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The Effects of Moderate Intensity Strength Training Coupled with Blood Flow Restriction: A 12 Week Intervention

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ABSTRACT

Blood flow restriction training (BFRT) has been suggested to increase muscle size and strength in trained and untrained individuals when using light load intensities (30 percent) one repetition maximum (1-RM). However, there is little data to support its use when working with moderate load intensities, specifically, above 50 percent of an individual’s 1-RM. The purpose of this study was to evaluate the effects of moderate load intensity BFRT on muscle size and strength of the elbow flexors after a 12 week strength training intervention. Nine, previously strength trained, participants performed an elbow flexion exercise at 70 percent of their individualized 1-RM, twice per week, while blood flow of the brachial artery was reduced by 50 percent in the dominant (right) arm. Elbow flexor muscle mass, and maximal isometric voluntary contractions were assessed before and after training. Elbow flexor muscle mass did not significantly increase after the 12 week training period in either arm, (BFRT arm = 1.85%, non-BFRT arm 3.01%), (p = 0.249). There were no significant differences in isometric arm strength between pre and post training, BFRT arm: (pre: 88.5 ± 16.6, vs. post: 87.2 ± 16 Nm), non-BFRT arm: (pre: 87.8 ± 18.8, vs. post: 85.6 ± 20.2 Nm), (p = 0.407). Therefore, we conclude that unlike low load intensity BFRT, performing BFRT at higher load intensities does not augment muscle growth or muscular strength in trained, young, men when compared to normal strength training alone.

Keywords: Elbow flexor, Blood flow restriction training, 1-repetition maximum, Isometric contraction, Maximal voluntary contraction, Strength training
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LIST OF ABBREVIATIONS

I: Type One Muscle Fiber
IIA: Type Two Muscle Fiber (oxidative)
IIB: Type Two Muscle Fiber (less oxidative than IIA)
IIX: Type Two Muscle Fiber (Mixed between IIA and IIB)
1-RM: One Repetition Maximum
ADP: Adenosine Di-Phosphate
ATPase: Enzyme decomposition of Adenosine Tri-Phosphate to Adenosine Di-Phosphate
ATP: Adenosine Tri-Phosphate
BFRT: Blood Flow Restriction Training
Ca²⁺: One molecule of Calcium
DB: Dumbbell
DXA: Dual Energy X-ray Absorptiometry
FG: Fast Glycolytic
FT: Fast Twitch Muscle Fiber
FOG: Fast Oxidative Glycolytic
H⁺: Hydrogen Ions
iEMG: Integrated Electromyography
IGF-1: Insulin Like Growth Factor 1
MVC: Maximal Voluntary Contraction
MPS: Muscle Protein Synthesis
MRI: Magnetic Resonance Imaging
MU: Motor Unit
NO: Nitric Oxide
NOS-1: Nitric Oxide Synthase
Pᵢ: Inorganic Phosphate
RPE: Rate of Perceived Exertion
SM: Skeletal Muscle
SO: Slow Oxidative
ST: Strength Training
Chapter 1

INTRODUCTION

The human body is made up of numerous adaptable systems that work in unison in order to sustain homeostasis. One major system is the musculoskeletal system. The musculoskeletal system consists of approximately 680 muscles. There are three types of human muscle which include: skeletal, cardiac and smooth muscle. All three types aid in different and vital roles within the human body. Skeletal muscle is responsible for the support as well as the movement of the body and is an essential component to survival. A sarcomere is a basic unit of skeletal muscle. Inside each sarcomere are contractile protein units, actin and myosin. The inclusion of the contractile proteins as well as myofibrils constitutes a sarcomere (Kraemer, Ratamess, & French, 2011). Within a sarcomere, intramuscular proteins can undergo numerous cascading reactions that lead to muscular contractions and hypertrophy. A muscle contraction allows each muscle to act as a mechanical mover. It is through the lengthening and or shortening of the protein units that permits muscle to function as a mechanical mover. It does this by pulling on tendons that are attached to bones. The torque created from a muscle contraction can then amount to movement around the joint (Alexander, 1991).

A muscle fiber is a single cylindrical cell and each individual muscle is made up of thousands of muscle fibers bundled together. Each muscle is wrapped in a protective connective tissue known as fascia, which serves as a compartmentalization tool (Structure of Skeletal Muscle, 2008). The fascia protects the soft and fragile muscle cell and also provides a protected pathway for blood vessels and nerves to run through. Muscle requires a constant supply of blood in order to survive. Blood vessels, in close proximity to the muscle, provide an avenue for nutrient transport as well as waste removal. Muscle is a post-mitotic tissue, meaning, it does not undergo cell replacement throughout life and because of this, there must be a symbiotic relationship between muscle protein synthesis (MPS) and degradation (Schoenfeld, 2010). Furthermore, muscle is constantly interchanging between hypertrophy (synthesis) and atrophy (degradation). Muscle hypertrophy occurs when MPS exceeds protein breakdown (Schoenfeld, 2010). The majority of exercise induced hypertrophy, resulting from strength training, is subsequent from an increase of sarcomeres that are added in parallel. A serial increase in sarcomeres can also result but this type of hypertrophy is less common (Schoenfeld, 2010). Other proposed mechanisms such as cell swelling, sarcoplasmic hypertrophy, and hormone release will be later discussed (section 2.3 and 2.6.1). In order to prevent muscle atrophy, it is common for individuals of all ages and sexes to engage in a strength training program that promotes muscle hypertrophy (Yasuda, Loenneke, Thiebaud, & Abe, 2015).

Strength training (ST) is defined as “any activity that enables muscles to contract against an external force” (Sundell, 2011). During a dynamic strength training exercise, there are several key movement components which include concentric and eccentric actions. Concentric actions occur when the muscle is shortening and eccentric actions occur when the muscle is lengthening (Schoenfeld, 2016). It is the interplay between continual concentric and eccentric contractions that promotes exercise induced muscle hypertrophy. If contractions are continually repeated until muscular failure is reached, significant increases in muscle size and strength can be achieved.
However, not all contractions involve the shortening or lengthening of a muscle. An isometric contraction is when the muscle does not change in length. To further explain, an isometric contraction is static, meaning the joint angle remains the same throughout the entire exercise (Haff et al., 2005). Maximal isometric strength is a product of the muscles length, where the muscle’s contractile proteins, actin and myosin, are overlapped at an optimal ratio (Haff et al., 2005). Isometric strength training can be added to a dynamic strength training program (Haff et al., 2005).

It is suggested that muscle tension is a primary proposed mechanism for muscle hypertrophy (Abe, Loenneke, & Fahs, 2012). The inducement of muscle tension can be accomplished through varying intensities i.e. loads, of different repetition ranges. Repetition ranges can be classified into three broad categories when strength training: low: one to five, moderate: six to 12 and high: 15 or more repetitions (Schoenfeld, 2010). For the purpose of this research paper, repetition ranges can be further classified by one repetition maximum (1-RM) intensity. Low intensity is categorized between zero to 50 percent, moderate intensity between 50 to 70 percent and high intensity is above 80 percent of an individual’s 1-RM. Research suggests that exercise induced muscle hypertrophy occurs most effectively when the exercise intensity is greater than or equal to 70 percent of an individual’s 1-RM. (Schoenfeld, 2010). It has been shown in previous literature that training within the moderate repetition range can promote muscle hypertrophy (Burgomaster et al., 2003; Dankel, Buckner, et al., 2016; Dankel, Jessee, Abe, & Loenneke, 2016; Laurentino et al., 2008; Schoenfeld, 2013; Scott, Loenneke, Slattery, & Dascombe, 2015). The moderate repetition range has been shown to evoke greater hypertrophy when compared to both low and high repetitions. The hypertrophy detected could be attributed to muscle tension, however, metabolite accumulation, hormone release, neural activation and cell swelling are also proposed mechanisms (Loenneke, Wilson, & Wilson, 2010). Repetitions performed at a lower intensity, less than 60 percent of an individual’s 1-RM, does not seem to generate enough muscle tension to produce gains of the same magnitude (Abe et al., 2012).

Furthermore, specific training exercises can be performed for specific body parts. An example is the dumbbell biceps curl. To perform an elbow flexion exercise, the weights are placed in both hands which are held at the individual’s side with arms straightened. In order to execute the exercise movement, the weights are raised upwards towards the shoulder while the forearm rotates around the elbow joint. Once the dumbbells are past 90 degrees, in comparison to the floor, a supination of the forearm is performed. The transition of the palms from neutral i.e. starting position, to supine, is referred to as the concentric action of an elbow flexion. Once the weight has reached the shoulder, the weight is then lowered back to the starting position. The downward movement of the elbow flexion is referred to as the eccentric action. Typically, when elbow flexion exercises are performed at an intensity greater than or equal to 70 percent of an individual’s 1-RM, hypertrophy can occur (Gentil, Soares, & Bottaro, 2015).

However, some populations’ might not be able to perform an exercise safely with an intensity above or equal to 70 percent 1-RM. Individuals who are in rehabilitation, or individuals in the aging population may need to use intensities that are lighter than the suggested load percentage. The aforementioned populations might not achieve adequate muscle tension and specific muscle fiber activation to augment muscle hypertrophy and strength, because of an reduced load intensity. Due to this predicament, a novel form of ST was invented to provide an
avenue for increasing hypertrophy and strength while using a lighter load intensity. Blood flow restriction training (BFRT) was developed to adhere to populations that fit the criteria of needing resistance exercise but cannot attain adequate load or muscle tension.

During the 1990’s, Yoshiaki Sato developed Kaatsu training which was later termed BFRT (Weatherholt, Beekley, Greer, Urtel, & Mikesky, 2013; Flesche, 2014). This form of training is a technique that has been used for more than 20 years. When training with BFRT, the application of a pneumatic cuff is applied to the most proximal end of the muscle being trained (Laurentino et al., 2008; Loenneke, Abe, et al., 2012; Yasuda, Loenneke, Thiebaud, & Abe, 2012; Weatherholt et al., 2013; Dankel, Jessee, et al., 2016). Blood flow restriction training is only used for the extremities of the body. To elaborate, the cuff is wrapped around the entire circumferences of the leg or arm where it is inflated to a pre-determined pressure (Jessee et al., 2016; Dankel et al., 2017). Once the cuff is inflated the exercise can begin. The purpose of cuff inflation during exercise is to allow arterial blood inflow to the working muscle while reducing venous outflow. Exercise with an inflated cuff also allows for the recruitment of additional motor units, which contain fast –twitch (FT) muscle fibers, that would not normally be recruited according to Henneman’s size principle, while working at a reduced exercise intensity (O’halloran, 2014). Inflation pressures can range from 50 to upwards of 200 mmHg when working with BFRT. The cuff typically remains inflated until the required amount of sets and or repetitions are completed (Dankel, Jessee, et al., 2016). However, intermittent cuff inflation where deflation occurs between sets has been used (Laurentino et al., 2008; Teixeira et al., 2017).

Within the literature, the quadriceps muscle is the most common muscle investigated when training with BFRT. The biceps brachii has also been studied but to a lesser extent (Dankel, Jessee, et al., 2016). Training with a reduced load intensity, 20 to 40 percent of an individual’s 1-RM, in combination with BFRT has been shown to increase muscle mass and muscle strength to a similar extent as heavy load training i.e. equal to or greater than 70 percent of an individual’s 1-RM (Dankel, Jessee, et al., 2016; Poveda, Arenas, Ibáñez, García, & Márquez, 2017). Moreover, BFRT has been shown to be effective in increasing strength in the upper extremities, Dankel and colleagues (2016) as well as the lower extremities (Loenneke et al., 2012). However, the majority of BFRT studies have used loads lighter than 50 percent of an individual’s 1-RM, to train acutely or chronically. There are limited studies in the current literature that have attempted to use a heavier load intensity i.e. greater than 65 percent 1-RM, in combination with BFRT (Laurentino et al., 2008; Cook, Kilduff, & Beaven, 2014; Dankel et al., 2017; Teixeira et al., 2017). The gap in the literature provides a unique opportunity to combine BFRT with a chronic moderate intensity strength training program to investigate the effects on muscle hypertrophy and strength.
1.2 **Purpose**

The purpose of the study was to develop and evaluate the effects of moderate load intensity blood flow restriction training on muscle size and strength of the elbow flexors after a 12 week strength training intervention. Participants will perform an elbow flexion exercise twice per week with the dominant arm occluded at the most proximal end. All participants in the study were right handed, therefore the right arm was trained with blood flow restriction for the duration of the training intervention.

1.3 **Objectives**

1. To implement a 12 week intervention that combines the use of blood flow restriction training at moderate load intensities, 70 percent one repetition maximum, while performing an elbow flexion exercise.

2. To measure maximal voluntary isometric contractions of the elbow flexors using a Cybex dynamometer at two different time points, pre and post training.

3. To determine anthropometric changes in the composition of the elbow flexors as well as the whole body while using a dual-energy X-ray absorptiometry scan.

1.4 **Hypotheses**

The following hypotheses were tested:

1. The blood flow restriction trained arm of the participants will have greater muscle hypertrophy than the non-BFRT arm after the 12 week strength training program.

2. The blood flow restriction trained arm of the participants will have a greater increase in maximal voluntary isometric strength than the non-BFRT arm after the 12 week training program.
Chapter 2

LITERATURE REVIEW

2.1 Cross-Bridge Theory

Each muscle fiber contains contractile filaments, actin and myosin. In the early 1950’s, an in-depth analysis of A-Band dimensions revealed that myosin filaments were not significantly shortened under a plethora of contractile conditions and thus could not account for muscle contraction or the changed length of muscle tissue (Huxley, 1953). However, it has since been proposed that muscle contraction occurs not by shortening of the myosin filaments but due to a relative slide of two sets of filaments, actin and myosin (Huxley & Hanson, 1954). In 1954, Huxley proposed how this relative sliding motion occurred and provided a framework for the now known cross-bridge theory. In the cross-bridge model, contraction and force production of the muscle are achieved by the extension of cross-bridges from the thick myosin filaments which interact intermittently with the thin, actin filaments. The interaction between the two produces a shortening action of the muscle. The regulation of SM force is governed exclusively by the two proteins (Herzog et al., 2015).

2.1.1 Cross Bridge Cycle

Each cycle of attachment and detachment of a cross-bridge is associated with the hydrolysis of one molecule of adenosine triphosphate (ATP) (Herzog, Powers, Johnston, & Duvall, 2015). ATP is responsible for the initiation of the binding process of the contractile proteins (Fitts, 2007). It is the release of inorganic phosphate (P_i) from ATP hydrolysis that cultivates the cross bridge between actin and myosin. After ATP has been hydrolyzed, the two proteins are transformed into a strongly bound high force state that can undergo a power stroke. The power stroke is the action of the muscle shortening. Fitts (2007) stated that ADP is released after the power stroke has occurred thus allowing the cross bridge complex to return to its original unbound state. When repeated muscle contraction occurs, the up-regulation of lowbound to high-bound states is accelerated by both cytoplasmic Ca^{2+} and by the number of highbound cross bridges formed (Fitts, 2007). In regards to ST, moderate to vigorous exercise can induce high rates of ATP hydrolysis within the working muscle which can cause increases in intracellular H^+, P_i, and ADP. The intracellular concentration changes are directly proportional to the exercise intensity used and the muscle fiber type present (Herzog et al., 2015).

2.2 Muscle Fiber Types

The physiological properties of SM are highly dependent on fiber type composition. According to Fitts & Widrick (1996) there are three distinct fiber types that are classified based
on their function and metabolic properties. Fast- twitch glycolytic (FT), fast- twitch oxidative glycolytic (FOG) and slow- twitch oxidative (SO). Each of these three muscle fibers are found within the human body. FT fibers and are classified based on their high amounts of ATP (ATPase) activity. During short intense bouts of exercise, FT muscle fibers hydrolyze and utilize ATP as well as other metabolites in an accelerated manner. FT fiber fuel utilization, in the form of ATP, is also up-regulated in response to contractions that involve maximal shortening velocities (Fitts, & Widrick, 1996). In SO, a contrast appears due to the substantially lower amount activity of ATP hydrolysis, ATPase activity and overall consumption of energy intracellularly when in use (Fitts, & Widrick, 1996).

Research conducted by Bottinelli et al. (1994) revealed a fourth fiber type in adult human SM. The researchers proposed that muscle could be classified into four distinct fiber type categories. The classifications outlined are as followed: I, IIA, IIB, and now IIX. Each fiber type represented includes: I (type I, slow twitch oxidative, SO), IIA (FT oxidative, FOG), IIB (FT glycolytic, FG) and IIX (mixed-FT). In support of Bottinelli’s findings, a review conducted by Schiaffino & Reggiani (2011) stated that they had also discovered a third FT fiber type composition different from IIA and IIB. Type IIX fibers have characteristics similar to those of IIA and IIB fibers, and their resistance to fatigue is intermediate between that of IIA and IIB. Human SM contains a different ratio of each of the four major fiber types which could be due to the functionality of specific muscles. For example in the posterior compartment of the leg where the soleus is located, the majority of muscle fibers are SO. The soleus muscle is typically used over longer durations and at lower exercise intensities, such as when walking. Whereas, the biceps brachii, located on the anterior portion of the proximal arm, contains a mix of type I and type IIA, IIB and IIX fibers, which may be used for faster and shorter exercise movements such as an elbow flexion (Evangelidis et al., 2016). Muscle fibers have different responses to exercise and differ in hypertrophy and strength categories, metabolic demand, fuel usage and metabolic accumulation.

2.3 Skeletal Muscle Hypertrophy

Muscle hypertrophy can be referred to as the growth and increase in size of individual muscle cells (Schoenfeld, 2016). Muscle in humans, specifically in males, accounts for roughly 45 percent of the total body mass (Rodriguez et al., 2017). In order to remain fit, healthy and independent, maintenance of muscle is of utmost importance. Skeletal muscle functions as the largest disposal site for ingested glucose, plays a vital role in lipid oxidation and is one of the greatest contributors to resting metabolic rate (Loenneke, Abe, et al., 2012). Muscle is a highly plastic tissue capable of responding to an appropriate stimulus by various signaling pathways for hypertrophy and strength (Loenneke et al., 2012). “The majority of exercise induced hypertrophy subsequent to traditional strength training programs results from an increase of sarcomeres and myofibrils added in parallel.” (Schoenfeld, 2010). When skeletal muscle is subjected to an overload stimulus, it can cause disruptions in the myofibers or the extracellular matrix. Due to this, a chain of myogenic events can occur which ultimately leads to an increase in the amount of contractile protein units, actin and myosin, and the total number of sarcomeres that are in parallel. In turn, the augmentation of individual muscle fibers causes an increase in muscle cross-sectional area (CSA), (Schoenfeld, 2010). However, there are other proposed mechanisms for
muscle growth. An expansion of the extracellular matrix has been suggested as an avenue to support contractile protein enlargement, thus supporting hypertrophy (Schoenfeld, 2010). Hypertrophy that occurs in series is suggested, however, it is less common. “In-series hypertrophy has been shown to occur when muscle is forced to adapt to a new functional length” (Schoenfeld, 2010). Another possible mechanism for muscle hypertrophy is sarcoplasmic hypertrophy. During sarcoplasmic hypertrophy, it is suggested that growth occurs from an increase in various non-contractile elements and fluids. Because muscle tissue is post mitotic, satellite cells are thought to facilitate hypertrophy in several ways (Schoenfeld, 2010). Through the donation of extra nuclei to muscle fibers, the up-regulation of mRNA production or the expression of myogenic regulatory factors, are proposed mechanisms in which satellite cells promote hypertrophy.

2.3.1 Muscle Hypertrophy and Progressive Overload

As an individual becomes more strength trained, there is a point in time when it is harder to achieve muscular hypertrophy. When this happens, a very common training principle called progressive overload is added to a strength training program. Progressive overload is the addition of extra volume (reps x sets x weight lifted) to the workout in order to provide an augmented stimulus to the muscle. With this principle, it is possible to create additional hypertrophy after an extended amount of time. However, the amount of progressive overload needed to achieve hypertrophy is individualized and not well understood within the literature.

Hypertrophy can occur from repetitive muscular contractions which involve eccentric, concentric or isometric movements. Possible avenues for augmenting hypertrophy take into consideration the enlargement of contractile proteins, a change in the extracellular matrix, satellite cells, myogenic pathways, cell swelling, hypoxia, mechanical tension, muscle damage, metabolic stress and exercise training variables to create additional muscle growth (Schoenfeld, 2010).

Progressive overload can cause increased perturbations in myofibers as well as the expansion of the extracellular matrix. An overload stimulus can provide a cascade effect of myogenic events that can lead to an increase in the size as well as the amount of myofibrillar contractile proteins. From an additional muscle stimulus, the up-regulations of mTOR and MAPK pathways can occur (Schoenfeld, 2010).

2.3.2 Muscle Hypertrophy, and Muscle Fiber Type

Muscle hypertrophy can differ pending on the method of training executed. A repetition range above 15 has been shown to increase hypertrophy in SO fibers, however, to a lesser extent than FT fibers (Thorstensson, Hultén, von Döbeln, & Karlsson, 1976). SO fibers with a high oxidative capacity are relatively small in diameter when compared to fibers with a lower oxidative capacity such as IIA, IIB, and IIX (van Wessel, de Haan, van der Laarse, & Jaspers, 2010). Under mechanical tension, such as that with strength training, SO fibers typically do not yield as
significant hypertrophy when compared FT muscle fibers. As muscle fiber CSA increases from I to IIA, IIX and IIB, endurance capacity decreases. Moreover, performing ST within the eight to 12 repetition range, fiber types IIA, IIX and IIB can experience muscular hypertrophy. The size differentiation as well as the hypertrophic effects observed between type I, and IIA, IIX and IIB is not well understood. Wessel et al. (2010) proposed that in SO fibers, the rate of protein degradation and protein synthesis is much greater than in the other muscle fiber types. It is suggested that SO fibers have an increasingly greater rate of MPS in order to maintain equilibrium. In turn, greater protein degradation in SO fibers could be an important factor limiting the size and hypertrophic effects observed while under mechanical tension. Furthermore, insulin like growth factor 1 (IGF-1) concentrations are differentially regulated in both high and low oxidative fibers. IGF-1 stimulates muscle hypertrophy in all four fiber types. However, when training in the moderate repetition range, mechanical loads induce changes in intracellular Ca^{2+} concentrations and increase expression of growth factors, mainly growth hormone (GH), which could contribute to an increased hypertrophic effect observed in the muscle fibers IIA, IIX and IIB when compared to type I (van Wessel et al., 2010). Specifically, when completing a strength training program, IIA, IIX and IIB fibers have been shown to increase their CSA greater than type I fibers. Another possible explanation for the hypertrophy observed is Henneman’s size principle. If exercise intensity or duration increases, additional muscle fibers are recruited to maintain force output. The order of activation follows the order of, small SO fibers activated first, followed by the activation of larger FT fibers. During moderate repetition range exercises, FT muscles fibers are activated which has been suggested to induce hypertrophy (Schoenfeld, 2010).

2.3.3 Muscle Hypertrophy and Strength Training

In the pursuit of exercise-induced muscle hypertrophy, it has been suggested that one must work with an external load that is approximately 70 percent of an individual’s 1-RM. To elaborate, it has been almost extensively recommended within the literature that strength training must be executed with a moderate to high load intensity to produce hypertrophy (Ozaki, Loenneke, Buckner, & Abe, 2016).

In ST, methods and modalities are often classified according to the type of training exercise performed (Wernbom, Augustsson, & Thomeé, 2007). Training exercises, as previously mentioned can be organized by using an intensity that is measured from calculating an individual’s 1-RM. Fluent throughout the literature, using a repetition range between eight to 12 has been shown to produce beneficial hypertrophy when compared to lower repetition ranges, one to six and repetitions above 15.

According to an eight week intervention conducted with 32 untrained middle aged men, ST was performed in two different repetition ranges. One group performed the exercise in the moderate repetition range, while the second group worked in an elevated range, above 15. The moderate range produced greater muscle hypertrophy when compared to the group that performed higher repetitions (Campos et al., 2002). It was concluded that ST within the moderate range was more beneficial for hypertrophy. Furthermore, another study used youngmiddle aged men that
were recreationally trained prior to the 12 week training program. McCall et al. (1996) used a three set, 10 repetition training protocol while targeting the biceps brachii. Magnetic resonance imaging (MRI) scans revealed an increase in the biceps brachii muscle CSA (from 11.8 ± 2.7 to 13.3 ± 2.6 cm$^2$, p < 0.05) after the training program. It was concluded that participants increased hypertrophy in the biceps brachii while training within the moderate repetition range (McCall, Byrnes, Dickinson, Pattany, & Fleck, 1996). The study also found a 25 percent increase in 1-RM preacher curl strength following the training protocol.

2.4 Isometric Strength Compared to Dynamic Strength Training

Maximum strength and power are major factors influencing performance in a variety of sports and activities. A 2010 study investigated the relationship between isometric and dynamic strength in recreationally trained men (Mcguigan, Newton, Winchester, & Nelson, 2010). Each participant was tested for peak force, rate of force development, vertical jump performance and 1-RM strength. Peak force was tested using an isometric mid-thigh pull exercise. A 1-RM for the squat and bench press were determined as a measure of dynamic strength. Correlations between exercise variables were calculated using Pearson product moment correlation coefficient. The researchers found that peak isometric force was highly correlated between 1-RM squat (r = 0.97, p < 0.05) and 1-RM bench press (r = 0.99, p < 0.05). It was suggested that isometric peak force testing provides an efficient method for assessing strength in recreationally trained individuals while providing non time intensive data collection (Mcguigan et al., 2010).

Similar results were reported in a study investigating the relationship of maximum strength in weight lifting performance. A 2005 study assessed the relationship of maximum dynamic strength and isometric contractions (Stone et al., 2005). Pearson’s product moment correlation coefficient was used to determine the correlation between dynamic strength during a 1-RM squat and 1-RM snatch when compared to an isometric mid-thigh pull. Researchers found a strong correlation (r = 0.84) between isometric and dynamic strength. It was suggested that when collecting isometric data, maximum strength is strongly related to weightlifting performance which is independent of body mass and height differences (Stone et al., 2005).

2.5 Blood Flow Restriction Training

As previously stated, using moderate to high intensity exercise was once thought to be the only way to obtain hypertrophy when strength training. However, a growing body of evidence has arose supporting the use of BFRT combined with low-load ST. The use of low load BFRT has been shown to produce muscle hypertrophy similar to that of moderate intensity training (Neto et al., 2016; Scott et al., 2015). Moreover, BFRT has been used for a variety of scenarios which include; rehabilitation, augmenting muscle hypertrophy, augmenting muscle strength, specificity to the athletic population and lastly, providing an avenue to reduce exercise time to muscular failure (Scott et al., 2015).
2.5.1 Blood Flow Restriction Training in Rehabilitation

A 2017 meta-analysis examined BFRT in clinical MSK rehabilitation and found positive results for increasing strength (Hughes, Paton, Rosenblatt, Gissane, & Patterson, 2017). The rehab categories included were reconstruction (n=3), knee osteoarthritis (n=3), older adults at risk of sarcopenia (n=13), and patients with sporadic inclusion body myositis (n=1). The analysis revealed that low load BFRT had a moderate effect on increasing strength (p < 0.001). Due to limited data for muscle hypertrophy with BFRT in the aforementioned rehab categories, the focus of the meta-analysis remained only on muscular strength (Hughes et al., 2017).

A study involving rehabilitation patients used BFRT to investigate the size of thigh muscles in patients who underwent reconstructive ACL surgery. Between day three and 14 postoperation, BFRT was used on the quadriceps. Results showed that without a BFRT stimulus, the CSA of the knee extensors and flexors decreased by (20.7 ± 2.2%) whereas the BFRT leg decreased less, by (9.4 ± 1.6%), (Takarada, Takazawa, & Ishii, 2000). Thus implementing BFRT with low-load, suggested an attenuation of muscle atrophy post-operation of more than 100 percent.

2.5.2 Low Load Intensity Blood Flow Restriction Training: Biceps Brachii Muscle Hypertrophy

A meta-analysis investigated muscle adaptation in the upper body musculature in response to low-load BFRT (Dankel, Jessee, et al., 2016). Dankel and colleagues (2016) quantitatively compared increases in muscle size and strength occurring from low-load BFRT with that of volume-matched unrestricted low-load training. The meta-analysis provided inclusion criteria for the studies involved. All study protocol must have a pneumatic cuff applied to the upper arm before exercise and the working muscle must remain restricted until the exercise is completed. A second criteria was, the study had to be chronic and consist of at least five sessions to allow sufficient time for measurable muscle adaptation. Lastly, pre and post measurements of muscle size and/or strength must be have been provided. A total of nineteen articles met the inclusion criteria for this review. In order for hypertrophy measurements to be included, measurements had to be recorded from MRI, ultrasound or computed tomography scans. Studies that measured strength using either 1-RM or maximal voluntary contraction (MVC) were also included. Results indicated that eighteen of the nineteen studies reported increased biceps brachii hypertrophy when training was coupled with BFRT. It was also stated that the control groups performing volume matched low-load ST, in the absence of BFRT, did not report an increase in hypertrophy of the biceps regardless of the exercise performed. One study did examine moderate load strength training with low-load BFRT but muscle strength was not reported and therefore no comparisons for upper
extremity strength could be made (Lowery et al., 2014). According to Dankel et al. (2016) results from the meta-analysis are difficult to compare due to unstandardized protocols varying in intensity, volume, duration and frequency for the upper body exercise performed. The sets taken to volitional fatigue were not volume matched and thus limited the ability to compare low-load BFRT to moderate load training (Burgomaster et al., 2003; Moore et al., 2004; Dankel et al., 2016).

2.5.3 Blood Flow Restriction Training and Muscle Failure

Within the current literature, training to volitional muscle failure results in similar MPS responses when compared to low-load BFRT which is independent of load intensity. However, the time it takes to reach muscular fatigue can be manipulated through BFRT. A study looked to determine if knee wraps, in replacement of a pneumatic cuff, could provide a stimulus to decrease time to training failure during a 30 percent 1-RM leg extension exercise (Loenneke, Balapur, Thrower, Barnes, & Pujol, 2012). This study used 20, healthy, individuals in a randomized crossover study. Participants were assigned to a BFRT group or to a control group. It was concluded that the knee wraps provided an avenue for the BFRT group to reach muscular failure quicker than the control group. The number of repetitions until failure was significantly lower (p < 0.001) with BFRT than without (BFRT: 26 ± 1.31 vs. control: 36 ± 2.54). There were no reported differences between the control and BFRT groups for rate of perceived exertion (RPE). Metabolic stress was measured via whole blood lactate and was greater immediately after muscular failure in the control group when compared to the BFRT group. However, after three minutes post exercise, lactate levels were greater in the BFRT group. Displaying elevated lactate levels three minutes post exercise are similar to the findings conducted by Takarada & Nakamura (2000) in which lactate was also observed to be greater under BFRT exercise conditions. An increase in metabolic pooling post BFRT exercise could be an avenue for muscular hypertrophy (Takarada et al., 2000; Suga et al., 2012).

Another study investigated low load intensity BFRT vs. free-flowing traditional strength training performed to volitional fatigue during a six week period (Farup et al., 2015). Ten, healthy, young males performed elbow flexor exercise to failure with 40 percent 1-RM with and without BFRT. MRI was used to estimate biceps brachii muscle volume and water accumulation. It was reported that both the BFRT and low-load volume match group produced similar muscle hypertrophy. However, the BFRT group was able to achieve the same muscle hypertrophy with less repetitions completed and less time spent under muscular tension (Farup et al., 2015). This suggests that BFRT could help individuals achieve muscular failure while still gaining muscle size.
2.5.4 Blood Flow Restriction Training within the Athletic Population

Blood flow restriction training can further promote muscle hypertrophy in the athletic population. A study looked at the hormonal and inflammatory responses to low load BFRT in a trained male population that performed a leg extension exercise (Takarada, et al., 2000). Blood samples were measured before and after the pneumatic cuff was released from the working muscle to assess metabolite concentrations. Concentrations of GH, norepinephrine, and lactate were considerably elevated under the exercise with BFRT when compared to the exercise without BFRT (Takarada, et al., 2000). The increase in GH concentration is similar to the GH response found when working with moderate load training (Takarada et al., 2000). Training within the moderate repetition range while using short rest periods has also been proposed to increase GH release post exercise. (Takarada, et al., 2000).

2.6 Blood Flow Restriction Hypertrophy: Proposed Mechanisms

As outlined above, BFRT at low-loads can augment muscle hypertrophy and strength in the lower and upper extremities. However, the underlying mechanisms of BFRT are equivocal. A 2010 paper investigated the underlying proposed mechanisms in which BFRT produces its hypertrophic and strength gaining effects. The primary mechanisms include: metabolic accumulation such as lactate, GH release, FT muscle fiber recruitment, MPS through mTOR and MAPK pathways, nitric oxide synthase-1 (NOS-1), myostatin and cell swelling (Loenneke et al., 2010).

2.6.1 Lactate, GH and Metabolic Products

Blood flow restriction has been shown to increase whole blood lactate, plasma lactate and muscle cell lactate after a single bout (Takarada et al., 2000; Loenneke et al., 2012). It has been suggested that an increase in lactate levels is beneficial to GH secretion due to the fact that GH release can be augmented by an acidic intramuscular environment (Loenneke et al., 2010). The accumulation of metabolites may increase cell swelling, increase intramuscular anabolic/anabolic signalling, and increase muscle fiber recruitment. An increase in the three previously mentioned categories can be beneficial for hypertrophy (Scott et al., 2015).

It is hypothesized that the cause for an increase in lactate and GH is from local hypoxia which can create a more anaerobic intracellular environment (Takarada et al., 2000). Additionally, the suppression of lactate clearance in the directly worked muscle is a proposed mechanism when using BFRT conditions. An acidic intramuscular environment has been shown to stimulate sympathetic nerve activity through a chemoreceptive reflex mediated by intramuscular metabo-receptors as well as type III and IV afferent fibers (Takarada, Nakamura, et al., 2000). Because the chemoreception pathway was recently shown to play an important role in the regulation of GH secretion, it was also hypothesized that BFRT could increase GH release because of decreased intracellular pH levels. (Takarada, et al., 2000).
In contrast, changes in blood lactate are not always a savvy predictive measure of changes in GH secretion. A 2006 study showed that BFRT resulted in a greater GH response than low-load training but no significant changes in blood lactate levels were determined between groups (Reeves et al., 2006). Early evidence has been collected that GH as well as IGF1, play vital roles in growth, development as well as maintenance of muscle (Takarada et al., 2000). Takarada et al. (2000) stated that, although relatively controversial within the literature, current results suggest the intramuscular conditions observed during BFRT could evoke positive effects in potentiating muscle hypertrophy in humans.

A 2003 study investigated the effect of low-load training with and without BFRT on resting metabolites in the biceps brachii (Burgomaster et al., 2003). The study also investigated elbow flexor strength. Eight, healthy, male participants, who took part in aerobic training two to three times per week but had no formal ST experience, completed an eight week intervention. One arm occluded using blood flow restriction while the other arm was not occluded and served as the control. Both arms were volume matched Subjects performed a unilateral biceps exercise using a load equivalent to 50 percent 1-RM. Each workout consisted of three to six sets of eight to 10 repetitions. A final set was performed to volitional muscle failure. Muscle biopsies were obtained before and 72 hour after the final training bout. It was concluded that concentrations of intramuscular glycogen were increased in both groups, however, the BFRT arm potentiated greater metabolic changes; (BFRT arm: 501 ± 12; control arm: 452 ± 20 mmol.kg-1 dry weight), (p ≤ 0.05). Additionally, resting ATP concentration were lower (p ≤ 0.05) in both arms following the training protocol: (BFRT: 18.2 ± 0.6, control arm: 20.5 ± 0.5 mmol.kg-1 dry weight), however, the decrease in ATP concentration was larger in the BFRT arm (p ≤ 0.05). Maximal isokinetic and isotonic elbow strength increased after the training and were similar between arms (p < 0.05) (Burgomaster et al., 2003).

2.6.2 Fiber Type Recruitment with BFRT

When the force or duration of a muscular contraction increases, muscle fiber recruitment adheres to Henneman’s size principle during normal strength training. However, under BFRT conditions, Henneman’s size principle can be manipulated. The size principle suggests that under normal training conditions, SO fibers are recruited first and as the load intensity increases, larger diameter, FT fibers are recruited (Loenneke et al., 2010). A novel aspect of BFRT is that FT muscle fibers are recruited even though the load intensity used is much lower. In a 1992 study, oxygen availability and motor unit (MU) activity were observed in order to determine if an interrelationship exists. It was suggested that decreased oxygen availability, which is seen under BFRT conditions, resulted in a progressive recruitment of additional MU’s (Moritani, Sherman, Shibata, Matsumoto, & Shinohara, 1992). Moreover, in a study conducted by Takarada et al. (2000), integrated electromyography (iEMG) were recorded during unilateral knee extension. The relative iEMG during BFRT was 1.8 times as large as that during non BFRT training (p < 0.01). When comparing the control and BFRT groups, the force generated and the mechanical work produced were similar, however, muscle activation was greater with BFRT. The elevated iEMG at low level force generation could be due to a previous discussed topic involving a
hypoxic intramuscular environment, in which FT fibers are recruited despite the lower load intensity (Takarada et al., 2000). Increasing training load intensity has been shown to produce greater EMG activity and is associated with an increase in blood lactate concentration, indicating greater muscle metabolic demand. As previously mentioned a rise in blood lactate and H⁺ ion concentration may also increase GH release enhancing muscle hypertrophy in FT muscle fibers.

### 2.6.3 mTOR Pathway

Increased rates of MPS help to fuel muscle hypertrophy responses within the human body. The literature suggests that training in the moderate repetition range can have many benefits in regards to up-regulating the mTOR pathway. Less known, are the effects of low and moderate to high load BFRT on the underlying cellular mechanisms of the mTOR pathway. Fujita et al. (2008) investigated whether an acute bout of low-load BFRT would enhance mTOR signalling and stimulate MPS. After the exercise, stable isotope techniques were used to determine phosphorylation status of signalling proteins. Ribosomal S6 kinase 1 (S6K1) phosphorylation, a downstream target of mTOR, increased concurrently with a 46 percent increase in MPS (p < 0.05), (Fujita et al., 2007). These findings suggest that under low-load BFRT conditions, the mTOR pathway is up-regulated which could enhance muscle hypertrophy.

### 2.6.4 Nitric Oxide Synthase (NOS-1)

Nitric oxide synthase (NOS-1) is an enzyme responsible for converting L-arginine into nitric oxide (NO), (Loenneke et al., 2010). Muscle functions regulated by NOS-1 include; force production, cross-bridge formation, as well as glucose homeostasis. In muscle, NOS-1 is located beneath the sarcolemma of FT muscle fibers. Neural NOS (nNOS), a similar molecule, is found in the transmembrane protein complex of muscle. Under resting conditions, nNOS produces low levels of NO which has been shown to maintain satellite cell inactivity (Loenneke et al., 2010). However, during exercise, muscular contractions induce nNOS activation via mechanical shear force coupled with an increased intracellular Ca²⁺ influx. An increase in nNOS is hypothesized to increase the activity of satellite cells. Currently, within the BFRT literature, it is not well understood how BFRT affects NOS-1 and nNOS activation and its subsequent effect on muscular hypertrophy. In an animal study, nNOS concentrations were increased in conjunction with BFRT. It was also proposed that changes in muscle blood flow may affect muscular size through actions of NOS-1 and nNOS (Shigeo Kawada & Ishii, 2005). However, there is a lack of literature on whether NOS-1 can augment hypertrophy when coupled with BFRT. Therefore, more studies are needed to further investigate the potential effects.
Myostatin Gene Expression

Myostatin, also known as growth differentiation factor 8 (GDF-8), is a protein produced and released by myocytes which regulates muscle growth. Myostatin is a negative regulator of muscle growth, and a mutation of this gene can result in overgrowth due to increased cell proliferation. The suggested function of decreasing myostatin is to up-regulate satellite cell activity which has been shown in a study conducted by McCroskery et al. (2003). A 2012 study examined whether muscle hypertrophy and strength responses were changed after a low-load BFRT exercise or high load exercise without BFRT. Both groups were examined for changes in messenger RNA expression of the selected genes involved in myostatin signalling (Laurentino et al., 2012). Researchers found that myostatin mRNA expression was significantly decreased in both high load training and BFRT groups (40 %, p < 0.0004, and 45 %, p < 0.0001, respectively). It was also concluded that BFRT produced similar muscle (CSA), and strength gains when compared to high-load training alone.

Muscle Cell Swelling

In the literature there are situations in which the benefits of BFRT are observed without a large accumulation of metabolites and/or large increases in FT fiber type recruitment (Loenneke, Fahs, Rossow, Abe, & Bemben, 2012). Cell swelling is proposed to be the possible mechanism for the observed muscle hypertrophy. Loenneke and colleagues (2012) suggested that BFRT may be able to induce cell swelling through blood pooling, accumulation of metabolites and/or reactive hyperemia following the removal of the cuff. “Cell swelling is able to inhibit catabolism, shifting the protein balance towards anabolism” (Loenneke, Fahs, et al., 2012). To elaborate, blood pooling caused by BFRT, may be able to shift intracellular and extracellular water balances. An increased pressure gradient which is observed during BFRT would create a greater influx of water into the cell to drive the possible anabolic processes (Leonneke, Fahs, et al., 2012). It is proposed that an increase in cell water volume can create a cascade effect for intracellular signalling wherein G-protein activation, by a currently unidentified tyrosine kinase, can lead to the activation of the mTOR and MAPK pathways.

Blood Flow Restriction and Cuff Pressure on the Quadriiceps

A 2011 study investigated the differences in cuff pressure for two types of pneumatic cuffs commonly used within the BFRT literature (Loenneke, Fahs, et al., 2012). One hundred and sixteen participants were measured once in a laboratory setting in which mid-thigh muscle and fat CSA were assessed using peripheral quantitative computed tomography. The same participants then underwent, in a randomized order, arterial occlusion pressure testing using both a narrow (5cm) and wide (10cm) pneumatic cuff. The cuff was inflated at the most proximal portion of each leg. Significant difference were observed between the cuff type and the occlusion pressure needed to obtain a 100 percent reduction in the blood flow of the tibial artery (narrow: 235 (42) mmHg
vs. wide: 144 (17) mmHg; (p < 0.001). It was concluded that wider pneumatic cuffs reduce arterial blood flow at a lower pressure than a narrower cuff. (Loenneke, Fahs, et al., 2012). This study provided evidence for both wide and narrow cuffs and the pressures needed to achieve 100 percent reduction in blood flow for the lower extremities. However, the cuff pressures calculated in this study could differ when considering occlusion of the upper body due to differences in arm circumference and arm composition.

2.8 Blood Flow restriction, Cuff Width and Pressure on the Bicep Brachii

A recent study by Laurentino et al. (2016) investigated the influence of different cuff widths on muscle size and strength of the biceps brachii (Laurentino et al., 2016). Eleven, physically active, male participants had their arms randomly divided into two separate conditions. The two groups included, a low-load BFRT with a narrow (5cm) cuff and low-load BFRT group with a wide (10cm) cuff. Muscle mass was measured with MRI. Strength was assessed during a unilateral elbow flexion exercise. In both groups the cuff was inflated up to the point at which the auscultatory pulse was no longer present (Laurentino et al., 2016). Cuff pressure in the narrow (5cm) group was 185 ± 31 mmHg. Cuff pressure in the wider (10cm) group was 137 ± 11 mmHg. All participants underwent a 12 week training program while performing the exercise at 20 percent of their 1-RM. The blood pressure cuff remained inflated during the entire exercise for both groups and was only deflated after exercise protocol was finished. Total training volume and RPE were measured at the end of each training bout. Post training results showed that elbow flexion 1-RM and CSA significantly increased in both conditions (BFRT + narrow = 13.5% and 9% vs BFRT + wide = 11.9% and 11.2%, respectively). There were no significant differences in the training volume and RPE between conditions (p > 0.05).

Recently, researchers investigated relative pressures that would result in a 40 percent reduction in normal arterial blood flow of the brachial artery (Mattocks et al., 2017). The study characterized the cardiovascular and perceptual responses to different levels of occlusion while performing a unilateral elbow flexion exercise using 30 percent of the participant’s 1-RM. Twenty-six trained individuals performed four sets of elbow flexion exercise while occluded that relative applied pressures (0%, 10%, 20%, 30%, 50% and 90%). RPE and discomfort were taken prior to the beginning of the exercise and following each set. It was found that applying greater pressures resulted in an elevated cardiovascular response, higher RPE and a greater decrease in exercise volume when compared to lower restriction pressures. It can be suggested that RPE and discomfort from lower relative pressures i.e. less than 50 percent full occlusion, may be more appealing and provide a more tolerable stimulus for participants (Mattocks et al., 2017). The majority of low-load BFRT studies are performed at an occlusion pressure that is greater than 60 percent of full brachial artery occlusion which could compromise comfort and potentially the continuation of exercise.
2.9 Exercise Intensity and Occlusion Pressure

In 2015, a study investigated the effect of exercise intensity and occlusion pressure after a 12 week intervention (Lixandrão et al., 2015). Specifically, different occlusion pressures were coupled with different exercise intensities to observe changes in muscle size and strength. Twenty-six participants had each leg allocated to two of five protocols. BFRT protocols were performed at either 20 or 40 percent 1-RM with 40 or 80 percent occlusion pressure. The groups were divided as follows; BFRT 20/40, 20/80, 40/40 and 40/80. A fifth and final group was a conventional strength training group which performed exercises at 80 percent 1-RM without BFRT. Maximum dynamic strength and quadriceps CSA were assessed at baseline and after 12 weeks. It was found that, increasing occlusion pressure was effective only at very low exercise intensities for increase hypertrophy. No additional increase in hypertrophy was observed at the higher exercise intensities including the strength training group. Furthermore, exercise intensity played a role in CSA when comparing groups with similar occlusion pressure. Muscle strength was similarly increased across all BFRT groups (12.10 %) but to a lesser extent than training at 80 percent 1-RM with BFRT (21.60 %). It was concluded that BFRT protocols can benefit from higher occlusion pressure i.e. 80 percent, when exercising at very low intensities. The incremental increase of occlusion pressure coupled with heavier weights suggested no added benefit.

As presented, increasing cuff width and pressure does not seem to augment muscle hypertrophy and strength for the upper and lower body extremities while under BFRT conditions. However, cuff pressure can affect study outcomes such as total exercise volume, time until muscular fatigue as well as RPE. During each of the prior three studies, BFRT was applied continuously throughout the exercise and only deflated immediately after the exercise was completed. To build upon this knowledge, studies have investigated whether continuous or intermittent cuff inflation effects muscle hypertrophy and strength.

2.10 Blood Flow Restriction Continuous vs. Intermittent Cuff Inflation

In 2016, researchers conducted a study to compare the acute effects of low intensity strength training with continuous or intermittent BFRT (Neto et al., 2016). Ten, recreationally trained men, performed an upper arm exercise in three experimental protocols in a randomized order; Group one performed a low-load BFRT at twenty percent 1-RM with intermittent BFRT. Group two performed a low-load BFRT at twenty percent 1-RM with continuous cuff inflation and group three worked at a high load intensity of 80 percent 1-RM without BFRT. Blood lactate, heart rate, double product (heart rate x systolic blood pressure) and RPE were measured. It was concluded that a greater change in lactate and double product was observed for continuous BFRT when compared to intermittent BFRT. However, RPE was lower in the intermittent group (Neto et al., 2016). Furthermore, it has been shown by Takarada et al. (2000) that when under continuous BFRT conditions, metabolites such as lactate can accumulate, thus providing a possible hypertrophic benefit.
2.10.1 Blood Flow Restriction Continuous vs. Intermittent on Muscle Activation

In 2000, strength training was combined with BFRT to investigate the effects on muscular activation. Changes in iEMG and plasma lactate concentration were measured during or after an elbow flexion exercise. The cuff was inflated prior to exercise and remained inflated until exercise completion. One set of exercise was performed during the study (Takarada, Takazawa, Sato, Takebayashi, Tanaka, & Ishii, 2000). The mean iEMG and plasma lactate concentration were elevated with an increase in occlusion pressure at low intensity exercise whereas, these variables were unchanged with an increase in pressure at the high load intensity.

Tomohiro and colleagues (2013) explored the effects of continuous and intermittent BFRT on muscle activation during a unilateral arm curl exercise performed at 20 percent 1-RM (Tomohiro, Yasuda, Loenneke, Ogasawara, & Abe, 2013). Eight, physically active, participants that had not participated in regular strength training for a minimum of one year prior to the study, performed three different exercise protocols. Within each protocol participants performed multiple sets of unilateral elbow flexion. Each exercise was volume matched. EMG were recorded from the biceps brachii muscle and integrated iEMG were analyzed. During the unilateral elbow flexion exercise, iEMG increased progressively in both the continuous as well as intermittent BFRT groups. Both conditions were greater in muscle activation (p < 0.05) than the control group, without BFRT, at the third and fourth set of exercise. However, there were no differences (p > 0.05) in iEMG between continuous and intermittent BFRT exercise (2.45 and 2.40 times, respectively). Therefore it was suggested that the magnitude of increased muscle activation may be similar between continuous and intermittent BFRT exercise when performed at a high level of cuff pressure. Both BFRT groups had inflation pressures of approximately 160 mmHg suggesting complete occlusion was obtained. This study also provided an important reduction within the literature for examining multiple sets of BFRT under continuous versus intermittent occlusion regarding the upper body musculature which had not been previously studied.

2.11 Blood Flow Restriction Training at Moderate to High-Load Intensities

Researchers investigated moderate load intensity strength training coupled with BFRT and attempted to determine if it produced an additive effect on muscle hypertrophy and strength (Laurentino et al., 2008). Sixteen physical active, men were divided into two groups. Group one performed a moderate intensity exercise that was roughly comparable to a six –RM. A second group exercised at a moderate intensity that correlated to a 12- RM. A pneumatic cuff was attached to the proximal end of the right quadriceps prior to the beginning of the exercise. The left leg was trained with identical weight but without a pneumatic cuff. Knee extension 1-RM and quadriceps CSA, via MRI, were evaluated at two time points, pre and post intervention. The length of the intervention was eight weeks. It was concluded that BFRT in combination with moderate intensity strength training did not augment muscle hypertrophy when compared to moderate intensity strength training alone; pre 12–RM group (occluded 75 ± 9.5, control 75.1 ± 10.5) compared to post, (occluded 79.3 ± 12.3 vs. control 79.7 ± 12.4 cm²). Likewise, BFRT did
not significantly increase muscle strength when compared to the control leg; pre 12- RM (occluded 80.6 ± 17.0 vs. control 79.3 ± 16.1 kg) compare to post (occluded 108.4 ± 17.6 vs. control 108.6 ± 18.9 kg). 12- RM and six -RM groups were not significantly different for both muscle hypertrophy and strength between time points. However, muscle hypertrophy and strength, when comparing the same leg, significantly increased after the intervention, muscle CSA (p = 0.005) and strength (p < 0.001) for both groups.

A second study examined the effect of moderate load exercise, 70 percent 1-RM, with and without BFRT on strength, power, repeated sprint ability, as well as acute and chronic salivary hormonal parameters (Cook et al., 2014). Twenty semi-professional, male rugby players underwent a three week training program. Participants were randomized into a BFRT group, in which an occlusion cuff was pressurized to 180 mmHg and worn bi-laterally on the proximal quadriceps only during the exercise, and a control group that trained without occlusion. Five sets of five repetitions of bench press, squat and pull-ups were completed during each training session. The sessions were performed three times per week. It was concluded that greater improvements were observed (BFRT vs control) in bench press (5.4 ± 2.6 vs 3.3 ± 1.4 kg), squat (7.8 ± 2.1 vs 4.3 ± 1.4 kg), maximum sprint time (-0.03 ± 0.03 vs -0.01 ± 0.02 s), and leg power (168 ± 105 vs 68 ± 50 W). Greater exercise-induced salivary testosterone and cortisol responses were observed in the BFRT group. However, the acute cortisol increases were attenuated across the training block (Cook et al., 2014). It is suggested that the intermittent application of the pneumatic cuff to the lower extremities enhanced upper body strength, as seen in the bench press. The phenomena is suggestive of a systemic mechanism that is not limited to localized hypoxia or metabolic accumulation. In a previous study conducted by (Madarame et al., 2008), they demonstrated a cross transfer effect similar to that found by Cook et al. (2014). However, Fahs et al. (2015) has refuted the idea of a systemic hormonal effect during BFRT.

In 2017, a study investigated whether applying BFRT can augment muscle activation when combining it with traditional moderate load intensity training (Dankel et al., 2017). Ten resistant trained, individuals completed two sets of elbow flexion exercise to volitional fatigue at 70 percent 1-RM. The study design outlined that the control arm rested for three minutes between sets while the experimental arm had a cuff inflated to 180 mmHg and applied for three minutes while still resting. During the second set, the experimental group remained under BFRT conditions while the control arm did not. The BFRT arm completed significantly fewer reps in the second set in comparison with the first set (set 1: 9, set 2: 4), (p < 0.001), whereas no differences were observed in the control arm (set 1: 8, set 2: 7), (P = 0.057). Surface EMG indicated no differences in muscle activation between the BFRT arm and the control arm. However, only two sets of biceps curls were performed and only one set of biceps curls were performed with the pneumatic cuff inflated. It was concluded that BFRT did not augment additional muscle activation when training at 70 percent 1-RM. No measurements of muscle growth were recorded during the study.

Teixeira and colleagues (2017) investigated differences in metabolic stress, specifically lactate and muscle activation when moderate load intensity training was coupled with BFRT. Twelve, untrained participants were split into three different training groups. The first group trained with BFRT applied only during the rest periods. A second group trained with BFRT only during the exercise and lastly, a third group trained without BFRT. In each of the three training
conditions, participants completed three sets of eight repetitions while performing a unilateral knee flexion with 70 percent 1-RM. It was concluded that lactate increased in all three protocols but was greater in the BFRT group that had cuff inflation applied during the rest intervals. There was a decrease in EMG amplitude when observing the second and third sets when compared with the first set wherein the difference in EMG was not significant between the experimental protocols. No measurements for muscle hypertrophy and/or strength were recorded during this study.

Thus far, BFRT studies have investigated low-load intensity BFRT on the lower and upper extremities. Studies have also specifically investigated the biceps brachii and proposed several mechanisms for the changes observed in muscle size and strength. However, there currently exists a gap in the literature in regards to moderate to high load BFRT and its effects on muscle hypertrophy as well as muscular strength from a chronic study point of view. Only a handful of studies have attempted to couple moderate load strength training with BFRT (Laurentino et al., 2008; Cook et al., 2014; Dankel et al., 2017; Teixeira et al., 2017) and none of the existing studies have looked specifically at the elbow flexors muscle size or strength. Based on the scarcity of moderate load intensity training with BFRT, a 12 week intervention was implemented to investigate the effects of muscle size and strength.
Chapter 3

METHODS

3.1 Population and Study Design:

A prospective pre-post one way group study design of nine \( n = 9 \) healthy, highly trained male participants aged 21 to 35 years old were recruited from the Western University population or from local fitness clubs in London, Ontario, Canada was conducted.

3.2 Eligibility

Participants Inclusion:

1. Eligibility was determined by a minimum strength training frequency of two times per week for the previous one year.
2. Participants must have performed at least one exercise per week that directly targeted the elbow flexors.

Participants Exclusion:

1. Participants were excluded if they had a metabolic or bone disorder,
2. had a previous injury to the biceps brachii or surrounding musculature,
3. had a neuromuscular degenerative disorder,
4. or used pharmaceutical supplementation such as anabolic steroids.
5. All participants were instructed to refrain from consuming alcohol 24 hours prior to all visits.
6. Participants were also instructed to not perform any upper body exercises targeting the biceps brachii 24 hours before pre and post testing.

3.3 Outcome Measures

Prior to enrolment in the study, participants were asked to read and sign a letter of information outlining the study details. Participants were also asked to fill out a DXA scan questionnaire to determine if they were eligible to participate (see appendix A). The study protocol was approved by Western University’s Ethics Board for Health Science Research involving human subjects (see appendix B). This study conformed to the Declaration of Helsinki.

Participants were required to make two visits to the Arthur and Sonja Labatt Health Science Building where MVC and DXA scans were completed on the same day. Before isometric MVC data were recorded, each individual was fitted into the Cybex dynamometer to
ensure all testing protocols were standardized. Both the left and right elbow flexors were tested for isometric strength. Individual’s arms were randomized for order of testing at pre and post time points. Participants then performed three separate isometric holds that targeted the elbow flexors. Each contraction lasted three seconds in duration. Participants rested for three minutes between each MVC. After MVC data was collected, participants underwent a single DXA scan. Participants began the strength training program within five days of completing all baseline tests. All participants in the study were right handed, therefore the right arm trained with blood flow restriction for the duration of the training intervention. Furthermore, participants completed three sets of 10 repetitions while performing a seated dumbbell biceps curls at approximately 70 percent 1-RM twice per week for the first six weeks of training. During each training session the dominant arm was occluded, at the most proximal end, with the cuff at an inflated pressure of 60 mmHg. The cuff remained inflated during the entire exercise. Blood flow was not manipulated in the non-dominant training arm, however biceps curls were still performed and volume matched to the BFRT arm. At week six of the intervention, participants total workout volume increased by one set for the remaining six weeks of training. After 12 weeks, participants underwent post isometric strength testing as well as completed a second DXA scan. Participants were all tested and scanned within five days of completing the 12 week intervention.

3.4 Anthropometry

Body mass and height were measured using a professional scale 550KL (Health O Meter, Balance Beam Scale) and rounded to the nearest 0.1 pound and nearest 0.1 centimeter for all measurements. Total body weight was converted from pounds to kilograms by dividing the total body weight by 2.2. Both height and weight were measured without foot wear and participants emptied pockets entirely before stepping onto the scale.

3.5 Dual-Energy X-ray Absorptiometry: Muscle and Fat Mass Image Analysis

Participants underwent two DXA scans, pre and post training. A manual calibration test was completed prior to each participant scan. If multiple scans were performed on the same day, only one calibration test was completed. Participants removed footwear, headwear and emptied pockets before being placed on the scan table. During scan preparation, participants were placed horizontal lying supine with palms placed directly to the side of the body in a prone position. After aligning the body to fit within the boundaries of the scanning table, the participants were instructed to remain motionless until the scan was completed. All DXA scans were conducted by a trained DXA specialist. The same DXA specialist was used for pre and post intervention scans. Each DXA scan lasted no longer than 12 minutes in duration.

Both pre and post DXA scans were used to investigate muscle mass and fat mass of the left and right elbow flexors. A customized region of the upper arm was constructed and
measured in cm² (see figure 3.1) using Lunar iDXA software. The customized area within the outlined box was then used to determine the anthropometric composition of the elbow flexors. Each participant’s proximal upper arm area was standardized by using a cm² measurement wherein pre and post areas were identical. The scans were also used to calculate total body lean mass and total body fat mass (see figure 3.2). Participants total body lean and fat mass were calculated using a total body scan that was individually matched for each individual’s height in both pre and post scans. Two images of the full body were obtained, one of the bones and the other of soft tissues. Only the image of the soft tissue was used in the study. To calculate total body muscle mass and fat mass the system automatically divided the body into regions of interests. The corresponding regions of interest were: from under the chin up to the top of the skull, arms separated from the body with the lines passing through the armpits, legs separated from the arm and the medial cut lines located between both legs, pelvis lines; upper line cut immediately above the pelvis and cut lines through the femoral neck without touching the pelvis (see figure 3.2). The summation of all outlined regions of interest were then used to determine total body compositions. Lastly, a GE Healthcare (Lunar encore) X-ray bone densitometer was used for all the scans performed in this study.
Figure 3.1. Dual-energy X-ray absorptiometry image of a supine participant wherein elbow flexors are sectioned. Region 1: left elbow flexors. Region 2: right elbow flexors. For each participant, region 1 and 2 were area matched, in cm$^2$, between pre and post intervention scans. Area 1: 55cm$^2$. Area 2: 55cm$^2$. Images of the left and right sectioned elbow flexors for all nine participants were used in the analysis.
Figure 3.2. Illustrates a sample DXA scan determining total body lean mass as well as total body fat mass and BMI. Top left image of the full body outlines the automatically divided regions of interest.
3.6 Strength Training: Seated Dumbbell Biceps Curl

Participants individual 70 percent 1-RM biceps curls were calculated by performing a unilateral 1-RM test, three to five days prior to starting the training protocol. 1 –RM test results were then multiplied by 0.7 to determine the participants 70 percent 1-RM. Participants performed a warm up prior to 1-RM testing consisting of three sets. The first warm up set was performed with 20 percent 1-RM for 10 repetitions. A second set was performed with 50 percent 1-RM for six repetitions. And lastly, a third warm up set was performed at roughly 70 percent 1RM for four repetitions. All warm up weights were approximated and divided by 60 seconds of rest. During the 1- RM test, it was deemed a successful biceps curl if a full range of motion (ROM) was completed (see figure 3.3). The curl must have travelled a full ROM of 170 to 180 degrees. All 1- RM testing was supervised by a certified personal trainer.

In the subsequent intervention workouts, participants then engaged in three sets of 10 repetitions of a seated dumbbell biceps curls for weeks one to six. At week six, participants performed four sets of 10 repetitions for the remaining six weeks. The elbow flexion exercise was performed twice per week at the start of the participant’s workout. The introduction of an additional set was to provide a progressive overload stimulus to the muscle. Additionally, a new 70 percent 1-RM was obtained via the identical one repetition maximum testing used in pre intervention testing. Each training session was separated by a minimum of 48 hours.

During the training program, participants were instructed to aim for 10 repetitions per set. However, if muscular failure occurred in the BFRT arm before ten repetitions was reached, the exercise was terminated for both arms to control for total workout volume. If participants were unable to reach a minimum of eight repetitions for a single set, the weight was decreased by two and a half percent. In the following sets, the lower calculated weight was then used. Participants with the ability to perform more than 10 repetitions per set increased the elbow flexion weight by two and a half percent for each successive set. After each set, a timer was activated to monitor the rest periods. A rest period of 90 seconds was completed between each set. During the rest period, participants were instructed to remain seated but not obligated to hold onto the weights. After each set, the cuff pressure was checked manually to maintain a consistent 60 mmHg throughout the entire exercise. After all sets were completed, the cuff was then deflated and normal blood flow resumed in the participants BFRT arm. Additional workouts of the participants were not recorded. Participants were not permitted to use the cuff more than twice per week or use knee wraps or tourniquets to perform additional BFRT sessions on the lower or upper extremities.
Figure 3.3. A seated dumbbell biceps curl. Left picture: starting and ending position of the movement displaying zero degrees in elbow flexion angle. Right picture: Dumbbells are located at the top of the movement. After the completion of the concentric portion of the movement, the joint angle is approximately 170 to 180 degrees.
3.7 Cybex Isokinetic Dynamometer: Isometric Strength Testing

The Cybex Isokinetic dynamometer was used to determine the isometric MVC of the left and right elbow flexors. Participants were individually fitted in the Cybex chair to maintain consistent pre and post measurements. Arm length, drum height, and elbow angle were all individually fitted for each participant. The backrest of the chair was set to 90 degrees and this, however, remained consistent for each participant. The lever arm was measured from the lateral epicondyle of the individual to the straight bar placed in the center of the participant’s hand. The lever arm of the Cybex was situated parallel to the participant’s lever arm during all tests. Joint angle, mentioned as the fulcrum point, was measured from the acromioclavicular joint intercepting at the lateral epicondyle to the styloid process of the radius. The lever arm was then manipulated to produce a joint angle of 90 degrees for each participant. The testing arm was then placed directly against the back of the seat while the participants remained in an upright position. Joint angle was measured a second time to ensure accuracy. Having the participants arm placed directly against the back of the seat was done to make sure that the force generated during the contraction would be directly related to the elbow flexors and not to external forces. The elbow joint of the participants were height matched and directly parallel to the fulcrum of the Cybex drum for all tests. Lastly, subjects were buckled in to ensure safety while performing the contractions. After all the settings were confirmed and deemed correct, participants began the isometric strength testing protocol. Participants performed three separate isometric MVC’s on each arm wherein each contraction lasted three seconds in duration (see Figure 3.4). Between each MVC, participants rested for three minutes while remaining seated. Identical procedures for both the left and right arm were used. All three MVC were performed on the same arm before switching sides. Arm selection was randomized to decide which arm would be tested first for pre and post testing. For testing reliability each MVC was measured in newton meter’s (Nm) and rounded to the nearest 0.1. It was determined that an isometric contraction was reported as an individual’s maximum if, two out of the three MVC’s were within five percent of each other. The highest value was then recorded. Lastly, all isometric strength training sessions were conducted and supervised by the same individual.
Figure 3.4. Sample isometric maximal voluntary contraction (MVC) of the elbow flexors measured in Nm. The Y-axis represents force in Nm and the X-axis represents time. Each contraction was held for approximately three seconds.
3.8 Doppler Ultrasound Pilot Test for Pneumatic Cuff Pressure

Before the commencement of the BFRT intervention, four, healthy, male participants underwent Doppler ultrasound testing to determine a cuff pressure that created a 50 percent reduction in resting blood flow of the brachial artery. Resting blood flow was measured by having the participants in a seated position with their right arm extended forward and rested on a table. The pneumatic cuff was then placed around the most proximal portion of the biceps brachii. Once the cuff was in place, the ultrasound probe was then used and placed on the brachial artery. For the entirety of the test, the probe remained on the brachial artery. The test began by measuring resting blood flow of the brachial artery for one minute with zero mmHg inflated into the cuff. The cuff was then inflated in increments of 20 mmHg. Following each successive 20 mmHg incremental increase, blood flow was assessed and recorded for one minute to allow any physiological changes in blood flow to be detected. Cuff pressure was increased until a blood flow reduction in the brachial artery of 100 percent was achieved. Doppler ultrasound unit (GE Vingmed, System Five) was used. A 4-5 MHz probe was also used to determine resting blood flow of each participant. The pneumatic cuff used during the pilot test was the same cuff used during the study. Two out of the four pilot test volunteers participated in the BFRT program. Lastly, the cuff used was a dual port, five centimeter width Easi-Fit tourniquet cuff 18’ (Medical Innovations Inc).

3.9 Statistical Analysis

All statistical analysis were conducted using RStudio and R software (version 2.13.0). Paired t-tests were used to determine within group differences for baseline elbow flexor muscle mass, right elbow flexor muscle mass differences between pre and post training, left elbow flexor muscle mass differences between pre and post training and differences between left and right elbow flexor muscle mass pre and post training. A total of four independent paired t-tests were used to analyze elbow flexor muscle mass. Paired t-tests were also used to determine within group differences for baseline biceps fat mass and differences between left and right elbow flexors fat mass pre and post training. Additional paired t-tests were used to determine within group differences between pre and post training for total body lean mass and total body fat mass. Pearson’s product moment correlation was used to test for correlations between, elbow flexors muscle mass, elbow flexors fat mass, isometric arm strength, total body muscle mass, and total body fat mass. All tests were two tailed, and were considered significant when p values were less than 0.05. Data is reported as mean ± standard deviations.
Chapter 4

RESULTS

Table 4.1 Subject Characteristics

<table>
<thead>
<tr>
<th>Strength Training Participants (n = 9)</th>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Body mass (kg)</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>27.55 ± 3.91</td>
<td>181.22 ± 8.61</td>
<td>85.25 ± 10.14</td>
<td>26.16 ± 2.20</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation; n number of subjects; ST strength trained; BMI body mass index.

4.1 Dual-Energy X-ray Absorptiometry Image Analysis: Elbow Flexor Muscle Mass

Based on a paired t-test there were no significant differences between the left and right elbow flexors muscle mass pre intervention (p = 0.6135). A paired t-test of the right arm between pre and post time points showed that there were no significant within group differences (p = 0.507); (pre: 1610.22 ± 342g), (post: 1640.44 ± 306g). The muscle mass of the left elbow flexors between pre and post training were also not significant (p = 0.249), (pre: 1600.77 ± 336g), (post: 1650.44 ± 299g). Lastly, based on a paired t-test, there were no significant within group differences between the left and right elbow flexors muscle mass post intervention (p = 0.807). (Figure 4.1) illustrates the muscle mass of the elbow flexors at pre and post training. (Figure 4.2) illustrates elbow flexors muscle mass change from pre to post training.

Using Pearson’s product moment correlation, muscle mass of the right arm was correlated to right arm strength (r = 0.827, p < 0.01) and left arm muscle mass was correlated to left arm strength (r = 0.819, p < 0.01). Furthermore, muscle mass between the left and right arm were highly correlated (r = 0.988, p < 0.01). (Table 4.4) illustrates correlation data overview.

4.2 Dual-Energy X-ray Absorptiometry Image Analysis: Elbow Flexor Fat Mass

Based on a paired t-test, there were no significant within group differences (p = 0.598) between the left and right elbow flexors fat mass pre intervention. Based on paired t-test there were no significant difference between the left and right elbow flexors fat mass post intervention.
(p = 0.391), (right BFRT arm: 22.44 ± 34g), (left control arm: 19.89 ± 28g). Differences in the left and right elbow flexors fat mass after the 12 week training period are shown in (figure 4.3).

Using Pearson’s product moment correlation elbow flexors fat mass was highly correlated to full body fat mass for both left and right arms; right arm (r = 0.899, p < 0.01) and left arm (r = 0.897, p < 0.01) respectively. Correlations between right and left arm fat mass were also highly correlated (r = 0.969, p < 0.01). Elbow flexors fat mass correlation to isometric strength was negative and weak; left arm (r = -0.280, p > 0.05), right arm; (r = -0.186, p > 0.05), respectively. Table (4.4) illustrates correlation data overview.

4.3 Dual-Energy X-ray Absorptiometry Image Analysis: Total Body Lean Mass

Based on a paired t-test for total body lean mass between pre and post training, no significant differences were found (p = 0.094), (pre: 68879 ± 10912.5g), (post: 69859.1 ± 11396.5g). Total body lean mass increased 982.55 grams after the 12 week intervention.

Based on Pearson’s product moment correlation, total lean body mass was positively correlated with elbow flexors muscle mass left arm (r = 0.898, p < 0.01), right arm (r = 0.861, p < 0.01) as well as isometric strength, left arm (r = 0.715, p < 0.05), right arm (r = 0.753, p < 0.05), (table 4.4). (Figure 4.4) illustrates total body lean mass at pre and post training.

4.4 Dual-Energy X-ray Absorptiometry Image Analysis: Total Body Fat Mass

Based on a paired t-test, no significant differences were found between pre and post training for total body fat (p = 0.077), (pre: 14456.9 ± 4230.5g), (post: 15299.4 ± 4759.5g). Total body fat mass increased 842.55 grams after the 12 week intervention.

Pre and post values for total body fat mass are displayed in table (4.2). As previously stated, full body fat mass was correlated to elbow flexors fat mass (table 4.4) based on Pearson’s product moment correlation. There was no correlation between total body fat mass and isometric arm strength.
Figure 4.1  Sectioned left and right elbow flexors muscle mass in (g) of participant’s at pre and post training time points. The left and right elbow flexors muscle mass between pre and post training were not significant based on a paired $t$-test ($p = 0.807$).
Figure 4.2 Differences in elbow flexor mass from pre to post intervention. Based on a paired $t$-test, the left and right elbow flexors muscle mass differences between pre and post training were not significant ($p = 0.778$).
Figure 4.3  Differences in elbow flexor fat mass from pre to post intervention. Based on a paired $t$-test, differences between left and right elbow flexors fat mass were not significant ($p = 0.391$).
Figure 4.4 Differences in total body lean mass from pre to post intervention. Based on a paired $t$-test differences between pre and post total body lean mass were not significant ($p = 0.094$).
Figure 4.5  Differences in total body fat mass from pre to post intervention. Based on a paired $t$-test differences between pre and post total body fat mass were not significant ($p = 0.077$).
### Table 4.2  Total Body Lean Mass, Total Body Fat Mass, BMI and Total Body Weight

<table>
<thead>
<tr>
<th></th>
<th>Baseline (T₀)</th>
<th>Post Training (T₁₂)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Body Lean Mass (g)</td>
<td>68879 ± 10912.5</td>
<td>69859.1 ± 11396.5</td>
</tr>
<tr>
<td>Total Body Fat Mass (g)</td>
<td>14456.8 ± 4230.5</td>
<td>15299.4 ± 4759.8</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>26.2 ± 2.2</td>
<td>26.6 ± 2.2</td>
</tr>
<tr>
<td>Total Body Weight (Kg)</td>
<td>85.7 ± 10.1</td>
<td>87.3 ± 11.1 *</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation; g grams; kg kilograms.

* . Difference is significant at the (p < 0.05) level

### 4.5 Isometric Strength

Based on a paired t-test, the left and right elbow flexors isometric strength differences between pre and post intervention were not significant (p = 0.407). Isometric arm strength decreased slightly for both arm after the 12 week training period, right arm (-1.21 ± 8.38 Nm), left arm (-2.19 ± 9.15 Nm), respectively. Right arm isometric strength post training: (88.5 ± 16.6 Nm) and left arm (85.6 ± 20.2), (Table 4.3).

A positive correlation was found between isometric elbow flexors strength and muscle mass; right arm (r = 0.806, p < 0.01) and left arm (r = 0.821, p < 0.01). Isometric strength was moderately correlated to full body lean mass; right (r = 0.795, p < 0.05) and left (r = 0.765, p < 0.05). Lastly, isometric strength was highly correlated to height (r = 0.969, p < 0.01). All correlations were based on Pearson’s product moment correlation. Table (4.4) illustrates correlation data overview.
Table 4.3  Maximal Isometric Strength Testing

<table>
<thead>
<tr>
<th></th>
<th>Pre Training</th>
<th>Post Training</th>
<th>Percentage Change From Pre to Post Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non BFRT: Left Arm</td>
<td>87.8 ± 18.8 Nm</td>
<td>85.6 ± 20.2 Nm</td>
<td>-2.51 %</td>
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<tr>
<td>BFRT: Right Arm</td>
<td>88.5 ± 16.6 Nm</td>
<td>87.2 ± 16 Nm</td>
<td>-1.4 %</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation; g grams; kg kilograms; Nm Newton Meters.

* Difference is significant at the (p < 0.05) level

4.6  Doppler Ultrasound Pilot Test

From our four volunteers, it was determined that an average of 60 mmHg was sufficient to create a 50 percent reduction of blood flow in the brachial artery when in a seated position. More specifically, the cuff pressure average determined from the test was 58.8 ± 16.1 mmHg but for functional purposes this value was rounded to the nearest 5 mmHg.
Table 4.4: Outcome Correlations at Post Training: An Overview

<table>
<thead>
<tr>
<th>Post</th>
<th>Muscle mass left arm</th>
<th>Muscle mass right arm</th>
<th>Fat mass left arm</th>
<th>Fat mass right arm</th>
<th>Strength left arm</th>
<th>Strength right arm</th>
<th>Total body lean mass</th>
<th>Total body fat mass</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle mass left arm</td>
<td>0.935*</td>
<td>0.902*</td>
<td>0.155</td>
<td>0.077</td>
<td>0.857*</td>
<td>0.819*</td>
<td>0.898*</td>
<td>-0.14</td>
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<tr>
<td>Muscle mass right arm</td>
<td>0.901*</td>
<td>0.925*</td>
<td>0.230</td>
<td>0.160</td>
<td>0.811*</td>
<td>0.827*</td>
<td>0.861*</td>
<td>0.77</td>
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<tr>
<td>Fat mass left arm</td>
<td>-0.380</td>
<td>-0.266</td>
<td>0.928*</td>
<td>0.940*</td>
<td>-0.280</td>
<td>-0.296</td>
<td>-0.30</td>
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<tr>
<td>Fat mass right arm</td>
<td>-0.265</td>
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* Correlation is significant at the (p < 0.05) level
Chapter 5

DISCUSSION

5.1 Overview

Blood flow restriction training has been suggested to increase muscle size and strength in trained individuals when using light load intensities (30 percent 1-RM). However, there is little data to support its use when working with moderate load intensities, specifically, above 50 percent of an individual’s 1-RM. The purpose of this study was to evaluate the effects of moderate load intensity BFRT on muscle size and strength of the elbow flexors after a 12 week strength training intervention. Participants performed an elbow flexion exercise at 70 percent 1RM while blood flow of the brachial artery was reduced by 50 percent. The dominant arm of each participant was occluded during each workout. Brachial artery blood flow was manipulated using a cuff inflated to a pre-determined pressure of 60 mmHg. The cuff remained inflated during the entire exercise. The exercise consisted of three consecutive sets of seated bilateral dumbbell biceps curls. At week six of the intervention the amount of sets was increased to four. The exercise protocol was performed twice per week. Based on previous studies combining blood flow restriction and low intensity exercise, it was hypothesized that the BFRT arm would show greater muscle hypertrophy compared to the control arm. This was not observed. There were no significant differences in the elbow flexors muscle mass between the BFRT arm and the control arm post training. It was also hypothesized that the BFRT arm would show greater gains in strength when compared to the control arm. This was also not observed. There were no significant differences in strength between the BFRT arm and the control arm post training. The main finding of this paper was that unlike low intensity BFRT, performing BFRT at greater intensities does not augment muscle growth or muscular strength in trained, young, men when compared to normal strength training alone.

5.2 Blood Flow Restriction Training and Muscle Hypertrophy

To our knowledge, there is only one study within the literature that measured muscle hypertrophy when investigating chronic moderate load intensity BFRT (Laurentino et al., 2008). The findings of our study are consistent with Laurentino and colleagues (2008) wherein, training at 70 percent 1-RM with BFRT did not augment muscle hypertrophy when compared to moderate intensity training alone. Laurentino et al. (2008) reported no significant differences in muscle hypertrophy in the BFRT leg when compared to the control leg after the training program. However, Laurentino et al. (2008) did report significant muscle hypertrophy differences between the same leg when observing pre and post values. A possible explanation for the observed difference in hypertrophy of the same leg following the training intervention could be that the participants in the study were untrained. Because the participants completed the exercise with a moderate load intensity, it is supported within the literature that the muscle tension produced from the exercise i.e. 70 percent 1-RM, would be sufficient to increase muscle hypertrophy (Schoenfeld, 2010). It is also plausible that a release of GH, from an increase in
lactate concentration post exercise, could have augmented hypertrophy (Laurentino et al., 2008). Both muscle tension and GH secretion are proposed mechanisms for muscle hypertrophy (Schoenfeld, 2010). However, metabolites were not measured in our study and only speculations can be made. Furthermore, our participants did not show significant hypertrophy in either arm following the training period, 3.01 percent lean mass gain in the left arm and 1.85 percent gain in the right arm, respectively. An explanation could be that our participants were highly trained, total number of year’s strength training; 8.2 ± 6.33 years. For an individual who is highly trained, exercising at 70 percent 1-RM might not have the same hypertrophic effects as it does for an untrained individual. Therefore, a muscle hypertrophy plateau could have been reached. A 2017 review elaborated on this idea (Counts et al., 2017). The study reported that muscle growth responses will plateau and additional growth is not likely to occur appreciably beyond this initial plateau when engaging in ST for participants who are trained. To build upon the idea of a muscle growth plateau, our participants could have had a dampened anabolic response to MPS. This is supported in a 2016 study which stated, “individual’s with greater training experience appear to have an attenuation in intramuscular anabolic signaling and MPS rates after training thus suggesting muscular hypertrophy might be mitigated” (Gonzalez, 2016). Even though we did not measure MPS, it is a speculative reason for our un-observed muscle growth. Therefore, exercise training with BFRT did not produce an avenue to overcome a potential muscle growth plateau.

It appears that moderate intensity BFRT is not as effective as low intensity BFRT for muscle hypertrophy when combining it with a chronic strength training program. Lowery et al. (2014) examined the effects of low intensity BFRT on muscle hypertrophy when added to a moderate load intensity training program (Lowery et al., 2014). Twenty college aged, male participants who had at least one year strength training experience, were randomized into a crossover protocol. The first group had BFRT implemented into their training program during weeks one to four. The second group had BFRT implemented during weeks four to eight. Regardless of whether the BFRT was performed at the start or end of the intervention, the results indicated, for the first time, that light load intensity (30 percent 1-RM) BFRT showed similar muscle hypertrophy as a volume matched, high intensity exercise bout. It was postulated that light intensity BFRT resulted in increased water content of the muscle cells which induced a cascade of anabolic intracellular signalling to occur (Loenneke, Fahs, et al., 2012). Through cell swelling, increased muscle size has been recorded by measuring arm circumference (Fry et al., 2010). However, whether this proposed mechanisms occurs during moderate intensity BFRT remains ambiguous. Furthermore, Dankel and colleagues (2016) quantitatively compared increases in upper body muscle size occurring from low-load BFRT with that of volumematched unrestricted low-load training (Dankel, Jessee, et al., 2016). Results indicated that eighteen out of the nineteen studies included in the meta-analysis showed increased biceps muscle hypertrophy when training was coupled with BFRT. It was also reported that the control groups performing volume matched low-load strength training in the absence of BFRT, did not report an increase in muscle hypertrophy regardless of the exercise performed. It is proposed by Dankel et al. (2016) that it is unlikely that an exercise performed at 20 percent of an individual’s 1-RM, consisting of just three sets of 15 repetitions, as that performed by the control groups, would produce any measurable increase in muscle size in the absence of blood flow restriction. Therefore, unless a low intensity exercise without blood flow restriction is taken volitional
fatigue, muscle hypertrophy is doubtful (Farup et al., 2015). Another study conducted in 2000 found that participants performing an elbow flexion exercise under low to moderate intensity BFRT conditions (50 percent 1-RM), increased muscle CSA of the biceps brachii when compared to light load ST and sedentary controls (p < 0.05), (Takarada, Takazawa, et al., 2000). Based on the literature, it appears that the hypertrophic responses from BFRT seem to be attenuated when the exercise intensity used is greater than 50 percent 1-RM and our data also suggests this.

An explanation for the unobserved hypertrophy when BFRT is coupled with intensities above 50 percent of an individual’s 1-RM could be a muscle activation plateau. It has been proposed by Dankel et al. (2017), that the application of BFRT coupled with moderate intensity training does not augment muscle activation which would in turn seem unlikely to induce greater muscle growth. Taken a step further, a 2017 study found that moderate intensity BFRT increased metabolic stress but decreased muscle activation during exercise (Teixeira et al., 2017). Teixeira et al. (2017) reported a decrease in EMG amplitude in the second (8.5% ± 7.7%) and third set (12.5% ± 11.0%) when compared to the first (p < 0.05) under BFRT conditions. A reason for their findings could be that when training with a moderate load intensity, muscle activation is already at a maximum and by implementing BFRT, it does not create an additive effect for increased EMG activity to greater than possible neurological levels. It also appears that the addition of BFRT may be detrimental to force production during strength training at higher intensities (Teixeira et al., 2017). Due to our null findings in regards to muscle hypertrophy, it is speculated that maximal muscle activation was already attained. Contrary to moderate load intensity BFRT, low load appears to augment muscle activation when using consecutive sets. Yasuda et al. (2014) found that two sets of biceps and triceps exercises increased muscle activation progressively (p < 0.05) under BFRT (46% and 69%) but not under the control condition when working at 30 percent 1-RM (12% and 23% respectively). The muscle activation discrepancy between low and moderate load intensity BFRT is likely due to the different exercise intensities used. It is plausible that there is a 1-RM intensity limit in which BFRT will not augment muscle activation and it appears that the limit is approximately 50 to 70 percent.

Increased muscle activation observed with lower intensity BFRT is proposed to be from reduced oxygen availability and metabolic accumulation (Takarada et al., 2000; Kawada, 2005; Loenneke, Fahs, et al., 2011; O’halloran, 2014; Yasuda et al., 2014). Through the stimulation of group III and IV afferent neurons, metabolic accumulation may cause inhibition of the alpha motor neuron, resulting in an increased muscle fiber recruitment to maintain force (Loenneke et al., 2011). Yasuda et al. (2014) found blood lactate concentration post exercise were elevated (p < 0.05) with light intensity BFRT than with the control setting without BFRT (3.6 and 2.1 mmol/L, respectively). Blood lactate concentration post exercise were also reported to be correlated with increased iEMG in biceps flexion exercises (r = 0.52, p < 0.05). Another study conducted by Takarada et al. (2000) found that peak concentration of lactate after low load, less than 50 percent 1-RM, exercise with BFRT, were twice as large as that after the exercise without. The accumulation of lactate is suggested to be an avenue to increase the recruitment of higher threshold motor units, containing FT muscle fibers, thus increasing muscle activation. By using low intensity BFRT the recruitment of FT muscle fibers is possible despite the lighter load.
However, with higher intensity BFRT this may not be the case, as Teixeira et al. (2017) reported. With the addition of BFRT at greater exercise intensities, metabolic accumulation could be detrimental to muscle activation (Teixeira et al., 2017). It is important to note that the recruitment of additional FT muscle fibers is not the only possible mechanism for hypoxic induced muscle hypertrophy. Mechanisms involving metabolite accumulation (Takarada et al., 2000; Yasuda et al., 2014), cell swelling (Lowery et al., 2014a; Loenneke et al., 2012), MPS and MAPK pathways (Loenneke et al., 2011), NOS-1 or NO release (Anderson, 2000; Loenneke et al., 2010) and anabolic hormone release (GH), (Takarada et al., 2000; Seo, So, & Sung, 2016) can augment muscle hypertrophy at low load intensity BFRT. These proposed mechanisms are less known during moderate to high load intensity BFRT.

5.3 Strength Testing

To our knowledge, only two studies have measured muscular strength when coupled with chronic moderate intensity BFRT (Laurentino et al., 2008, Cook et al., 2014). Both studies used a dynamic strength protocol for the determination of 1-RM data. Laurentino et al. (2008) used a dynamic leg extension movement to determine participant’s 1-RM for pre and post training testing. During the intervention, an identical leg extension exercise was used. Laurentino and colleagues (2008) did not report any significant difference in their participant’s strength after the intervention when comparing legs but reported significant increases in strength when observing the same leg. Cook et al. (2014) used dynamic strength testing with a barbell squat and bench press as their method for 1-RM data collection. Researchers found that greater improvements were observed (BFRT training vs. control) in squat (7.8 ± 2.1 vs. 4.3 ± 1.4kg) and bench press (5.4 ± 2.6 vs. 3.3 ± 1.4kg). The control group performed the identical exercises without occlusion. Because both studies used dynamic movements in pre testing as well as during the intervention, specificity to the movement is partially plausible for the strength gains observed. By practicing the same dynamic movement over an allotted amount of time, it is reasonable that there would be a greater chance to see strength gains in post testing. Nonetheless, our findings indicate that isometric strength did not increase in either arm after the training period. A possible reason why our participant’s did not see an increase in strength is that they were highly trained. A strength training study looked at the effect of a one year training period on 13 elite weight lifters and investigated changes in EMG, muscle fiber and force production characteristics (Häkkinen, Komi, Alén, & Kauhanen, 1987). The study found that there is limited potential for strength development in elite strength athletes. The study also suggested that the magnitude and time course of neural adaptations in the neuromuscular system during their training may differ from previously reported untrained subjects (Häkkinen et al., 1987). Therefore, the same attenuation for the muscle hypertrophy can be applied to our participants in regards to strength, wherein neurological adaptation could be mitigated to a training stimulus when BFRT is added.
During low intensity BFRT, both isometric as well as dynamic strength testing has been used. One study used isometric strength testing to determine the MVC of the soleus muscle after a four week BFRT intervention (Colomer-Poveda et al., 2017). Results showed that MVC increased 33 percent (p < 0.001) and 22 percent (p < 0.01) in the trained BFRT leg and light load strength training groups, respectively. An increase in MVC after the training period could be due to specificity of the training protocol which involved an isometric hold. However, an increase in muscle thickness cannot be ruled out as an avenue for the increased MVC observed, BFRT 9.5 percent (p < 0.001) and light load without BFRT, 6.5 percent (p < 0.01), respectively. The contribution of muscle hypertrophy to strength following resistance training was investigated in another study (Erskine, Fletcher, & Folland, 2014). The study found that muscle hypertrophy explained a significant portion of the inter-individual variability in isometric strength gains following a 12 week elbow flexor strength training program. Because we did not observe muscle hypertrophy in our participants, mitigated strength is plausible. Moreover, a 2015 study used a dynamic movement involving a leg extension to determine participants 20 and 40 percent 1-RM (Lixandrão et al., 2015). The 1-RM data was then used to work dynamically during a 12 week period. The researchers found that BFRT was able to induce gains in 1-RM similar to those observed in traditional high load training (BFRT 40.1 percent vs. high load training 36.2 percent). Taken a step further, Fahs et al. (2014) measured three different muscle strength properties under low load BFRT conditions after a six week period. Dynamic strength, muscular power and muscular endurance were all measured pre, mid and post intervention. Unilateral knee extensor exercise taken to volitional fatigue while using 30 percent 1-RM was used each week. The researchers reported significant increases in all of the three muscle testing categories, except mean power at 90 percent 1-RM, for both BFRT and non BFRT limbs. An improvement in all but the highest 1-RM percentage could suggest a specificity to training effect because the participants worked only at 30 percent 1-RM. It is of interest to note, that the BFRT and control group increased strength similarly in this study. A similar increase in strength could be because the exercise in the control group was taken to volitional muscle failure. An exercise taken to volitional failure, regardless of the load intensity, has been shown to increase muscle fiber activation (Yasuda, Fukumura, Iida, & Nakajima, 2015). An increase in muscle fiber activation, when training to volitional fatigue, could attribute to the strength gains observed without BFRT.

### 5.4 Muscle Imaging

Multiple studies involving low load BFRT have measured changes in muscle mass while using different technology. Dankel et al. (2016) conducted a meta-analysis involving upper body BFRT with low intensity and reported the different techniques used for muscle measurement. Eight out of the seventeen studies included have used MRI, four have used ultrasound, another study used water displacement and lastly, one study used pQCT (Dankel, Jessee, et al., 2016). It is clear that the main method for the assessment of muscle hypertrophy is MRI but other techniques have been used.
Within the moderate intensity BFRT literature, only Laurentino et al. (2008) investigated muscle hypertrophy. The study used MRI to determine changes in muscle CSA of the quadriceps. During our study we used a DXA scan for the assessment of muscle mass as well as fat mass. In order to determine the reliability of DXA measurements, a 2013 study compared MRI to DXA for muscle size and age related atrophy in thigh muscles (Maden-Wilkinson, Degens, Jones, & McPhee, 2013). It was found that DXA and MRI scans were highly correlated ($R^2 = 0.88$, $p < 0.001$). The reliability of muscle mass measurements of DXA compared to MRI were also reported in a 2002 study. Kim and Colleagues (2002) found that total body skeletal muscle can be accurately predicted from the DXA when compared to MRI, thus affording a practical means of quantifying the large and clinically important muscle mass compartments (Kim, Wang, Heymsfield, Baumgartner, & Gallagher, 2002). Furthermore, a study reported that DXA is very accurate, with a margin of error of two to six percent for body composition (Ramos et al., 2012). Therefore, it is plausible that our findings from the DXA scan involving the full body as well as the elbow flexors lean mass and fat mass are accurate.

5.5 Occlusion Pressure

Both low and moderate intensity BFRT studies have used a wide range of cuff pressures. Low load intensity BFRT studies have used pressures between 80 and 270 mmHg. Previous moderate load intensity studies have differing reported cuff pressures Laurentino et al. (2008) used 128 mmHg and Cook et al. (2014) 180 mmHg. Teixeira et al. (2017) reported that when cuff inflation was implemented intermittently, blood lactate concentration increased greater than with continuous inflation or high intensity exercise alone. However, the findings from Teixeira et al. (2017) have not been replicated. The findings provide a different insight when compared to studies conducted by Takarada et al. (2000), and Yasuda et al. (2014) which found continuous BFRT showed increased levels of blood lactate when exercising at a lower intensity. As presented, it is plausible that with low intensity BFRT, continuous cuff application during consecutive sets of exercise might provide greater levels of blood lactate (Takarada et al., 2000; Yasuda et al., 2014). A moderate load intensity study used a cuff pressure that fully occluded arterial blood flow to the quadriceps (Laurentino et al., 2008). The pressure used in the study was relatively high, 128.4 ± 13.8 mmHg, and therefore, continuous cuff inflation during exercise had to be modified to intermittent, wherein cuff pressure was released during the rest periods. This was due to an intolerable burning sensation in the legs of the participants when resting between sets. Because of the modification, it may have equalized the metabolic overload, and the training load, between the BFRT and non BFRT conditions producing similar hypertrophy and strength gains (Laurentino et al., 2008). Based on the findings from Laurentino et al. (2008), prior to our BFRT intervention, we conducted a pilot test to determine a 50 percent reduction in the blood flow of the brachial artery in order to have our participants perform continuous BFRT. We did not collect blood samples and therefore we cannot speculate whether continuous occlusion at moderate intensity exercise produced increased levels of lactate or GH to a greater extent than normal strength training alone. When compared to the pre-existing literature we did use a reduced occlusion pressure. A possible explanation for our reduced occlusion pressure is that inflation pressure used for the quadriceps has been shown to be on average greater in mmHg than the biceps brachii. This
is due to a larger circumference of the quadriceps (Hunt, et al., 2016). Because of the smaller circumference of the biceps, a lower occlusion pressure was determined. Findings from a 2015 study suggested that relatively high pressures may not be needed to maximize the acute or chronic responses to BFRT and therefore a lower pressure could be sufficient (Counts, Dankel, et al., 2015). It seems likely that a greater cuff pressure is tolerable when using a lighter load intensity. However, inflation pressure to allow for continuous cuff inflation at moderate intensity BFRT has not been studied nor has metabolites or other proposed mechanisms for muscle hypertrophy. Lastly, blood flow was not measured between sets and therefore, it cannot be speculated whether full occlusion of the brachial artery was obtained during consecutive sets of strength training.

5.6 Conclusions

Several methodological considerations contributed to the novelty of this study, distinguishing it from previously published work. In terms of training, moderate intensity BFRT has been combined with strength training, but this is the first study to extend chronic training past eight weeks. Current study durations are a limitation when observing muscle growth and strength (Counts et al., 2017). This study was also the first study to investigate muscle hypertrophy and strength of the elbow flexors when using moderate intensity BFRT. In terms of muscle imagery, this is the first study to use a DXA scan. While studies have used MRI (Laurentino et al., 2008; Yasuda et al., 2012; Yasuda et al., 2011; Farup et al., 2015), and others ultrasound, Counts et al. (2016), this study offers a welcome addition to the extant BFRT literature for compositional analysis of muscle and fat mass.

In regards to the hypotheses presented, the study was unsuccessful in increasing muscle size and strength of our trained participants. To further elaborate, there were no significant differences in muscle size and strength between the arms of the participants after the chronic training period. The same null effect regarding muscle hypertrophy was also observed in the only other moderate intensity BFRT study to measure hypertrophy (Laurentino et al., 2008). However, muscle mass of the elbow flexors did increase marginally in our participants. Within the context of elite athletes, a minor increase in muscle could prove significant. Our second hypotheses involving muscle strength also proved to be unsuccessful. Participants did not increase elbow flexor strength after the training program. However, muscular strength was maintained after the training period. From an athletic population point of view, maintenance of strength could be very beneficial when navigating through rigorous season play. In the context of the general public, the use of moderate intensity BFRT would seem irrelevant. The use of low intensity BFRT could be beneficial for the general public, rehabilitation, elderly populations and for individuals who would potentially benefit from reduced joint tension. However, the main objective of this study was not to create another rehabilitation program using light intensity BFRT. Instead, we attempted to create a novel training protocol for athletes that would create additive muscle growth and strength that is not currently observed with traditional strength training. In summation, our data suggests that when strength training at 70 percent 1-RM, the implementation of BFRT does not augment additive muscle hypertrophy or isometric strength in young, trained male individuals. The underlying reasons for our undetected changes in muscle
size and strength are not well understood in the literature. However, several proposed mechanisms such as, maximum muscle fiber activation with moderate intensity BFRT (Dankel et al., 2017), metabolite pooling that is detrimental to muscle force production (Teixeira et al., 2017), and lastly, the highly trained nature of our participants (Häkkinen et al., 1987; Gonzalez, 2016) could be potential reasons. Cell swelling, mTOR and MAPK pathways as well as hormonal responses should be investigated when working with moderate intensity BFRT. Individuals who are looking to add to their current strength training program to enhance muscle hypertrophy and strength would be advised to implement BFRT at a lower intensity between 20 and 40 percent of their 1-RM.
Chapter 6

LIMITATIONS

The present study is not without its limitations. First, it is not possible to generalize the findings, and apply conclusions made within this study to the general population. For example, Gonzalez et al. (2016) stated that highly trained individuals could have mitigated anabolic responses to exercise training. Because the majority of BFRT studies use untrained individuals, our findings could further complicate comparisons. Therefore, untrained participants may benefit from strategies with elevated load intensity BFRT differently than trained participants. Secondly, isometric strength testing methods in this study may have also had an influence on the strength data collected. Although the test, re-test reliability of the Cybex dynamometer is high, Alvares et al. (2015), our participant’s did not train specifically for an isometric strength hold. Instead, our participant’s performed dynamic movements that were aimed at increasing muscle hypertrophy. Due to this discrepancy, any strength gains from a dynamic point of view could have been overlooked. Moreover, this study did not account for total workout volume of the participants outside of the BFRT program. Because of this, there could have been a large variability in frequency, volume and duration of weekly workouts. Based on that, muscle hypertrophy could have also deviated somewhat between participants. However, the BFRT protocol was volume matched for each arm during the intervention which provided a controlled intervention setting. A weekly standardized strength training protocol in addition to a BFRT program would create a training volume that is consistent between all participants. Within the athletic population, strength training programs might have to be modified specifically for that sport in order to achieve high study adherence. Nutrition could have also been an important determinant for muscle size and strength. In this study weekly nutrition logs were not recorded before, during or after the training period. Creating another standardized meal plan based on individualistic lean muscle tissue could prove effective for muscle hypertrophy over an extended training period. A final potential limitation of this study could be the cuff pressure obtained from the pilot study. Although we did find individualized pressures for two out of the nine participants in the study, and four total, not all study participants were involved due to time constraints. Because of this, varying pressures could have been needed to reach a 50 percent blood flow reduction of the brachial artery, at rest.
Chapter 7

FUTURE INVESTIGATIONS

Future investigations examining moderate intensity BFRT and the effects on muscle hypertrophy and strength are needed. Specifically, chronic studies investigating metabolite pooling before and after occlusion are necessary. Our study was the first study to use continuous cuff inflation, over an extended period of time, at 70 percent of an individual’s 1-RM. However, we were not able to oversee and examine blood samples. Future studies should use blood sampling as a tool to determine metabolic pooling after a chronic training period. According to the literature, only Teixeira et al. (2017) has investigated metabolic pooling with moderate intensity BFRT and this was after an acute bout of BFRT. Lactate concentrations have been recorded but these recordings were from systemic circulation. Future studies should take direct measurements from the working muscle which could create different concentrations when compared to systemic recordings. Furthermore, moderate intensity BFRT studies should investigate other proposed mechanisms of muscle hypertrophy, such as hormone release, cell swelling, mTOR and MAPK pathways, NOS-1 function and satellite cell proliferation. A 2014 study did investigate the effects of moderate intensity BFRT on plasma testosterone and cortisol levels (Cook et al., 2014). It was found that BFRT did significantly increase free circulating testosterone which produced greater muscular strength. However, to date no studies have been able to replicate the Cook et al. (2014) data reporting a systemic hormonal effect for muscle hypertrophy from BFRT. Furthermore, future studies should consider the application of the cuff bi-laterally. Cook et al. (2014) applied the occlusion cuff to both legs at the same time. A comparison between bi-lateral and unilateral cuff application could provide a different insight as to why muscle growth occurred from a suggested systemic point of view. In doing so, it would advance our understanding of skeletal muscle adaptations and or alterations when placed under BFRT conditions at heavier loads. Furthermore, it could provide possible explanations for any changes in muscle hypertrophy, specifically, for trained individuals. To our knowledge, our study is currently the only study to assess muscle size and strength of the elbow flexors after a three month period. Because of this, the implementation of additional chronic studies would allow sufficient time for muscle adaptations, which may not be observed from acute or short term interventions. Moreover, future chronic studies of highly trained individuals should take into account daily nutrition. Specifically, daily macro and micro-nutrient intake as well as meal timing. The addition of nutrition to future studies would allow for a greater understanding of the mTOR and MAPK pathways when using moderate intensity BFRT. In turn, studies could investigate the hypertrophic pathways at a cellular level. Lastly, future studies should attempt to measure each participant individually for cuff pressure. Having individualized cuff pressure would increase the accuracy of each study providing more consistent data for the changes in muscle size and strength that are observed at the incremental increases in cuff pressure and their complementary exercise intensity.
REFERENCES


APPENDIX A

DXA Screening Questionnaire

Descriptive Data

Subject ID:
Age:
Sex:
Weight (Kg):
Height (cm):

Have you completed a DXA scan before? Y or N
Do you have any pins or screws placed inside your body? Y or N
Are you currently wearing a necklace or earrings? Y or N
APPENDIX B

Ethics Approval Form

Western University Health Science Research Ethics Board
HSREB Full Board Initial Approval Notice

Principal Investigator: Dr. Gregory Marsh
Department & Institution: Health Sciences/Kinesiology, Western University

Review Type: Full Board
HSREB File Number: 108106
Study Title: Moderate intensity strength training coupled with blood flow restriction: A 12 week intervention.
HSREB Initial Approval Date: July 22, 2016
HSREB Expiry Date: July 22, 2017

Documents Approved and/or Received for Information:

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The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above named study, as of the HSREB Initial Approval Date noted above.

HSREB approval for this study remains valid until the HSREB Expiry Date noted above, conditional to timely submission and acceptance of HSREB Continuing Ethics Review.

The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCP52), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice Practices (ICH E6 R1), the Ontario Personal Health Information Protection Act (PHIPA), 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.

Members of the HSREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Signature:

Ethics Officer, on behalf of Dr. Joseph Gilbert, HSREB Chair

Ethics Officer: Erika Basile __ Katherine Harris __ Nicole Kanik __ Grace Kelly __ Vikki Tran __ Karen Cogans __

Western University, Research, Support Services Bldg., Rm. 5150
London, ON, Canada N6G 0G9 t 519.661.3036 f 519.855.2466 www.uwo.ca/research/ethics
APPENDIX C

Isometric Strength Data Collection Sheet

Descriptive Data
Subject ID:
Pre Testing Date____________
Post Testing Date____________

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<td>3.</td>
</tr>
<tr>
<td></td>
<td>Maximum MVC in Nm:</td>
<td>Maximum MVC in Nm:</td>
</tr>
</tbody>
</table>

Note: For the maximum attempt to be officially recorded, two isometric contractions must have been within five percent of each other
APPENDIX D

DXA Scan Data Collection Sheet

Descriptive Data
Subject ID:
Age:
Height (cm):
Mass (kg):

<table>
<thead>
<tr>
<th>DXA Outcome Variables</th>
<th>BMI</th>
<th>Total fat mass of left upper arm (g)</th>
<th>Total fat mass of right upper arm (g)</th>
<th>Total lean mass of left upper arm (g)</th>
<th>Total lean mass of right upper arm (g)</th>
<th>Total Body Lean Mass (g)</th>
<th>Total Body fat mass (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre -</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post -</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference Between Pre and Post Measurements (g)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CURRICULUM VITAE

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