

EFFECTS OF ACUTE BLOOD FLOW RESTRICTION
EXERCISE ON METABOLIC FUNCTION
IN UNTRAINED INDIVIDUALS

by

TIFFANY L. ADAMS
LEE J. WINCHESTER, COMMITTEE CHAIR
HAYLEY V. MACDONALD
MICHAEL R. ESCO
BRETT C. BENTLEY

A THESIS

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ABSTRACT

INTRODUCTION: RE decreases the symptoms of metabolic disorders due to its ability to increase glucose disposal and uptake by myofibrils, thus, RT resulting in hypertrophy is beneficial for disease management. BFR can be a beneficial addition to an exercise protocol as it can induce hypertrophic gains with lower exercise loads and chronically can improve glucose uptake. An acute bout of RE with BFR in untrained individuals may have the ability to improve insulinogenic and glycemic regulation. **PURPOSE:** The purpose of this study is to determine the systemic effects of blood flow restriction exercise in untrained individuals on glucose uptake and utility, and insulinogenic response compared to a non-BFR session. **METHODS:** 11 non-resistance trained individuals participated in three laboratory visits in a randomized, crossover, repeated measures experimental design. After the first familiarization session, the proceeding exercise sessions included 4x15 body-weight air squats with control and BFR conditions. BFR was inflated to 60% LOP during exercise. Blood lactate (mmol/L), glucose (mg/L), and insulin (mU/L) concentrations were taken before and after exercise. RPE and perceived pain were collected at the end of each set. Data analysis was done in SPSS with a significance level of 0.05. **RESULTS:** There was a significant effect of time for blood lactate ($p < 0.001$), but no significant effect of condition. There was an effect of condition on the change in lactate ($p < 0.05$). There was no significance for any other variable. There was a significant effect of time ($p < 0.001$) and condition ($p = 0.049$) for RPE, but no significant interaction of time x condition. There was a significant effect for time ($p < 0.001$), condition ($p = 0.002$), and time x condition ($p = 0.017$) for pain. **CONCLUSION:** Lactate significantly increased in both conditions between

resting levels and immediately post-exercise, and decreased post-exercise. Glucose and insulin had no significant changes over time or differences between conditions. These results indicate that a light-intensity RE with BFR, while fasted, produces similar metabolic outcomes as a session without BFR and does not produce any extreme glycemic or insulinemic changes while fasted in a healthy untrained population.

Keywords: Metabolism, Occlusion, Exercise, Glucose Regulation, Hemodynamics

DEDICATION

This thesis is dedicated to every individual who guided me and helped me through this entire research process. Especially to my professors, fellow graduate students, and undergraduate students who aided me in the data collection process. This thesis is also dedicated to the family and friends in all areas of my life who have contributed an integral part in my success of completing this degree.

LIST OF ABBREVIATIONS AND SYMBOLS

AMPK:	adenosine monophosphate-activated protein kinase
ANOVA:	analysis of variance
BFR:	blood flow restriction
BFRE:	blood flow restriction resistance exercise
BP:	blood pressure
CVD:	cardiovascular disease
DBP:	diastolic blood pressure
ELISA:	enzyme-linked immunosorbent assay
eNOS:	endothelial nitric oxide synthase
FPG:	fasting plasma glucose
GLUT4:	glucose transporter 4
IGF-1:	insulin-like growth factor
LOP:	limb occlusion pressure
mTOR:	mechanistic target of rapamycin
PA:	physical activity
PTP:	personal tourniquet pressure
RE:	resistance exercise
RT:	resistance training
SBP:	systolic blood pressure
SPSS:	Statistical Package for the Social Sciences

T1-T3: timepoint 1 – timepoint 3 (blood analysis)

T2D: Type II Diabetes

1RM: 1- repetition maximum

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CHAPTER 1 – INTRODUCTION

The loss of muscle mass due to aging and inactivity-induced atrophy is associated with increased mortality, due to the energy imbalance it causes (1). Regular physical activity (PA), both aerobic and resistance exercise (RE), can play a role in not only preventing metabolic disorders, but also the related micro-and macrovascular complications by improving chronic low-level inflammation associated with hyperglycemia and insulin resistance (2). Resistance exercise, which is exercise performed against external resistance, is beneficial in decreasing metabolic disorder symptoms, such as increasing glucose disposal and control (3-5). Resistance training alone improves glycemic control by mechanisms of enhancing GLUT4 translocation, which increases glucose disposal independent of insulin, therefore reducing abnormalities associated with metabolic disorders such as Type II Diabetes (T2D) (6). Resistance training that results in muscular growth and hypertrophy should be included in a training program for most able-bodied individuals to improve or maintain blood glucose control; however, these benefits are not indicated until a high exercise load of about 70% of 1 repetition maximum (1RM) is reached (7, 8). As loads this high may be intimidating or impose potential joint strain in a sedentary population, blood flow restriction (BFR) training may be a beneficial addition to an exercise program for sedentary individuals. Blood flow restriction (BFR), performed with an inflatable cuff much like a typical blood pressure cuff, has recently piqued scientific interest due to its ability to generate significant hypertrophy even at low exercise intensity. Some results of this practice include stimulation of the body's natural repair mechanisms, increases in strength, and increases in glucose uptake compared to non-BFR exercise. BFR has been shown to induce

similar gains in muscle mass and strength with mechanical loads as low as 20-40% of 1RM (9). The application of BFR alone can effectively stabilize muscle mass and reduce atrophy in a chronically sedentary population (10). BFR has a more pronounced effect on counteracting atrophy than low-intensity isometric training by suppressing protein breakdown and can be a beneficial addition to low-load training to induce hypertrophy and strength gain without heavy resistance loads (11). BFR use has also been shown to improve glucose uptake through glucose transporter 4 (GLUT4) translocation to the sarcolemma, a critical step toward reversing metabolic disorder pathologies (9).

Adding BFR into a training protocol may benefit those with low-mobility and those who live sedentary lifestyles. Since mobility and joint health can become limiting in older sedentary populations, BFR may be a way to introduce an effective low-intensity resistance program into their routine, as lower mechanical loads with BFR can elicit similar muscular performance gains as typically observed with higher resistance loads (9). Therefore, a combination of BFR with resistance training in untrained populations has the potential to be a beneficial modality to aid in glycemic control.

The purpose of this study is to determine the systemic effects of blood flow restriction exercise training in untrained individuals.

Hypothesis: This study hypothesized that a decreased concentration of glucose and increased levels of insulin would be reflected in the BFR visit compared to the non-BFR visit

Specific Aim 1: To determine if BFR during low-load resistance exercise increases glucose uptake and utility more than non-BFR low-load resistance exercise training in

untrained populations. Circulating glucose and lactate levels were compared before and after exercise during both conditions.

Specific Aim 2: To determine whether insulin-dependent glucose uptake, as assessed by changes in blood insulin, is enhanced under BFR exercise when compared to standard exercise alone. Circulating insulin levels were compared before and after exercise during both conditions.

This study evaluated how BFR in combination with resistance exercise affects metabolic markers in the fasted state in untrained individuals.

CHAPTER 2 – LITERATURE REVIEW

Introduction

Responses to exercise may vary for people due to medical conditions, training status, or other variables; however, it is widely accepted that physical activity (PA) and exercise decrease the risk of all-cause mortality and cardiovascular disease (CVD) in all populations. The chronic energy imbalance often accompanying physical inactivity is a major risk factor for prediabetes and other CVD comorbidities and progression to type II diabetes (T2D), leading to cellular maladaptation. One maladaptation is how skeletal muscle can have impaired insulin-stimulated glucose transport, manifested as insulin resistance in T2D and prediabetic individuals (9). In general, impaired glucose metabolism is associated with an increased risk factor for CVD, specifically elevated fasting plasma glucose (FPG). A FPG well outside of normoglycemic ranges is an independent risk factor for coronary artery disease, and it is indicated that practitioners should include FPG in their prognosis and risk stratification for their patients' cardiovascular mortality risk (12). In doing so, the prevalence of fasted exercise has increased, with the intention to not only increase lipolysis, but to also counteract increased FPG levels (13).

BFR with resistance exercise is as effective as high-load RT for improving hypertrophy, and to a lesser extent, muscle strength, despite lower training loads (14). However, current BFR research has only investigated postprandial metabolite levels; therefore, it is important to analyze how BFR affects acute metabolite levels in a fasted state.

Acute and Chronic Exercise Effects

Even a single bout of exercise is a sufficient stimulus to increase cellular glucose uptake, rapidly reducing hyperglycemic abnormalities (6, 9). Typically, mild to moderate intensity exercise decreases blood glucose levels and helps to maintain reduced glycemic levels for 2-48 hours after a single exercise bout (7, 15). The magnitude of reduction blood glucose levels is related to the duration and intensity of exercise being performed (8). Higher intensity or prolonged exercise has a greater magnitude of reduction, and thus, a more effective postexercise glycemic control (16). However, acute exercise effects on glucose regulation subsides after 48 hours (15). Current recommendations suggest that even individuals with hyperglycemia undergo successive exercise bouts within a 48-hour span to maintain the glycemic benefits.

Improvements in muscular strength and endurance, flexibility, and body composition can decrease the risk of CVD, all while increasing the amount of insulin-sensitive muscle mass (8, 17, 18). Indeed, participation in regular PA can play a role in not only preventing diabetes but the related micro-and macrovascular complications by improving the chronic low-level inflammatory state that is associated with hyperglycemia and insulin resistance (2).

Resistance Exercise

Resistance exercise (RE), defined as exercise performed against external resistance, is recommended for almost every individual because it can improve a myriad of physiological variables. Indeed, maintaining or increasing muscle mass decreases the risk of all-cause mortality and improves one's quality of life (19, 20). Chronic RE can also increase the responsiveness of skeletal muscle to insulin and resting blood glucose uptake (8). The mechanisms through which aerobic exercise and RE increase glucose utilization are similar, for example, RE increases GLUT4 translocation and insulin sensitivity, contributing to an increased capacity for insulin-stimulated glucose transport (16, 21). However, RE has a greater ability than aerobic to increase

muscle mass, therefore, providing a greater ability to increase glucose storage. In order to achieve hypertrophic and strength benefits from RT, loads of at least 70% of a 1-repetition maximum (1RM) are often recommended (22). Despite the potential benefits of RT, exercising with higher loads may not be feasible for sedentary populations with reduced muscular strength (1).

Blood Flow Restriction Exercise

BFR is a training modality that involves partial vascular occlusion of a muscle using inflatable cuffs, similar to a blood pressure cuff. BFR is typically used in conjunction with resistance loads as low as 20-40% of 1RM, consisting of 2-4 sets of RE performed to near volitional failure (23). BFR alone, without exercise, is effective in mitigating atrophy and strength loss resulting from limb immobilization post-operation and during periods of bed rest (10, 24, 25). The use of BFR during muscular contractions has been shown to increase insulin-independent glucose uptake and endothelial function because of induced muscle hypoxia (26-28). As noted earlier, high RT loads of 70% of 1RM (or higher) are often necessary to achieve RT-induced hypertrophic and strength benefits for glycemic control. Therefore, BFR combined with low-load RT may serve as a viable and effective alternative for previously sedentary or deconditioned individuals.

BFR with low-load resistance exercise is as effective as high-load RT for improving hypertrophy, and to a lesser extent, muscle strength, despite lower training loads (14). When training to failure, hypertrophy was shown to be similar for a BFRE group compared to a non-BFR group; however, the exercise volume required to achieve similar hypertrophic results was lower with the application of BFR (29). The increase in muscle mass and improvements in

hypertrophy observed with BFR, despite using lower loads, may also translate to improved muscular glucose uptake, an important mechanism for addressing metabolic maladaptation (30).

BFR produces venous blood pooling in the exercising limb through a complete occlusion of venous outflow and partial reduction of arterial inflow, inducing cell swelling. Accumulation of metabolites creates an oncotic pressure that draws fluid into the cell, increasing cell volume. Metabolite accumulation and cell swelling are inducers of mechanistic target of rapamycin (mTOR) signaling pathways that increase in protein synthesis to promote hypertrophy(31). Blood lactate accumulation in response to BFRE is a key metabolite, inducing the secretion of anabolic hormones such as growth hormone, insulin-like growth factor 1 (IGF-1) and testosterone (31). Loenneke et al. hypothesized that muscle swelling may be the primary mechanism that results in the observed benefits of BFR, independent of exercise (31). Additionally, research has delineated that reactive hyperemia, an increase in blood flow post-occlusion, does not seem responsible for stimulating muscle protein synthesis following BFRE (32).

Exercise, Glucose, Insulin, and Lactate Interactions

Exercise improves glucose uptake into the skeletal muscle by way of three simplified, sequential steps: enhanced delivery of blood glucose to the muscle, enhanced transport of glucose across the myocyte (muscle cell) membrane, and enhanced phosphorylation of glucose within the muscle (16). Exercise increases central and peripheral blood flow (hyperemia), which increases capillary recruitment and increases GLUT4 translocation throughout the myocyte membrane, among other exercise-induced adaptations. The sum of these mechanistic improvements results in an increase of glucose disposal from the blood and its uptake into the muscle (16). Exercise-induced glucose uptake is effective at maintaining interstitial glucose in

insulin-resistant populations. An increase in muscle perfusion is necessary for contraction-induced glucose uptake and is strongly correlated to muscle blood flow of the working limb (16).

In muscle cells, there are two distinct mechanisms to stimulate glucose uptake, both during and after an exercise bout: insulin-dependent, which predominates at rest, and insulin-independent, which results from muscular contraction. (15). During a bout of exercise, skeletal muscle contraction serves as a cell-signaling mechanism to increase GLUT4 translocation without the need for glucose-mediated signaling (16). An increase of GLUT4 translocation can also occur in response to the activation of AMPK and eNOS during exercise (16). This exercise-induced increase in GLUT4 translocation is especially important for insulin-resistant prediabetes and T2D, as individuals with these disorders are resistant to the stimulatory effects of insulin. Through muscular contraction and insulin-independent pathways, the stimulatory effects of exercise are effective for enhancing glucose uptake, and individuals maintain the ability to translocate GLUT4 as a response (33).

Exercise can also improve the insulin sensitivity of skeletal muscle through an insulin-dependent signaling pathway. Exercise and insulin are synergistic in terms of glucose utilization for a population not fully insulin resistant. Exercise causes hemodynamic adjustments that increase flow through the capillary beds surrounding skeletal muscle, increasing insulin exposure to the tissue. Increased surface area contact enhances the action of insulin directly at the working muscle through activation of GLUT4 receptors post insulin signaling. This process stimulates glucose uptake and can be observed after exercise cessation by an increase in insulin concentration (16). This is done because there is an increased need after exercise for increased substrate oxidation for refueling, specifically the glycogen stores in the muscle, as exercise necessitates fuel sources to be mobilized and oxidized (34).

The effects of insulin are not limited to during exercise, but also continue through the recovery period (34). Insulin is not required for glucose uptake and oxidation via the muscle during exercise; however, the fall in plasma insulin levels during exercise is necessary for glucose to mobilize from the liver and adipose tissue (34). Exercise-induced decrease in plasma insulin is because of α -adrenergic inhibition of pancreatic β -cells, if contraction mediated glucose uptake is sufficient for the short-term energy oxidation needs of the exercise being performed (35).

The body maintains glucose homeostasis by multiple mechanisms and pathways, as both hypo- and hyperglycemia can be detrimental to numerous bodily processes. Because of this, an increase in hepatic gluconeogenesis and/or glycogenolysis accompanies increased glucose uptake via skeletal muscle during exercise (34, 36). This hepatic glucose production partially elevates plasma glucagon and is associated with a fall in plasma insulin concentrations as both pancreatic β -cells and the liver are sensitive to glucose availability (37, 38). The amount of hepatic glucose production during exercise is also associated with pre-exercise hyperinsulinemia, an important pre-exercise measure for control (39). Pre-exercise hyperinsulinemia has been shown to reduce hepatic glucose output at rest. Exercise will increase hepatic glucose output, but it remains lower than what is observed at normal insulin levels prior to exercise (39).

As skeletal muscle is the main site of contraction-mediated glucose uptake, it is also the site of lactate production and utilization (40, 41). Moderate intensity exercise causes a marked increase in lactate oxidation with a connected decrease in plasma glucose oxidation, as it's an intermediary in carbohydrate metabolism and a major component in gluconeogenesis (36, 40, 42). When there is an increased carbohydrate demand during exercise, lactate can spare blood

glucose for other tissues; therefore, lactate stands as not only a valuable oxidative substrate, but also a means of shuttling carbohydrates for metabolism (42).

The Effect of Blood Flow Restriction on Glucose Metabolism

Preserving muscular function and strength is essential for the metabolic health of individuals as a decrease in muscle mass and function impair capacity to uptake glucose (9, 43). BFR training promotes contraction mediated GLUT4 translocation, increasing glucose uptake via activating calcium and AMPK pathways. Christiansen et al. reported that BFR training 3 times per week for 6-weeks led to a net increase in glucose uptake compared to control (44). The occlusion mediated hypoxia from BFR training can induce angiogenesis and help capillary recruitment, which could aid individuals at the early stages of endothelial dysfunction (9). BFR training may improve metabolic control in individuals by improving muscle mass, muscle metabolism, decreasing resting insulin levels, and/or increasing GLUT4 translocation while utilizing a lighter resistance load, especially with its ability to increase systemic lactate and metabolite levels (31). As of this study, research has only been conducted in BFR training studies on its effects on glucose regulation when included in a RE protocol. Therefore, it is important to address how a singular bout of BFR resistance exercise will affect acute glucose levels, insulinogenic response, and lactate.

Purpose

The combination of BFR with resistance exercise has the potential to be an effective strategy to aid in glycemic control. Given the paucity of data on the acute effects of BFR and RE on glucose regulation and insulinogenic responses, the purpose of this study is to determine the

systemic effects of BFR and low-load RE on glucose uptake and utility, and insulin-dependent glucose uptake in non-resistance trained adults.

CHAPTER 3 – METHODS

Participants

Participants were required to be non-smokers, classified as non-resistance trained (not having engaged in consistent resistance training in the past three months), and have no contraindications to exercise training according to the standards set by the American College of Sports Medicine (ACSM). This required the participants to not have any signs or symptoms of metabolic, cardiovascular, or renal disease as outlined by the ACSM pre-participation health screening guidelines (45). Previously published research on the acute effects of resistance exercise RE and metabolic responses (46) informed our *a priori* power analysis conducted in G*Power (Version 3.1) with the provided Cohen's *d* effect size of 0.72 for glucose change on an acute bout of RE. To account for the within-subject repeated measures design of the present study, our power analysis used a repeated measures model with 2 conditions and 3 measurements, that assumed a moderate correlation among repeated measures ($r = 0.60$), an alpha level of 0.05, and a power level of 0.8. Based on the power analysis, we recruited 11 male and female adults for participation (Table 1).

Overview of Research Design

This study was conducted using a randomized, crossover, repeated measures experimental design. Recruited participants engaged in a familiarization session with two different data collection sessions, 7-9 days apart. Sessions were no less than one week apart to ensure adequate recovery time, while limiting the training effect from neuromuscular adaptation. The conditions for each visit were randomized, with each participant performing the exercise protocol with the control condition and with BFR, the experimental condition. Participants were

asked to refrain from any strenuous exercise within 3 days of the first study session. Participants were asked to arrive at the lab for each exercise session and refrain from eating or drinking anything other than water (fasted) for at least 3 hours before arrival.

Procedures

Initial Visit

Participants received an email with a copy of the informed consent document 24 hours before arrival for the initial visit to review. During the first session, participants were formally consented and evaluated for their ability to engage in a light resistance training activity using a standard Physical Activity Readiness Questionnaire Plus (PARQ+) and a 24-hour history recall form, in that order. The information provided was used to indicate if the participant can participate in a moderate intensity exercise program without medical clearance, according to ACSM's pre-participation health screening. After clearance, baseline data for anthropometric measures and body composition by bioelectrical impedance (Tanita BWB-800, Tanita©, Arlington Heights, IL) was obtained. Height was obtained using a stadiometer (SECA 67310, SECA©, Chino, CA) and weight was measured on a digital scale (Tanita BWB-800, Tanita©, Arlington Heights, IL), with shoes off the participant for both measures. Supine resting blood pressure (BP) and arterial stiffness measurements (SphygmoCor® Xcel, Colson, U.S.A.) were collected after 5-minutes of rest. The exercise protocol, consisting of air squats, was explained, and demonstrated to the participant with the proper form and technique, if needed, to confirm that the participant was comfortable performing such movements. At the end of this session, the participant and researcher determined an adequate date for the first exercise session.

Exercise Sessions

The exercise sessions (second and third visits) were randomized to either the control condition or the BFR condition in a crossover design. Data collection for each exercise session included continual HR monitoring, rating of perceived exertion (RPE) and pain (Borg CR-10 and Discomfort Scale), as well as blood analysis of glucose, lactate, and insulin. Upon arrival at both exercise sessions, the participant completed a 24-hour history form and reaffirmed consent. Resting blood pressure (BP) was obtained using an automated BP monitor (Omron HEM-907XL, Omron Healthcare, Bannockburn, IL) after 5 minutes of seated rest, in accordance with the 2017 ACC/AHA High Blood Pressure Clinical Practice Guidelines for Adults (47). BP was measured 3 times, 1 minute apart in the dominant arm with the cuff at heart level. BP measurement took place in a quiet environment, with the participants instructed to keep their feet flat on the floor, with their legs uncrossed, and their back supported by the chair. The participant was asked to refrain from talking for the duration of BP measurements. The average BP was determined by averaging the 3 readings that are no more than 5 mmHg apart for both SBP and DBP. Additional BP readings were performed until an agreement was reached. The purpose of the BP measurement before the exercise session was to ensure that the participant did not have stage 2 hypertension. This would be indicated by a systolic and/or diastolic measure that reads ≥ 140 mmHg and/or ≥ 90 mmHg. If the average BP readings result in a measure higher than this cutoff, the participant would have been asked to reschedule at least 24 hours later for repeated baseline and BP measurements. If the participant's BP remains outside of this threshold, they would have been excluded from the study; however, none of the participants screened were hypertensive. This was repeated after the exercise protocol, before the participant left the laboratory. Before exercise, a venous blood draw and capillary finger prick was taken to obtain baseline blood glucose, lactate, and insulin levels (T1). Due to difficulties with the phlebotomy procedure on

some participants, venous blood draws were only successful on 8 of the 11 total participants, for the assessment of plasma insulin.

After BP measurements and a blood draw, the participant was fitted with a Polar heart rate monitor (Polar H10, Polar Electro, Kempele, Finland), secured by a chest strap, to continuously monitor and record the participant's HR for the exercise sessions.

Both exercise sessions entailed 4 sets of 15 repetitions of body-weight air squats. There was a 1-minute rest between each set. Because this protocol requires the participant to work the legs at an endurance volume, it is expected to be a sufficient stimulus to produce adequate changes in the markers being measured. Within five minutes of exercise cessation, another venous blood draw, capillary finger prick, and blood pressure measure was taken (T2). One hour after exercise, an additional finger-prick was performed for additional glucose and lactate measurements, concluding the visit (T3).

BFR Session

The protocol for the BFR session is identical to the protocol for the control exercise session but with the addition of the BFR apparatus. The Delfi Personalized Tourniquet system (Delfi PTS II, Owens Recovery Science, Vancouver, B.C.) is an FDA-approved Blood Flow Restriction device commonly used in physical therapy, athletic training, and research. This BFR device uses an inflatable tourniquet to induce vascular occlusion in the limb. The system first determines information to calculate a user-specific occlusion percentage, also called personal tourniquet pressure (PTP). This specific device system has a pressure-regulating sensor to maintain constant pressure during muscular movement, rather than allowing a pressure spike during muscular contraction. For BFR application, the BFR cuffs were applied to the proximal half of both thighs, but distal to the fold of the gluteal muscles and distal to the inguinal

crease. The cuff was then inflated to a limb occlusion pressure (LOP), 60% of PTP, for 1 minute prior to beginning exercise and stayed inflated until the completion of the exercise protocol (48). Based on the entire protocol, the BFR cuffs were inflated for about 10 minutes or less, which is standard for BFR use.

Perceived Exertion and Pain

A rating of perceived exertion and pain was assessed using the Borg CR-10 scale. Rest was associated with a rating of 0 and complete fatigue with a rating of 10. Immediately after the completion of each set of exercise, participants rated the level of effort needed to complete the set on a scale of 0 to 10 and the amount of pain experienced.

Analysis of Glucose, Lactate, and Insulin

Venipuncture took place prior to exercise and within 5 minutes of exercise cessation for analysis of insulin from the participant's cubital vein. Approximately 10 mL of venous blood was drawn to measure glucose and insulin expression levels, using an enzyme-linked immunosorbent assay (ELISA) kit (AFG Bioscience, EK710804) to measure the blood concentration of insulin. Whole blood samples were centrifuged at 1500xg for 15 minutes for isolation of blood plasma, then aliquoted into multiple microcentrifuge tubes for storage.

The capillary blood sample was analyzed using a handheld glucose analyzer (Contour® Next Gen, Ascensia Diabetes Care, Parsippany, U.S.A.) and a handheld lactate analyzer (Lactate Plus, Nova Biomedical, Waltham, U.S.A.) prior to exercise, within 5 minutes of exercise cessation, and one-hour post-exercise cessation. The distal anterior portion on fingers 2-4 were used for this protocol. The finger was first be cleansed with an alcohol wipe, then dried using a sterile gauze pad. An auto-lancet was utilized, allowing for the surfacing of capillary blood. The initial blood was wiped away by a sterile gauze and the finger was squeezed gently to create a

new blood droplet to be aspirated by the device test strip. Once blood glucose and lactate analysis were complete, a sterile gauze was applied to the affected fingertip to ensure the cessation of bleeding.

Data Analysis

Since this was a repeated measures design study, a repeated measures ANOVA was utilized to evaluate whether there are significant differences in variables between the different trials for blood lactate and glucose between timepoints T1, T2, and T3. Insulin and BP were analyzed between conditions and timepoints T1 and T2. RPE, pain, and average HR were analyzed during each set. Due to the multiple timepoints, a paired samples t-test was performed between groups and between each timepoint for lactate, glucose, and insulin. Mauchly's Test of Sphericity was conducted for each ANOVA, and if homogeneity of variance was found, Huynh-Feldt correction was applied. If homogeneity of variances could not be assumed, Greenhouse-Geisser correction was applied, and is indicated in each respective table. If significance was found, a Tukey's Honest Significant Differences *post-hoc* analysis determined where significant differences occur in the data. Analysis was completed using SPSS (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp). Data is summarized as Mean \pm Standard Deviation unless specified. An alpha level of 0.05 is used to determine statistical significance.

CHAPTER 3 – RESULTS

Participants and Pre-Exercise (Resting) Measures

Thirteen subjects initiated the study but only eleven participants completed all three visits. Overall, participants were young, healthy men and women, who were normal – to overweight (based on body mass index [BMI] = 25.9 ± 4.6 kg/m²), with normal SBP and DBP (BP; $109 \pm 7/65 \pm 7$ mmHg), and normal blood glucose (95.3 ± 5.6 mg/dL) and insulin (11.9 ± 3.0 mmol/L), respectively. Pre-RE measures of resting BP, HR, and blood biomarkers (lactate, glucose, and insulin) were not different at T1 across conditions (Table 3; $p > 0.05$ for all).

Table 1: Participant Characteristics

	Age	Height (cm)	Weight (kg)	BMI	BF %	Muscle Mass (kg)	BP (mmHg)	HR (bpm)	PWV (m/s)
N	11	11	11	11	10	10	11	11	11
Mean	26.9	171.9	73.5	24.9	25.7	51.2	109/65	61.5	6.0
Std. Deviation	7.9	8.1	14.96	4.6	6	11.6	7.3/6.9	10.3	0.7
Min	19	160	53.95	18.5	14.4	38.9	96/56	43	4.8
Max	39	187	94.8	32	35.5	67.8	121/77	79	7

BMI: body mass index (kg/m²), BF%: body fat percentage, BP: systolic/diastolic (mmHg), HR: heart rate in beats per minute
 PWV: pulse wave velocity (m/s), cm: centimeters, kg: kilograms, m/s: meters per second, mmHg: millimeters of mercury

Main Effects: Blood lactate, Glucose, and Insulin

When conducting a two-way repeated measures ANOVA, there was a significant effect of time for lactate ($p < 0.001$), but no significant effect of condition. For both glucose and insulin, there was no significant effect found by time nor by condition. For the change between lactate and glucose, there was an effect of condition on the change in lactate ($p = 0.002$). There was no interaction of time x condition for any variable (Table 2).

Table 2: Two-way repeated measures ANOVA: Glucose, Lactate (N = 11), and Insulin (N = 8)

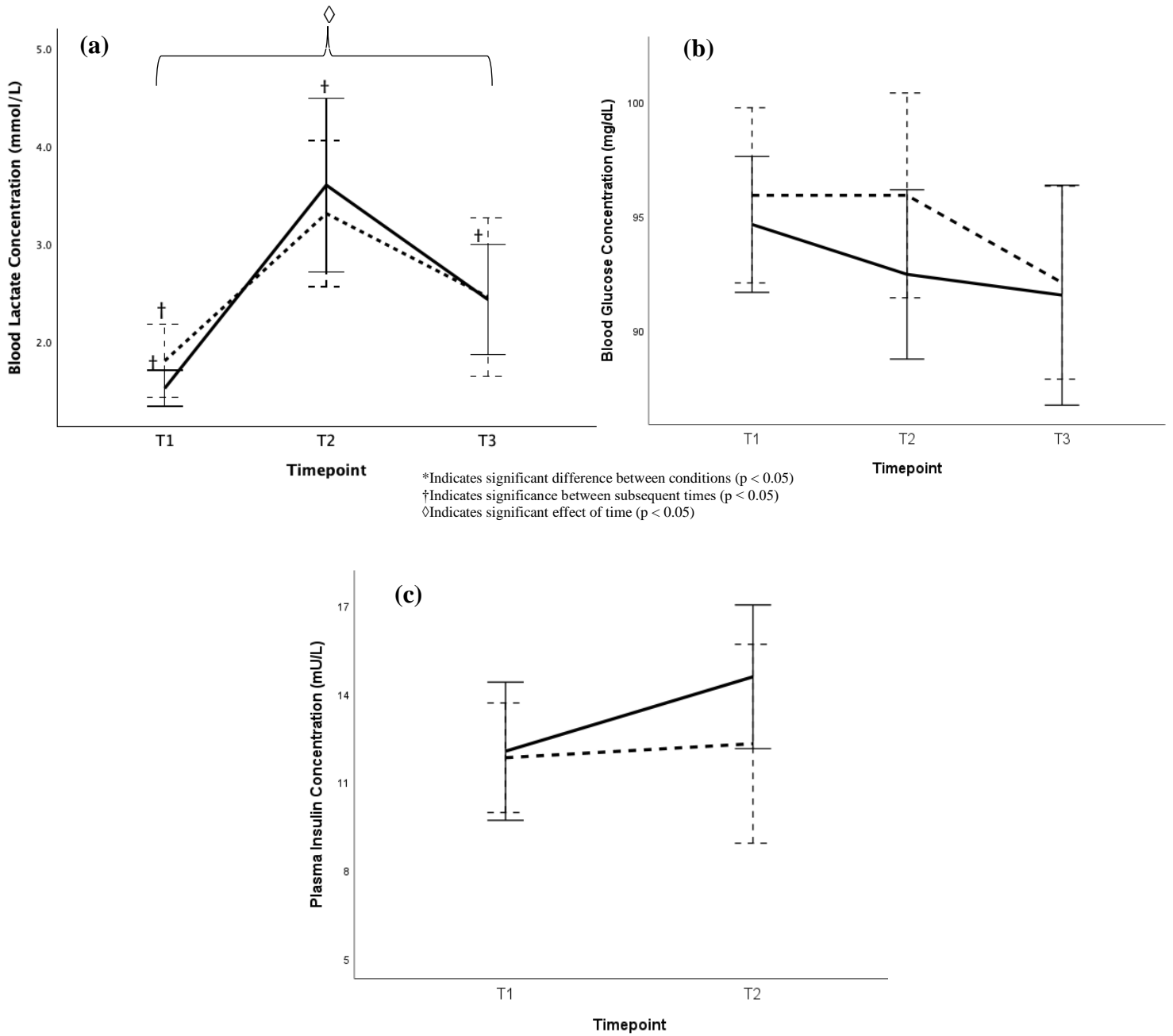
Variable	Time	BFR	Control	Time Effect			Treatment Effect			Interaction		
				F	η^2 partial	p	F	η^2 partial	p	F	η^2 partial	p
Lactate (mmol/L)	T1	1.5 ± 0.31	1.8 ± 0.62	15.61	0.61	<0.001	0.001	0	0.98	0.789	0.07	0.439
	T2	3.6 ± 1.48	3.3 ± 1.24									
	T3	2.4 ± 0.93	2.5 ± 1.35									
Glucose (mg/dL)	T1	94.6 ± 4.9	95.9 ± 6.3	3.15	0.24	0.065	1.6	0.14	0.23	1.03	0.09	0.366
	T2	92.5 ± 6.1	95.9 ± 7.4									
	T3	91.6 ± 7.9	92.1 ± 6.9									
Insulin (mU/L)	T1	12.0 ± 3.3	11.8 ± 2.6	2.06	0.23	0.194	1.4	0.17	0.276	1.16	0.14	0.317
	T2	14.8 ± 3.5	12.2 ± 4.8									
Lactate Change	T2-T1	2.1 ± 1.5	1.5 ± 1.3	0.372	0.036	0.555*	16.8	0.63	0.002*	1.03	0.094	0.338*
	T3-T2	-1.2 ± 1.6	-0.9 ± 1.4									
	T3-T1	0.9 ± 0.8	0.7 ± 1.2									
Glucose Change	T2-T1	-2.2 ± 4.1	0.0 ± 5.2	1.14	0.1	0.327 *	0.105	0.01	0.753*	1.99	0.17	0.184*
	T3-T2	-0.91 ± 5.3	-3.8 ± 6.8									
	T3-T1	-3.1 ± 7.3	-3.8 ± 5.6									

Blood Flow Restriction (BFR), Control (Control session)
 * Greenhouse-Geisser Correction applied

Paired Samples T-Test

Both the mean values at each timepoint and the mean change between conditions lactate, glucose, insulin, were analyzed through a paired samples T-test (Appendix 3). For lactate, all three timepoints of the BFR session had a significant change in lactate concentration ($p < 0.05$), and the control session had a significant change between T1 and T2 ($p = 0.003$) (Figure 1a). For glucose, only the control session produced a significant difference between timepoints T1 and T3 ($p = 0.048$), and there was a significant difference between conditions at T2 ($p = 0.048$) (Figure 1b). Paired samples t-test found no significance between timepoints or conditions for insulin, however, there was a trending towards significance difference between conditions at T2 ($p = 0.052$) (Figure 1c).

Figure 1: (a), Lactate (mmol/L), (b) Glucose (mg/L), (c) Insulin (mU/L)



RPE, Pain, Average Heart Rate, BP

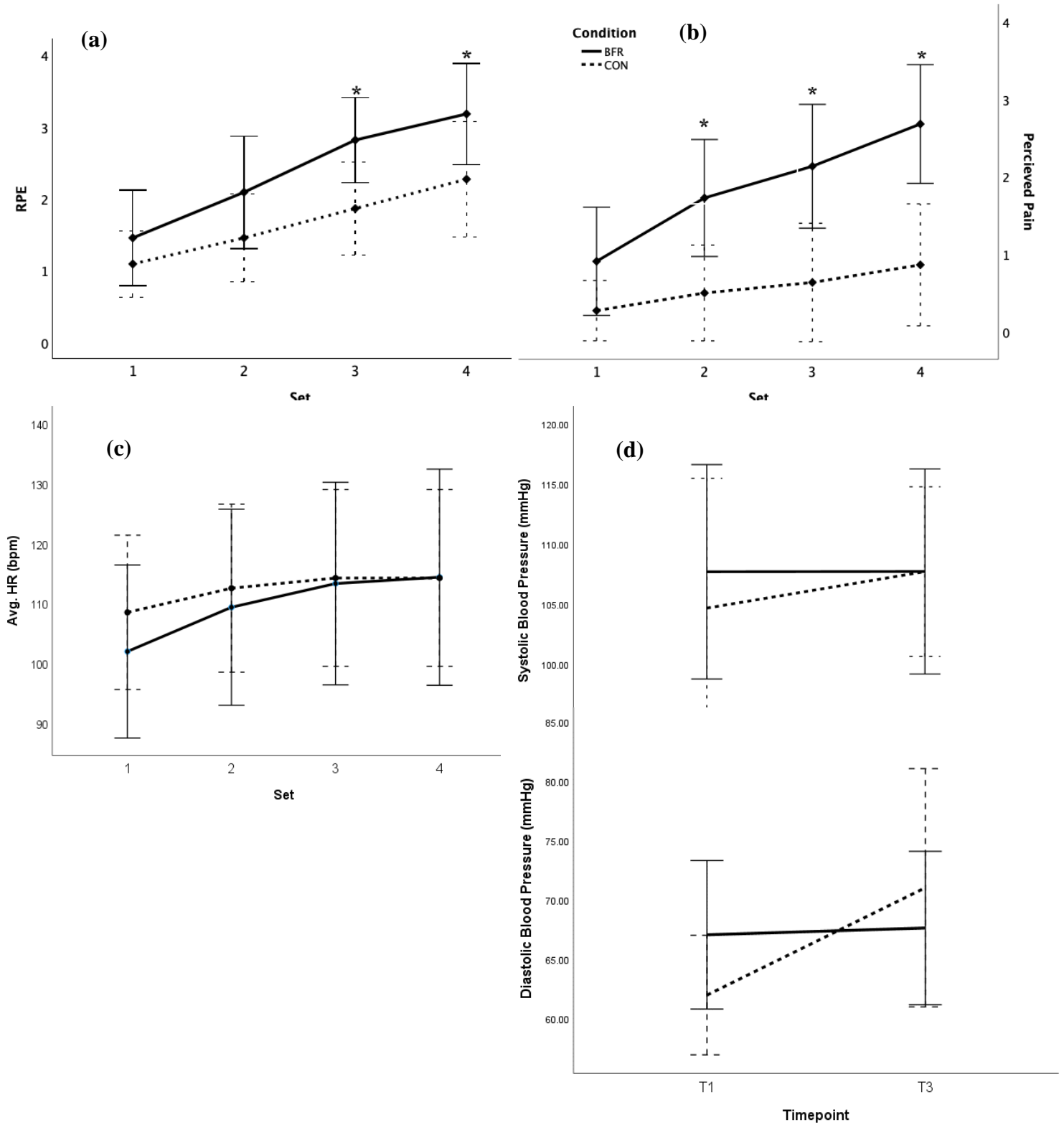
When conducting a two-way repeated measures ANOVA, there was a significant effect of time ($p < 0.001$) and condition ($p = 0.049$) for RPE, but no significant interaction of time x condition (Table 3) (Figure 2a) between RPE and each set. There was a significant effect for time ($p < 0.001$), condition ($p = 0.002$), and time x condition ($p = 0.017$) (Table 3) (Figure 2b) between pain and each set. There was a significant effect for time ($p = 0.002$) for the average HR during each set, but no significant effect for condition nor time x condition was found (Table 3) (Figure 2c). There was no significant effect of time, condition, or time x condition on SBP. DBP had a significant effect of time ($p = 0.039$), but no other significant effects were found (Table 3) (Figure 2d).

Table 3: Two-way Repeated Measures ANOVA: RPE, Pain (N = 11), Average HR, SBP, DBP (N = 9)

Variable	Set/Time	BFR	Control	Time Effect			Treatment Effect			Interaction		
				F	η^2 partial	p	F	η^2 partial	p	F	η^2 partial	p
RPE	1	1.45 ± 1.11	1.09 ± 0.77	20.377	0.67	<0.001*	5.01	0.334	0.049*	1.739	0.148	0.211*
	2	2.09 ± 1.30	1.45 ± 1.01									
	3	2.82 ± 0.98	1.86 ± 1.07									
	4	3.18 ± 1.17	2.27 ± 1.33									
PAIN	1	0.91 ± 1.16	0.27 ± 0.65	19.523	0.661	<0.001*	16.084	0.017	0.002*	5.199	0.342	0.017*
	2	1.73 ± 1.25	0.50 ± 1.03									
	3	2.14 ± 1.33	0.64 ± 1.27									
	4	2.68 ± 1.27	0.86 ± 1.31									
Avg HR (bpm)	1	101.9 ± 21.7	108.5 ± 19.3	10.996	0.579	0.002*	0.127	0.016	0.731*	1.328	0.142	0.292*
	2	109.3 ± 24.5	112.5 ± 21.1									
	3	113.3 ± 25.4	114.2 ± 22.1									
	4	114.4 ± 27.1	114.2 ± 22.1									
SBP (mmHg)	T1	107.7 ± 10.7	104.6 ± 12.9	0.415	0.056	0.54	3.828	0.091	0.091	0.517	0.069	0.495
	T2	107.7 ± 10.2	107.7 ± 8.5									
DBP (mmHg)	T1	67.1 ± 7.5	61.9 ± 6.0	6.385	0.477	0.039	0.189	0.026	0.677	4.002	0.364	0.086
	T2	67.6 ± 7.7	71.0 ± 11.9									

Blood Flow Restriction (BFR), Control (Control session), RPE: Perceived Rating of Exertion, HR: heart rate (beats/minute), SBP: systolic blood pressure (mmHg), DBP: diastolic blood pressure (mmHg)
* Greenhouse-Geisser Correction applied

Figure 2: (a) Rating of Perceived Exertion (RPE), (b) Perceived Pain, (c) Average Heart Rate (bpm), (d) Blood Pressure (mmHg)



CHAPTER 4 – DISCUSSION, LIMITATIONS, & CONCLUSION

Discussion

The primary purpose of this study was to determine the systemic effects of blood flow restriction exercise training in untrained individuals on glucose uptake and utility, and insulin-dependent glucose uptake compared to a non-BFR session. This was accomplished by analyzing circulating glucose, lactate, and insulin concentrations after a bout of low-load resistance exercise (RE), with or without blood flow restriction (BFR).

Blood lactate concentration differences were evaluated via repeated measures ANOVA. A significant effect for time ($p < 0.05$) (Table 2) was found, and the paired samples t-test indicated a significant difference for all three timepoints in the BFR condition (Appendix 3). Lactate (mmol/L) increased significantly for both conditions between T1 and T2, where only the BFR group had significant changes between every timepoint. However, there was a significant effect of condition when comparing the change between timepoints (Table 2), BFR condition had a greater change in lactate concentration between timepoints. There were no significant time x condition interactions. These results indicate that an acute light-intensity bout of resistance exercise with or without BFR, significantly increases the metabolic stress response, with the BFR condition causing a higher rate of lactate accumulation compared to the control condition.

This is not surprising, as prior research has indicated that BFR significantly increases lactate concentrations when compared to a control group (31, 49). While this study did not find a significant difference in lactate concentrations between conditions (Appendix 3), the significantly higher rate of lactate accumulation than control (Table 2), and the significant

change in lactate concentration between every timepoint (Appendix 3), indicates that BFR likely creates a more pronounced metabolic stressor. The lack of direct significance between BFR and control could be due to a multitude of reasons. It is plausible that there would be a significant difference in lactate between condition if the exercise protocol was of higher volume. Takano et al. had 11 untrained individuals perform an acute BFR exercise bout and saw a significant increase in lactate in the BFR group compared to control; however, these individuals exercised until failure (49). This discrepancy indicates the possibility that the total volume of this protocol, significantly lighter than exercising to failure, affected the rate of lactate accumulation when using BFR specifically.

It is possible that the insignificant differences in lactate between conditions is due to a lower LOP of the BFR cuff, as 60% LOP was utilized in this protocol rather than the traditional 80% LOP. Hornikel et al. previously found that there is not a significant difference in volume flow change between pressures above 40% LOP, with no significant differences between 60% and 80% LOP (48). Therefore, it is unlikely that the 60% LOP used had a direct effect on the rate of lactate accumulation between conditions.

In this present study, no significant effect for time, condition, nor time x condition for blood glucose concentration was observed, though the effect of time had a trend towards significance ($p = 0.65$) (Table 2), indicating that a larger sample size might have resulted in significant findings. When evaluating changes between conditions at each timepoint using t-tests, the control session at T2 had a significantly higher glucose concentration than the BFR session ($p = 0.048$) and only the control session was found to be different between T1 and T3 ($p = 0.048$) (Appendix 3).

These findings compare well to a similar research protocol with 7 participants after an acute bout of light intensity walking with BFR while fasted (50). Although that study utilized an aerobic exercise protocol, and this present study is focused on RE, the results are similar with no significant interaction for time or time x condition (50). Their participants showed a greater increase in glucose when collapsed for time (50), but our study indicated a decrease in glucose, though not significant (Figure 1b). Longer-term BFR training protocols with light-intensity RE have shown increases in contraction mediated GLUT4 translocation, thus lowering of blood glucose concentrations (51). However, research thus far, including this present study, has not shown a significant difference between conditions for glucose reduction during in acute light-intensity RE with BFR.

The blood glucose responses observed in this study may be explained by a few variables. The initial glucose values (T1) were already low due to the fasted state of participants, preventing change of glucose concentration due to the body's desire to tightly maintain glycemic homeostasis (36). Therefore, an increase in hepatic gluconeogenesis or glycogenolysis could accompany increased glucose uptake via skeletal muscle, resulting in an insignificant change in glucose concentration over time (36, 52). Furthermore, when there is an increase in carbohydrate demand, such as the case with this exercise protocol, lactate can spare blood glucose utility by other tissues, as it is an intermediary in carbohydrate metabolism (36, 42). Thus, it is plausible that glucose uptake was elevated during exercise, but blood glucose values were able to be maintained due to the low intensity of the protocol.

There were no significant effects for time, condition, nor time by condition for insulin in the present study. An increasing trend was indicated for the fasting T1 values of insulin, though it did not quite reach significance ($p = 0.052$) (Appendix 3) (Figure 1c). Ozaki et al. saw an

insignificant increase in insulin during light-intensity aerobic exercise with BFR, and our results are found to be similar. Exercise improves insulin sensitivity of the muscle as exercise and insulin are synergistic for glucose uptake via translocation of GLUT4 receptors post insulin signaling (16). Facilitated glucose uptake by GLUT4 can be reflected after exercise by a decrease in blood glucose concentration. Prior research has indicated an increase in GLUT4 translocation after a 6-week BFR training program, however, our protocol was investigating if this was observed acutely after a single RE bout. While both conditions had a trend for increased insulin concentration throughout exercise, the change was not significant. When considering the effect of time on insulin concentration, a blood insulin concentration measurement at an hour post exercise (T3) did not occur in this protocol due the necessity of installing an intravenous catheter if collecting more than 3 venous blood samples in one session. Future research should ensure to include a later post-exercise collection of insulin in order to fully analyze its effect on glucose uptake during recovery.

There was a significant effect for time ($p < 0.001$, $p < 0.001$) and condition ($p = 0.049$, $p = 0.002$) for both RPE and perceived pain respectively, while only pain had a significant interaction for time x condition ($p = 0.017$) (Table 3). For both RPE and pain, the BFR condition had significantly higher perceived values compared to control, that increased for each set over time (Figure 2a-b). These results are consistent with the overall research on BFR use and perceived exertion and pain. A systematic review and meta-analysis concluded that overall, low-load BFR exercise produces significantly higher perceived exertion and discomfort than without BFR use, even when controlling for the volume of exercise (53).

Though it was not a main effect of the study, the cardiovascular response to light-intensity BFRE reflected the same responses as without BFR. For each set, HR was averaged and

compared between set and condition with a repeated measures ANOVA (Table 3) (Figure 2c). A significant effect for time ($p = 0.002$) was found, but no significance for condition or time x condition were observed. Average HR per set increased consistently throughout the four sets, with no difference between BFR and control conditions. BP was measured at rest, before blood draws and exercise, and right before the final (T3) finger prick for lactate and glucose. There was a significant effect of time ($p < 0.001$) for diastolic BP, but no effect of condition or time x condition for SBP or DBP (Table 3) (Figure 2d). DBP increased significantly between T1 and T3 and was relatively the same between the two conditions. These cardiovascular responses are consistent with the rest of literature, as findings suggest there are no greater acute effects of BFR with resistance exercise for HR and BP when compared to a matched load control group (53, 54).

Limitations

The purpose of this study was to determine if an acute bout of RE with BFR had comparable metabolic effects in the fasted state as RE without BFR; however, this study was not without its limitations. The recruited sample size of participants was small, but matched other similar studies (49, 50). While the total number of participants was 11 individuals, only 8 individuals were included in the venous blood draw samples for insulin concentration. This discrepancy was due to phlebotomy issues and participant withdraw of consent for further venous draw, but they continued to consent to the remainder of the study. While this study determined the acute metabolic response to light-intensity BFRE, the exercise stimulus may not have created a great enough stress response to elicit substantial metabolic demand. One or more additional timepoints of blood analysis would have been beneficial on delineating the outcome of RE between BFR and non-BFR conditions on insulin production and glucose uptake. Further

research should be done to investigate how acute bouts of moderate to vigorous intensity BFR affect fasted metabolic responses.

Conclusion

The findings of this study reveal how an acute bout of BFR exercise affects metabolic function in non-resistance trained individuals. As expected, increases in HR, pain, and RPE from set 1 to set 4 in both conditions, and higher ratings of perceived pain with BFR were observed. Lactate levels increase with RE in both conditions, whereas glucose and insulin levels remained fairly stable during and between each RE condition. These results suggest that a single bout of light-intensity RE, regardless of BFR use, while fasted, produces similar HR and metabolic responses in healthy non-resistance trained adults when performed following an overnight fast. If optimizing glucose regulation and insulinemic responses is the goal, this combination of BFR and RE does not elicit superior responses compared to other modalities. Conversely, the lack of extreme glycemc or insulinemic changes with BFR and light-intensity RE underscores its safety and utility in a variety of settings.

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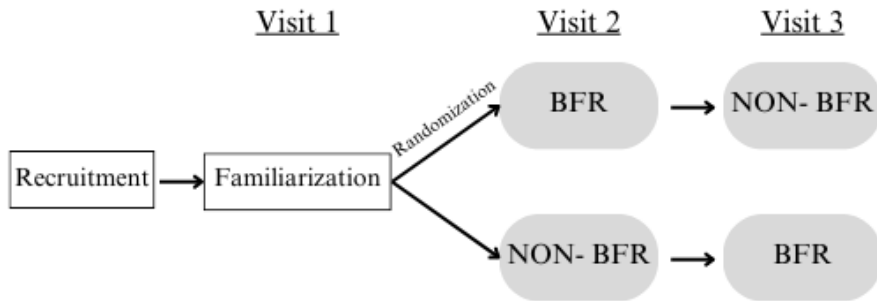
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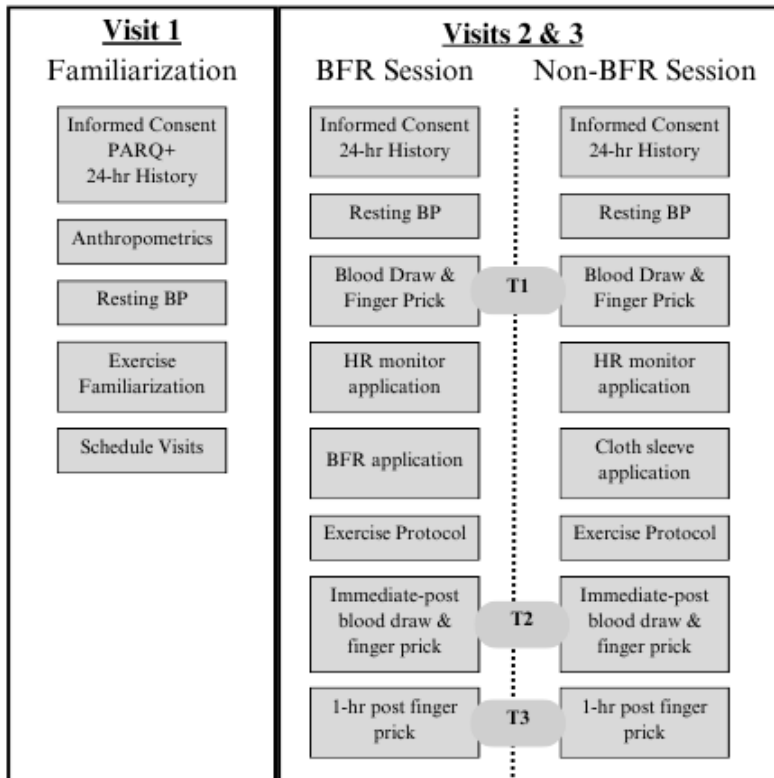
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APPENDIX

APPENDIX 1: STUDY TIMELINE



APPENDIX 2: METHODOLOGY



APPENDIX 3: PAIRED SAMPLES T-TEST: LACTATE, GLUCOSE, & INSULIN

Variable			Mean	Std. Deviation	t-stat	Significance
Lactate (mmol/L)	BFR:	T1 - T2	-2.08	1.49	-4.64	<0.001
		T2 - T3	1.17	1.57	2.48	0.033
		T1 - T3	-0.91	0.79	-3.77	0.004
	CON:	T1 - T2	-1.51	1.23	-3.92	0.003
		T2 - T3	0.85	1.36	2.08	0.064
		T1 - T3	-0.65	1.22	-1.78	0.106
	BFR T1 - CON T1		-0.01	1.16	-0.03	0.976
	BFR T2 - CON T2		0.29	1.12	0.94	0.368
	BFR T3 - CON T3		-0.03	1.67	-0.05	0.958
Glucose (mg/dL)	BFR:	T1 - T2	2.18	4.07	1.78	0.106
		T2 - T3	0.91	5.32	0.57	0.583
		T1 - T3	3.09	7.33	1.39	0.192
	CON:	T1 - T2	0	5.18	0	1
		T2 - T3	3.82	6.84	1.85	0.09
		T1 - T3	3.82	5.62	2.25	0.048
	BFR T1 - CON T1		-1.76	6.05	-1.67	0.105
	BFR T2 - CON T2		-3.46	5.09	-2.25	0.048
	BFR T3 - CON T3		-0.55	7.29	-0.248	0.809
Insulin	BFR T1 - T2		-2.53	4.37	-1.64	0.14
	CON T1-T2		-0.48	4.63	-0.29	0.78
	BFR T1 - CON T1		0.22	2.38	0.26	0.8
	BFR T2 - CON T2		2.28	4.58	1.41	0.2

BFR: Blood Flow Restriction, CON: Control session

APPENDIX 4: IRB APPROVAL LETTER



January 12, 2024

To: Tiffany Adams
Department of Kinesiology
College of Education
The University of Alabama
Box 870312



Re: **Notice of Approval**
IRB Application #: e-Protocol 22-11-6113-R1
Project Title: "Comparison of Exercise with or without Blood Flow Restriction on Physiological Outcomes in Prediabetic Populations"
Submission Type: Renewal
Approval Date: January 12, 2024
Expiration Date: January 10, 2025
Funding Source: None
Review Category: Full Board
Approved Documents: Informed Consent, Waiver of Documentation of Informed Consent

Dear Ms. Adams:

The University of Alabama Medical Institutional Review Board has granted approval for your proposed research. Your application has been given full board approval according to 45 CFR part 46.

The approval for your application will lapse, as noted above. If your research will continue beyond this date, please submit the Continuing Review to the IRB as University policy requires before the lapse. Please note any modifications made in research design, methodology, or procedures must be submitted to and approved by the IRB before implementation. Please submit a final report form when the study is complete.

Please use reproductions of the IRB approved stamped consent form to obtain consent from your participants.

All the best with your research.

166 Rose Administration | Box 870127 | Tuscaloosa, AL 35401 | 205-348-8461 | rscompliance@ua.edu

Consent to Participate in a Research Study

Please read this informed consent carefully before you decide to participate in the study.

Consent Form Key Information:

- This study aims to determine if blood flow restriction (BFR) during exercise increases the body's ability to use the sugar in the blood more than non-BFR exercise in prediabetic populations compared to non-prediabetic populations.
- This study involves 3 different visits to the lab, two visits including exercise. One exercise visit is with blood flow restriction, and one is without. Each session will take about 2 hours.
- An OPTIONAL visit for 24 hours after each exercise will be offered for an additional blood draw. This is OPTIONAL and is not needed for participation in the study.
- The exercises are air squats and walking lunges. You will do 3 sets of each exercise. You will do 15 repetitions in each set.
- Consent is being sought for research only and participation is voluntary.
- The main risks in this research study are risks that come along with typical exercise. Blood flow restriction has low potential risks.
- You will be given a \$25 Visa Gift Card for participating. You will receive this at the end of the last session.

Purpose of the research study: The purpose of this study is to determine the whole-body effects of blood flow restriction exercise training in people with prediabetes. Information from this study can be used to help physical therapists, doctors, athletic trainers, and strength coaches by determining if the benefits of blood flow restriction training are similar in prediabetic and non-diabetic populations.

What you will do in the study: You will do things in the following order:

Information About You: Session 1

On the first visit, you will fill out the answers to questions that ask you about your age, height, weight, your overall health, any medicines you take, and any sickness you may have. Depending on your answers to the questions, you may not be able to take part in the study. If this happens, this will be explained to you and any questions you have will be answered. The investigator will remove you from the study. You will not be penalized in any way.

**If you meet the criteria and you agree to take part in this study,
you will be asked to do these things:**

You will fill out a form that tells us what exercise you did and how much sleep you got during the previous day. We will measure your height and weight.

You will have your body fat estimated by a special scale that uses bioelectrical impedance. You will hold a device the size and shape of a game controller. Your hands will be on a special area for full-body measurement. Your arms will be held straight out in front of you for a few seconds only. We will take a measure of heart health during this session. A machine using a blood pressure cuff and a wand will be used. It is noninvasive and will measure the blood flow speed of your arteries from your neck to your legs.

Exercise: Sessions 1 and 2

The same base methods will take place at both exercise sessions. You will be doing a short exercise session both times you come to the lab. One session will have "control" conditions. "Control" conditions are with no blood flow restriction. The other session will have "BFR" condition. "BFR" stands for blood flow restriction. It involves having a blood pressure cuff-like device inflated to 50% of the pressure it would take to stop your own personal blood flow.

Each exercise session will include:

Before

- Checking blood pressure before the exercise. This will make sure you are at a healthy level to exercise that day. If we think exercising that day may not be the best for you, we will ask you to reschedule your visit.
- We will do a simple blood draw from one arm. This draw takes 10 milliliters (about a tablespoon) of blood. There are two blood draws at each session.

Exercise Portion

- Four sets of ten repetitions of body-weight air squats
- You will wear a loose-fitting soft cloth leg sleeve during each exercise visit that will sit between your skin and the cuff. The leg sleeve will be washed after each participant.
- Another blood draw will be taken less than 5 minutes after your last repetition.
- A finger prick will be taken one hour after the last repetition. This is how we can tell what hormones (like insulin) are responding in your body.
- You will be asked to rank your effort from 1-10 and your pain 1-11.

BFR addition

- In the BFR session, the BFR systems figures out the pressure needed for 100% of blocking of blood flow. It then uses this information to calculate your personal pressure needed to block 50% of blood flow.
- This system regulates pressure during movement. This prevents a spike in pressure during exercise.
- Once the cuff is inflated, you will wait for 30 seconds before starting the exercise session.
- The cuff will remain inflated until the completion of exercise. It will be cleaned with alcohol after each participant

Time required: The study will require 4-5 hours of your time. Each session will take around 2 hours.

Risks: The main risk of being in this study are risks associated with the type of exercise. Weight training can cause muscle or bone injury. This includes bruising, muscle cramps or soreness, muscle strains and sprains or muscle tears. There is also a risk of feeling lightheaded, nauseous, or even fainting after performing exercise. The blood draw process can potentially cause fainting, minor bruising, infection, and slight discomfort during the sampling procedure.

Potential BFR risks associated with this study are very low. Based on a review of previous BFR studies there been very few reports of health issues related to its use. This is not different from the chance of experiencing these issues without the use of BFR. This suggests that BFR is not likely to be the cause of these problems. There is a great deal of research available showing that BFR use actually improves blood vessel health and blood flow, which are very good effects. Previous studies, as well as surgeons, have completely stopped blood flow for up to 2 hours without problems. For this study, we will only be partially stopping blood flow for the duration of the exercise, about 10 minutes or less. Therefore, the risk for any problems is small. You may also experience possible slight numbness or "pins and needles", which will be gone when the cuff is removed. You may find use of the blood flow restriction device to be uncomfortable and you may experience some pain. There is also a small risk of muscular injury. There may be unknown risks that could occur during this study, as there are with any study involving exercise.

The Exercise Physiology lab has an emergency response plan in place and all the research staff have been trained in appropriate response procedures.

You will be observed during and after testing, and testing will be stopped if you show negative signs/symptoms such as chest pains, lightheadedness, confusion, nausea, or cold, clammy skin, or if you feel for any other reason you need/want to stop. In case of accident or illness, a CPR certified individual will provide proper care, until emergency medical services arrive.

How will risks be minimized? Risks will be minimized by:

- Only allowing you to participate in the study if you are healthy and without diabetic complications.

4

UNIVERSITY OF ALABAMA IRB
CONSENT FORM APPROVED: 1-12-24
EXPIRATION DATE: 1-11-25

-
- Following the BFR protocol.
 - Using only well-trained people to draw your blood.
 - Stopping a test if you show any signs or symptoms of possible illness.
 - Asking you how you are feeling during the test.

Someone trained in CPR will be present for all sessions, and we are only 5 minutes from a hospital if an emergency occurs. In the event that this research activity results in an injury, treatment will be available, including first aid and emergency treatment as needed. Care for such injuries will be billed in the ordinary manner to you or your insurance company. We will not confirm whether you have health insurance coverage. Therefore, if you are not covered and you become injured as described above, you will be responsible for any costs you incur for treatment. Neither the Principal Investigator nor the University of Alabama will provide payment of costs associated with any injury due to your participation in this study.

You will be informed if significant new findings arise that might affect your desire to continue in the study.

Benefits: You will be given a \$25 Visa Gift Card for participation in the study. You will receive this at the end of the last session. You may or may not believe that information about your strength and fitness as well as an estimate of your body fat percentage as a benefit. This study will help scientists figure out better ways for fitness professionals, physicians, and therapists to prescribe exercise and potential treatment conditions that are used.

Confidentiality: Your privacy will be protected by asking you medical related questions in a private room or a site of your choosing. During exercise, your privacy will be protected by limiting the entrance of individuals into the laboratory to only those people who are working on the study and/or those people who normally work in the laboratory and have a desk there.

Medically-related information collected about you while you are exercising will not have your name on it.

Voluntary participation: Your participation in the study is completely voluntary. You can choose not to be in the study. If you start the study, you can stop at any time. There will be no effects on your care or your relations with the University of Alabama.

Right to withdraw from the study: You have the right to withdraw from the study at any time without penalty.

How to withdraw from the study: If you want to withdraw from the study, you may tell the researcher and leave the room as you deem fit. There is no penalty for withdrawing.

Compensation/Reimbursement: You will receive no payment for participating in the study.

If you have questions about the study or need to report a study related issue please contact, contact:

Principal Investigator: Tiffany Adams

Title: Student Research Assistant

Department Name: Department of Kinesiology

Telephone: (317) 378-3103

Email address: tladams5@crimson.ua.edu

Faculty Advisor: Dr. Lee Winchester

Department Name: Department of Kinesiology

Telephone: (205) 348-9522

Email address: ljwinchester@ua.edu

If you have questions about your rights as a participant in a research study, would like to make suggestions or file complaints and concerns about the research study, please contact: The University of Alabama Office for Research Compliance (205)-348-8461 or toll-free at 1-877-820-3066. You may also ask questions, make suggestions, or file complaints and concerns through the IRB Outreach Website at <https://research.ua.edu/compliance/irb/>. You may email the Office for Research Compliance at rscompliance@ua.edu.

Agreement:

- I agree to participate in the research study described above.
- I do not agree to participate in the research study described above.

Signature of Research Participant

Date

Print Name of Research Participant

Signature of Investigator or other Person Obtaining Consent

Date

Print Name of Investigator or other Person Obtaining Consent