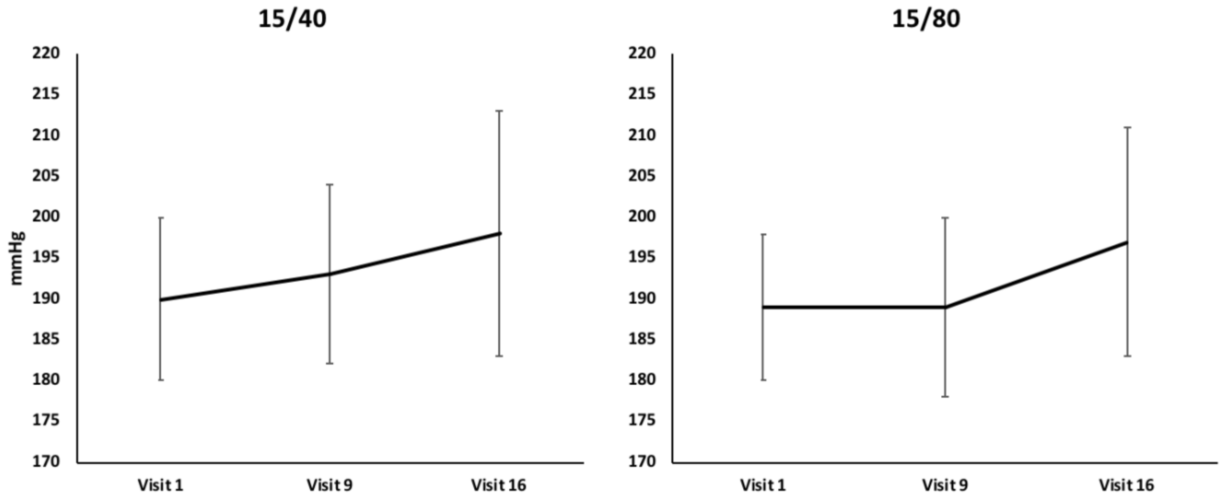


Figure 22. AOP (mmHg) across time. Values presented as means (95% CI)



CHAPTER V: DISCUSSION

The results of the current study showed that blood pressure increased following an acute bout of lower body resistance exercise independent of the level of blood flow restriction and external load. Additionally, blood flow increased in the 15/0 and 15/40 conditions but not the other conditions. When examining the chronic adaptations to these different protocols, calf blood flow and vascular conductance increased in conditions 15/80 and 70/0. However, there were no statistically significant changes in calf venous compliance in any of the conditions following 8 weeks of lower body resistance training. RPE ratings were greater with a higher restriction pressure and load. Discomfort ratings were generally higher with blood flow restriction.

Main Findings

1. All conditions increased systolic blood pressure pre-post following one bout of knee extension exercise. However, condition 15/80 had the lowest change in systolic blood pressure while conditions 15/0, 15/40, and 70/0 had a similar change.

2. All conditions increased diastolic blood pressure similarly following one bout of knee extension exercise.

3. All conditions increased heart rate similarly following one bout of knee extension exercise.

4. Blood flow only increased in conditions 15/0 and 15/40 following one bout of knee extension exercise.

5. Calf blood flow and calf vascular conductance increased in conditions 15/80 and 70/0 following 8 weeks of resistance training

6. There was no increase in calf venous compliance following 8 weeks of resistance training.

7. RPE significantly decreased in condition 15/40 by the end of the training study while all other conditions remained similar.

8. Discomfort ratings significantly decreased in conditions 15/0, 15/40, and 70/0 by the end of the training study while condition 15/80 remained similar.

9. RPE had generally higher ratings with increased pressure and load.

10. Discomfort had generally higher ratings with blood flow restriction

10. Arterial occlusion pressure did not significantly change over the 8 week training study.

Acute Experimental

Blood Pressure

Overall, systolic blood pressure increased pre-post which agrees with previous literature on resistance exercise with and without the application of blood flow restriction (24, 28, 88, 94). The change in systolic blood pressure was greatest for the 15/0 condition and was not augmented by the application of blood flow restriction. Interestingly, the 15/80 condition had the smallest change from baseline. Our results differ when compared to Downs et al. (88) who found that the blood flow restriction condition with the highest restriction pressure increased systolic blood pressure by 38 mmHg pre-post while the current study observed a 5 mmHg increase. Additionally, our results differ from Takano et al. (24) who observed that blood flow restriction augmented the blood pressure response. One possible explanation for the difference is that participants performed unilateral knee extension exercise in the current study while the previous studies performed bilateral exercise (24, 88). It has been shown that performing bilateral exercise results in a greater cardiovascular response when compared to unilateral exercise (19, 95).

Additionally, the greater amount of muscle mass involved in the exercise could have played a role. It is also possible that the additional exercise could have influenced the greater systolic blood pressure response while the current study only employed one exercise. Downs et al. (88) performed leg press exercise followed by calf raises exercise (both exercises performed bilaterally) while the current study only performed one exercise. The 15/0 condition induced the highest systolic blood pressure change which is in contrast to what Downs et al. (88) observed. One possible explanation for the differences between studies is the amount of exercise performed (e.g. number of repetitions). A study by Gjovaag et al. (96) examined the acute hemodynamic response following 4 sets of bilateral knee extension exercise to two different protocols (4RM vs 20RM). The authors found that systolic and diastolic blood pressure increased more following the 20RM protocol. This is in agreement with MacDougall et al. (19) which found a progressive increase in blood pressure with each subsequent repetition. These findings suggest that the acute blood pressure response is related to the numbers of repetitions performed and not the load. In the current study, participants performed 4 sets to volitional failure/90 repetitions while Downs et al. (88) performed 3 sets to failure. Therefore, the greater number of repetitions following unrestricted resistance exercise could have played a role when comparing the current study and Downs et al. (88). Additionally, this could also explain why the 15/80 condition observed the smallest systolic blood pressure change.

Diastolic blood pressure observed a slight increase in all conditions but not to the same magnitude as systolic blood pressure which agrees with previous literature on resistance exercise with and without the application of blood flow restriction (19, 24, 28, 88, 95). The current study observed an increase in heart rate in all conditions which agrees with previous research following resistance exercise with and without blood flow restriction (19, 24, 28, 88, 96, 97). The increase in heart rate response to an acute bout of exercise may be explained by an increase in sympathetic nervous activity and vagal withdrawal (98). In addition, with blood flow restricted exercise, heart rate is often augmented due to the decrease in venous return (24, 72). Interestingly, the heart rate values following blood flow restricted exercise in the current study produced similar values to unrestricted exercise. These similar heart rate responses may be due to all conditions exercising to failure and not being matched for work/repetitions.

Blood Flow

At the onset of exercise, blood flow increases to deliver oxygen to the active region to meet the increased metabolic demands (32, 99). This increase in blood flow is regulated by an increase in cardiac output and peripheral vasoconstriction (17, 34). Furthermore, mechanical and vasodilatory factors also contribute to the rise in blood flow during dynamic muscular contractions (34, 37, 42, 100). The mechanical factor for the increase in blood flow is referred as the muscle pump (34, 36, 37) while K^+-stimulated vascular hyperpolarization, nitric oxide, vasodilating prostaglandin, endothelium-derived hyperpolarizing factor, and possibly ATP are vasodilatory factors (18, 49, 91, 101). In the current study, there were no statistical differences in blood flow at pre or at post between conditions. However, a Wilcoxon signed rank test revealed that blood flow increased in conditions 15/0 and 15/40. Rådegran and Saltin (36) examined the blood flow response to a 3-minute one-legged knee extensor model bout at four different intensities. They saw that blood flow increased from resting values at different intensities and that this response was intensity dependent. Although the intensity was low (15% 1RM), the nature of the exercise protocol itself could be intensive. It is puzzling why condition 15/80 did not observe an increase in blood flow following exercise. One possible reason for the lack of blood flow increase in the 15/80 condition is that the mechanical compression of the cuff decreased the amount of blood flow during exercise below baseline values which has been observed previously (23, 24, 88, 102). Further, the post exercise hyperemic response after cuff deflation could have been affected by the number of repetitions. The combination of a decreased blood flow during resistance exercise and decreased repetitions may have affected the post exercise hyperemic response in the 15/80 condition.

Chronic Experimental

Calf Blood Flow and Calf Vascular Conductance

When examining cardiovascular health, basal limb blood flow and vascular conductance are often measured as a reduction in limb blood flow is associated with the development of metabolic syndrome (44). It has been demonstrated that low load resistance exercise (89) and traditional high load resistance exercise (43) increases basal limb blood flow and vascular conductance following 13 weeks of resistance training. One proposed mechanism for this effect is an increase in capillarization.

When examining the blood flow restriction literature, we observed a similar response in calf blood flow and vascular conductance as Fahs et al. (92). They examined three different resistance training protocols (low load blood flow restriction, moderate load, and high load resistance exercise) for 6 weeks and observed that calf blood flow and vascular conductance increased. In the current study, we observed that conditions 15/80 and 70/0 increased calf blood flow and calf vascular conductance following 8 weeks of lower body resistance training. The increase in calf blood flow and vascular conductance from the current study suggests that there may have been an increase in arteriole numbers and/or capillaries in parallel. Some variables that play a role in vascular remodeling include the muscle contraction itself, metabolism, reduced oxygen tension, and shear stress (21, 100). Shear stress is raised when blood flow increases which can lead to an increase in nitric oxide formation and upregulation of endothelial nitric oxide synthase (eNOS) (100). The increase in nitric oxide interacts with vascular endothelial growth factor (VEGF) which may promote angiogenesis (formation of new capillaries) (103). A recent study by Ferguson et al. (104) examined VEGF following an acute bout of knee extension exercise with and without blood flow restriction. They observed that VEGF increased following blood flow restriction at 2 hours and 4 hours post exercise which has been previously found (24). The blood flow restriction condition utilized 100 mmHg of pressure with a 13 cm wide cuff and may have decreased muscle oxygen levels which has been displayed previously within the literature (88, 105). Thus, this environment can upregulate HIF-1α which has been demonstrated to signal VEGF (106). Therefore, with repeated exercise training sessions, the increase in arterioles numbers and/or capillaries in parallel may cause an increase in limb blood flow.

The increase in blood flow was only observed in the high restriction condition and high load condition; however, this was not observed in the other conditions (15/0 and 15/40). A previous study by Fahs et al. (27) saw that blood flow increased following resistance exercise in the lower body while lifting 30% 1RM to volitional failure without blood flow restriction. In the current study, we did not observe an increase in blood flow when utilizing a load of 15% 1RM without blood flow restriction. It is possible that the combination of lifting at 30% 1RM and exercise to failure caused the participants to contract their calf muscle and may have been enough to induce angiogenesis. A possible explanation for why there wasn't an increase in the 15/40 condition is that the restriction pressure may not have been high enough when combined with a very low load (15% 1RM). Previous literature have investigated the metabolic activity to low load blood flow restriction resistance exercise and compared it to traditional high load resistance exercise. (107, 108). For instance, a study by Yasuda et al. (107) examined metabolites levels following low load resistance exercise (20% 1RM) with blood flow restriction at two different restriction pressures (100 mmHg and 160 mmHg) using a 3 cm wide cuff and compared the changes with traditional high load (70% 1RM) resistance exercise. They observed that the production of lactate and inorganic phosphate was augmented with the higher restriction pressure. Additionally, EMG amplitude was increased with the higher restriction pressure which could lead to increased energy demand. Furthermore, Suga et al. (108) also observed a similar response in which low load resistance exercise with continuous blood flow restriction (130% SBP; 18.5 cm wide cuff) and traditional high load resistance exercise induced a similar metabolic stress. Although the low load conditions were not performed to failure, these studies suggest that a high restriction pressure augments metabolite accumulation and energy demand. Further a high restriction pressure may be necessary to see adaptations when lifting a load less than 30% 1RM (14).

Calf Venous Compliance

Approximately 70% of the total blood volume is stored in the venous system which plays an essential role in maintaining cardiovascular homeostasis (26, 109, 110). The veins play an important role in determining cardiovascular stress from orthostasis. As blood volume shifts from the thoracic region to the lower extremities when standing up, there is an increase in heart rate and peripheral arterial resistance (47, 109). Additionally, lower limb muscular contractions along with venous valves promote blood flow towards the right atrium (111). A change in compliance may represent structural changes within the vessel wall (e.g. a decrease in the elastin-to-collagen ratio) or an increase in nitric oxide and/or decreased sympathetic adrenergic tone (45, 46). Increasing venous compliance may be important for blood mobilization to the central circulation; however, if the veins become too compliant, it may also lead to greater incidence of orthostatic intolerance (47). Moreover, a low venous compliance may serve as a protective mechanism against orthostatic hypotension but could also be detrimental (46, 112). It seems that venous compliance is on a continuum and that there seems to be a range for individuals. To determine venous compliance, a pressure-volume slope is calculated during the deflated period from various cuff inflated pressures (20,40,60, and 80 mmHg) to reflect venous pressure.

Within the blood flow restriction literature, there is limited data looking at venous compliance (26, 27). Following 6 weeks of lower body resistance training to volitional failure with or without blood flow restriction, calf venous compliance did not increase (27). This is similar to the results in the current study where there were no increases in calf venous compliance in any of the groups. In contrast, Iida et al. (26) did observe an increase in calf venous compliance following 6 weeks of walking 5 days per week. The discrepancies between the current study and Iida et al. (26) findings could be explained by the modality of exercise. In the current study, the mode of exercise was knee extension which primarily involves the quadriceps muscles and does not directly involve the calf muscles whereas walking directly involves the calf muscles. Other potential reasons for the lack of increase in venous compliance is the number of training sessions (16 sessions vs. 30 sessions), duration under blood flow restriction (12 minutes vs. 20 minutes), and the measurement location. The measurement of venous compliance is taken at the calf and not the quadriceps. It is plausible that if the measurement was taken at the upper thigh in the current study, there may have been an increase in venous compliance.

Maximum venous outflow is calculated as the slop of the tangent line to the curve 0.5 s after deflation of the cuff. Further, this variable is described as the ability of the vein to carry blood out of the limb (113). It has been previously observed that maximum venous outflow can decrease (27) or increase (26) following blood flow restricted exercise. Since the goal of blood flow restriction is to reduce arterial inflow and occlude venous outflow, it has been suggested that venous pooling may alter the hydrostatic forces and affect the venous properties (26, 114) such as the venous wall. A study by Fahs et al. (27) observed a decrease in maximum venous outflow at 20 mmHg in the blood flow restricted condition which may indicate there is a reduced in elastic recoil of the venous wall (115). However, Iida et al. (26) observed an increase of maximum venous outflow at 80 mmHg which suggests that there were alterations in the hydrostatic forces. In the current study, there were no significant changes in maximum venous outflow which suggests that blood flow restriction did not affect any of the venous properties. It is plausible that the load and/or type of exercise played a role in the discrepancies of the previous studies (26, 27).

Perceptual Responses

Previous studies that use blood flow restriction with a relative restriction pressure will often use a moderate pressure (40% arterial occlusion pressure) or a high pressure (80% arterial occlusion pressure) (13, 14, 87, 116). When comparing the perceptual responses to these two relative restriction pressures, a higher restriction pressure generates a greater discomfort (13, 29, 116) while ratings of perceived exertion (RPE) are either similar (83, 87) or higher (29, 116).

When compared to high load resistance exercise, RPE is either lower (107) or higher (117) while discomfort is often greater (83). A study by Martin-Hernández et al. (84) examined RPE to determine if ratings were altered following six training sessions and how it compared to traditional high load resistance exercise. They observed that RPE decreased in both training conditions over time; however, RPE was greater in the traditional high load condition. In the current study, condition 15/40 observed the greatest decrease in RPE by the end of training study while all other conditions remained consistent. This suggests that possibly the relative intensity decreased over the course of the training protocol. In general, condition 15/80 and 70/0 observed higher RPE ratings. It is possible that the 15/80 condition had an exacerbated RPE rating by stimulating cutaneous afferent nerves which increased central descending drive; thus, exaggerating the perception of work (118). Additionally, an increased corollary discharge rate may also be playing a role as blood flow restriction produces muscle fatigue quicker compared to unrestricted resistance exercise with a similar load (119, 120). Furthermore, high mechanical loading may have increased the strain in the thigh muscles, tendons, and joints in the 70/0 condition which may have caused an increase in perceived exertion (121).

Previous investigations have shown that the level of discomfort is higher with blood flow restriction compared to unrestricted resistance exercise (82, 85). Additionally, a higher restriction pressure is also associated with higher discomfort ratings when compared to moderate restriction pressure (13, 29, 116). In the current study, discomfort ratings decreased by the end of the study for conditions 15/0, 15/40, and 70/0 while condition 15/80 remained similar. Kim et al. (81) and Martin-Hernández et al.(84) have observed that blood flow restriction caused high discomfort/pain ratings initially but decrease over time. In the present study, this was only observed in the 15/40 condition but not the 15/80 condition in the current study. A possible reason why the 15/80 condition did not observe a significant decrease in discomfort is that the high restriction pressure increased metabolites and reduced oxygen in the tissue which may have stimulated group III and IV afferent fibers (107, 122). Although condition 15/40 observed a decrease in discomfort rating by the end of the training study, both blood flow restriction conditions displayed greater discomfort ratings compared to the unrestricted conditions (15/0 and 70/0). In general, RPE were greater with higher loads and pressure. Moreover, discomfort was generally greater with the application of blood flow restriction. These perceptual responses to different restriction pressures may be important as individuals may be less likely to perform this mode of training if it is perceived as less tolerable.

Arterial Occlusion Pressure

The current study observed no significant changes in arterial occlusion pressure by the end of the 8 week resistance training protocol. Ingram et al. (12) suggested that applying a relative restriction pressure should be based on arterial occlusion pressure for each training visit rather than applying pressure based on one measurement time point. Moreover, the authors observed that arterial occlusion pressure differed (albeit small) depending on the time of day. The current study measured arterial occlusion pressure for each training visit prior to exercise to account for oscillatory patterns. Although there were no statistically significant changes over the course of the study, arterial occlusion does appear to trend upwards over the 8 weeks. Some possible explanations for an increase could be that we did not control for caffeine intake and did not have the participants rest prior to exercise. Additionally, some participants could have trained at a different time than they were scheduled resulting in a different arterial occlusion pressure as previously stated (12). Although there was an upwards trend which would increase the applied restriction pressure, this trend would not be a matter of concern as the current study applied a percentage (40% or 80% arterial occlusion pressure) based on arterial occlusion pressure for that specific visit. This would ensure that all participants received a similar stimulus to lessen their risk for a potential cardiovascular event.

CHAPTER VI: CONCLUSION

The purpose of this study was to examine the acute changes in blood pressure and blood flow following exercise with and without different levels of blood flow restriction while using a very low load (15% 1RM) and traditional high load (70% 1RM). Additionally, we wanted to determine the chronic changes of calf vascular conductance, calf venous compliance, and perceptual responses (RPE and discomfort) following 8 weeks of resistance training in the lower to these different protocols.

Hypotheses

1. It was hypothesized that blood pressure would be greatest following traditional high load resistance exercise compared to other exercise conditions. Further, blood pressure would be greater at a restriction pressure of 80% arterial occlusion pressure compared to a restriction pressure of 40% arterial occlusion pressure. Resistance exercise at very low loads without blood flow restriction would have the lowest blood pressure change.

The hypothesis was moderately supported by the data. Conditions 15/0, 15/40, and 70/0 had a similar blood pressure response to acute resistance exercise and was significantly different to the 15/80 condition. The blood pressure response in the condition with 80% arterial occlusion pressure (15/80) observed an attenuated response compared to other conditions.

2. It was hypothesized that participants performing very low load resistance exercise with blood flow restriction (40% and 80% AOP) would have similar post-exercise blood flow

values compared to low load resistance exercise without blood flow restriction and traditional high load resistance exercise.

The hypothesis was partially supported by the data. Only conditions 15/0 and 15/40 statistically changed from pre-post while 15/80 and 70/0 did not. Condition 15/0 observed the greatest change in blood flow response to lower body resistance exercise compared to all other conditions.

3. It was hypothesized that calf vascular conductance would increase in all conditions following 8 weeks of resistance training.

The hypothesis was moderately supported by the data. Conditions 15/80 and 70/0 were the only conditions that increased calf blood flow and calf vascular conductance following 8 weeks of resistance training in the lower body.

4. It was hypothesized that calf venous compliance would not change in any of the conditions but would remain similar to their respective baseline values following 8 weeks of resistance training.

The hypothesis was fully supported by the data. Calf venous compliance did not change significantly from baseline values. However, it does look like there was a trend for an increase in calf venous compliance in condition 15/80.

5. It was hypothesized that RPE and discomfort ratings would be greatest for traditional high load exercise compared to very low load resistance exercise alone or combined with blood flow restriction. Also, a restriction pressure of 80% arterial occlusion pressure would

produce a greater RPE and discomfort rating compared to a restriction pressure of 40% arterial occlusion pressure.

The hypothesis was moderately supported by the data. Traditional high load exercise (70/0) had a high RPE rating; however, a restriction pressure of 80% arterial occlusion pressure produced a similar value. A restriction pressure of 80% arterial occlusion pressure did have a greater RPE rating to a restriction pressure of 40% arterial occlusion pressure. When observing discomfort ratings, condition 15/80 observed the greatest rating. Additionally, condition 15/80 had a greater discomfort rating compared to condition 15/40. Traditional high load exercise (70/0) had the lowest discomfort rating out of all conditions.

Significance

The current study showed that the acute blood flow response is higher following resistance exercise without blood flow restriction while lifting a very low load and lifting a very low load with moderate restriction pressure (40% arterial occlusion pressure). Chronic vascular adaptations of the current study agree with some of the previous literature with and without blood flow restriction; however, there are some conflicting results. We did not observe an increase in calf blood flow and vascular conductance in the 15/0 and 15/40 conditions. It may be that lifting a load of 15% 1RM without blood flow restriction or at a moderate pressure does not have an impact on the vascular network over time and that a higher restriction pressure may be necessary to observe changes in calf blood flow and vascular conductance. These results add to the hypothesis that a higher restriction pressure is necessary when utilizing a load less than 30% 1RM. This study provides information to the cardiovascular and perceptual response to lifting at 15% 1RM with or without blood flow restriction and how it compares to traditional high load resistance exercise. These findings may be beneficial for individuals in the clinical setting following ACL surgery, athletes, and the elderly.

Future Research

Follow up studies could investigate the signaling pathways of angiogenesis to these conditions to gain a better understanding of the mechanisms involved in the vascular adaptations observed in the current study. Additionally, other prospective studies could examine the response to different exercises (e.g. back squat, leg press). The current study design was a within/between subject design. Future study designs can perform a between subject design comparing the same conditions. Additionally, including a control group may be beneficial to account for the random biological error occurring over the 8 weeks. This study may also serve as a reference for future studies examining the impact of load and cardiovascular adaptations and may want to examine how low of a load can be effectively applied.

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- EL 151 Weightlifting: Spring 2016 (1 section)
- EL 124 Racquetball: Fall 2015 (3 sections), Spring 2016 (3 sections)

- ES 349 Physiology of Exercise Lab: Fall 2015 (1 section), Summer 2016 (1 section), Spring 2017 (1 section)

This course consisted of teaching and demonstrating laboratory methods such as VO_2max, skinfold measurements, Wingate test, flexibility, muscular strength/endurance, and blood pressure. In addition, the laboratory included a practical exam to ensure that the students followed correct procedures to test their skills.

- ES 457 Exercise Testing and Prescription Lab: Spring 2016 (2 sections), Fall 2016 (3 sections), Spring 2017 (4 sections), Fall 2017 (3 sections)

This laboratory consisted of demonstrating and providing methods for exercise testing such as VO_2max, skinfold measurements, YMCA submaximal protocols, flexibility, and muscular strength/endurance. In addition, the laboratory included a practical exam to ensure that the students followed correct procedures and to test their skills. A case study was also incorporated into the class by having the students write out a detailed exercise program (cardiovascular and resistance training) for an individual based on exercise test classifications.

- ES 456 Exercise Testing and Prescription: Fall 2017 (1 section), Spring 2018 (1 section)

This class was to provide scientific foundations for exercise testing and prescription for a variety of populations. Proper methods of exercise testing such risk stratification, informed consent, and contraindications and test terminations points were overviewed as well as the FITT-VP principle for prescribing exercise for healthy and at-risk populations.

- HP 203 First Aid & CPR: August 2016 (1 section), Fall 2016 (1 section)

This class was to provide information on how to prevent accidents, care for individual self and others, know what to do in an emergency, and to provide up to date methods of accident preventions and first-aid techniques. Moreover, this class consisted of practical examinations of different CPR and first-aid situations to test the knowledge of the students.

- ES 394 Therapeutic Exercise and Fitness: Summer 2017 (1 section)

This class provided an overview of therapeutic exercise and fitness components for at-risk populations with an emphasis in the exercise response, exercise training effects, and exercise programming. Additionally, this class provided the pathophysiology to the diseases discussed in the course.

EXPERIENCE

University of Mississippi, Oxford MS **(August 2015 – Present)**

Graduate Assistant

- Performed arterial occlusion pressure measurements relating to blood flow restriction exercise
- Isokinetic dynamometer (Biodex Quickset System 4) tests
- Measured blood flow using pulsed-wave Doppler ultrasound
- Measured skeletal muscle via ultrasound (B-mode ultrasound)
- Measured blood flow via forearm and calf plethysmography

LA Fitness **(August 2013 – June 2015)**

Personal Trainer

- Designed and implemented resistance and cardiovascular exercise programs to clientele from ages 18-75
- Provide one hour fitness assessments for members to identify their level of fitness
- Educate clientele and club members on the importance of health, exercising, and quality of life
- Assist and monitor members with the proper use of free weights, machines, and cardiovascular equipment

University of Oklahoma, Norman OK **(April 2013 – June 2013)**

Research Assistant Internship
Neuromuscular Laboratory

- Learned the methodology of Blood Flow Restriction training
- Assisted in data collection (RPE, Lactate, Hematocrit, MVC)
- Isokinetic dynamometer (Biodex System 3) tests
- Imaged skeletal muscle via ultrasound
- Assisted in the development of a research paper based on previous investigations

University of Pittsburgh, Pittsburgh PA **(August 2012 – August 2013)**
Exercise Specialist
Bairel Student Recreation Center/Trees Hall/Bellefield Hall

- Personal trained for Healthy U Fitness program
- Assisted and monitored students, faculty, and staff with the proper use of free weights, machines, and cardiovascular equipment
- Provided fitness assessments for Fitt at Pitt program

West Virginia University, Morgantown, WV **(May 2011-August 2011)**
Public Health Internship
The Wellness Program of the WVU Health Sciences Campus

- Developed and modified a new HRA for WVU health employees
- Supervised and co-coordinated Farmer's Market
- Assisted and monitored Ornish patients during exercise
- Provided orientations to new members on fitness center policies, procedures, and proper use of equipment
- Designed posters and contributed monthly articles for the monthly newsletter
- Assisted in new employee orientation presentation

Slippery Rock University, Slippery Rock, PA **(January 2010 – December 2011)**
Exercise Specialist
Aebersold Student Recreation Center/Russell Wright Fitness Center

- Performed maintenance on cardio and weight machines (Cybex, Life Fitness, Paramount, Hammer Strength)
- Assisted and monitored members, students, and faculty with the proper use of free weights, machines, and cardiovascular equipment
- Provided orientations to new members on policies and procedures and proper use of equipment
- Provided exercise programs for "Rock Teen Fit" program
- Communicated with Fitness, Welcome Center, Rockwall, and Aquatic staffs to ensure a safe environment

PEER-REVIEWED RESEARCH PUBLICATIONS

1. Loenneke JP, Fahs CA, Rossow LM, Thiebaud RS, **Mattocks KT**, Abe T, Bemben MG: *Blood Flow Restriction Pressure Recommendations: A Tale of Two Cuffs.* Front Physiol 201;4:249.

2. Jessee MB, Buckner SL, Mouser JG, **Mattocks KT**, Loenneke JP: *Letter to the editor: Applying the blood flow restriction pressure: the elephant in the room*. Am J Physiol Heart Circ Physiol 2016;310(1):H132-3 01/2016; 310(1).

3. **Mattocks KT**, Dankel SJ, Buckner SL, Jessee MB, Counts BR, Mouser JG, Laurentino GC, Loenneke JP: *Periodization: What is it Good For?*. Journal of Trainology 2016;5:6-12.

4. Counts BR, Buckner SL, Dankel SJ, Jessee MB, **Mattocks KT**, Mouser JG, Laurentino GC, Loenneke JP: *The acute and chronic effects of "NO LOAD" resistance training*. Physiol Behav 2016;164(Pt A):345-52.

5. Buckner SL, Dankel SJ, Counts BR, Jessee MB, Mouser JG, **Mattocks KT**, Laurentino GC, Abe T, Loenneke JP: *Influence of cuff material on blood flow restriction stimulus in the upper body*. J Physiol Sci 2017;67(1):207-205.

6. Dankel SJ, Buckner SL, Jessee MB, **Mattocks KT**, Mouser JG, Counts BR, Laurentino GC, Abe T, Loenneke JP: *Post-exercise blood flow restriction attenuates muscle hypertrophy*. Eur J Appl Physiol 2016;116(10):1955-63.

7. Buckner SL, Jessee MB, **Mattocks KT**, Mouser JG, Counts BR, Dankel SJ, Loenneke JP: *Determining Strength: A Case for Multiple Methods of Measurement*. Sports Med 2017;47(2):193-195.

8. Buckner SL, Dankel SJ, **Mattocks KT**, Jessee MB, Mouser JG, Counts BR, Loenneke JP: *The problem of muscle hypertrophy: Revisited*. Muscle Nerve 2016;54(6):1012-1014.

9. Counts BR, Rossow LM, **Mattocks KT**, Mouser JG, Jessee MB, Buckner SL, Dankel SJ, Loenneke JP: *Let's talk about sex: where are the young females in blood flow restriction research?* Clin Physiol Funct Imaging 2016; [Epub ahread of print] DOI: 10.1111/cpf.12394

10. Dankel SJ, Jessee MB, **Mattocks KT**, Mouser JG, Counts BR, Buckner SL, Loenneke JP: *Training to fatigue: the answer for standardization when assessing muscle hypertrophy?* Sports Med 2017;47(6):1021-1027.

11. Dankel SJ, **Mattocks KT**, Jessee MB, Buckner SL, Mouser JG, Counts BR, Laurentino GC, Loenneke JP: *Frequency: the overlooked resistance training variable for inducing muscle hypertrophy?* Sports Med 2017;47(5):799-805.

12. Dankel SJ, Mouser JG, **Mattocks KT**, Counts BR, Jessee MB, Buckner SL, Loprinzi PD, Loenneke JP: *The widespread misuse of effect sizes*. J Sci Med Sport 2017;20(5):446-50.

13. Mouser JG, Dankel SJ, Jessee MB, **Mattocks KT**, Buckner SL, Counts BR, Loenneke JP: *A tale of three cuffs: the hemodynamics of blood flow restriction*. Eur J Appl Physiol 2017;117(7):1493-9.

14. Buckner SL, Dankel SJ, **Mattocks KT**, Jessee MB, Mouser JG, Loenneke JP: *Muscle size and strength*: *another study not designed to answer the question*. Eur J Appl Physiol 2017;117(6):1273-4.

15. **Mattocks KT**, Buckner SL, Jessee MB, Dankel SJ, Mouser JG, Loenneke JP: *Practicing the test produces strength equivalent to higher volume training*. Med Sci Sports Exerc 2017 (Epub ahead of print) doi: 10.1249/MSS.0000000000001300

16. Dankel SJ, Buckner SL, Counts BR, Jessee MB, Mouser JG, **Mattocks KT**, Laurentino GC, Abe T, Loenneke JP: *The acute muscular response to two distinct blood flow restriction protocols*. Physiol Int 2017;104(1):64-76.

17. Buckner SL, Mouser JG, Dankel SJ, Jessee MB, **Mattocks KT**, Loenneke JP: *The general adaptation syndrome: potential misapplications to resistance exercise*. J Sci Med Sport 2017; (Epub ahead of print) doi: 10.1016/j.jsams.2017.02.012

18. Jessee MB, **Mattocks KT**, Buckner SL, Mouser JG, Counts BR, Dankel SJ, Laurentino GC, Loenneke JP: *The acute muscular response to blood flow-restricted exercise with very low relative pressure*. Clin Physiol Funct Imaging 2017 (Epub ahead of print) doi: 10.1111/cpf.12416

19. Dankel SJ, Buckner SL, Jessee MB, **Mattocks KT**, Mouser JG, Counts BR, Laurentino GC, Loenneke JP: *Can blood flow restriction augment muscle activation during high-load training?* Clin Physiol Funct Imaging 2017 (Epub ahead of print) doi: 10.1111/cpf.12414

20. **Mattocks KT**, Jessee MB, Counts BR, Buckner SL, Mouser JG, Dankel SJ, Laurentino GC, Loenneke JP: *The effects of upper body exercise across different levels of blood flow restriction on arterial occlusion pressure and perceptual responses*. Physiol Behav 2017;171:181-6.

21. Buckner SL, Mouser JG, Jessee MB, Dankel SJ, **Mattocks KT**, Loenneke JP: *What does individual strength say about resistance training status?* Muscle Nerve 2017:55(4):455-7.

22. Buckner SL, Dankel SJ, **Mattocks KT**, Jessee MB, Mouser JG, Counts BR, Laurentino GC, Loenneke JP: *Differentiating swelling and hypertrophy through indirect assessment*

of muscle damage in untrained men following repeated bouts of resistance exercise. Eur J Appl Physiol 2017:117(1):213-24.

23. Counts BR, Buckner SL, Mouser JG, Dankel SJ, Jessee MB, **Mattocks KT**, Loenneke JP: *Muscle growth: to infinity and beyond?* Muscle Nerve 2017. (Epub ahead of print) doi: 10.1002/mus.25696

24. Dankel SJ, Mouser JG, Jessee MB, **Mattocks KT**, Buckner SL, Loenneke JP: *Post-exercise blood flow restriction attenuates hyperemia similarly in males and females.* Eur J Appl Physiol. 2017;117(8):1707-12.

25. Jessee MB, Dankel SJ, Buckner SL, Mouser JG, **Mattocks KT**, Loenneke JP: *The cardiovascular and perceptual response to very low load blood flow restricted exercise*. Int J Sports Med. 2017:38(8):597–603.

26. Mouser JG, Laurentino GC, Dankel SJ, Buckner SL, Jessee MB, Counts BR, **Mattocks KT**, Loenneke JP: *Blood flow in humans following low-load exercise with and without blood flow restriction*. Appl Physiol Nutr Metab 2017 (Epub ahead of print) doi: 10.1139/apnm-2017-0102

27. Dankel SJ, **Mattocks KT**, Jessee MB, Buckner SL, Mouser JG, Loenneke JP: *Do metabolites that are produced during resistance exercise enhance muscle hypertrophy?* Eur J Appl Physiol. 2017 (Epub ahead of print) doi: 10.1007/s00421-017-3690-1

28. Dankel SJ, Buckner SL, Jessee MB, Mouser JG, **Mattocks KT**, Abe T, Loenneke JP: *Correlations do not show cause and effect: not even for changes in muscle size and strength*. Sports Med. 2017 (Epub ahead of print) doi: 10.1007/s40279-017-0774-3

29. Dankel SJ, Jessee MB, Buckner SL, Mouser JG, **Mattocks KT**, Loenneke JP: *Are higher blood flow restriction pressures more beneficial when lower loads are used?* Physiol Int. 2017:104(3):247-257

30. Buckner SL, Dankel SJ, Mouser JG, **Mattocks KT**, Jessee MB, Loenneke JP: *Chasing the top quartile of cross-sectional data: is it possible with resistance training?* Med Hypotheses. 2017:Oct;108:63-68.

31. Dankel SJ, **Mattocks KT**, Mouser JG, Buckner SL, Jessee MB, Loenneke JP: *A critical review of the current evidence examining whether resistance training improves time trial performance*. J Sports Sci. 2017:Nov;1-7 (Epub ahead of print) doi: 10.1080/02640414.2017.1398884

32. Dankel SJ, Mouser JG, **Mattocks KT**, Jessee MB, Buckner SL, Bell ZW, Abe T, Loenneke JP. *Changes in muscle size via MRI and ultrasound: are they equivalent?* Scand J Med Sci Sports. 2017 (Epub ahead of print) doi: 10.1111/sms.13011

33. Abe T, Dankel SJ, Buckner SL, Jessee MB, **Mattocks KT**, Mouser JG, Bell ZW, Loenneke JP. *Differences in 100-m sprint performance and skeletal muscle mass between elite male and female sprinters*. J Sports Med Phys Fitness. 2018 (Epub ahead of print) doi: 10.23736/S0022-4707.18.08267-1

34. Jessee MB, Mouser JG, Buckner SL, Dankel SJ, **Mattocks KT**, Abe T, Loenneke JP. *Effects of load on the acute response of muscles proximal and distal to blood flow restriction*. J Physiol Sci. 2018 (Epub ahead of print) doi: 10.1007/s12576-018-0593-9.

35. Mouser JG, Jessee MB, **Mattocks KT**, Bell ZW, Buckner Sl, Dankel Sj, Abe T, Loennek JP. *Blood flow restriction: methods matter*. Exp Gerontol. 2018:Apr;104:7-8.

36. Abe T, Buckner Sl, Dankel SJ, Jessee MB, **Mattocks KT**, Mouser JG, Loenneke JP. *Skeletal muscle mass in human athletes: what is the upper limit?*. Am J Hum Biol. 2018 (Epub ahead of print) doi: 10.1002/ajhb.23102.

37. Mouser JG, Dankel SJ, **Mattocks KT**, Jessee MB, Buckner SL, Abe T, Loenneke JP. *Blood flow restriction and cuff width: effect on blood flow in the legs.* Clin Physiol Funct Imaging. (Epub ahead of print) doi: 10.1111/cpf.12504.

38. Buckner SL, Jessee MB, Dankel SJ, Mouser JG, **Mattocks KT**, Loenneke JP. *Comment on: "the general adaptation syndrome: a foundation for the concept of periodization"*. Sports Med (Epub ahead of print) doi: 10.1007/s40279-018-0887-3.

39. Buckner SL, Jessee MB, Dankel SJ, **Mattocks KT**, Abe T, Loenneke JP. *Resistance exercise and sports performance: the minority report*. Med Hypotheses. 2018:Apr;113:1-5.

SCIENTIFIC ABSTRACTS

1.) Counts BR, Buckner SL, Dankel SJ, Jessee MB, **Mattocks KT**, Mouser JG, Laurentino GC, Loenneke JP. The Acute Response to No Load Exercise: Is it Sufficient? ACSM National Conference, May 2016, Boston, Massachusetts.

2.) Laurentino GC, Mouser JG, Buckner SL, Counts BR, Dankel SJ, Jessee MB, **Mattocks KT**, Loenneke JP, Tricoli V. The influence of cuff width on regional muscle growth: Implications for Blood Flow Restriction Training. ACSM National Conference, May 2016, Boston, Massachusetts.

3.) Loenneke JP, Buckner SL, Dankel SJ, Jessee MB, Counts BR, Mouser JG, **Mattocks KT**, Laurentino GC, Abe T. The Influence of Cuff Material on the Acute Muscular Response to Blood Flow Restricted Exercise in the Upper Body. ACSM National Conference, May 2016, Boston, Massachusetts.

4.) **Mattocks KT**, Buckner SL, Dankel SJ, Counts BR, Jessee MB, Mouser JG, Laurentino GC, Abe T, Loenneke JP. The Influence of Cuff Material on the Blood Flow Restriction Stimulus in the Upper Body. ACSM National Conference, May 2016, Boston, Massachusetts.

5.) Mouser JG, Buckner SL, Counts BR, Dankel SJ, Jessee MB, **Mattocks KT**, Laurentino GC, Loenneke JP. Venous versus Arterial Blood Flow Restriction: The Impact of Cuff Width. ACSM National Conference, May 2016, Boston, Massachusetts.

6.) **Mattocks KT**, Jessee MB, Counts BR, Buckner SL, Mouser JG, Dankel SJ, Laurenntino GC, Loenneke JP. Effects of Different Levels of Blood Flow Restriction on Arterial Occlusion Pressure and Perceptual Responses. ACSM National Conference, May 2017, Denver, Colorado.

7.) Mouser JG, Laurentino GC, Dankel SJ, Buckner SL, Jessee MB, Counts BR, **Mattocks KT**, Loenneke JP. Blood Flow in Humans During Low-Load Exercise with and without Blood Flow Restriction. ACSM National Conference, May 2017, Denver, Colorado.

8.) Buckner SL, Dankel SJ, **Mattocks KT**, Jessee MB, Mouser JG, Counts BR, Laurentino GC, Loenneke JP. Differentiating Swelling and Hypertrophy Following Repeated Bouts of Resistance Exercise. ACSM National Conference, May 2017, Denver, Colorado.

9.) Dankel SJ, Jessee MB, Buckner SL, Mouser JG, **Mattocks KT**, Loenneke JP. Cardiovascular and Perceptual Responses to Various Blood Flow Restriction Pressures and External Exercise Loads. ACSM National Conference, May 2017, Denver, Colorado.

10.) Jessee MB**, Mattocks KT**, Counts BR, Buckner SL, Mouser JG, Dankel SJ, Laurentino GC, Loenneke JP. The Acute Muscular Responses to Blood Flow Restricted Exercise Using Low and High Relative Pressures. ACSM National Conference, May 2017, Denver, Colorado.

11.) Loenneke JP, Dankel SJ, Jessee MB, Buckner SL, Mouser JG, **Mattocks KT**. Are Higher Blood Flow Restriction Pressures More Beneficial When Lower Loads Are Used? ACSM National Conference, May 2017, Denver, Colorado.

12.) Mouser JG, **Mattocks KT**, Dankel SJ, Buckner SL, Jessee MB, Bell ZW, Abe T, Loenneke JP. Cardiovascular Responses to Blood Flow Restriction and Very Low Load Resistance Exercse in the Upper Body. ACSM National Conference, May 2019, Minneapolis, Minnesota.

13.) Jessee MB, Buckner SL, **Mattocks KT**, Mouser JG, Dankel SJ, Bell ZW, Abe T, Loenneke JP. Very Low Load Resistance Exercise Is Augmented by Blood Flow Restriction In the Lower Body. ACSM National Conference, May 2019, Minneapolis, Minnesota.

14.) **Mattocks KT**, Mouser JG, Jessee MB, Dankel SJ, Buckner SL, Bell ZW, Abe T, Loenneke JP. Acute Hemodynamic Response to Very Low Load Resistance Exercise With or Without Blood Flow Restriction. ACSM National Conference, May 2019, Minneapolis, Minnesota

15.) Dankel SJ, Mouser JG, **Mattocks KT**, Jessee MB, Buckner SL, Abe T, Loenneke JP. The effects of cuff width on hemodynamics in the legs during blood flow restriction. ACSM National Conference, May 2019, Minneapolis, Minnesota.

16.) Buckner SL, Jessee MB, Dankel SJ, Mouser JG, **Mattocks KT**, Bell ZW, Abe T, Loenneke JP. Muscular responses to very low load resistance exercise with blood flow restriction in the upper body. ACSM National Conference, May 2019, Minneapolis, Minnesota.

17.) Bell ZW, Buckner SL, Jessee MB, Mouser JG, **Mattocks KT**, Dankel SJ, Abe T, Loenneke JP. Perceptual And Cardiovascular Responses To Very Low Load Exercise With And Without Blood Flow Restriction. ACSM National Conference, May 2019, Minneapolis, Minnesota.

GRANTS

Loenneke JP. Principal Investigator (2016). Does low load exercise in combination with blood flow restriction attenuate muscle damage and/or confer a protective effect to a subsequent bout of high load exercise in statin users? National Institutes of Aging (RO3). $144,000 (Not Funded).

- Intellectually contributed to this grant

Loenneke JP. Principal Investigator (2017). The muscular and vascular effects of very low loads with and without different levels of blood flow restriction. American College of Sports Medicine $10,000 (Not Funded).

- Intellectually contributed to this grant

Loenneke JP. Have improper analyses cost us millions: reassessing inter-individual responses to exercise. National Institutes of Aging (R15). $300,000 (In Review)

- Intellectually contributed to this grant

SERVICE

University of Mississippi's Rebel Man Sprint Triathlon volunteer – Spring 2016, Spring 2017

Student Group Advisor – Fall 2015 – Present
Graduate Student Council Member – Fall 2016 – Spring 2017
Science Fair Judge at the Lower Science Fair (Oxford, MS) – Spring 2017, Spring 2018
Graduate Student Fair volunteer – Spring 2017
Reviewer for Journal of Trainology

PROFESSIONAL MEMBERSHIPS

American College of Sports Medicine, 2012 - Present

CERTIFICATIONS

CPR/AED	January 2016 – Present
First Aid	January 2016 – Present
ACSM CPT (ID 704564)	March 2012 – December 2016