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BLOOD FLOW RESTRICTION TRAINING: A POTENTIAL ADJUNCT TO ORTHOBIOLOGIC PROCEDURES

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Abstract

Blood flow restriction (BFR) is an augmented training method that utilizes a proximal extremity tourniquet to occlude the venous and partially occlude the arterial blood flow during specific exercise programming or at rest. BFR training (BFRT) has gained popularity among the exercise science and rehabilitation professions as a means of stimulating anabolic responses with reduced tissue overload and resistance. This manuscript presents an overview of BFRT and its utility for both performance and clinical applications. The clinical efficacy as well as the cellular and molecular mechanisms will be discussed as it may apply to patients with musculoskeletal conditions. Treatment parameters will be introduced for patients and clients with injuries and those seeking improvement in conditioning parameters. Moreover, the utilization of BFRT for patients receiving orthobiologic procedures will be highlighted as BFR serves as a synergistic regenerative rehabilitation intervention and a means of augmenting resistance training for individuals with lower exercise tolerance and post-procedural precautions.

Keywords: *resistance training*; *tourniquet*; *hypertrophy*; *musculoskeletal*; *rehabilitation*

INTRODUCTION

Blood Flow Restriction training (BFRT) may be defined as an intervention that applies a tourniquet or blood pressure cuff to the proximal portion of the arm or thigh to occlude the venous outflow and partially occlude arterial inflow.[1] The origins of blood flow restriction (BFR) began in Japan around the 1960s with personal experiments by Dr. Yoshiaki Soto following a skiing injury that involved the use of tourniquets and tubes meant to improve physical fitness and decrease muscle loss. As time progressed, research emerged and BFR became more well-known within the rehabilitative and fitness communities.

It is well known that moderate to high intensity training stimulates anabolic adaptations (e.g., hypertrophy and strength) through both cellular and molecular responses, however, similar evidence for achieving these benefits with low intensity training is quite limited as it lacks the necessary overload. This paucity of evidence for anabolic responses from low intensity training has limited the efficacy of exercise programming for ameliorating atrophy in post-operative patients or those with exercise precautions or co-morbidities precluding high intensity training. Fortunately, a growing body of evidence has identified BFRT as a mechanism to induce similar benefits of moderate to high intensity training while utilizing a low intensity programming model. By limiting the amount of blood flow to the working muscles and heart during low intensity exercise, an environment that mimics high intensity exercise is created. The result is the ability to exercise at lower intensities while simultaneously creating local and systemic responses within the body that are traditionally only produced at higher loads and intensities.[2] Locally, the pooling of blood within the working muscle increases the number of metabolic byproducts and, in turn, stimulates specific processes that are conducive to muscle growth, strength gains, and increased nutrient delivery. Proximal systemic effects are also seen, such as increased aerobic capacity and increased release of hormones necessary for muscle growth and repair.[2]

Applications of BFR combined with low-intensity exercise may be used across a continuum of care ranging from individuals who are unable to exercise or weight-bear, to individuals who want to increase muscular hypertrophy or sport performance. BFR can be applied to a variety of populations including but not limited to bed ridden, casted or braced, pre/post-operative, elderly, and athletic populations.[3] Research findings indicate that BFR may be efficacious for increasing strength and muscle hypertrophy, improving cardiovascular function, attenuating muscle loss following injury, and aiding in recovery.[4] The purpose of this article is to provide an overview of the evidence underpinning BFR as well as practical applications for use in a wide range of patient and client populations A discussion of methods to integrate BFR into the post-procedural care of patients who have received orthobiologic interventions will be presented.

BLOOD FLOW RESTRICTION EVIDENCE

A brief overview of the evidence underpinning the use of BFR is presented to support the recommended practical applications. Specifically, research supporting molecular and cellular effects will be presented as well as evidence for improving clinical outcomes and athletic performance.

Molecular and Cellular

A body of evidence suggests that low intensity resistance training (LIRT) with BFR (LIBFR) has the ability to produce hypertrophy based outcomes that exceed LIRT without BFR, and are similar to moderate to high intensity resistance training (MHIRT).[5–7] Explanations for these outcomes likely reside in the molecular and cellular benefits of applying a BFR tourniquet during training, which by way of a hypoxic effect and the accumulation of metabolites and cell swelling mimics a high intensity environment. While MHIRT possesses a specificity to sports or activities that require greater muscle activation that lower intensity training does not, it is clear that adding LIBFR is a desirable option for those individuals with a low exercise tolerance such as patient populations and those undergoing surgical and orthobiologic procedures.

The benefits of LIBFR range from acute hormonal responses and acute phosphorylation of proteins involved in hypertrophy signaling pathways (e.g., mammalian target of rapamycin pathway [mTOR]) to the expression of ribosomal RNA transcription factors, increases in biomarkers associated with satellite cell activity, and mRNA expression of genes related to skeletal muscle mass regulation (e.g., MuRF1).[5,6,8–15] Moreover decreased bone resorption markers, increased interleukin-6 (which may assist with skeletal muscle remodeling) and vascular endothelial growth factor (VEGF), and increased blood lactate occur from LIBFR.[11,13,15,16]

A majority of the evidence for acute hormonal secretions following LIBFR is related to growth hormone secretions. In one study, a HIRT program was compared to LIBFR for 10-adults who performed squats and chest presses using both programs.[6] Blood samples were collected at baseline, immediately after, and 15-minutes after completion of the exercise routine. The results indicated that the LIBFR program was associated with significantly greater growth hormone serum concentrations at the 15-minute assessment when compared to the HIRT group. No significant differences were otherwise measured between the groups for testosterone, insulin like growth factior-1 binding protein, and cortisol indicating the ability of LIRT to have comparable hormone responses to HIRT when BFR is added. In another study, LIBFR was compared to HIRT among 13 healthy women.[8] In this study, fasting cortisol, growth hormone, and blood lactate responses were measured pre and post exercise session with increases in both growth hormone and cortisol found after the exercise program in both groups with no significant between-group differences. In contrast, blood lactate and ratings of perceived exertion were higher in the HIRT group. In a study by Patterson et al., seven healthy older men performed both LIRT and LIBFR with blood samples taken at rest prior as well as at 30-,60-, and 120 minutes post exercise.[15] Results indicated greater increases in growth hormone with the LIBFR protocol when compared to the LIRT program. Furthermore, a study by Manini et al., compared LIBFR to HIRT in both younger and older men[12] and found that growth hormone responses to LIBFR are slightly higher than HIRT and that the younger men had a more pronounced increase. Lastly, in another study that compared LIBFR with electrical stimulation to LIBFR without electrical stimulation on individuals performing isometric exercise, acute growth hormone responses were only increased in the group that received the electrical stimulation.

With regard to muscle morphology, numerous studies exist to elucidate the evidence underpinning hypertrophy following LIBFR. Davids et al., compared changes in muscle function, morphology and signaling pathways in twenty-one subjects who performed LIBFR or over the course of 9-weeks.[5] In this study it was found that muscle strength was superior in the HIRT group as expected given the specificity of training. However, acute phosphorylation of key proteins involved in hypertrophic pathways as well as expression of ribosomal RNA transcription factors were relatively comparable between the groups, suggesting the mechanisms for hypertrophy may be stimulated by LIRT when augmented with BFR. In regard to different training modes, one study compared 3 groups which included rest only, BFR with rest, and LIBFR, and found that no differences in anabolic signaling or myofibril protein synthesis rates were observed between the rest only group and BFR with rest.[10] However, when comparing LIBFR to BFR with rest, anabolic signaling (mTOR), increased myofibril synthesis rates, and elevated expression of MuRF1 was identified in the LIBFR group. Further supporting the option of LIBFR is a study that compared the number of visible satellite cells per muscle fibre as well as myogenin (a muscle transcription factor that regulates myogenesis) in a group that performed LIBFR on one leg and LIRT on the other leg.[14] In both groups satellite cells and myogenin were increased, however, the LIBFR group had greater increases in protein signaling and factors associated with the mTOR pathways.

Other interesting findings concerning BFRT include changes in bone cells and cytokines. Bittar et al., analyzed LIBFR and HIRT's effect on bone metabolism markers in a systematic review.[16] In the review, 4 studies identified increases in the expression of bone formation markers and decreased bone resorption markers after aerobic and anaerobic exercises. With regard to cytokines, a study by Patterson et al., found that LIBFR leads to increases in VEGF and interleukin 6; however, changes in VEGF were only seen in the LIBFR group.[15]

While numerous molecular and cellular benefits occur from the overload and metabolic effects of higher-intensity resistance-type exercise, the plausible explanations for these responses in LIBFR range from the ability to train more frequently without muscle soreness, cellular swelling, and to the intermittent hypoxic effects produced by the restriction in arterial flow.[1,17] While a detailed discussion is beyond the scope of this article, it should be mentioned that evidence suggests that intermittent hypoxic environments are associated with the migration of very small embryonic-like stem cells (VSELs) from the bone marrow to peripheral circulation.[18] A benefit of VSELs is that they are pluripotent and may play an important role in healing from injuries and recovery. Additional evidence suggests that intermittent hypoxia may reduce inflammatory factors (c-reactive protein, TNF-alpha, and IL-4), improve blood oxygen transport, increase nitric oxide, and promote the upregulation of VEGF.[19–21]

In summary, when the goal of hypertrophy is desired, LIBFR is an alternative to HIRT for those individuals who may have post-procedural precautions or an intolerance to high intensity loading. BFRT with dynamic and isometric resistance seems to offer comparable changes in factors associated with muscle hypertrophy that were previously only seen with HIRT, however, changes in strength are likely to be less. With regard to hormones and cytokines, anabolic changes in growth hormone seem to underpin many of the anabolic benefits of BFRT and may explain changes seen proximal to the torniquet.

Clinical Evidence

To promote hypertrophy and strength gains, traditional heavy resistance training with loads between 67–85% of one repetition maximum (1-RM) is recommended to assist patients in developing their functional capacity before their injury or operation.[2] However, traditional heavy resistance training can be difficult for individuals unfamiliar with traditional weight lifting exercises such as the barbell back squat, which can be contraindicated with elderly patients with chronic diseases, such as hypertension and osteoporosis. It can cause further injury in athletes recovering from their initial injury.[2]

A growing body of evidence supports the use of BFR for increasing bone formation factors, increasing Achilles tendon cross sectional area (CSA) and stiffness, increased strength and decreased pain in patellofemoral syndrome, and with attenuating muscle atrophy in post-op ACL patients. A study performed by Linero and Choi highlighted the efficacy of BFR as a training modality for individuals with menopause based on improvements in markers of bone formation.[22] Specifically, the study consisted of 26 women who were post-menopausal that were randomly assigned into a MHIRT group, and LIBFR group, LIRT group, or control group. Exercise groups performed leg press, biceps curl, and triceps extension 3 times a week for 12 weeks at a training intensity of 60% 1RM for the MHIRT group and 30% 1RM for the LIBFR and LIRT groups. Results showed that while the LIRT group did not have any responses on bone turnover markers, the LIBFR group showed a significant increase in bone formation markers (P1NP) by about 7.05 ng/ml, while the MHIRT group showed no changes.[22] The results of the aforementioned study suggest that BFR may be a training option for those with an inability to perform MHIRT who require loading at a level necessary to improve bone formation.

Centner et al., evaluated the effect of LIRT combined with BFR on Achilles tendon adaptations when compared to high load (HL) resistance training.[23] Fifty-five untrained healthy males with an average age of 27.9 ± 5.1 years were randomly assigned into 3 groups: low load blood flow restriction (LLBFR) with loads 20–35% 1RM, high load group at 85%1RM, and a control group. Tendon stiffness and tendon CSA over the course of a 12-week resistance training program was evaluated. At the end of the 12-week training program it was found that tendon stiffness and tendon CSA significantly increased in both the HL and LLBFR groups. Tendon CSA increased by 7.8% in the LLBFR group compared to an increase of 4.6% in the HL group.[23] Thus, augmenting BFR with lower load training may produce comparable changes in tendon stiffness and greater increases in CSA than HL which may be of value for those individuals who are intolerant to HL training.

Karabulut et al., conducted a study of healthy older men (mean age 56.8 ± 0.6 years) randomized into 3 groups: high intensity resistance training (HI-RT), LIRT plus BFR at the most proximal portion of the thighs, and a control group. Results indicated that the HI-RT and LIRT plus BFR groups both showed increased bone specific alkaline phosphate and type 1 collagen uptake compared to the control group.[24] This suggested that low load resistance training with BFRT could be an alternative to high intensity exercise for bone health in older men.

When evaluating pain reduction, BFR combined with low-intensity training (LIT) has been shown to have comparable effects to light-intensity and high-intensity training.[25] The following four studies show the potential benefits of utilizing BFR with low-load resistance training (LLRT) to reduce individuals' pain and increase function. A study conducted by Giles, Webster, and McClelland compared quadriceps strength with and without the use of BFR applied to the proximal thigh when treating patellofemoral pain. Sixty-nine participants completed the double-blind, randomized trial, which showed a 93% greater reduction in pain and a 49% increase in knee extensor torque for the BFR group compared to the group without BFR.[26] Another clinical trial evaluated the application of BFR combined with LLRT in reducing anterior knee pain (AKP).[22] The study was made up of 40 males that were randomized into a LLRT-BFRT group (N = 20) and a LLRT group (N = 20). Before starting the study, all participants performed baseline testing that involved a shallow single-leg squat (SLSS), a deep single-leg squat (DSLS), and a 20cm step down (SDT) and were asked to rate their pain on an 11-point numeric rating scale (NRS 0–10) after performing each test. Both groups performed 4 sets of open kinetic chain knee extensions (90 degrees - 0 degrees) and performed each repetition (2 seconds concentric, 2 seconds eccentric) to the pace of a metronome. The first set of knee extensions was performed for a maximum number of repetitions and was terminated when an individual could not match the pace of the metronome or if they failed to fully extend the patellofemoral joint. The first set was followed by 3 sets of 15 repetitions with 30 seconds of recovery between sets. The only difference between both testing groups was the BFR LLRT group had a BFR cuff applied to the proximal thigh of the affected lower extremity and had the cuff set to 80% to each individual's limb occlusion pressure (LOP), which is the amount of occlusion necessary to restrict arterial and venous flow. LOP was determined by using a doppler ultrasound over the popliteal artery until the pulse was no longer heard. After performing 4 sets of leg extensions, both groups performed the same functional tests at baseline and rated their pain on the NRS 0-10 scale to see if there was any difference in their AKP. At the end of the trial, Korakakis and his colleagues found that the BFR LLRT group had significant immediate pain reduction in the SLSS, DSLS, and SDT post-BFR LLRT, and had reduced pain for an additional 45 minutes. The LLRT group, on the other hand, did not have any difference in pain between baseline and post-intervention testing. Additionally, 20% of participants within the LLRT group reported that their knee pain was worst after performing 4 sets of knee extensions and performing the functional assessments at the end of the session.[27]

An RCT conducted by Karanasios and his colleagues, investigated the effects of LLRT with BFR on patients with lateral elbow tendinopathy (LET).[23] The study consisted of 46 patients randomly assigned into a LLRT-BFR group that performed exercises at 30–50% LOP and a sham LLRT-BFR group that performed exercises at <20% LOP (where the BFR cuff would just fit comfortably on the patient's arm). Both groups within the study participated in a six-week program that consisted of soft tissue massage, supervised exercises for LET (two 30–45-minute sessions a week), education on LET, and a home exercise program. The primary outcome measures that were used in this RCT to see if LLRT with BFR has any impact on LET were pain intensity, patient-rated tennis elbow evaluation (PRTEE) score, pain free grip strength, and global rating of change. All primary outcome measures were measured at baseline, 6 weeks, and 12 weeks. The training program involved 2 stages. In the first stage all participants performed the same exercises. Both groups performed 4 sets (30/15/15/15 repetitions) of elbow flexion and extension at 30% of 1RM using dumbbells. After completing the first set of exercises both groups performed wrist extension, wrist flexion, supination, and pronation exercises (3 sets of 10 repetitions per muscle group) with the heaviest free weight possible that did not cause pain ≥ 2/10 on the affected upper extremity. At the end of every session, all participants performed three repetitions with 30 second holds of stretching exercises that targeted the wrist extensors and wrist flexors. As patient's in both groups progressed in the first stage of training, the amount of resistance per exercises was increased by 0.5–1 kg on a weekly basis depending on a patients strength/ pain level with performing the exercises within the program. Patients started the second stage of the training program after having at least two weeks of training and reported no LET pain during, or after performing the exercises within the training program. During the second stage patients continued to perform exercises under

BFR and sham-BFR, as well as performing other exercises without BFR and sham-BFR. The only difference between both training groups in the 6-week program was the LLRT-BFR group did all of their exercises with BFR, while the sham-BFR group did their exercises with the blood pressure cuff placed comfortably on their affected upper extremity. All exercises were paced by an exercise metronome (2 seconds concentric phase + 2 seconds eccentric phase = 1 repetition) to ensure that all repetitions performed in the LLRT-BFR group and the sham-BFR group had equal time under load, so that there were no load differences between the groups. Both groups were given a 30 second break between sets of a given exercise and had a 1-minute break between different exercises. The BFR Cuff in both groups was inflated for the entire duration of a given exercise and was deflated between different exercises. The study results found that the LLRT-BFR group had a reduction in pain intensity at the 12 weeks follow up, had increases in pain-free grip strength at the 6 weeks follow up, and had a reduction in their PRTEE scores at the 6 and 12 weeks follow ups compared to the LLRT-Sham BFR group. Additionally, subjects within the LLRT-BFR group had greater odds at reporting complete recovery or significant improvement of LET at the 6 weeks follow up and 12 weeks follow up compared to the LLRT-Sham BFR group.[28] This study shows that BFRT can potentially serve as an effective intervention to increase functional outcomes in individuals diagnosed with LET.

The impact of BFRT on individuals that have a clinical presentation of subacromial impingement syndrome (SAIS) has been reported in a case series.[24] The case series consisted of a 51-year-old female (patient A) and a 46-year-old male (patient B) that were referred for physical therapy for gradual onset of shoulder pain. Patient A was right hand dominant but had pain at the posterior lateral aspect of the left shoulder, and had difficulty performing dressing activities behind her back, and difficulty with reaching overhead due to left shoulder pain. Patient A's goal for physical therapy was to be able to reduce her left shoulder pain in order to be able to perform dressing activities behind her back and increase her ability to perform reaching and lifting activities overhead. Patient B was right hand dominant and had pain at the anterior lateral aspect of his right shoulder and had difficulty with lifting > 50 pounds to shoulder height and lifting > 10 pounds overhead. Additionally, patient B had to modify his gym exercises and the frequency that he played tennis during the week due to his right shoulder pain. Patient B's goal was to decrease his right shoulder pain in order to perform lifting, carrying and reaching activities without any pain, and to return fully to his recreational activities. Several outcome measures were used to measure baseline shoulder pain and post shoulder pain after going through a BFRT program. The Pennsylvania Shoulder Score (PENN) was used to assess pain and satisfaction with current function, the American Shoulder and Elbow Surgeon Shoulder Assessment Form (ASES) was used to assess upper extremity function, activities of daily living (ADLs) and pain, the single Alpha-numeric Evaluation was used to compare patient's current functional level to pre injury functional level, and the Patient Specific Functional Scale to see what the three most important activities to the patient's was limited due to their shoulder pain. Pain pressure threshold (PPT) is another outcome measure that was used in the case series to assess local and remote pain sensitization during BFRT sessions and between BFRT sessions. PPT was measured with a handheld digital pressure algometer at the ipsilateral supraspinatus, ipsilateral thenar eminence, and contralateral web space (between toes 1 & 2). The three sites were selected to specifically measure PPT locally (ipsilateral supraspinatus) and PPT remotely (ipsilateral thenar eminence and contralateral space between toes 1 and 2). PPT was measured prior to and after BFRT sessions. During the initial examination patient, A demonstrated limitations in both active range of motion (AROM) and passive range of motion (PROM) of the shoulder due to pain and weakness (with pain) when performing shoulder strength testing. Patient A also tested positive for the Neer impingement test, Hawkins-Kennedy test, Empty Can test, External rotation test, and had a painful arc sign. Unlike patient A, patient B had no limitations in right shoulder AROM and PROM but had pinching at the end range of shoulder external rotation and shoulder extension. Patient B demonstrated right shoulder weakness due to pain. Just like patient A, patient B also tested positive in the Neer impingement test, Hawkins-Kennedy test, Empty can test, External rotation test, and had a painful arc sign. Based off of the subjective reports and objective measures collected during the examination, SAIS was the suspected clinical diagnosis that caused both individuals to have shoulder pain. After completing the examination, patient A was seen for three visits for 3 weeks and did a follow up on the phone, while patient B had four visits over 4 weeks. Before undergoing BFRT, both subjects did a six-minute warm-up on an upper body ergometer. They performed maximal isometric strength testing in scaption, external rotation at the side, and prone horizontal adduction using a handheld dynamometer to determine 20% of their isometric strength in each movement. The physical therapists performed these strength tests in the exact order before the start of every session to reduce variability in the study, and to progress loads appropriately for each individual exercise. Once done with strength testing, both patient's LOP of the affected upper extremity was taken in supine and set to 50% LOP for the patients to perform their exercises. The three exercises that both patients performed under BFR was side-lying external rotation, prone horizontal abduction, and standing scaption. For each exercise patients completed one set of 30 repetitions followed by 3 sets of 15 repetitions at 50% LOP with 20% of their maximal isometric strength. Patients rested 30 seconds between sets with the BFR cuffs still inflated and rested 1 minute between exercises with the cuffs deflated. Both patients were given a home exercise program (HEP) to perform on days not receiving treatment in order to achieve the volume necessary to achieve hypertrophy and compliment the use of BFRT. The HEP consisted of performing the same exercises that were used in the BFRT sessions for three sets of 12 repetitions. At the study conclusion, both patients were able to achieve their goals and had clinically meaningful improvements in all self-report outcome measures, pain sensitization (locally and remotely), and resting-pain levels. In addition to improvements in outcome measures, both patients also showed improvements in strength gains in their affected shoulders, patient A had gains in AROM of the left shoulder, and patient B reported less pain at end range of right shoulder external rotation and right shoulder extension.[29]

Preservation of skeletal muscle is a key determinant for an individual's health and impacts the quality of their life due to the fact of having an impact on the ability to ambulate and perform ADLs. One of the biggest challenges for rehabilitation professionals and other healthcare professions is the preservation of muscle mass in individuals that have undergone surgery such as an ACL reconstruction or sustained an injury, since the patient will be limited in activity with the involved extremity in order to promote healing. This leads to rapid atrophy, reduced exercise capacity, and decreased ability to perform ADLs.[2] Studies have shown BFRT to be an effective tool to prevent atrophy in individuals that have undergone surgery or sustained injuries limiting function, as the mechanism of BFR promotes similar levels of hypertrophy and strength gains that are associated with traditional heavy resistance training.

One study of interest investigated the effects of BFR on three groups of healthy patients that had their left lower extremity immobilized and restricted to non-weight bearing for two weeks.[15] The BFR group completed five sets of 5-minute intervals of passive BFR with 3 minutes of rest between sets twice a day. The isometric group performed 20 isometric exercises with five second holds per repetition that involved the knee extensors, knee flexors, and plantar flexors and did not involve any BFR. The control group did not receive any therapeutic intervention.[30] At the end of the two weeks, the BFR group had experienced no changes in leg or thigh circumference, the isometrics group had experienced decreased leg circumference and strength in the knee extensor and flexor muscles with no changes in thigh circumference, and the control group had significant decreases in both thigh and leg circumference as well as decreased strength in knee extensor and flexor muscles.[30]

A study conducted by Takarada and colleagues analyzed the effects of BFR on 16 patients (8 male and 8 female) that had undergone ACL reconstruction.[31] The 16 subjects were split into two groups, a BFRT group and a control group comprising 4 males and 4 females. MRI scans were performed on the 3rd and 14th day after the initial ACL reconstruction to determine if there was a difference in CSA of the affected lower extremity between the BFRT and the control group. For two weeks patients in the experimental group performed five sets of 5-minute intervals of passive BFR with 3 minutes of rest between sets twice a day, while the control group did not receive an intervention. At the end of the study, patients that had undergone BFR only had a decreased CSA in the knee extensors by 9.4 ± 1.6% and a decreased CSA in the knee flexors by 9.2 ± 2.6%. Conversely, the control group had a decreased CSA in the knee extensors by 20.7 ± 2.2% and a decreased CSA in the knee flexors by 11.3 ± 2.6%.[31]

Spada, Paul, and Tucker[32] conducted a systematic review to determine if BFRT can limit the loss of knee extension and knee muscle torque during early recovery from ACL reconstruction in comparison to traditional ACL post-operative rehabilitative methods. The researchers only analyzed studies that were level 1 RCTS, and measured knee flexion and knee extension using an isokinetic device as their primary outcome measure. Out of 55 studies, only 2 studies met the inclusion criteria for the systematic review. The 2 RCTs demonstrated that BFRT groups had less of a decline in knee extension/knee flexion torque after ACL reconstruction compared to groups that followed traditional post operative ACL reconstruction protocols.[32] The two aforementioned studies suggest that BFRT could potentially help increase post-operative function and reduce atrophy in patients that have undergone ACL reconstruction.

A systematic review and meta-analysis of research studies on BFR in combination with light exercise found that young adults and elderly frail patients were able to increase strength in 1-RM, isometric, and isokinetic tests similar to individuals that underwent a heavy traditional weightlifting program.[33] In the studies examined, subjects that performed BFRT trained at intensities equivalent to 20–30% of 1-RM using BFR, while subjects that underwent a traditional weightlifting program trained at intensities equivalent to 60–90% of 1-RM.[33]

The aforementioned studies and reviews have indicated that BFR has promising evidence in preserving muscle mass post operatively, despite not using typical exercises that are prescribed to patients post operatively, such as isometrics of the lower extremity. As a result, BFR has become a popular method for rehabilitation and medical professionals due to being able to simulate similar strength and hypertrophy gains at a lower intensity without the risks associated with heavy resistance training.

Performance & Conditioning

In addition to the evidence underpinning the ability of BFR to prevent atrophy after reinjury and induce strength and hypertrophy gains in a clinical population, BFR has shown to be advantageous for athletes in terms of increasing athletic performance despite training at lower intensities. Specifically, BFRT can be an attractive therapeutic intervention that increases muscular strength and size in clients, while providing low mechanical stress on contractile and non-contractile tissue that is associated with traditional weight training. Additionally, evidence suggests that BFR can also induce changes in aerobic performance.

Yamanaka, Farley, & Caputo conducted a study to examine the effects of a 4-week BFRT program on the upper and lower extremities on muscular hypertrophy and strength in NCAA Division 1 (DIA) college football players.[34] The study comprised 32 (D1A) football players randomized into a BFRT group and a control group (did not have BFR). Both groups participated in resistance training sessions in addition to the off-season workouts designated for their team. To be included in the study, all participants needed to have had at least five years of experience in heavy resistance training, have high levels of strength equivalent to the 93.2–94.4% percentile for their height and body mass, and have no medical conditions that can potentially cause complications if selected for the BFRT group. Before starting the study, all participants took part in pre-test measurements that involved resting blood pressure, girth measurements (upper/lower chest, upper/lower arm, and thigh), height, body mass, 1RM barbell bench press, and 1RM of the barbell back squat. Once the 4-week training program, all participants performed the same testing to compare pre-test and post-test data.[34] The sessions conducted by the researchers involved the barbell bench press and barbell back squat and was performed 3 times a week with each individual athlete training at the same time they were designated on the three days of training they had to perform throughout the week. The BFRT group had an exercise protocol that involved one set of 30 repetitions and 3 sets of 20 repetitions with a 45-second rest period with 20% of their initial 1RM. These exercises' concentric and eccentric phases for the BFRT group were guided by a metronome, with the eccentric phase lasting twice as long as the concentric phase. The control group, on the other hand, performed the same exercise regime as the BFRT group without BFR cuffs and without the metronome determining the length of both exercises' concentric and eccentric phase in the training regime. At the end of the 4 weeks, both groups had no changes in height or body mass but had significant increases in strength and hypertrophy in the upper/lower chest and left upper arm. However, the BFRT had significantly greater gains in strength and hypertrophy in the upper/lower chest than in the control group. Regarding strength, the BFRT group increased their 1RM in the barbell bench press by 7% and their 1RM in the barbell back squat by 8%. The control group increased their 1RM in the barbell bench press by 3.2% and their 1RM in the barbell back squat by 4.9%. Regarding hypertrophy, the BFRT group had an increase in upper chest girth by a mean of 3.7 cm, an increase in lower chest girth by 2.6 cm, and an increase in left upper arm girth by a mean of 0.8cm. Contrastingly, the control group had an increase in upper chest girth by a mean of 1 cm, an increase in lower chest girth by a mean of 1.2 cm, and an increase in left upper arm girth by 1.5cm.[34]

Another study examined the effects of a BFR walking program on lower extremity muscle size and strength.[35] The study included a BFR group and a control group (did not have BFR) that participated in a walking program 2 times a day, 6 days a week, for three weeks. Before testing, participants performed unilateral (UL) leg press and bilateral (BL) hamstring curl 1-RM tests, isokinetic strength testing of the knee flexors and extensors using a dynamometer and had circumference measurements of the mid-thigh. At the end of the study, the BFR group had increased their 1-RM in the UL leg press and BL press by 7.4% and 8.3%, accordingly, and increased their maximal isometric knee extension strength by 10.4%. Additionally, the BFR group had a 5.3% increase in the mid-thigh circumference, which included hypertrophy in the quadriceps, hamstrings, and adductors. The control group in this study had no increases in any strength testing or increases in CSA of the mid-thigh.[35]

In addition to inducing gains in muscular strength and hypertrophy, BFRT has also been able to help improve aerobic capacity and athletic performance. As previously stated, BFRT restricts some arterial blood flow and completely occludes venous blood flow. By doing so, the body is placed in a high stress environment due to decreases in the body's ability to deliver oxygen to the working muscles, as well as the ability to clear out metabolic byproducts of exercise that hinder performance. As a result, the body is forced to make physiological adaptations in order to overcome the stressful stimulus.

The effects of low-intensity cycling with and without BFR in 19 young adult males aged 20–26 has been evaluated.[36] In the study, subjects were randomized into a BFRT group (N = 9) and a control group (N = 11) of subjects with no BFR. Before testing, all subjects performed isometric testing of the knee flexors and extensors, a VO2 test on a bicycle ergometer, and had measurements of the cross-sectional area of the quadriceps/thigh using MRI. Both groups trained 3 days a week for 8 weeks. Each individual within the BFR group trained at an intensity of 40% of their VO2 max for 15 minutes. The BFR group wore BFR cuffs on both thighs when performing their cycling sessions and started with a LOP of 160mm Hg. As the subjects within the BFRT group adapted to BFRT, cuff pressure was increased by 10mm Hg each week until a final LOP of 210mm Hg was achieved. For each session, individuals within the BFRT group were subjected to 18 minutes of BFR (3 minutes to get LOP and

15 minutes training with LOP). Individuals within the control group trained at 40% of their VO2 max for 45 minutes. At the end of the study the BFRT group had significant increases in quadricep/thigh CSA (3.4–5.1%), isometric knee extension strength (7.7%), VO2 max (6.4%) and exercise time until exhaustion (15.4%). The control group at the end of the study only had an increase in knee extension isometric strength (1.4%) and had no changes in VO2 max, time until exhaustion, and quadricep CSA. There was no change in isometric knee strength for either group at the end of the study.[36]

Another study investigated the effects a 5-week BFRT program would have on the VO2 max of elite rowers.[37] The study consisted of 8 female and 23 male elite rowers randomized into a BFRT group (4 females and 12 males) and a control group (4 females and 11 males that did not have BFR). All rowers did a VO2 max ramp test on a rower and a 1RM squat before and after the study to see the potential effects between the group that underwent BFRT and the group that did not undergo BFRT. Throughout the 5-week program, the BFR and control groups were subjected to the same training regimen, including cross-training (running and cycling), strength training, and rowing at low, moderate and high intensity. Every participant within the study performed their training sessions at similar times every day to minimize the impact of circadian effects on performance. The BFRT group was subjected to BFRT three times a week during low-intensity rowing sessions that consisted of two bouts of 10-minute rowing intervals, with a 10-minute break between intervals. After both groups completed the five-week training program, it was found that there where was no significant increase in the 1RM barbell back squat in either group, with the BFRT group going from 106.2 kg ± 20 kg from pre-testing to 111.9 kg ± 20.9 kg post-testing, and the control group going from 99.1 kg ± 25.1 kg from pre-testing to 103.7 kg ± 25.4 kg. Although there were no significant changes in 1RM barbell back squats between both groups, the BFRT group had significantly increased their VO2 max at the end of the study compared to the control group. At the end of the study the BFRT group increased their VO2 max from 63 ± 7 mL/min/kg to 69.7 ± 9.4 mL/min/kg, whereas the control group increased their VO2 max from 63.2 ± 8.5 mL/min/kg to 64.9 ± 8.6 mL/kg/min.[37]

When considering the evidence of the aforementioned studies in regard to improvements in performance and conditioning, it should be taken into consideration that the study consisting of college football players and elite rowers are high level athletes that have significant experience in the realms of strength and conditioning. In summary, BFRT when combined with LIT can induce significant changes in strength, hypertrophy, and aerobic performance, which are vital attributes in improving an individual's performance and level of conditioning.

PRACTICAL APPLICATIONS

When applying BFRT it is critical to understand LOP as well as the different methods for performing BFR. Specifically, a discussion of utilization of BFR with isometric and dynamic resistance training as well as passive BFR is provided. Furthermore, a brief discussion of utilization with aerobic training is presented. Lastly, post procedural recommendations will be presented for patients who have undergone orthobiologic procedures.

Limb Occlusion Pressure

BFR can be clinically applied in a variety of methods based on the individual circumstance. The four main methods of BFR application are passive, isometric exercise, dynamic exercise using LIRT, and aerobic exercise. Depending on the patient's presentation or the intent of the occlusion, these methods can be utilized in isolation or in combination. An example of using these methods in combination would be utilizing BFRT dynamically during exercise as well as using it passively for recovery after the exercise session has occurred. It is recommended to perform BFR at a predetermined percentage of the patient's LOP, which is the minimum amount of pressure needed to occlude arterial blood flow.[1] By using individualized percentages of the patient's LOP, this eliminates the need to account for other variables that may affect blood flow, such as the cuff width, limb size, and blood pressure. Some

BFR cuffs may be used with devices, such as the one seen in Figure 1, that can calculate the individualized LOP within the device, while others cannot. If an automated devise is not available, the LOP can be calculated by using a doppler ultrasound device on the distal pulse (radial or posterior tibial arteries) while manually inflating the cuff and finding the pressure in each limb where the occlusion is 100%. Once the LOP is determined manually, programming can be based on a percentage of the LOP. As previously stated, the automated devices calculate LOP within the device without a doppler and provide an option to select a percentage of LOP for training within the device.

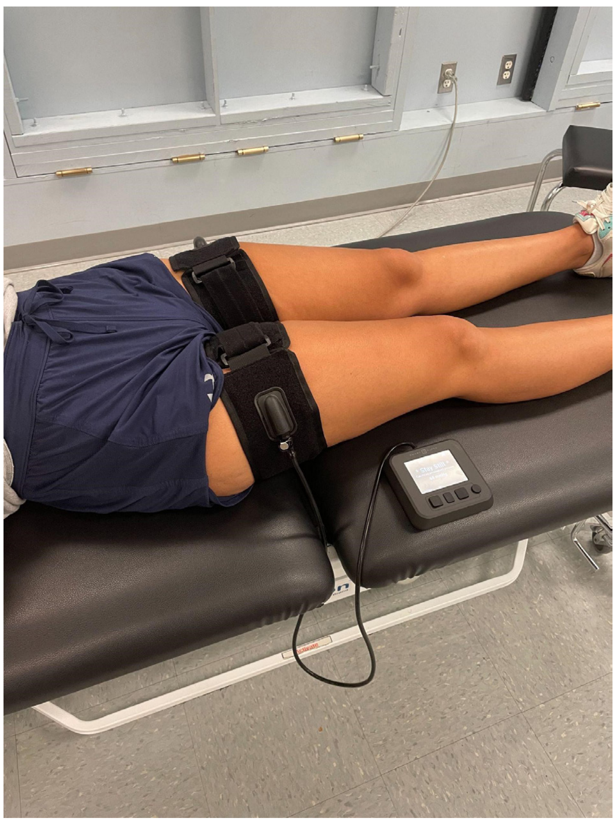

Figure 1. Measuring limb occlusion pressure (LOP) of both lower extremities. This is performed unilaterally at rest. The LOP is then used to determine percent occlusion for exercise. Depending on the blood flow restriction device used this may be calculated through an automated device or may be calculated using blood flow restriction cuffs and a doppler unit.

To determine a patient's LOP, the practitioner has the patient lie supine and places the cuff proximally on the targeted extremity as seen in Figure 1. For example, if a practitioner wanted to determine a patient's LOP of both upper extremities, the practitioner would place both cuffs on the proximal arm. It is recommended to determine the LOP on one limb at a time and to deflate the cuff before calculating LOP of the next limb. Figure 1 shows the placement of the blood pressure cuffs to determine the LOP of both lower extremities. For dynamic and isometric BFR exercises, around 50–80% occlusion for the lower extremities and 30–50% for the upper extremities should be performed.[1,17] Aerobic BFRT exercises are recommended at 40–50% of LOP/occlusion. Passive BFRT is recommended to be performed at 80–100% occlusion.[1,17]

Passive BFRT

Passive BFRT, also known as ischemic preconditioning or the passive cell swelling protocol, can be utilized when a patient is not yet mobile after an acute injury and/or during recovery from bouts of exercise when the patient is resting. This may be considered in cases where post-procedural pain prevents the performance of isometric or dynamic resistance training or in situations whereas a patient has muscle inhibition from effusion or other mechanisms seen with intra-articular injections of combination orthobiologics (e.g., bone marrow and lipoaspirate or platelet rich plasma). It is hypothesized that the occlusion causes cell swelling which creates a pseudo overload effect on the cells as they are technically stressed by the swelling. Goals of cell swelling include accumulation of lactate which increases growth hormone circulation and collagen synthesis, down regulation of myostatin, and increased recruitment of muscle fibers. It is recommended to perform passive BFR up to two times per day. Volume is recommended to be up to 5 sets of 5 minutes on with a 3-minute rest between sets.[17] During the rest time, the cuff should be deflated and other interventions may be performed, such as range of motion or manual soft tissue work. If performing for the first time it is advisable to perform only 2 sets of 5-minutes as a means of acclimating patient to BFR.

Isometric Training with Blood Flow Restriction

Isometric exercises can be combined with BFRT in stages where a patient has been cleared to begin strengthening but cannot move through a joint's range of motion or is experiencing pain or a low therapeutic tolerance to dynamic exercises. Isometrics can also be performed as a bridge between passive BFRT and dynamic exercises. A common exercise performed for patients who have undergone surgical procedures or sustained injuries to their lower extremities is quad sets (Figure 2). It is recommended to perform the exercises 1–2 times per day using a 5-minute duration for 5-sets with a 3-minute rest between sets with deflated cuff. When the cuff is inflated, the patient would alternate by performing isometrics for varying duration followed by set rest periods. For example, with a work/rest ratio of 3:1 or may simplify by performing 10-second isometric followed by 10-seconds rest. Two common isometric exercises that can be used with BFR are quad isometrics (quad sets) and elbow flexion isometrics (Figures 2 and 3).

Another option to explore at this stage is combining isometric exercise with neuromuscular electrical stimulation (NMES). NMES can also be combined with passive BFR or active movements such as isometrics or dynamic isolation movements. In this case, it is recommended for NMES settings to be set

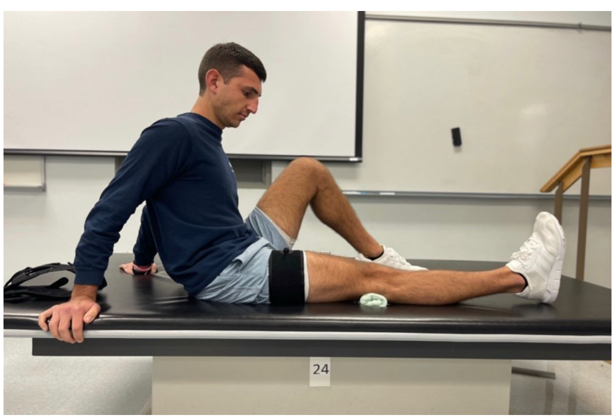

Figure 2. Quadriceps isometrics (quad sets) exercise with blood flow restriction cuff at proximal thigh.

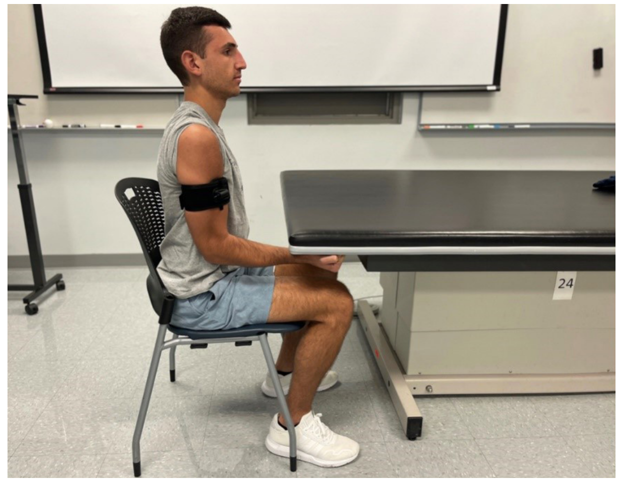

Figure 3. Elbow flexion isometric with blood flow restriction cuff at proximal arm.

at a frequency of 20 Hz, a pulse duration of 400 ms, and a work-to-rest ratio of three to one.[13] A meta-analysis by Coombes et al., included 4 comparative studies showing that NMES combined with BFRT elicits a significantly greater increase in skeletal muscle mass than control groups without intervention. This suggests that this combination of NMES and BFRT could provide a safe means of hypertrophy as a passive intervention but that more research needs to be performed to compare NMES plus BFR to BFR or NMES alone to make more conclusive statements on its effectiveness.[38] Moreover, evidence suggests that combining NMES with BFR using an on: off ratio of 3:1 seconds during an isometric quadriceps activity resulted in increased serum immunoreactive growth hormone secretions when compared to BFR without NMES.[13]

Dynamic Exercise (Isolated and Compound Movements)

Once the patient can tolerate low load resistance training, it can then be combined with BFRT to promote strength and hypertrophy adaptations. It has been shown that BFRT does not promote additional muscle adaptations when combined with high-load resistance training.[39] Teixeira et al., found that regardless of the BFRT protocol used, there were similar increases in maximal voluntary contraction, 1RM, and quadriceps CSA when comparing BFRT alone and high-load resistance training.[39] It is recommended to perform this type of BFRT 2–3 times per week with body weight or up to 15–50% 1RM when it is safe or based on patient tolerance. In cases where it is not convenient to estimate a 1RM, completion of desired repetitions may gauge the intensity. An estimated 1 rep max (RM) can be found using a 10RM test (Table 1). The patient can begin with isolated open chain movements such as leg extensions and shoulder external rotation and progress to compound closed chain exercises such as squats or push-ups (Figures 4 and 5). The patient should perform 4 total sets, with set 1 including 30 repetitions and sets 2, 3, and 4 including 15 repetitions.[17] There should be 30 seconds of rest between each set and at least 1 minute of rest before completing a different exercise. Slowly deflate the cuff at 10 mmHg increments after all 4 sets have been completed.

Table 1. Estimated 1-Repetition Maximum (1RM) Conversion

Calculating Estimated 1RM
Example: Goal is to do 30% of 1RM of squat using BFRT Patient was able to squat 135 lbs for 10 Reps 135 × 1.33 = 180 lbs estimated 1RM 180 × .3 = 54 lbs.

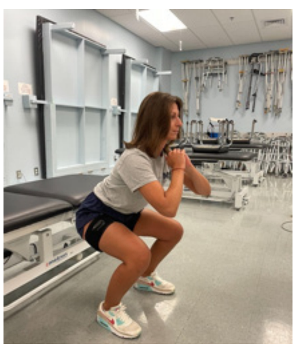

Figure 4. Squat exercise with blood flow restriction cuff at proximal thigh.

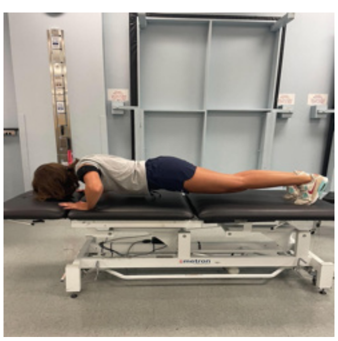

Figure 5. Push-up exercise with blood flow restriction cuff at proximal arm.

Aerobic

Aerobic capacity training can be performed by utilizing BFRT with aerobic exercise, such as treadmill, upper body ergometer, rower, and stationary bike. An example of cuff placement and individual performing BFR on a stationary bike is demonstrated in Figure 6. This method can be used for patients who can tolerate low-intensity (20–40% 1RM) loads of traditional exercise. Some benefits to using BFRT in combination with aerobic exercise include attenuating disuse atrophy, increasing muscle lactate tolerance, and increasing VO2 max demands. It is recommended to perform this type of BFRT for a frequency of 2–5 times per week at an intensity of 30–65% of the heart rate reserve (HRR). Begin the patient at lower intensities (30% HRR) for shorter amounts of total time (5–20 minutes) and gradually increase their intensity and total time to 65% HRR and 20 total minutes, respectively.

POST-PROCEDURAL CONSIDERATIONS

Owing to the synergistic effects of orthobiologic and BFR interventions, incorporation of BFRT may be considered early in the post-procedural phase.

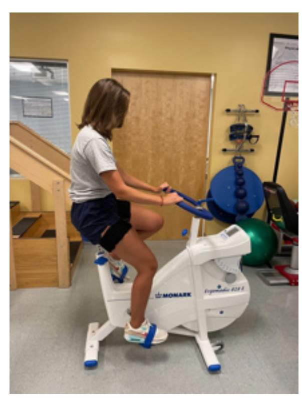

Figure 6. Stationary cycle utilizing blood flow restriction cuffs at proximal thighs.

While there are no scientific protocols published to date a reasonable and safe approach includes consideration of the patient diagnosis, co-morbidities, and post-procedural side effects or events. Since BFRT is often incorporated with exercise, the time since injection and pre-morbid activity levels should be considered.[40] Given the likelihood of variation amongst physicians in their post-procedural recommendations, BFR incorporation recommendations will be based on a milestone approach as opposed to week-based timelines.

After an orthobiologic procedure, return to activity considerations should be commensurate with the phases of healing and an individualized approach based on the specific patients' recovery. In the immediate post-procedural phase (0–3 days), patients are often prescribed active rest, and in some cases a sling or boot/brace may be implemented.[41] Active rest is generally movement as needed to complete ADLs and rest to allow healing. Ice and analgesics may be prescribed based on physician preference in this stage. While some physicians recommend avoiding ice and anti-inflammatory medications, it is the authors experience that ice and analgesics/anti-inflammatory medications allow an earlier return to activities.[42,43] In the authors' experience, it is best to avoid adding BFRT to a patients recovery in the immediate post-procedural phase as there may already be ecchymosis and swelling that is being managed physiologically and ideally, patients will return for a follow-up visit within the week to determine activity progressions.

In the late-acute and early subacute phases of healing, it is important to stimulate anabolic responses and begin efforts to mitigate muscle morbidity. In this stage, passive BFRT may be performed for 1–2 sessions using a 5-minute duration for 2 sets. This will allow patients to acclimate to BFRT and prepare them for the next phase of BFRT with isometrics. If isometrics are contraindicated, it is advised to continue passive BFRT for 5 minute sessions increasing the sets to 3–5 times each for 5 minutes. Please note the cuff should always be deflated between sets when applying passive BFRT.

Early progression into the sub-maximal isometric phase is recommended with the goal of progressing to maximal effort isometrics as appropriate into the early sub-acute phase. For isometric training, the authors recommend performing the exercises at a frequency of 1 time per day using a 5-minute duration for 5-sets with a 3-minute rest between sets with cuff deflated. When the cuff is inflated the patient would alternate by performing isometrics for varying duration followed by set rest periods. A work/rest ratio of 3:1 (or may simplify by performing 10 second isometric followed by 10-seconds rest) is recommended. In cases where a patient has their own BFR cuffs, the frequency may be increased to twice a day. One consideration that would likely increase the benefit is to use electrical current to the muscle being contracted to increase muscle activation. Incorporating electrical stimulation may be advantageous in cases where a patient has joint effusion or difficulty recruiting motor units. The electrical current, often referred to as Russian stimulation or NMES, would be set to turn on during isometric contraction and turn off during rest. As stated previously, the cuff should be fully deflated between sets.

Once it is appropriate to perform low-resistance progressive dynamic exercises, the BFR cuffs should be utilized 2–3 times per week with body weight (push-ups or squats) or up to 15–50% 1RM when it is safe to do so, or based on patient tolerance and stages of healing. An estimated 1 rep max (RM) can be found using a 10RM test (Table 1). The patient can begin with isolated open chain movements such as leg extensions or shoulder external rotation and progress to compound closed chain exercises such as squats, leg press, or push-ups (Figures 4 and 5). In cases where it is not convenient to estimate a 1RM, completion of a weight or resistance that allows 4 total sets, with set 1 including 30 repetitions and sets 2, 3 and 4 including 15 repetitions should be prescribed. It is strongly recommended to avoid heavy loading and intense training with BFR cuffs, as once a patient can progress to pre-injury training levels BFRT may be discontinued or be used for recovery days.

Lastly, during the post-procedural recovery phases, BFR may be used for activities such as stationary cycling, treadmill, elliptical, or upper body ergometer. Generally, these activities may be initiated in line with the phases where sub-maximal isometrics are introduced. Times range typically from 5–20 minutes and while the benefits of movement and aerobic training are well known, additional benefits may be derived with the addition of BFR cuffs. Readers seeking more detailed post-procedural guidelines refer to specific publications that outline staged post-procedural interventions from the perspective of a case report and narrative review.[40,41]

ADVERSE EVENTS

Since its conception, BFRT has been an efficacious intervention to improve fitness and therapeutic outcomes with a relatively low risk of adverse outcomes. Absolute contraindications for BFRT have not yet been established since it is a relatively new therapeutic intervention in clinical practice, which limits the ability to definitively determine precise evidence-based precautions and contraindications.[44-46] To clarify the safety of BFRT, Anderson, Rask, and Bates conducted a thorough literature review consisting of ten case reports, five case series, two national surveys, two questionnaires, six randomized controlled studies, and one systematic review.[44] From the studies analyzed, 1,672 people were reported to have an adverse event after undergoing BFRT out of 25,813 people. The most commonly reported adverse events that occurred in people that underwent BFRT were extremity tingling, delayed onset muscle soreness (DOMS), subcutaneous hemorrhaging, and rhabdomyolysis[44,47]

In a cross-sectional study consisting of 113 professionals in the fields of physical rehabilitation and exercise science, the health professionals reported using BFRT on multiple age groups ranging from youth (≤18 years), young adults (20 to 29 years old), and older adults (60–80 years old).[47] The Health professionals within this study reported that only 3.5% of youth, 74.6% of young adults, and 30.7% of older adults they saw in their respective fields were subjected to BFRT. Furthermore, 99.1% of professionals participating in this study stated that BFR was combined with resistance exercise. About 60.9% of professionals utilizing BFRT reported using BFRT for less than 5 minutes. Professionals within the study determined LOP only using brachial blood pressure to determine the intensity of all resistance and aerobic exercises for individuals deemed appropriate to undergo BFRT. Regarding numbness and tingling, the health professionals reported seeing 71.2% of individuals that underwent BFRT experience these symptoms. Despite reporting numbness and tingling occurring in subjects that underwent BFRT, professionals in this study stated that numbness and tingling disappeared once pressure was released from the blood pressure cuffs.[47] A possible explanation for numbness and tingling disappearing once pressure is released from blood pressure cuffs can be seen in a study conducted by Clarke and colleagues.[48]

A study conducted by Clarke and colleagues consisted of 16 young healthy adults (ages 18–30) performing 4 weeks of bilateral knee extension exercise for 3 days a week.[48] The 16 young adults were split into light-intensity BFRT and high-intensity exercise groups. The high-intensity group performed bilateral knee extension at 80% of 1RM for 3 sets with repetitions ranging from 8–12 repetitions (2 second concentric and 2 second eccentric) as needed to achieve volitional failure (training until the individual can no longer perform another repetition) with 90 seconds of rest between sets. Individuals within the BFRT training group performed the same protocol except bilateral knee extension at 30% of their 1RM with the blood pressure cuffs inflated to 130% above their resting brachial SBP. Weight was progressively increased for both groups as needed throughout the 4 weeks, to ensure all participants trained to volitional failure when they had increased strength. Individuals within the BFRT group reported experiencing acute bouts of numbness and tingling, when performing bilateral extension under BFR. However, once the pressure of the cuffs was released, individuals within the BFRT group no longer had these symptoms. Clarke and colleagues suggested that the acute bouts of numbness and tingling experienced within the BFRT group, can be due to a possible nerve conduction block when undergoing BFR with resistance exercise. As a result, Clarke and colleagues found this possible side effect of BFRT to be relatively safe since it had no chronic effect on nerve conduction in a 4-week program.[48]

Concerning DOMS experienced with BFRT, this particular report or symptom should not be a major concern for health professionals since BFRT induces muscle damage, and most participants that underwent BFRT were not used to exercise.[47] DOMS was found to usually disappear within a few days, as the individuals subjected to BFRT became accustomed to the physiological and biological demands of BFRT. Professionals reporting cases of subcutaneous hemorrhaging with BFRT stated that the subcutaneous hemorrhaging was transient and resolved quickly even if individuals continued their training session.[47] An effect that wasn't reported by Anderson and his colleagues but was reported to be seen by the cross-sectional study conducted by De Queiros and his associates was fainting.[47] Regarding witnessing individuals faint from BFRT, healthcare professionals found fainting to be linked to the decrease in venous return induced by BFRT, which can cause a reduction in cardiac preload, which can lead to decreased blood flow to the brain.[47,49]

Although there have only been a few cases of rhabdomyolysis occurring with BFRT, the possibility of rhabdomyolysis occurring with BFRT should not be neglected due to the seriousness of this particular condition. Rhabdomyolysis is a condition where the breakdown of muscle tissue leads to the release of muscle fiber contents into the blood, which can lead to serious kidney damage.[50] The key indicator medical professionals use to determine if an individual has rhabdomyolysis is creatine kinase levels (CK). Normal CK levels are found to be between 45–260 U/L, but when an individual has rhabdomyolysis, these levels can be between 10,000–200,000 U/L.[51] In a case report conducted by Iversen and Rostad, a 31-year-old ice hockey player underwent BFRT to induce hypertrophy and strength in his right quadricep 11 months after knee articular cartilage resection due to a microfracture.[52] In the initial treatment session, the patient performed a 10-minute warm-up on a stationary bike and then performed a single leg extension. The patient performed 12 kg for one set of leg extensions for 30 reps followed by 4 sets of 15 repetitions with the same weight and had a rest period of 45 seconds between sets. The patient performed all leg extension sets under BFR with a 14 cm cuff inflated to a pressure of 100 mmHg for the entire exercise duration. Two days after the initial treatment session, the patient developed extreme muscle soreness in his right quadricep and was admitted to the hospital. Upon examination, the patient did not have a deep vein thrombosis (DVT) but had a CK level of 12,400 U/L. The patient was diagnosed with rhabdomyolysis as a result.[52] Clark and Manini analyzed a case report in which a healthy sedentary 20-year-old male participated in a BFRT research study of kidneys.[50] Before participating in the study, the young male completed 2 strength testing sessions. Based on his strength testing, the subject performed BFRT consisting of 3 sets of bilateral knee-extension along with 3 sets of BL elbow flexion at 25% intensity, with the BFR cuffs inflated to 167mmHg. In the first set the subject was asked to complete 30 repetitions and for the 2nd/3rd sets to do until volitional failure. The subject had 30 seconds to recover between sets and had the blood pressure cuff inflated for the entire duration of the exercises. 48 hours after the initial BFRT session, the subject sought medical care due to having a 7.5 out of 10 pain in his thigh and had difficulty ambulating. After seeking medical care, the subject had a CK level of 18,022 U/L and was hospitalized for rhabdomyolysis.[50] In a case report conducted by Tabata, Suzuki, Azuma, and Matsumoto, a 30-year-old obese male with no serious health history developed rhabdomyolysis after performing 3 sets of 20 repetitions of squats for his first day of training after being sedentary since he graduated from university.[53] After completing his first BFRT session, the subject had pain in his upper and lower extremities, accompanied by a fever and pharyngeal pain. The following evening, the subject was admitted to a hospital due to worsening muscle pain and myoglobinuria. After obtaining lab results, the patient had a serum CK level of 56,475 U/L and was diagnosed with rhabdomyolysis.[53] Fortunately, rhabdomyolysis is a rare occurrence in individuals that performed BFRT. Nonetheless, it is important for health professionals not to neglect the possibility of this occurring with any exercise.[44,45,47] To avoid the possibility of rhabdomyolysis, it is suggested that healthcare professionals perform the most conservative parameters of BFRT to allow individuals of various activity levels to get accustomed to this style of training. By doing so, this will reduce the amount of muscle damage induced by BFRT and allow individuals that undergo BFRT to have adequate recovery between training sessions. Healthcare professionals should not have individuals perform exercises to volitional failure like in the case report conducted by Clark and Manini, since this has been linked as the main aggravating variable for exercise induced muscle damage.[47,50]

Due to the nature of BFRT, the literature review conducted by Anderson and his colleagues found that when BFRT was implemented in a patient who has a co-morbidity or condition that compromises the circulatory system such as diabetes, thromboembolisms, atherosclerosis, or hypertension, individuals may have an increase in developing adverse effects when undergoing BFRT.[44,47] When implementing BFRT, these conditions have served as precautions for healthcare professionals when utilizing this therapeutic intervention, since these conditions can potentially cause stasis and increase the rate of thrombogenesis within an individual. However, a study conducted by Clark, Manini and Hoffman, as well as a study conducted by Madarame and Kurano, did not identify any negative effects of BFRT in hemostasis when appropriate BFRT parameters were followed.[48,54]

In the authors' experience, many healthcare professionals express concerns over BFR and the potential risk of a DVT due to the external compression and occlusion of the venous system. While this and any other adverse events require serious monitoring, the risk of a DVT is physiologically low, provided guidelines are adhered to and people with known risk factors for DVT are excluded from this treatment. In fact, acute studies have not demonstrated an increase in D-Dimer, prothrombin fragment, and thrombin-antithrombin III complex following BFRT, suggesting minimal to no changes in coagulation profiles outside of normal clinical ranges.[48,55–57] Studies looking at chronic models of repeated BFR application reported no changes in D-Dimer and fibrinogen, as well as unremarkable duplex ultrasound scans for DVT.[48,49,56,58,59]

In summary, patients can participate in a BFRT program when they are deemed medically appropriate, when appropriate BFRT parameters are followed, and when monitored by healthcare professionals who recognize the potential risk factors and signs and symptoms of an adverse event of individuals that are performing BFRT.

PRECAUTIONS/CONTRAINDICATIONS

Healthcare professionals are often made aware of contraindications for BFRT based on certification course recommendations,[17] which are grounded in concepts related to the presence of vascular conditions (e.g., age-related risk, arterial disease, venous insufficiency, and bleeding disorders, etc.), co-morbidities, and overtraining. To reduce the risk of adverse events from BFRT, practitioners must pay attention to diagnostic findings, the medications their patients are taking, and conditions the patient has that would make them inappropriate for BFRT. Table 2 is an example of possible diagnostic findings, contraindications, and medications that may indicate an individual is at high risk for an adverse response to BFRT. Table 3 provides a point system used by the Smart tools BFR course to help healthcare professionals determine whether an individual is appropriate for BFRT.[17] While Tables 2 and 3 have not yet been validated, they can still offer direction for practitioners determining an individual's risk category.

CONCLUSION

The utilization of BFRT in both the general and symptomatic populations is growing in popularity due to promising cellular and molecular changes that were once only thought to be achieved with high-intensity exercise. BFRT, when utilized appropriately, allows individuals to experience similar benefits of high-intensity training from low-intensity/lower load training. The benefits of BFRT are most promising amongst those individuals with a low exercise tolerance due to injury or co-morbidities and patients with post-procedural

Table 2. Diagnostic Findings and Contraindications for Blood Flow Restriction Training

Diagnostic Findings	**Contraindications**
Poor circulation	Acidosis
Poor capillary refill time	Cancer
Varicose veins	Extremity with dialysis port
Abnormal clotting times	Excessive swelling in post-surgical limb, most often UE (lymphedema)
Atherosclerotic vessels	Infection within extremity
Arterial calcification	Increased intracranial pressure
Diabetes	Impaired circulation
Cardiopulmonary conditions	Lymphedema (on Limb)
Hypertension	Open fracture/open wound
Infection	Pregnancy
Sickle cell trait	Previous revascularization of limb
	Sickle cell anemia
	Severe hypertension
	Severe crush Injury
	Vascular graft
	Venous thromboembolism
	Mastectomy (on affected arm)
	Hemodialysis with arterial venous fistulas
Medications	
Anti-hypertensive, Anti-coagulants, Any medication that increases clotting risk	

**Adapted from SmartCuffs® Course manual p. 69 with permission. The authors of this paper also recommend avoiding BFRT for any patient with an un-healed fracture*

Table 3. Safety Recommendation Point Scale

1 Point	**2 Points**	**3 Points**	**4 Points**	**5 Points**
Age 40–59	Age > 60	Varicose Veins	Pregnancy	History of deep vein thrombosis
Female gender	BMI > 30 Kg/m^2	Prolonged inactivity		Acute sickness or Fever
BMI 25–30 Kg/m^2	Malignancy	Atrial fibrillation		Blood pressure > 180/100 mm Hg
	Hyperlipidemia	Heart failure		Early post-operative period
	Oestrogen therapy	Blood Pressure 160–179/95–99 mm Hg		Higher class arrhythmia or coronary ischemia

**Adapted from SmartCuffs® Course manual p. 70 with permission. It is recommended that any individual scoring greater than 4 points on the criteria be excluded from blood flow restriction training.*

precautions precluding high-intensity exercise. Healthcare providers treating patients with conditions or situations precluding high-intensity exercise should consider augmenting their patient management model with BFRT. Despite the well-established benefits of BFRT, healthcare providers should recognize that the patient population is heterogeneous, and individual programming should consider both the diagnosis and previous treatments. Patients who are in the post-operative and post-procedural phases of care should progress gradually to ensure tolerance with the absence of side effects. It is recommended that healthcare providers receive formal education on applying BFRT as with any treatment modality to ensure efficacious and safe application. Lastly, clinicians treating musculoskeletal injuries should always consider clinical guidelines and current concepts evidence to design a comprehensive plan of care for their patients.[60]

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