COMPARING ACUTE HEMODYNAMIC RESPONSES TO ISOMETRIC EXERCISE INDUCED BLOOD FLOW RESTRICTION VS. PASSIVE CUFF BLOOD FLOW RESTRICTION WHEN BLOOD FLOW RESTRICTION IS MATCHED

By

Krista Cook

A thesis submitted to the faculty of
the University of North Carolina at Charlotte
in fulfillment of the requirements
for the degree of Master of Science
in Kinesiology

Charlotte

2019

Approved by:

____
Dr. Reuben Howden

____
Dr. Joseph Marino

____
Dr. Luke Donovan

____
Mr. David Verrill

ABSTRACT

KRISTA KAYLIN COOK. Comparing acute hemodynamic responses to isometric exercise induced blood flow restriction vs. passive cuff blood flow restriction when blood flow restriction is matched. (Under the direction of Dr. REUBEN HOWDEN, Ph.D.)

High blood pressure, also known as hypertension, is one of the most common disorders globally. Research has shown that anti-hypertensive medications alone are not universally effective in the treatment of high blood pressure. Isometric exercise training has been shown to be most effective at reducing blood pressure when compared to aerobic and resistance exercise training. The mechanisms responsible for the observed decrease in blood pressure following isometric exercise training are unknown. This study compared isometric exercise vs. cuff blood flow restriction when blood flow restriction was matched to determine if there was a similarity in acute hemodynamic and metabolic response. Eight men and twenty-two women, ages 18-25 years old, were recruited. Each subject participated in a baseline, isometric exercise, and passive cuff blood flow restriction session. Sessions were once a week for three weeks. Heart rate, blood pressure, oxygen consumption, carbon dioxide consumption, ventilation, respiratory quotient, metabolic equivalent, and blood lactate and glucose were measured. During the baseline session subjects pushed at their max on the Biodex dynamometer for 10 seconds with 10 seconds rest for three rounds. The isometric exercise session consisted of performing two-minute contractions at 30% maximal voluntary contraction with one minute rest for four rounds. The passive cuff blood flow restriction session experienced cuff pressure relative to the blood flow restriction experienced in an isometric exercise at 30% maximal voluntary contraction for two minutes with one-minute rest for four rounds. Significant changes in metabolic and acute hemodynamic response were only observed from an isometric exercise. Future research may compare isometric exercise against varying degrees of blood flow restriction to see if there are similarities in response. Individuals may be unwilling to perform isometric exercises because they are fatiguing and uncomfortable. Cuff blood flow restriction may be a more comfortable alternative to decrease resting blood pressure.

DEDICATION

To my grandmother, Kathryn Venturella,

and

my mother, Roxanne Cook

Thank you for your belief in my abilities, encouragement, and love.

ACKNOWLEDGEMENTS

I first would like to acknowledge and thank my research committee members: Dr. Reuben Howden, Dr. Joseph Marino, Dr. Luke Donovan, and Mr. David Verrill for their support and encouragement during this project, and throughout my undergraduate and graduate academic career. I would also like to thank my participants for their time and commitment. It was a pleasure getting to know each and every one of you.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1 : INTRODUCTION

About 75 million adults in the US population are affected by hypertension (HTN)[30]. HTN is a chronic condition in which blood pressure (BP) stays at an abnormally elevated pressure[40]. This increased pressure causes the arteries, heart, brain, and kidneys to work harder in order to maintain normal function. Over time, arteries become less elastic and damaged which may lead to atherosclerosis, coronary artery disease, scarring, aneurysm, or kidney failure[29]. Stress on the heart causes the left ventricle to hypertrophy which decreases the heart's ability to pump blood to the rest of the body. Declining functional capacity increases the risk of myocardial infarction or sudden cardiac death [5,39]. HTN affects the brain by causing transient ischemic attacks, stroke, vascular dementia, or mild cognitive impairments. It is essential to study the causes and possible treatments for HTN, since it has such a large impact on the human body. Blood Pressure reducing medications and non-pharmaceutical methods, such as exercise, have been used in an attempt to reduce HTN incidence in both healthy and special populations. Both aerobic and dynamic resistance exercise training have been shown to decrease resting BP, but not to the extent of isometric exercise training (IET) [7]. Reductions in systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) have been observed from IET[8]. An isometric exercise (IE) is performed at a percentage of a subject's maximal voluntary contraction (MVC) for a designated time period. IET may utilize a handgrip dynamometer, an isokinetic dynamometer, or body weight training exercises. IE require little to no equipment or space, making it accessible for everyone. Although IET requires a lower time commitment than aerobic or dynamic resistance exercise training, patients may be resistant to perform this type of exercise. IE can be fatiguing and uncomfortable making it unappealing to some individuals.

The reason for the reduction in BP following IET is unknown. However, it has been proposed that this reduction in BP following IET is stimulated by acute hemodynamic responses observed post exercise[11]. The current study investigated the proportion of responses induced by IE that are driven by blood flow restriction (BFR). Hemodynamic and metabolic responses from an IE vs. passive cuff BFR when BFR is matched were compared. We hypothesized that IE and passive cuff BFR would elicit similar hemodynamic and metabolic responses when BFR was matched. Cuff BFR is an example of passive BFR because the muscle is not contracting but BFR is still present. In other words, compression of the blood vessels is due to the cuff force applied around the limb, rather than muscle activation. An IE is considered active BFR, meaning the person is causing compression of the blood vessels by performing an isometric contraction. If cuff BFR and IE elicit a similar response, then BFR is a major contributing factor in reducing BP. If BFR is a contributing factor, future research will further investigate passive BFR training to reduce BP, which has been insufficiently studied before. More individuals may be willing to adopt the new method since ambulatory exercise will no longer be required. A vast portion of the world suffers from HTN, making it crucial to find a method that is efficient and effective at reducing BP.

CHAPTER 2: LITERATURE REVIEW

2.1 Hypertension

HTN is one of the most common risk factors for cardiovascular disease (CVD) and all-cause mortality [8]. Just a 2 mmHg increase in SBP increases the risk of stroke or heart disease by 7-10% [8]. Before 2017, HTN was defined as a SBP of ≥140 mmHg and/or DBP of ≥90 mmHg [5,37]. In 2017 the American College of Cardiology determined that these guidelines were no longer applicable. Stage one HTN is now considered to be a SBP of ≥ 130mmHg and/or DBP of ≥ 80 mmHg, which significantly increases the number of people who are considered hypertensive[5].

There are two classifications of HTN. Primary HTN accounts for approximately 95% of all cases and includes genetic and environmental influences [40]. There are two genetic forms of HTN; complex polygenic and monogenic disorder. Complex polygenic disorder is caused by a combination of genes, whereas monogenic disorder is when one gene influences BP[45]. Environmental risk factors include diet, physical activity, alcohol consumption, occupational exposure, and obesity[45]. The second classification is secondary HTN, which occurs in response to another medical condition. Certain diseases or side effects of pharmaceuticals may elicit this response[40].

Anti-hypertensive medications used to help control BP include the following: beta-blockers, diuretics, ACE inhibitors, angiotensin II receptor blockers, calcium channel blockers, alpha blockers, alpha-2 receptor agonists, combined alpha and beta-blockers, central agonists, peripheral adrenergic inhibitors, and blood vessel dilators. These medications may be used individually or in combination[2]. Hypertensive subjects in the United States who were treated with HTN medications demonstrated a 9 mm Hg difference in SBP and a 5 mm Hg difference in DBP[5]. Data suggests that HTN medications paired with lifestyle intervention may help decrease BP to a favorable amount, since HTN may not be significantly decreased by medications alone[5]. Physical activity has also been studied extensively as a possible intervention to lower BP. Aerobic and dynamic resistance exercise training have both been shown to lower long-term SBP by about 3 mm Hg [35]. IET studies have shown decreases in SBP of 10.4 mmHg, and greater [9,35,38]. Both hypertensive and non-hypertensive subjects have shown decreases in SBP, DBP, and MAP from IET [8]. Besides eliciting a greater BP reduction than either aerobic and dynamic resistance exercise, IE may be performed in less time, and may be performed anywhere[6].

2.2 The Effect of Isometric Exercise on Resting Blood Pressure

IET has been shown to decrease resting blood pressure (RBP) in both hypertensive and normotensive participants[8]. The intensity and duration used for IET protocols vary. The most common protocol involves performing an IE at 20-30% of MVC multiple times a week for six to eight weeks [4,7,11,34,35,41]. This time frame and intensity has been shown to elicit a reliable reduction in RBP in most participants[4,7,11,34,35,41]. The greatest decrease from the literature presented was 13 mmHg during a 6 week IET protocol[38]. Protocols lasting less than six weeks have shown significant changes in RBP, but not to as great of an extent[10,14].

Limited research has observed the difference in RBP response between men and women following IET[20,44,46]. Hunter et al. determined that women were more fatigue resistant than men during an IE protocol[20]. It is important to note that fatigue is not caused by a lack of blood flow but a change in excitation-contraction coupling, inhibition of metabolic contraction, and failed activation of the central and peripheral nervous system[46]. Women have greater fatigue resistance because they have more Type I fibers, a larger vasodilatory response, and less metabolite buildup from an IE[20]. Cardiac baroreflex sensitivity (cBRS) is reduced during IE and elevated post-exercise in males and females[43]. However, the increase in cBRS is greater in women than in men[44]. It has not been determined if IET has a greater effect on men or women.

The main mechanism responsible for a decrease in RBP from IET remains unknown. During IE SBP, DBP, and MAP are increased. However, post exercise BP levels drop to or below resting baseline levels[8,43]. Increased BP during IE was accounted for by increased cardiac output, not peripheral vascular resistance[8]. Over time, RBP is reduced as a consequence of performing IET. Hemodynamic responses of the heart pre- and post- IE include decreased left ventricular (LV) end systolic diameter, posterior wall thickness, and relative wall thickness decreased[27]. The IE participants experienced normal LV geometry and improved LV mechanics following IE[27]. Heart rate (HR) responses varied between studies [3,7, 27, 43,44]. Isometric exercise training protocols produced either no change in HR or a slight decrease after training[3,7, 27, 43,44]. IET had no effect on lowering cholesterol, however, there was a significant decrease in oxygen-centered radicals[38]. A decrease in RBP long-term from IET may be due to the resetting of the baroreceptors or immediate post exercise cardiovascular response [8,11].

Little is known about chronic BP reductions via baroreceptor resetting. IET elicits a greater response on RBP than either aerobic or dynamic resistance exercise training when performed for less time each week. Therefore, there may be an underlying mechanism from the exercise that isn't experienced from either aerobic or dynamic resistance exercise training. An IE is performed by holding a position or squeezing a piece of equipment for a period of time. This continuous squeeze or hold causes compression of the blood vessels, which stimulates slight BFR. Compression of blood vessels limits blood flow which stimulates the chemoreceptors within the muscle. This stimulation causes the blood vessels to dilate in an attempt to increase blood flow to the working muscle[33]. We hypothesized that BFR during IET may be a mechanism for reductions in RBP. Therefore, the contribution of BFR only responses was compared to IE.

2.3 Passive Blood Flow Restriction

Passive cuff BFR has been studied as a method to decrease muscle weakness or soreness[20,23, 32,36,42]. Cuff inflation of 180 to 200 mmHg has shown to decrease disuse atrophy and muscle weakness[23, 36,42]. Cuff BFR causes a decrease in creatine kinase within the restricted muscle, which decreases inflammatory responses[36]. This decrease correlates with reduced muscle edema and intramuscular pressure which reduces the effects of exercise induced muscle damage[36]. It is important to note that some protocols have not produced a decrease in muscle weakness or recovery time when utilizing total BFR[32]. When the BFR stimulus was decreased to 50 mm Hg, cuff BFR elicited only partial prevention of muscle weakness[24]. When compared to IE, Cuff BFR has shown a greater effect on preventing muscle weakness and atrophy[23].

Cuff BFR has been studied as a method to reduce recovery time after an injury or exercise, but little research has studied the hemodynamic response to cuff BFR. Loenneke et al. studied the effect of BFR on arterial and venous blood flow without exercise at 70% Cuff BFR. Although the BFR was relatively high, an increase in venous outflow was observed. This response may result in a countermeasure for orthostatic intolerance[27]. Cuff BFR has shown to have a significant effect on the human body[23, 24, 32,36,42]. However, more research needs to be performed in order to determine the total effect of cuff BFR.

Determining the amount of BFR needed for each subject in a protocol has been a topic of debate. Even though a cuff is inflated to the same pressure for all participants, the response to the pressure is different for each individual[19,26]. BFR pressure at first was thought to be reliant on SBP, cuff size, and limb size[26]. However, no significant differences in BF response were observed when using a 10 cm and 12 cm cuff at the tibial artery[31]. This suggests that cuffs of different sizes do not have a significant effect on BF as long as relative pressures are used[31]. For the current study, Loenneke's formula to find total cuff BFR was used to determine cuff BFR for each participant[25]. Limb circumference, SBP, and DBP were the main predictors in determining an individual's cuff BF[25]. These three variables influenced a participant's cuff pressure, but not the percentage of BFR experienced. Accounting for these variables reassured that all participants experienced 30% BFR.

2.4 Summary

The purpose of this study was to determine the difference in acute hemodynamic and metabolic responses between passive and active BFR. It has been suggested that local muscle anaerobiosis generated during an IE plays an essential part in a decrease in RBP[13]. Anaerobiosis may be able to be mimicked by passive BFR if BFR is matched. After reviewing the literature, we hypothesized that passive cuff BFR will elicit a significant portion of the acute hemodynamic and metabolic responses observed during active IE when BFR is matched. To our knowledge, the acute hemodynamic and metabolic responses of these two conditions have not been directly compared before. Pulmonary response has not been observed at all from an IE or cuff BFR. In order to achieve a better understanding of the acute hemodynamic and metabolic responses from an IE and passive cuff BFR protocol, HR, BP, blood lactate, blood glucose, oxygen consumption (VO2), carbon dioxide consumption (VCO2), ventilation (VE), respiratory quotient (RQ), and metabolic equivalent (METS) were recorded. Metabolic and hemodynamic responses were monitored throughout, and blood lactate and glucose was taken before and five minutes following the IE and BFR sessions [12,15].

CHAPTER 3: MATERIALS & METHODS

Eight males and twenty-two females (N=30) (age 21.5 ± 3.5 years) volunteered and participated in the study. Participants were included if they were a UNC Charlotte student, between the ages of 18 to 25 years old, not using tobacco products (including smokeless) within the preceding 6 months, not taking large doses (800 mg/day Ibuprofen, 1250-1375 mg/day Naxproxen) of non-steroidal anti-inflammatory medications like Advil or Aleve, no prescribed heart medications (including BP and other health conditions), no physical limitations causing pain or discomfort when using their legs, no acute illness or sickness within the past two weeks, was able to read and understand the details of the study, and was free once a week to participate.

3.1 Sampling Techniques and Recruitment

Subjects were recruited through in class presentations at UNC Charlotte during summer session one and two. The importance and procedures of the study were explained to the class. All participants who expressed interest were contacted during the same week by telephone. The investigator explained the procedures again and asked the subject a series of questions regarding eligibility. If eligible the investigator scheduled an initial session with the subject in the laboratory of systems physiology at UNC Charlotte. Participating students received an email containing the pre-session criteria at least 24 hours prior to their scheduled sessions. Criteria included the following: voiding urine prior to sitting for the BP measurement, no significant changes in diet, no caffeine, alcohol, or vigorous exercise within the last 24 hours, taking daily medications (if on a prescription), no changes in health within the last week, and no eating two hours prior.

Informed consent was discussed, read, and signed during the baseline session. The study was approved by the Institutional Review Board (18-0049).

3.2 Study Design and Methodology

Each participant participated in a baseline, IE, and cuff BFR session, acting as their own control. The baseline session was used to determine the participant's MVC and resting BP and HR. The IE and cuff BFR sessions were compared at each time point to determine the variation in metabolic and hemodynamic response. Blood flow restriction was matched for IE and cuff BFR at 30%. Sessions were separated by one week. Each participant visited the laboratory a total of three times. The dependent variables measured in the study were SBP, DBP, HR, VE, VO2, VCO2, METS, RQ, blood lactate, and blood glucose. The independent variables measured were IE and cuff BFR.

3.3 Baseline Session

All participants participated in a baseline session for the first day of the study. The investigator initially explained the informed consent, and then had the participant read through and ask questions before they signed. The participants were then asked if they followed the criteria sent to them by email prior to the session. If the participant failed to follow criteria, they were asked to reschedule the initial session. If the criteria were followed, the participant rested for 15 minutes, seated in the laboratory. After 15 minutes passed, the investigator took three BP measurements from the brachial artery. Each measurement was separated by one minute of rest. Once the measurements were taken, the participant stood from the chair so the thigh circumference could be determined. Circumference was found by measuring from the groin to the top of the patella. The measurement number was multiplied by 0.33. The investigator marked 33%

of this measurement from the top of the patella. Thigh circumference was measured at this mark. Participants were then invited to sit on the chair of the Biodex dynamometer. The investigator set up the Biodex dynamometer and strapped the participant into the seat. Once the subject was set up, the investigator explained how the session would work. The subject performed a leg extension at MVC for 10 seconds with 10 seconds rest for three rounds. After the subject completed the three rounds they were unstrapped, and the investigator recorded the subject's MVC.

3.4 Isometric Exercise Session

Summer session one students completed the IE session on day two of the study, and summer session two students on day three. Participants were asked the same criteria questions as before. If criteria was followed, the participant rested for 15 minutes on the Biodex dynamometer. While the participant rested, the investigator made sure the metabolic cart, Biodex dynamometer, sphygmomanometer, and blood glucose and lactate monitors were ready to use. The participant's BP was measured three times with a minute rest in between after the rest period. The investigator then measured blood lactate and glucose and fitted the mask for the metabolic cart on the participant. Once completed, the participant was strapped into the Biodex dynamometer and the protocol was explained. Besides instruction from the investigator, the Biodex dynamometer told the participant when to push against the limb, and how hard they were pushing. Visual and sound displays were utilized to help the participant follow along. A cartoon character on the screen pushed and rested with the participant, and a bell went off to let the participant know when to work or stop. The participant pushed continuously at 30% of their max for two minutes with one minute rest for four rounds. Blood pressure, HR, VO2, VCO2, VE, METS, and RQ were taken every minute throughout the protocol. When the four rounds were complete, the investigator had the participant rest for five minutes. At the end of this rest period, the investigator took one more BP, HR, and blood lactate and glucose measurement.

3.5 Passive Cuff Blood Flow Restriction Session

The passive cuff BFR session occurred on the third day for summer session one and on the second day for summer session two. Participants were asked the same criteria questions as before. If criteria was followed, the participant rested for 15 minutes on the Biodex dynamometer. While the participant rested the investigator made sure the metabolic cart, sphygmomanometer, and blood glucose and lactate monitors were set up to use. Once the 15 minutes was finished the subject's BP was measured three times with a minute of rest in between. After the three measurements were recorded, the investigator determined 30% BFR by using the formula: [5.983 (circumference) + 0.734 (DBP) + 0.912 (SBP) - 220.046] x 0.30[25].The cuff BFR was comparable to the BFR witnessed during the IE. Once the number was calculated the investigator measured blood lactate and glucose samples. Next, the metabolic cart mask was fitted to the participant, and BP thigh cuffs were strapped to each thigh. The protocol was explained to the subject, and then the thigh cuffs were inflated to 30%. Cuffs were inflated for two minutes with one minute rest for four rounds. Blood pressure, HR, VO2, VCO2, VE, METS, and RQ were taken every minute throughout the protocol. Once passive cuff BFR was completed, the investigator had the subject rest for five minutes. At the end of this rest period, the investigator took one more BP, HR, and blood lactate and glucose measurement.

3.6 Biodex Dynamometer Setup

The Biodex Isokinetic Dynamometer System 4 Pro (Biodex Medical Systems, Shirley) was utilized in the baseline and IE protocol. The investigator recorded the participant's information and calibrated the limb of the Biodex dynamometer to lock at 90 degrees. After the limb was adjusted, the participant was strapped into the chair at the waist and chest. Once secured the participant's ankles were strapped to the limb of the Biodex dynamometer. The investigator then explained how the session would work, and then the participant completed the protocol.

3.7 Metabolic Cart

A Cosmed metabolic cart (COSMED, Concord) was used in the IE and passive cuff BFR session. The investigator calibrated the metabolic cart using standard manufacturer calibration procedures. Mask size for each participant was determined in the second session by using the metabolic cart face measuring device. The cart was used to measure VO2, VCO2, VE, METS, and RQ.

3.8 Blood Lactate and Glucose

Blood lactate and glucose were measured before and after each IE and cuff BFR session from the fourth or fifth digit of the left hand. The investigator cleaned the area before pricking the finger. The first drop of blood was wiped away using gauze to avoid sample contamination. The investigator used the Nova Biomedical Lactate Plus monitor (Nova Biomedical, Waltham) and the Stat Strip Xpress Glucose monitor (Nova Biomedical, Waltham) to test the participant's blood. Once the participant's readings were collected the investigator applied a bandage to the area that was pricked. If the investigator was unable to attain enough blood for a reading, another finger was utilized.

If a reading was not attained by the fourth attempt, the investigator recorded the variable as missing data.

3.9 Statistical Analysis

The sample size for the experiment was determined by an online power analysis calculator. An alpha level of .05 was used to indicate significance. A two way repeated measures ANOVA was used to determine the difference within conditions and against conditions. SPSS assessed differences between SBP, DBP, HR, VO2, VCO2, RQ, VE, METS, and blood lactate and glucose. Standard deviation indicated the extent of deviation for each time point of the protocol. An effect size calculator was used to determine the magnitude of change between IE and cuff BFR. An effect size of 0.8 or greater was used to determine if a comparison had a large magnitude of change. The larger the effect size, the greater the variation in response. A paired t-test and two way repeated measures ANOVA was used to determine the effect size between IE and cuff BFR SBP, DBP, and HR. A paired t-test was used to determine the median of these three dependent variables during contraction and relaxation. During the end of the IE protocol, the sphygmomanometer had issues reading BP due to involuntary contraction of the bicep. This caused participants to have missing data points. SPSS did not include participants with one or more missing variables when performing the two way repeated measures ANOVA. Instead of having an N of 30, there was only an N of 14 for BP and HR. Since contraction and relaxation points were not significantly different, the median of the time points was determined, and the data was collapsed to create an N of 30. Microsoft Excel was used to determine outliers. Any number that was greater than 2 standard deviations from the mean was determined to be an outlier and was removed.

CHAPTER 4: RESULTS

4.1 Isometric Exercise and Cuff Blood Flow Restriction

Significant differences were found in acute hemodynamic and metabolic response between an IE and cuff BFR. Thirty participants finished the protocol out of 36. The six individuals who did not complete the protocol were unable to follow the criteria or make it into the lab once a week. Participants who completed the study were fully compliant with all criteria and had 100% adherence. All participants except for one were a part of the exercise science department at the University of North Carolina Charlotte. Every individual was at least moderately active and had a normal RBP. Demographic data may be observed in **Table 1** for the 30 participants. Informed consent and participant demographic information was collected in the initial baseline session.

Demographic information for the study's 30 participants is represented in **Table 1**.

Table 1: Study participant including average resting SBP, DBP, and HR, maximal voluntary contraction, and 30% maximal voluntary contraction on a Biodex dynamometer. All values are represented as a mean ± standard deviation.

Participants	**N = 30**
Men	**8**
Female	**22**
Average Resting SBP (mmHg)	**112.8 ± 9.2**
Average Resting DBP (mmHg)	**67.8 ± 8.3**
Average Resting HR (bpm)	**76.4 ± 14.0**
MVC (Newtons)	**224 ± 115.8**
30% MVC (Newtons)	**67.19 ± 34.8**

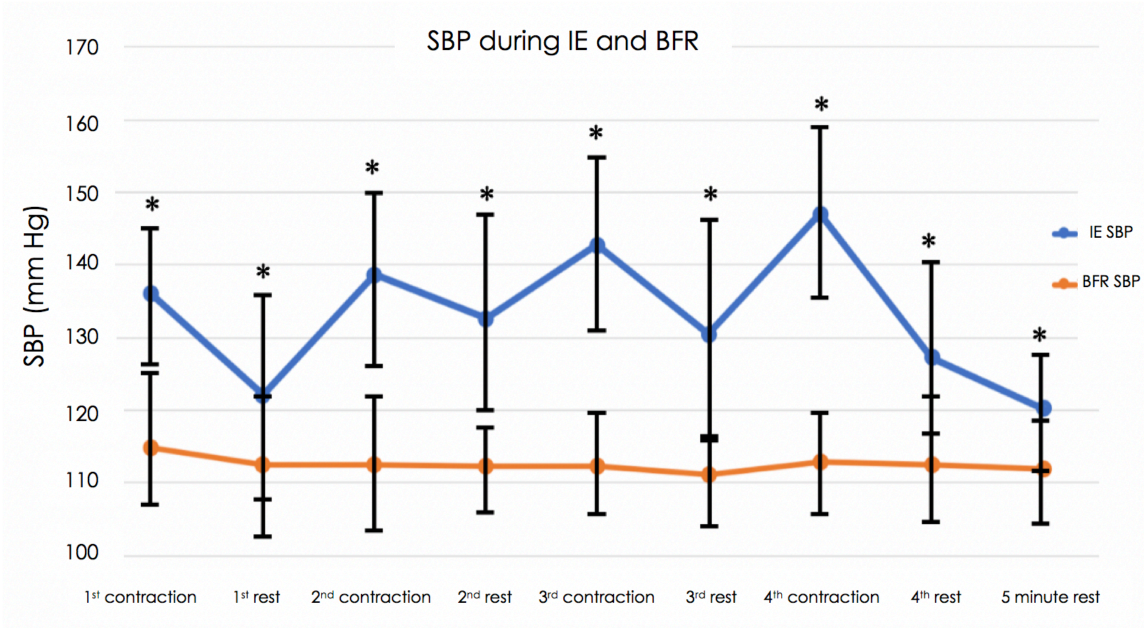

Figure 1A: Overall difference in SBP response between a double leg extension isometric exercise and double leg cuff blood flow restriction session. Paired t-test to determine missing variables. Two-way repeated measures ANOVA. * = Large magnitude of change between IE and BFR (Effect size > 0.8).

Isometric exercise			Cuff Blood Flow Restriction			Standard Error of E.S. estimate	Effect Size	Confidence Interval	
Mean	SD	n	Mean	SD	n			Lower	Upper
136.3	10.3	30	114.8	7.9	30	0.33	2.33	1.68	2.99
122.4	12.6	30	112.5	9.1	30	0.27	0.90	0.36	1.43
138.7	11.1	30	112.6	8.0	30	0.36	2.70	2.00	3.40
132.5	12.8	30	112.3	6.3	30	0.32	2.02	1.39	2.64
142.6	12.4	30	112.3	7.3	30	0.37	2.97	2.23	1.08
130.5	15.0	30	111.3	6.3	30	0.30	1.67	1.08	2.25
146.6	12.6	30	113.0	6.9	30	0.40	3.30	2.52	4.08
127.5	12.2	30	112.5	8.1	30	0.29	1.45	0.89	2.02
120.6	8.0	30	111.9	7.4	30	0.28	1.13	0.58	1.67

Figure 1B: Effect size calculator comparing IE vs. BFR systolic blood pressure

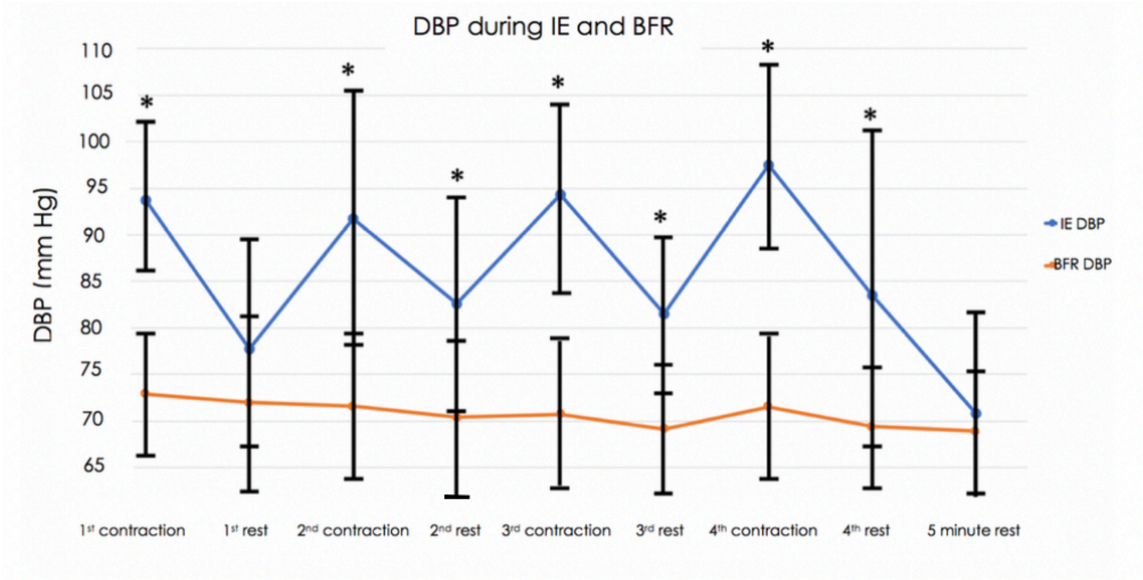

Figure 1C: Overall difference in DBP response between a double leg extension isometric exercise and double leg cuff blood flow restriction session. Paired t-test to determine missing variables. Two-way repeated measures ANOVA. * = Large magnitude of change between IE and BFR (Effect size > 0.8).

Isometric exercise			Cuff Blood Flow Restriction			Standard Error of E.S. estimate	Effect Size	Confidence Interval	
Mean	SD	n	Mean	SD	n			Lower	Upper
93.7	8.2	30	72.8	6.6	30	0.36	2.79	2.08	3.50
78.1	10.5	30	72.0	8.5	30	0.26	0.64	0.12	1.16
91.8	13.2	30	71.6	7.6	30	0.31	1.88	1.28	2.49
82.6	10.9	30	70.4	8.3	30	0.28	1.26	0.71	1.81
94.3	9.5	30	70.7	7.7	30	0.36	2.73	2.03	3.43
81.6	8.1	30	69.2	6.9	30	0.30	1.65	1.06	2.24
97.4	10.0	30	71.5	6.5	30	0.38	3.06	2.32	3.81
83.5	17.3	30	69.4	6.6	30	0.28	1.08	0.54	1.62
70.8	9.5	30	69.0	6.0	30	0.26	0.22	-0.28	0.73

Figure 1D: Effect size calculator comparing IE vs. BFR diastolic blood pressure

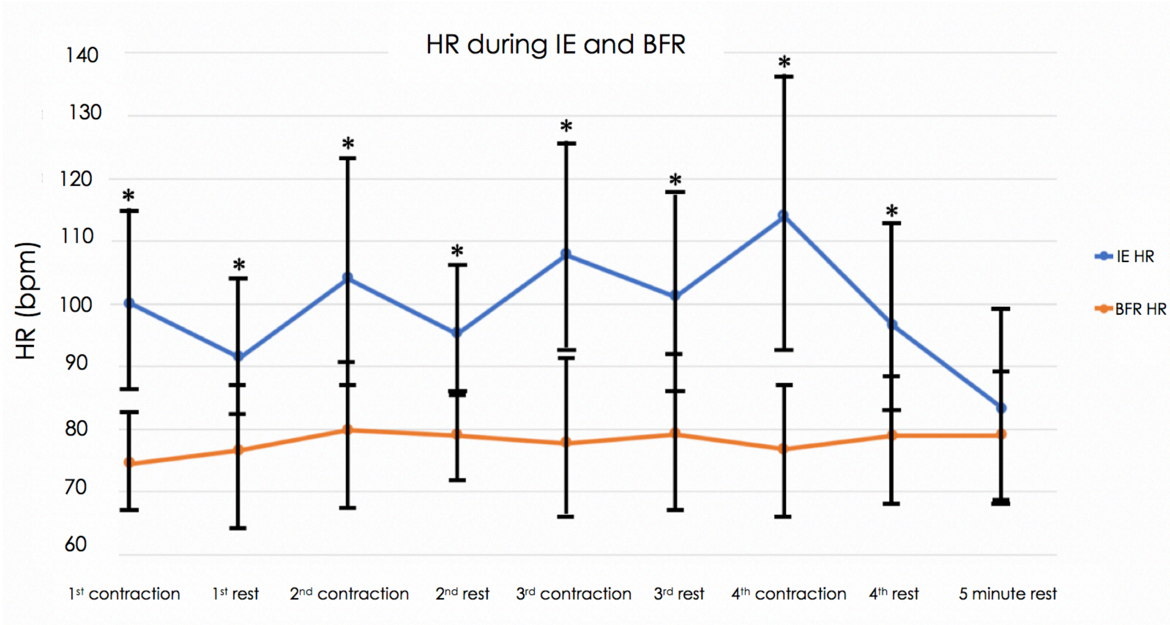

Figure 1E: Overall difference in HR response between a double leg extension isometric exercise and double leg cuff blood flow restriction session. Paired t-test to determine missing variables. Two-way repeated measures ANOVA. * = Large magnitude of change between IE and BFR (Effect size > 0.8).

Isometric exercise			Cuff Blood Flow Restriction			Standard Error of E.S. estimate	Effect Size	Confidence Interval	
Mean	SD	n	Mean	SD	n			Lower	Upper
100.1	12.1	30	74.8	8.1	30	0.34	2.46	1.79	3.13
91.9	11.0	30	76.6	11.0	30	0.29	1.39	0.82	1.95
104.1	15.9	30	79.6	10.0	30	0.31	1.84	1.24	2.44
95.3	12.5	30	78.9	7.6	30	0.30	1.59	1.01	2.17
107.7	15.9	30	77.8	12.9	30	0.32	2.07	1.44	2.70
101.1	15.8	30	79.1	11.7	30	0.30	1.58	1.00	2.16
114.0	23.5	30	76.8	10.3	30	0.32	2.05	1.43	2.68
96.7	15.3	30	78.9	9.5	30	0.29	1.40	0.84	1.97
83.2	15.3	30	79.0	9.8	30	0.26	0.33	-0.18	0.84

Figure 1F: Effect size calculator comparing IE vs. BFR heart rate

4.2 Acute Hemodynamic Responses to Isometric Exercise vs. Blood Flow Restriction

The data provided represents the difference in acute hemodynamic response during and after an IE and cuff BFR. Changes in SBP, DBP, and HR can be observed in **Figure 1A, 1C, and 1E**. The findings indicate a significantly higher response in SBP, DBP, and HR to IE. BFR at 30% caused insignificant changes in BP and HR during contraction and relaxation.

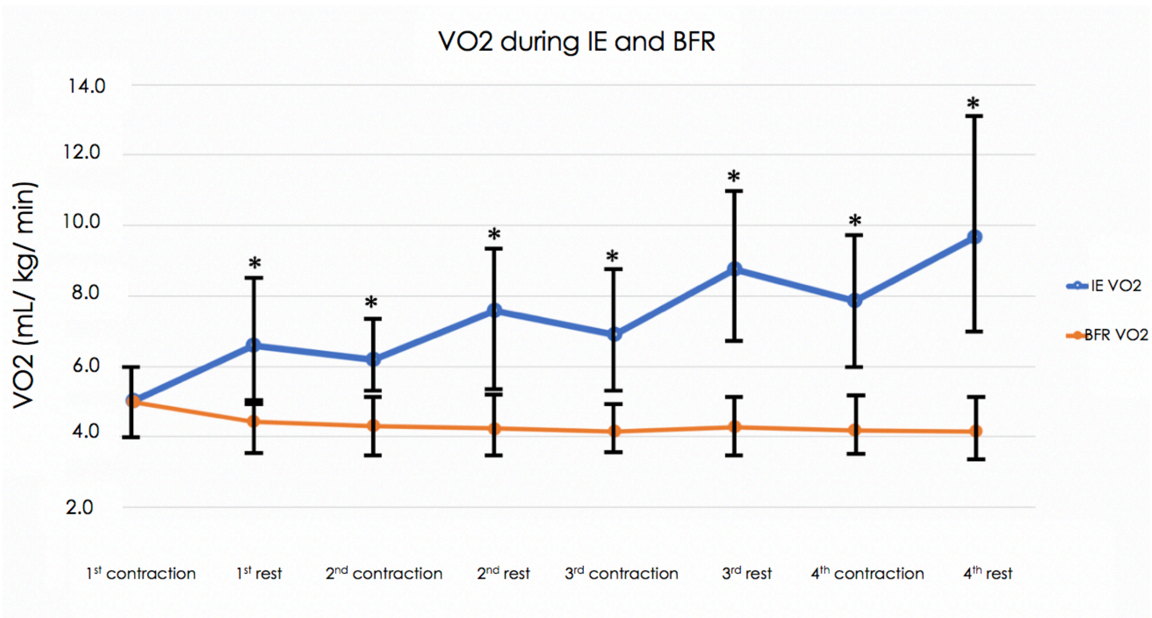

Figure 2A: Overall difference in VO2 response between a double leg extension isometric exercise and double leg cuff blood flow restriction session. Two-way repeated measures ANOVA. * = Large magnitude of change between IE and BFR (Effect size > 0.8).

Isometric exercise			Cuff Blood Flow Restriction			Standard Error of E.S. estimate	Effect Size	Confidence Interval	
Mean	SD	n	Mean	SD	n			Lower	Upper
5.2	1.3	26	5.0	1.0	26	0.28	0.17	-0.37	0.72
6.9	1.7	26	4.5	0.9	26	0.33	1.75	1.11	2.39
6.5	1.6	26	4.3	0.7	26	0.33	1.76	1.12	2.40
7.7	2.1	26	4.2	0.7	26	0.36	2.26	1.56	2.96
7.2	1.9	26	4.2	0.7	26	0.35	2.12	1.44	2.80
8.7	2.3	26	4.2	0.7	26	0.38	2.63	1.89	3.38
7.7	1.9	26	4.2	0.7	26	0.37	2.42	1.71	3.14
9.6	2.7	26	4.1	0.7	26	0.39	2.80	2.03	3.56

Figure 2B: Effect size calculator comparing IE vs. BFR oxygen consumption

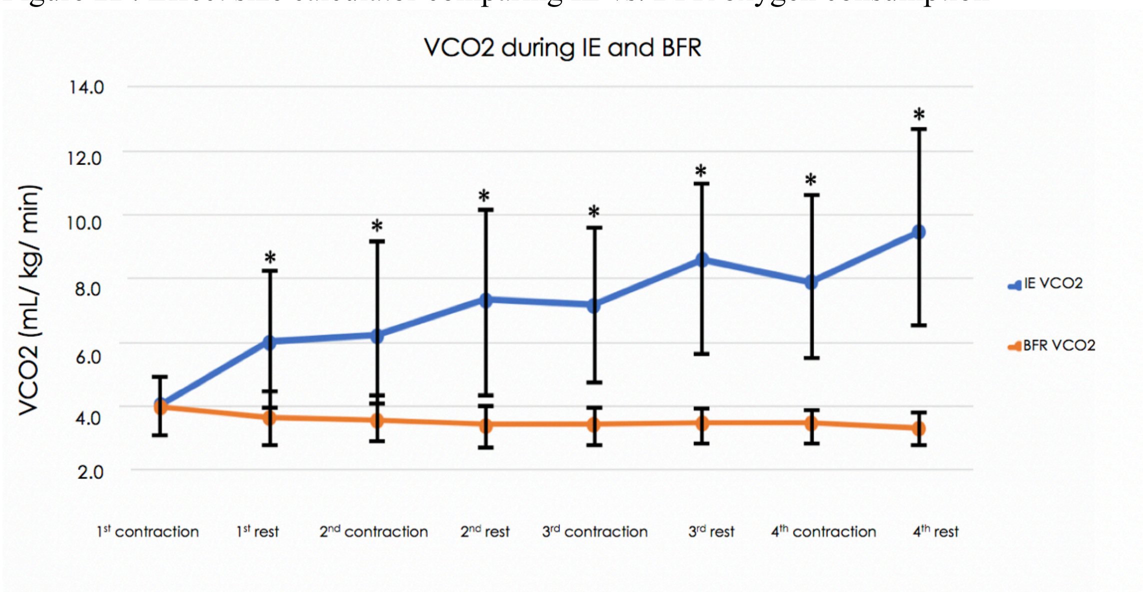

Figure 2C: Overall difference in VCO2 response between a double leg extension isometric exercise and double leg cuff blood flow restriction session. Two-way repeated measures ANOVA. * = Large magnitude of change between IE and BFR (Effect size > 0.8).

Isometric exercise			Cuff Blood Flow Restriction			Standard Error of E.S. estimate	Effect Size	Confidence Interval	
Mean	SD	n	Mean	SD	n			Lower	Upper
4.3	1.3	26	4.0	0.8	26	0.28	0.27	-0.28	0.82
6.2	2.0	26	3.7	0.7	26	0.32	1.66	1.03	2.30
6.3	2.1	26	3.6	0.6	26	0.32	1.72	1.08	2.35
7.3	2.8	26	3.4	0.5	26	0.34	1.98	1.32	2.65
7.1	2.4	26	3.5	0.5	26	0.35	2.12	1.44	2.80
8.5	2.9	26	3.5	0.5	26	0.36	2.40	1.69	3.11
7.8	2.5	26	3.5	0.5	26	0.36	2.41	1.69	3.12
9.4	3.2	26	3.3	0.5	26	0.38	2.63	1.89	3.38

Figure 2D: Effect size calculator comparing IE vs. BFR carbon dioxide consumption

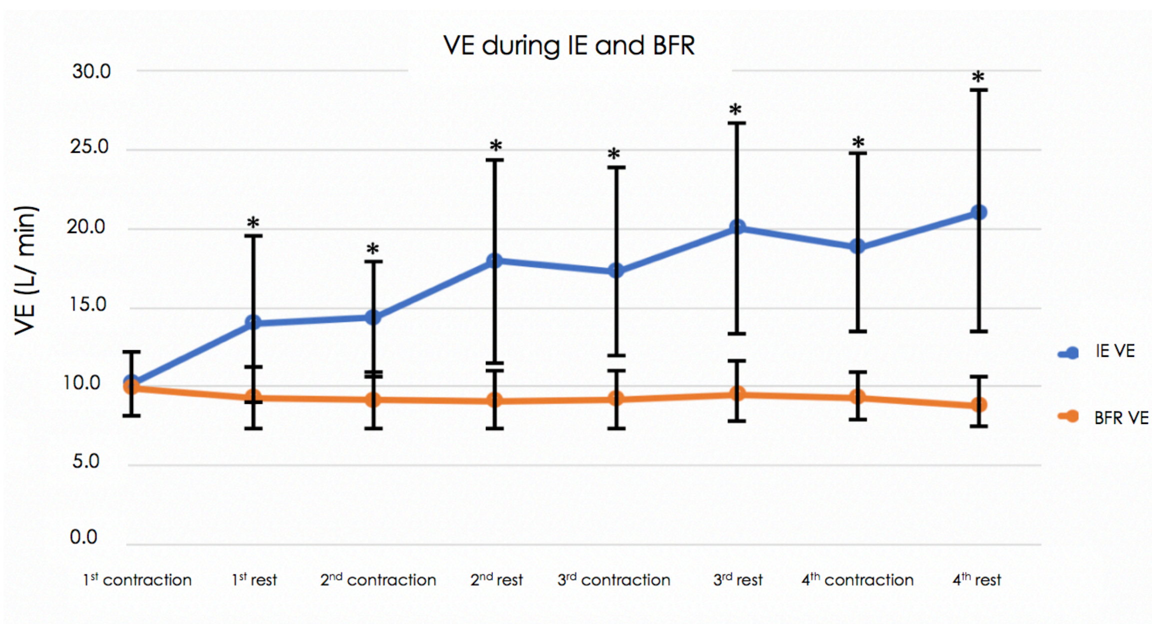

Figure 2E: Overall difference in VE response between a double leg extension isometric exercise and double leg cuff blood flow restriction session. Two-way repeated measures ANOVA. * = Large magnitude of change between IE and BFR (Effect size > 0.8).

Isometric exercise			Cuff Blood Flow Restriction			Standard Error of E.S. estimate	Effect Size	Confidence Interval	
Mean	SD	n	Mean	SD	n			Lower	Upper
11.0	3.1	26	10.1	2.3	26	0.28	0.32	-0.23	0.86
14.7	4.6	26	9.4	2.0	26	0.31	1.48	0.87	2.09
15.1	5.3	26	9.3	2.0	26	0.31	1.47	0.86	2.08
18.0	6.9	26	9.0	2.0	26	0.33	1.76	1.12	2.40
17.1	5.9	26	9.1	1.8	26	0.33	1.83	1.18	2.47
20.8	8.6	26	9.3	1.9	26	0.33	1.83	1.19	2.48
19.2	6.9	26	9.2	1.8	26	0.34	1.99	1.32	2.65
22.7	9.7	26	8.9	1.9	26	0.34	1.99	1.32	2.65

Figure 2F: Effect size calculator comparing IE vs. BFR ventilation

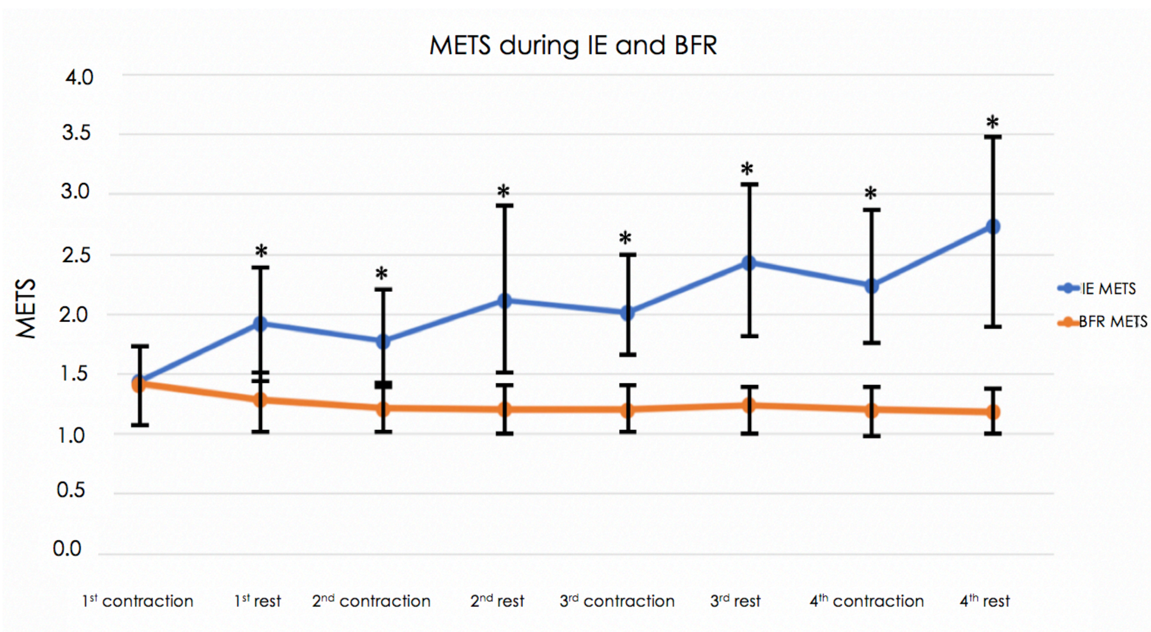

Figure 2G: Overall difference in METS between a double leg extension isometric exercise and double leg cuff blood flow restriction session. Two-way repeated measures ANOVA. * = Large magnitude of change between IE and BFR (Effect size > 0.8).

Isometric exercise			Cuff Blood Flow Restriction			Standard Error of E.S. estimate	Effect Size	Confidence Interval	
Mean	SD	n	Mean	SD	n			Lower	Upper
1.5	0.4	26	1.4	0.3	26	0.28	0.17	-0.37	0.72
2.0	0.5	26	1.3	0.2	26	0.33	1.76	1.12	2.40
1.8	0.5	26	1.2	0.2	26	0.32	1.68	1.05	2.31
2.1	0.7	26	1.2	0.2	26	0.33	1.88	1.23	2.54
2.0	0.5	26	1.2	0.2	26	0.35	2.12	1.44	2.80
2.4	0.7	26	1.2	0.2	26	0.36	2.31	1.60	3.01
2.2	0.6	26	1.2	0.2	26	0.37	2.43	1.72	3.15
2.7	0.8	26	1.2	0.2	26	0.38	2.65	1.90	3.39

Figure 2H: Effect size calculator comparing IE vs. BFR metabolic equivalent

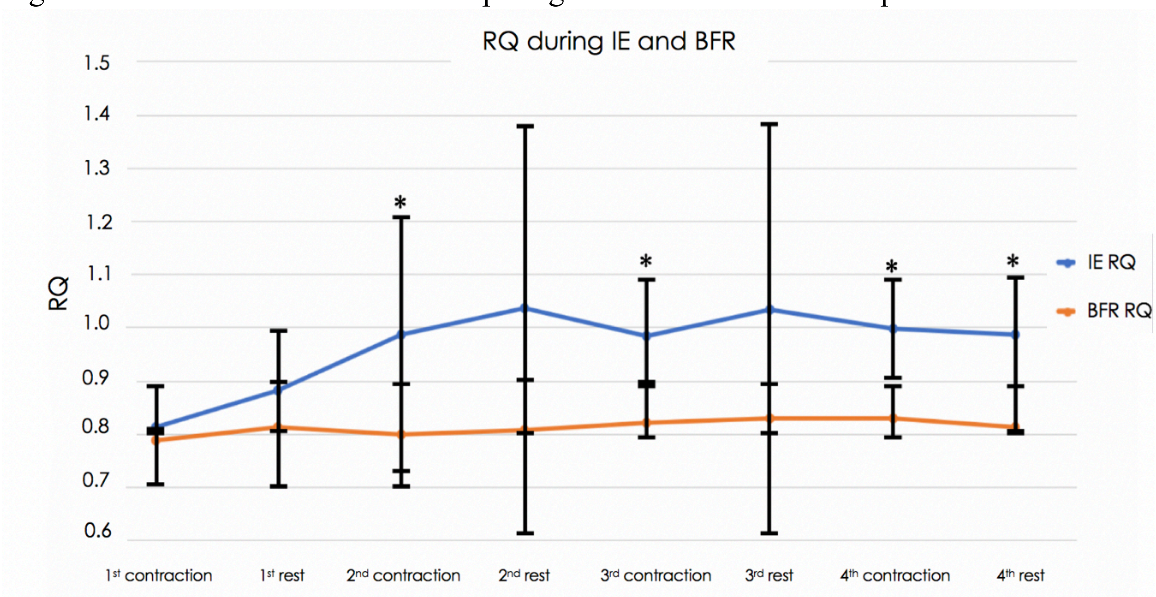

Figure 2I: Overall difference in RQ response between a double leg extension isometric exercise and double leg cuff blood flow restriction session. Two-way repeated measures ANOVA. * = Large magnitude of change between IE and BFR (Effect size > 0.8).

Isometric exercise			Cuff Blood Flow Restriction			Standard Error of E.S. estimate	Effect Size	Confidence Interval	
Mean	SD	n	Mean	SD	n			Lower	Upper
0.8	0.1	26	0.8	0.1	26	0.28	0.23	-0.31	0.78
0.9	0.1	26	0.8	0.1	26	0.29	0.74	0.18	1.30
1.0	0.2	26	0.8	0.1	26	0.29	1.01	0.43	1.59
1.0	0.4	26	0.8	0.1	26	0.29	0.78	0.22	1.35
1.0	0.1	26	0.8	0.1	26	0.32	1.61	0.98	2.23
1.0	0.4	26	0.8	0.1	26	0.29	0.71	0.15	1.27
1.0	0.1	26	0.8	0.1	26	0.32	1.69	1.06	2.32
1.0	0.2	26	0.8	0.1	26	0.31	1.49	0.87	2.10

Figure 2J: Effect size calculator comparing IE vs. BFR respiratory quotient

4.3 Comparing Pulmonary Response between Isometric Exercise and Blood Flow Restriction

The data provided represents the difference in pulmonary response during and after an IE and cuff BFR. Changes in VO2, VCO2, VE, METS, and RQ can be observed in **Figure 2A, 2C, 2E, 2G, and 2I**. The findings indicate a significantly higher pulmonary response to IE. Pulmonary response to IE was not significant from contraction to relaxation. Blood flow restriction did not elicit a significant change. Blood flow restriction stayed at a fairly consistent rate.

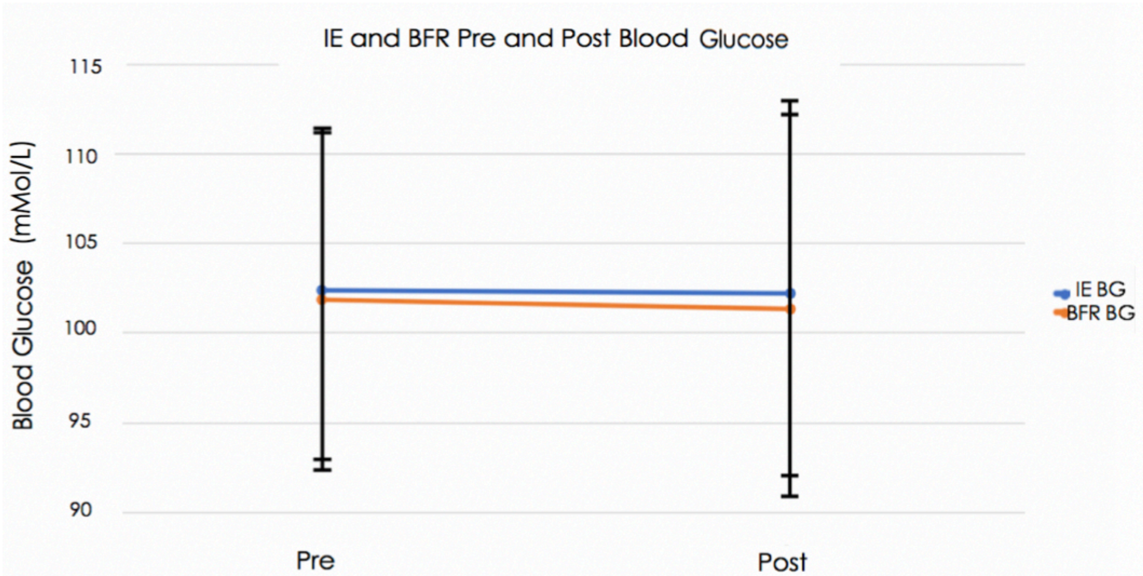

Figure 3A: The difference between pre and post exercise blood glucose response to a double leg extension isometric exercise and double leg cuff blood flow restriction session. Two-way repeated measures ANOVA. * = Large magnitude of change between IE and BFR (Effect size > 0.8).

	Isometric exercise			Cuff Blood Flow Restriction			Standard Error of E.S. estimate	Effect Size	Confidence Interval	
	Mean	SD	n	Mean	SD	n			Lower	Upper
Pre IE vs. BFR	103.5	10.9	28	103.9	12.1	28	0.27	-0.03	-0.56	0.49
Post IE vs. BFR	99.9	16.1	28	101.0	11.5	28	0.27	-0.08	-0.61	0.44
Pre IE vs. Post IE	103.5	10.9	28	99.9	16.1	28	0.27	0.26	-0.26	0.79
Pre BFR vs. Post BFR	103.9	12.1	28	101.0	11.5	28	0.27	0.24	-0.29	0.76

Figure 3B: Effect size calculator comparing IE vs. BFR pre and post blood glucose

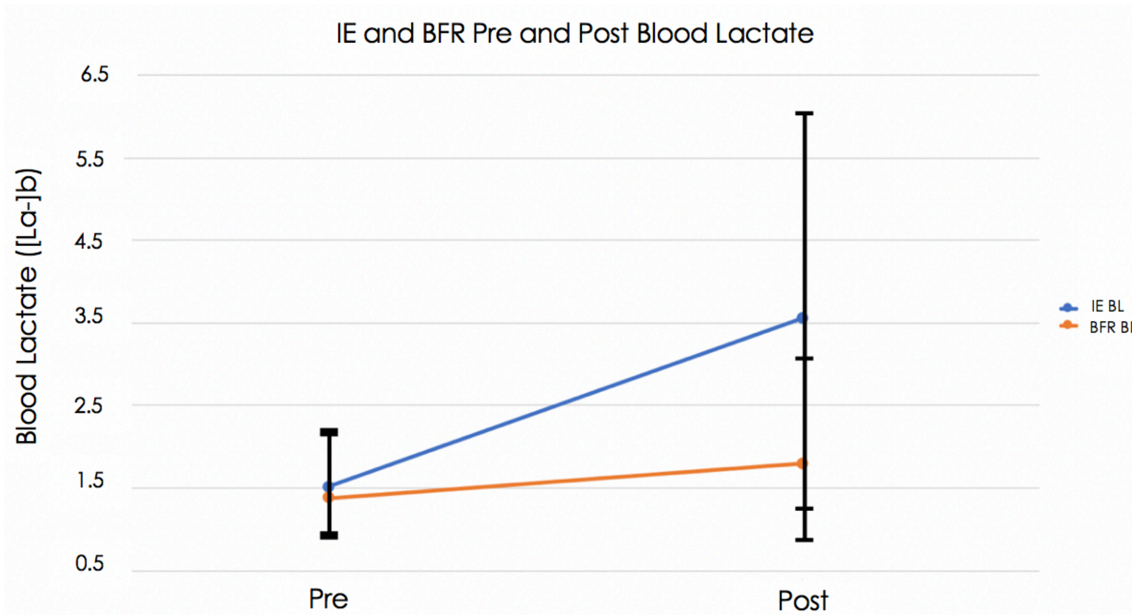

Figure 3C: The difference between pre and post exercise blood lactate response to a double leg extension isometric exercise and double leg cuff blood flow restriction session. Two-way repeated measures ANOVA.* = Large magnitude of change between IE and BFR (Effect size > 0.8).

	Isometric exercise			Cuff Blood Flow Restriction			Standard Error of E.S. estimate	Effect Size	Confidence Interval	
	Mean	SD	n	Mean	SD	n			Lower	Upper
Pre IE vs. BFR	1.6	0.9	28	1.5	0.9	28	0.27	0.04	-0.48	0.57
Post IE vs. BFR	4.0	3.3	28	2.2	2.0	28	0.28	0.69	0.15	1.23
Pre IE vs. Post IE	1.6	0.9	28	4.0	3.3	28	0.28	-1.02	-1.57	-0.46
Pre BFR vs. Post BFR	1.5	0.9	28	2.2	2.0	28	0.27	-0.41	-0.94	0.12

Figure 3D: Effect size calculator comparing IE vs. BFR pre and post blood lactate

4.4 Comparing Blood Glucose and Blood Lactate Response between Isometric Exercise and Blood Flow Restriction

The data provided represents the difference in pre and post IE and BFR blood glucose and blood lactate. The difference in blood glucose from pre to post session can be observed in **Figure 3A**. The difference in blood lactate from pre to post session can be observed in **Figure 3C**. No significant changes in blood glucose were detected within conditions and against conditions. Neither IE or BFR elicited significant changes in blood glucose. Blood lactate was significant from pre to post IE. BFR did not elicit a significant increase in blood lactate. IE vs. BFR was not significantly different for pre and post blood lactate.

CHAPTER 5: DISCUSSION

This study compared IE vs. cuff BFR to determine differences in acute hemodynamic and metabolic response. Passive cuff BFR at 30% occlusion was compared to IE at 30% MVC to determine if there was significant similarities in responses. Effect size was used to determine the magnitude of change between IE and cuff BFR. Variables that had a large effect size were SBP, DBP, HR, VO2, VCO2, VE, METS, and RQ. Post blood glucose had a small magnitude of change, and post blood lactate had a medium magnitude of change. IE and cuff BFR did not elicit similar acute responses when matched at 30% BFR.

IE BP and HR increased during contraction and decreased during relaxation. A gradual accumulation in BP and HR was observed as time progressed[41]. Blood flow restriction hemodynamic responses were not significant. The consistent BP and HR is due to the lack of sympathetic nerve activity witnessed during exercise.

Blood lactate was taken before and 5 minutes post exercise for the IE and BFR sessions[12,15]. Blood lactate significantly increased from pre to post IE. Accumulation of lactate was likely due to local muscle anaerobiosis stimulated by IE induced BFR[13]. Metabolite accumulation stimulated by BFR may be an important component relating to a decrease in RBP observed after weeks of IET [13]. Cuff BFR stimulated an upward trend in blood lactate that was not significant. The observed trend may be due to a small increase in muscle anaerobiosis during cuff BFR at 30%. If blood lactate accumulation is an important component of decreasing RBP, cuff BFR at a greater intensity may elicit a greater decrease in RBP. To our knowledge, this was the first study that looked at blood lactate and blood glucose responses to cuff BFR. Blood glucose did not change during either the IE or cuff BFR session[16]. During exercise insulin decreases in order to maintain blood glucose levels[16]. As intensity or time of exercise increases, blood glucose slowly decreases as it is metabolized as an energy substrate[16]. The lack of change in blood glucose in this study may be due to the intensity and/or duration of the IE and cuff BFR sessions.

VO2, VCO2, VE, and METS trends were as expected for the IE session. Metabolic response gradually accumulated as time continued. As exercise and intensity increased, pulmonary response increased as well to maintain adequate oxygen to the working muscles[17, 21]. The large increase in metabolic response during the first rest period was due to delayed response. Delayed response is when the body adjusts to the sudden action of exercise. During relaxation metabolic response increased and decreased during contraction. Compression of blood vessels during isometric contraction stimulated an increase in BP in order to deliver blood to the working muscle. When the muscle relaxed, blood flow and VE increased to make up for the deficit in oxygen experienced during contraction[22]. IE RQ was greatest during rest periods two and three. Participants claimed that contraction two and three were the most difficult out of the four. This increase in RQ may be due to unintentional breath holding (Valsalva manoeuvre) during the exercise and hyperventilation during the rest period[28]. BFR VO2, VCO2, VE, and METS was different than hypothesized. Pulmonary response to BFR at 30% occlusion was not significant. BFR started at a slightly higher point and slowly decreased as time progressed. This response may be due to the amount of time the participant was sitting on the Biodex dynamometer beforehand. This same phenomenon would be masked in the IE session by the exercise response.

Previous research comparing IE and BFR is limited. Cuff BFR research has focused on decreasing muscle weakness and soreness[20, 23, 25, 32,42]. When comparing blood flow restriction training (BFRT) against IET it was found that BFRT had a greater effect on preventing muscle weakness and decrease in thigh circumference[23]. Studies have shown that BFRT does have a significant effect on muscle damage, weakness, and recovery[20, 23, 24,25,42]. A single bout of BFR at 70% occlusion, stimulated a decrease in venous compliance and maximal venous outflow, but no significant changes in BP or HR[27]. Our study did not find any significant metabolic or hemodynamic changes from one bout of BFR. This nonsignificant response may be due to the level of intensity or time frame. Studies that showed a significant response from BFRT occurred more frequently, for a longer duration, or at a greater intensity[20,23,24,25,42]. 30% BFR does not elicit similar acute hemodynamic or metabolic responses to an IE at 30% MVC. Instead of comparing cuff BFR vs. IE at 30%, future studies should compare IE at 30% MVC with multiple percentages of cuff BFR. IET at 20-30% MVC has shown to elicit a decrease in RBP[4, 7, 8,11, 35,41]. However, the appropriate percentage of cuff BFR has not yet been determined. Exercise increases the sympathetic nervous system, which relates to increases in hemodynamic and metabolic responses. Therefore, it is not surprising that these responses are observed from an IE. BFR however does not have the aid of exercise to stimulate a response. Performing the study with larger percentages of cuff BFR would help determine if BFR is a mechanism for the decrease in RBP from IET.

The first limitation experienced during our study was associated with recruitment. Originally the study was designed to compare sex differences in responses to IE and cuff BFR. However, not enough males volunteered to make an appropriate comparison. A second limitation with recruitment was that all participants were active individuals that did not have HTN. Almost everyone who volunteered was part of the exercise science department on campus. Originally the study was designed to utilize both normotensive and hypertensive individuals to see if there was a variation in response when comparing IE vs. cuff BFR. The final limitation was with the sphygmomanometer. The sphygmomanometer had difficulty detecting pressure waves during rounds three and four of the IE session due to bicep tension. Instead of attaining 30 BP and HR readings, only 14 were found for the IE session. In order to make up for the lack of readings, the mean BP and HR was used in a paired t-test to determine the average for each variable missing.

Future research should further look into the effect of BFRT vs IET on hemodynamic and metabolic response. Although changes in BP were not observed from a single bout of BFR, changes may be observed following multiple bouts[27]. After a few weeks of IET, RBP reductions have been reported[7,8,11, 13,30, 33,38,44]. Time frame may play a role in response observed from passive and active BFR. Future research may also compare IE against varying BFR percentages. For the current study, IE and BFR were matched at 30% BFR. Previous research has acknowledged that IET at 20-30% MVC is an optimal range to observe responses in RBP [4, 7,8,11,18, 35,41,47]. However, 30% BFR may not be able to produce a large enough stimulus to induce a similar response to IE. Multiple studies that observed some type of response from BFRT were utilizing greater BFR percentages[20,23, 24,36,42]. IE and IET at 30% MVC should be measured against different percentages of BFR and BFRT to see if there are similarities in acute and long-term response.

In conclusion, IE and cuff BFR does not elicit similar acute hemodynamic or metabolic responses at 30% BFR. Our hypothesis was incorrect. Cuff BFR at 30% was not a strong enough stimulus to elicit changes in acute hemodynamic or metabolic response. Future research should compare IE at 20-30% MVC vs. cuff BFR at higher intensities to determine if BFR is a mechanism for the decrease in RBP from IET. Hypertensive individuals who are injured or ill may not be able to perform IET at 20-30% MVC. If cuff BFR at a higher intensity elicits a similar response to an IE, BFRT may be a less strenuous alternative.

REFERENCES

1) ACC. New ACC/ AHA High Blood Pressure Guidelines Lower Definition of Hypertension. *American College of Cardiology*. 13 Nov. 2017.

2) American Heart Association [internet]. Types of Blood Pressure Medications. 2017.

3) Baross, A.W., Hodgson, D.A., Padfield, S.L., Swaine, I.L. Effects of the Intensity of Leg Isometric Training on the Vasculature of Trained and Untrained Limbs and Resting Blood Pressure in Middle-Aged Men. *International Journal of Vascular Medicine*. 2012; 964697.

4) Baross AW, Hodgson DA, Padfield SL, Swaine IL. Reductions in Resting Blood Pressure in Young Adults When Isometric Exercise Is Performed Whilst Walking. *Journal of Sports Medicine*. 2017; 7123834.

5) Burt, V. L., Whelton, P., Roccella, E.J., Brown, C., Cutler, J.A., Higgins, M., Horan, M.J., Labarthe, D. (1995). Prevalence of Hypertension in the US Adult Population. Results from the Third National Health and Nutrition Examination Survey, 1988-1991 25(3): 305-313.

6) Cardoso, C. G., Gomides, R.S., Queiroz, A.C.C., Pinto, L.G., Lobo, F., S., Tinucci, D.M., Frojaz, C.L.M. Acute and Chronic effects of Aerobic and Resistance Exercise on Ambulatory Blood Pressure. Clinics. 2010; 65(3), 317-325.

7) Carlson D.J., Inder, J., Palanisamy, S.K.A., McFarlane, J.R., Dieberg, G., Smart, N.A. The efficacy of isometric resistance training utilizing handgrip exercise for blood pressure management: A randomized trial. *Medicine*. 2016; 95(52):e5791.

8) Chrysant, S. G. (2010). Current Evidence on the Hemodynamic and Blood Pressure Effects of Isometric Exercise in Normotensive and Hypertensive Persons. *The Journal of Clinical Hypertension*. 2010; 12(9): 721-726.

9) Cornelissen, V. A., & Smart, N. A. Exercise Training for Blood Pressure: A Systematic Review and Meta-analysis. *Journal of the American Heart Association: Cardiovascular and Cerebrovascular Disease*. 2013;2(1), e004473.

10) Devereux, G.R., Wiles, J.D., Swaine, I. Markers of isometric training intensity and reductions in resting blood pressure. *Journal of Sports Sciences*. 2011; 29(7): 715–724.

11) Devereux, G. R., Wiles J.D., Howden, R. Immediate post-isometric exercise cardiovascular responses are associated with training-induced resting systolic blood pressure reductions. *European Journal of Applied Physiology.* 2015; 115(2): 327-333.

12) Gass, G. C., Rogers, S., & Mitchell, R. Blood lactate concentration following maximum exercise in trained subjects. *British Journal of Sports Medicine*. 1981; 15(3), 172–176.

13) Gavin R. Devereux , Damian Coleman , Jonathan D. Wiles & Ian Swaine (2012) Lactate accumulation following isometric exercise training and its relationship with reduced resting blood pressure, *Journal of Sports Sciences*. 30:11, 1141-1148.

14) Gill, K.F., Arthur, S.T., Swaine, I., Devereux, G.R., Huet, Y.M., Wikstrom, E., Cordova, M.L., Howden, R. Intensity-dependent reductions in resting blood pressure following short-term isometric exercise training. *Journal of Sports Sciences*. 2015; 33:6, 616-621.

15) Goodwin, M.L., Harris, J.E., Hernández, A., & Gladden, L. B. Blood Lactate Measurements and Analysis during Exercise: A Guide for Clinicians. *Journal of Diabetes Science and Technology*. 2007; 1(4), 558–569.

16) Green. S.A., The Effects of Isometric Exercise on Immediate Post-Isometric Exercise Glucose Tolerance. University of North Carolina at Charlotte Masters Thesis. 2018.

17) Hazari, M.A., Arifuddin, M.S., Junaid, M.A., & Ali, M.A. (2016). Effect of on going isometric handgrip exercise on the inspiratory and expiratory reserve volumes.

18) Howden, R., Lightfoot, J. T., Brown, S. J. and Swaine, I. L. The effects of isometric exercise training on resting blood pressure and orthostatic tolerance in humans. *Experimental Physiology*. 2002; 87: 507–515.

19) Hunt JEA, Stodart C, Ferguson RA. The influence of participant characteristics on the reslationship between cuff pressure and level of blood flow restriction. *European Journal of Applied Physiology*. 2016; 116:1421–1432.

20) Hunter, S.K. Sex Differences in Fatigability of Dynamic Contractions. *Experimental Physiology*. 2016; 101.2.

21) Imms, F. J., Mehta, D. (1989). Respiratory responses to sustained isometric muscle contractions in man: the effect of muscle mass. *The Journal of physiology*, 419, 1-14.

22) Korthuis, R.J. Skeletal Muscle Circulation. San Rafael (CA): Morgan & Claypool Life Sciences; 2011. *Chapter 4, Exercise Hyperemia and Regulation of Tissue Oxygenation During Muscular Activity*.

23) Kubota, A., Sakuraba, K., Sawaki, K., Sumide, T., Tamura, Y. Prevention of Disuse Muscular Weakness by Restriction of Blood Flow. *Journal of the American College of Sports Medicine*. 2008; 40:529-534.

24) Kubota, A., Sakuraba, K., Koh, S., Ogura, Y., Tamura, Y. Blood flow restriction by low compressive force prevents disuse muscular weakness. *Journal of science and Medicine in Sport*. 2009; 95-99.

25) Loenneke JP, Allen KM, Mouser JG, Thiebaud RS, Kim D, Abe T, & Bemben MG. Blood flow restriction in the upper and lower limbs is predicted by limb circumference and systolic blood pressure. *European Journal of Applied physiology.* 2015; 115:397-405.

26) Loenneke, J.P., Fahs, C.A., Rossow, L.M., Thiebaud, R.S., Mattocks, K.T., Abe, T., Bemben, M.G. Blood flow restriction pressure recommendations: a tale of two cuffs. *Frontiers in Physiology*. 2013.

27) Loenneke J.P., Fahs, C.A., Thiebaud, R.S., Rossow, L.M., Abe, T., Ye, X., Kim, D., Bemben, M.G. The acute hemodynamic effects of blood flow restriction in the absence of exercise. *Clinical Physiology and Functional Imaging*. 2014; 10.1111.

28) Louhevaara, V., Smolander, J., Aminoff, T. Korhonen, O., Shen, N. (2000). Cardiorespiratory responses to fatiguing dynamic and isometric hand-grip exercise. *European Journal of Applied Physiology*, 82: 340.

29) Mayo Clinic staff [internet]. High blood pressure dangers: Hypertension's effects on your body. *Mayo Foundation for Medical Education and Research*. 2018.

30) Merai, R., Siegel, C., Rakotz, M., Basch, P., Wright, J., Wong, B; DHSc., Thorpe P. CDC Grand Rounds: A Public Health Approach to Detect and Control Hypertension. *MMWR Morbidity and Mortality Weekly Reports*. 2016 Nov 18;65(45):1261-1264.

31) Mouser, J.G., Dankel, S.J., Mattocks, K.T., Jessee, M.B., Buckner, S.L., Abe, T., Loenneke, J.P. Blood flow restriction and cuff width: effect on blood flow in the legs. *Scandinavian Society of Clinical Physiology and Nuclear Medicine*. 2018; 12504.

32) Northey, J.M., Rattray, B., Argus, C.K., Etxebarria, N., Driller, M.W. Vascular Occlusion and Sequential Compression For Recovery After Resistance Exercise. *National Strength and Conditioning Association*. 2016; 30 (2): 533–539.

33) Osada, T., Mortensen, S.P., Radegran, G. Mechanical compression during repeated sustained isometric muscle contractions and hyperemic recovery in healthy young males. *Journal of Physiological Anthropology*. 2015; 34(1): 36.

34) Osada, T., Katsumura, T., Murase, N., Sako, T., Higuchi, H., Kime, R., Hamaoka, T., Shimomitsu, T. Post-exercise Hyperemia after Ischemic and Non-ischemic Isometric Handgrip Exercise. *Journal of Physiological Anthropology and Applied Human Science*. 2003; 299-309.

35) Owen, A., Wiles J, Swaine I. Effect of isometric exercise on resting blood pressure: a meta analysis. *Journal of Human Hypertension*. 2010; 24(12): 796-800.

36) Page, W., Swan, R., Patterson, S.D. (2016). The effect of intermittent lower limb occlusion on recovery following exercise-induced muscle damage: A randomized controlled trial. *Journal of Science and Medicine in Sport*.

37) Pescatello, L. S., Franklin, B.A., Fagard, R., Farquhar, W.B., Kelley, G.A., Ray, C.A.American College of Sports Medicine position stand. Exercise and hypertension. *Medicine & Science in Sports Exercise*. 2004; 36(3): 533-553.

38) Peters, P. G., Alessio, H.M., Hagerman, A.E., Ashton, T., Nagy, S., Wiley, R.L. Short-term isometric exercise reduces systolic blood pressure in hypertensive adults: Possible role of reactive oxygen species. *International Journal of Cardiology*. 2006; 110(2): 199-205.

39) Poulter NR, Prabhakaran D, Caulfield M. Hypertension. *The Lancet*. 2015; 386(9995):801-12.

40) Powers S. K., Howley E.T. Exercise Physiology: Theory and Application to Fitness and Performance. *McGraw-Hill Higher Education*; 2008.

41) Sjogaard, G., Savard, G., Juel, C. Muscle blood flow during isometric activity and its relation to muscle fatigue. *European Journal Applied Physiology and Occupational Physiology*. 1988; 57(3): 327-335.

42) Takarada, Y., Takazawa, H., & Ishii, N. Applications of vascular occlusion diminish disuse atrophy of knee extensor muscles. *Medicine and Science in Sports Exercise*. 2000; 32(12):2035-9.

43) Taylor, K.A., Wiles, J.D., Coleman, D.D., Sharma, R., O'Driscoll, J.M.(2017). Continuous Cardiac Autonomic and Hemodynamic Responses to Isometric Exercise. *Medicine & Science in Sports & Exercise*. 1511-1519.

44) Teixeira, A.L., Ritti-Dias, R., Antonino, D., Bottaro, M., Millar, P.J., Vianna, L.C.. Sex differences in Cardiac Baroreflex Sensitivity following Isometric Handgrip Exercise. *Journal of the American College of Sports Medicine*. 2017.

45) Whelton P.K., Carey, R.M. (2017)Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. *American College of Cardiology*.

46) Wigmore, D.M., Propert, K., Kent-Braun, J.A. Blood flow does not limit skeletal muscle force production during. *European Journal of Applied Physiology*. 2006; 96: 370–378.

47) Yamada E, Kusaka T, Tanaka S, Mori S, Norimatsu H, Itoh S. Effects of vascular occlusion on surface electromyography and muscle oxygenation during isometric contraction. *Journal of Sport Rehabilitation*. 2004; 13: 287–299.