Capstone: Blood Flow Restriction in Older Adults

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Statement of Need

 As adults age, there is a tendency towards inactivity that results in a loss of maximum explosive power and strength, reducing their ability to respond to sudden losses of balance or meet the demands of daily living.1 For every decade after the age of 30, an estimated 3-8% of muscle strength and endurance is lost with inactivity.2 This loss of strength is the result of a changing metabolism as well as daily activities, but it can be attenuated with resistance training.2 The health benefits of resistance exercise are especially to older adults, as it can attenuate muscle loss, bone loss, and has protective effects against diabetes, and over all causes of mortality.1,2 However, resistance training in older adults can pose novel difficulties, as many may be returning to exercise post-surgery, or with levels of frailty that make traditional resistance training too difficult to demonstrate hypertrophy and strength gains. The LIFTMOR trials clearly demonstrated the safety and efficacy of high load resistance training, but largely amongst healthy adults with no injuries.3 However, not every adult may be able to safely function at such a high level immediately. High intensity training may not be tenable due to potential cardiac issues, osteoporotic conditions, or advanced sarcopenia, or simply lack of training with resistance training. The LIFTMOR trials, while successful, spent 4 weeks training their participants in traditional lifting technique and form, and monitored their participants for over 8 months to insure proper form.3

 Blood Flow Restriction combined with low load exercise is a novel intervention that has risen in popularity in the last decade because of its ability to demonstrate comparable strength and hypertrophy gains with high load intensity training.4,5 Rather than having to train at 70-80% 1 RM, BFR allows individuals to train at 20-30% 1RM while still gaining hypertrophic and strength benefits. While there is an abundance of data concerning the usefulness of BFR in younger individuals and athletes, such data cannot necessarily be applied to older adults because of their differences in physiology and potential comorbidities. Thus, separate data about concerning the safety and efficacy of BFR when combined with low load resistance training must be collected.

Proposed Mechanism of Action

 The typical mechanism of action for muscle hypertrophy revolves around moderate to high intensity resistance exercise with progressive overload.6 Blood Flow Restriction (BFR) is a novel intervention that involves reducing blood flow to an actively working limb as it performs low load intensity exercise.7 To be specific, venous outflow is inhibited while maintaining arterial inflow, that generates a hypoxic environment over time and drives anerobic metabolism.7 The exact mechanism of BFR’s action is as of yet unknown, and there are a variety of theories, including but not limited to: 1) changes in hormonal concentrations, 2) increases in intracellular components signaling muscle hypertrophy pathways like the mTOR pathway, 3) changes in fiber recruitment patterns, 4) increases in generative satellite cell activity, 5) increased anerobic metabolism, 6) and cellular swelling.6,7

 There are numerous proposed mechanisms of action, but three prominent ones focus on the changes in recruitment and changes in hormone production. The first posits that BFR preferentially recruits Type II fast twitch fibers due to the hypoxia of the environment.7 BFR generated a 1.8x muscle recruitment compared to controls in quadriceps tissue following knee extension exercise, with a compression over 200 mmHg.8 Type II fibers are more heavily recruited in a hypoxic environment, and driven to perform more vigorously, and this increased mechanical stress may be contributing to hypertrophy. There is also evidence to suggest that tissue hypoxia may drive new hormone synthesis; following BFR exercise, patient demonstrated almost 300x more growth hormone when compared to controls, even 24 hours after exposure to exercise.8 It is thought that the accumulation of cellular waste products, such as K+, H+, or lactate may change GH secretion rates, but it is not yet clear if these factors are initiatory in the cascade, or even if the presence of these hormones is contributing to localized growth of the muscle or not.6,7  However, it’s worth nothing that blood flow restriction *without* exercise has no impact on Growth Hormone levels, indicating they may still play a role.6 The third and final theory suggests that BFR increases the activity of mammalian target of rapamycin.9 This increased activity would increase cell proliferation, protein synthesis, and cell growth, all of which would contribute to hypertrophy.9 There is evidence to suggest that the downstream product of increased mTOR activity, S6K1, is also increased following BFR with resistance exercise, suggesting that there is a similar mechanism of action in humans as well as rats.10

 A final and important consideration in the mechanism of BFR relies on satellite cell activity. These cells are located beneath the basal lamina of muscle fibers, and are responsible for muscle regeneration and muscle hypertrophy.11 It is established that satellite cells are necessary for muscle hypertrophy, and that eccentric exercise promotes their proliferation.11 While it seems unlikely that BFR with its lighter loads would be stimulating satellite cell activation, there is evidence that the number of visible satellite cells in BFR tissue increases by 33-53% in the 48 hours post exercise.12 This particular study relied upon monitoring *active* satellite cells, and thus an increase in visible satellite cells represents an increase in satellite cell activity.12 What’s particularly fascinating is that this was the case in *both* legs,12 matching other reports that BFR promotes hypertrophy and strength in untrained limbs.6,7 This may suggest a more globalized hormone response, or BFR’s involvement with more neural pathways. This would be matched by data that BFR reduces MVC immediately following training,12 as well as the increased recruitment of Type II fibers;8 there are both neurological changes, and may be related to improvements on the untrained side, but there is no such evidence to confirm that conclusion.

 There is still some mystery to the exact mechanism of BFR; it’s clear that it generates changes in local hormones, including GH, as well as changes in recruitment of Type II fibers.6–8 It also increases the activity of the mTOR pathway,9,10 and promotes increases in satellite cell activity. How it is able to communicate changes to the untrained legs is as of yet still unclear, but beyond the scope of this paper.

Effects of Blood Flow Restriction on Hypertrophy, Strength in Older Adults

Given Blood Flow Restriction’s popularity as an up-and-coming modality, it is particularly important to know the strength of its outcomes. BFR set ups are complex and require specific equipment, so any investment of cost must have an equal or appropriate ‘pay-off’ in patient results. There are a variety of exercises that could be combined with BFR, including walking, resistance band training, and low-load resistance training. To properly assess the utility of BFR when combined with exercise, this paper will provide a brief discourse on known effects and outcomes for each intervention.

Walking Interventions

 Walking programs combined with blood flow restriction on one, or both legs appear in the literature with some frequency; of the 27 papers initially assessed, 5 included walking as their target intervention.13–17 Walking protocols have been found to increase strength, ranging from 3% to 21%. The greatest strength increase was found in the longest studying, suggesting strength improvements may continue well beyond a standard 8 week protocol.

 These walking studies also include assessment of functional outcomes. The experimental BFR-walking groups demonstrated improvements in Up&Go times, as well as the 30STS. The 30STS has an MDC of 3 reps in individuals with Parkinson’s, and 2 reps in individuals with COPD.18,19 The Clarkson and Ozaki papers reported an average increase of 6 and 4 reps, respectively, making these changes well within the sensitivity of these outcome measures. Only three studies reported strength changes in knee extension using a dynamometer, and at six weeks, reported an average of a 9.27% increase in knee extension torque compared to pre-trial values. 14,15,17

 The most important conclusion to take away from the combination of walking and BFR in combination is that increases in strength and functional outcomes occur within 6 weeks, when compared to inactive as well as walking control groups. These studies all used fairly high pressures, and had high frequencies which likely contributed to their success. BFR-Walking interventions may be appropriate in an acute rehab setting, where resistance training and equipment may not be as available, but a controlled walking space is.

Table 1: BFR Walking Protocols in the literature reviewed.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Author | N | Duration, Frequency | Occlusion Pressure | Walking Intervention  | Placement of Cuff | Outcomes | MVC |
| Natsume et al | 18 | Cross Sectional | 100 mmHg | Treadmill 20 min, 3-4 km/H | 33% Below Inguinal Crease | Acute increase of thigh musculature by 1 mm, Maximal isometric strength acutely decreased by an average of 8 Nm | -5.2% in the 20 minutes following intervention |
| Clarkson et al | 19 | 6 weeks,4x week | 134 +/- 4 | 10 min on track, 4 km/H w/ CON walking | Inguinal Crease | Both groups had increased steps, and improved strengthcompared to baseline. Difference TUG between CON an BFR by almost 1 sec at 6 weeks. 3+ reps in 30 STS at 6 weeks.  | NA |
| Abe et al | 19 | 6 weeks, 5x week | Progressive\*160 mmHg, 10 mmHg increase weekly to 200 mmHg.  | 20 min, 4 km/HControl group not walking.  | Inguinal Crease | Thigh CSA increased by 5% post 6 weeks, and 1.7% increase in mid thigh girth. 11.8% increase in isokinetic knee extension.  | NA |
| Ozaki et al | 18 | 10 weeks, 3x week | Progressive\*140 mmHg, 100 mmHg increase per week, to 160-200 mmHg.  | 20 min at 45% HRR reserve; The mean treadmill speed and grade were 4.5 ± 0.0 km/h and 1.6 ± 0.4 degrees in the BFR-Walk group and 4.4 ± 0.1 km/h and 1.5 ± 0.5 degrees in the CON-Walk group.  | “Most Proximal Leg”  | 3% increase in muscle CSA in BFR, 0.1% in CON, 3.7% increase in muscle volume, and 5.9% increase in isometric knee torque. 10% decrease in Up&Go times, and 20% increase in 30 STS reps.  | NA |
| Pereira et al | 20 | 12 weeks, 2x week | 80% full occlusion pressure.  | 65% Maximum HR, treadmill walking for 15 min.  | Proximal 1/3 of thigh | The Walking group had a 21.6% increase in maximum dynamic strength in 12 weeks, compared to 38% in HI, and 24% in LIBFR. A 10.1% increase at week 6.  | NA |

\*All values included were statistically significant.

Resistance Training Interventions

 Current literature assesses strength of the LE, including the quadriceps, hamstrings, and combined motions in the form of a leg press.4,5,20–22 Outcomes for strength are typically measured in 1RM, and iso-kinetic dynamometry measurements are not common. Muscle cross sectional area (mCSA) is another common outcome measure, either by ultrasound assessment or MRI. Two studies included in this review by Cook et al included assessments of maximum voluntary contraction.

Outcome measures come in the form of strength, muscle cross sectional area (mCSA, or CSA), and maximum voluntary contraction (MVC). The literature is of the consensus that LL-BFR has similar effects on mCSA and strength as compared to HL strength training.4,5,20–23 Walking when combined with BFR has also been found to promote increased torque and mCSA in older adults.14 However, the exact extent of these benefits is unclear.

 Cook’s 2017 paper concluded that BFR generated a 7.8% increase in quadriceps CSA, compared to a HL’s 6.5% (Figure 1).4 While quadriceps CSA increased more in BFR than in HL, hamstring CSA did not, though by only a 0.5%. This difference is statistically significant, but in terms of functional outcome, this 0.5% difference may not be noticeable when it comes to functional capacity.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Authors | N | Duration, Frequency | Exercises | BFR Intervention | HL | Change | CSA | MVC Changes |
| Cook et al, 2017 | 36 | 2x week, 12 weeks | LE, LC, LP | 2x 30 at 30% 1 RM + BFR with 184±25 mmHg, 66% Occlusion | 2x 15 at 70% 1 RM | HL: 31.7% increase in 1RM LP at 12 weeksBFR: 18.7% increase in 1RM LP at 12 weeks | HL: +2.86% BFR: +3.23% of Quads | 6 weeksHL: +20%BFR: -0.4%12 WeeksHL: 19.3%BFR: 11.2% |
| Cook et al, 2019 | 21 | 2x week, 12 weeks | LE, LC, LP (LP not reported)  | LE, LC at 2x 30 at 30%1 RM + BFR LP at 50% 1RM + BFRWith average 184±25 mmHg, 66% Occlusion | 2x 15 at 70% 1 RM | HL: 59% increase in LE 1RM at 12 weeksBFR: 35.8% increase in LE 1RM at 12 weeks  | HL: +6.5% BFR: +7.8 | HL: +23.1%BFR: +11.0% |
| Vechin et al, 2015 | 23 | 2x week, 12 weeks | LP | 1x 30, 3x 15 at 20% 1 RM for 6 weeks, then 30% 1RM for 6 weeks, with average pressure 71±9 mm Hg  | 4x 10 at 70% 1 RM for 6 weeks,4x 10 at 80% for 6 weeks | HL: 54% increase in LP 1RMBFR: 17% increase in LP 1RM\* | HL: +7.4%BFR: +5.9% | NA |
| Libardi et al, 2015 | 25 | 4x week, 12 weeks | LP | 1x30, 3x15 at 20% 1 RM for 6 weeks, 30% 1RM for 6 weeks67 ± 8.0 mmHg. 50% occlusion pressure.  | 4x10 at 70%1RM for 6 weeks80%1RM for 6 weeks | HL: 38.1% increase in LP 1RM BFR: 35.4% increase in LP 1RM.Not statistically different | HL: +7.3%BFR: +7.6%Not statistically different | NA |
| Yasuda et al, 2013 | 21 | 2x week, 12 weeks | LP, LE | 20-30% 1 RM with 75 reps split into 30, 20, 15, 10.120 mmHg. The pressure was increased by 10–20 mmHg at each subsequent training session until a pressure of approximately 270 mmHg was  | Performed daily ADLs | CON: NBFR: 26.1% increase in LP | CON: -0.5%BFR: +8.0% | NA |
| Karabulut | 37 | 6 weeks | LP, LE | 2x15 10% 1RM | Daily ADLS, RT80%  | CON: NBFR: 31.2RT80: 20.4 |  |  |

LE: Knee Extension

LC: Knee Flexion

LP: Leg Press

1RM = 1 Repetition Maximum

MVC = Maximum Voluntary Contraction

HL: High Load

\* = Accounting for Effect Size

Current Guidelines for Blood Flow Restriction, including pressure, duration, frequency

Frequency of Occlusion Pressure Used

 There are currently no standardized norms for occlusion pressure, duration, or frequency for Blood Flow Restriction. In the literature, occlusion pressure can be defined as the pressure itself. Some studies determine the pressure based upon the ‘percent occluded,’ which is in reference the amount of blood flow detected at arteries downstream of the femoral artery, including the tibial anterior artery. This reduction in volume is measured with a doppler scanner. The lowest occlusion pressure used in the surveyed literature was 50% occlusion pressure, in the works done by Libardi and Vechin.5,21 Both Vechin and Libardi found that LL-BFR was comparable to high load resistance training in its strength and CSA outcomes. So, while there may be more, or less benefits at high pressures, practitioners should have a minimal guarantee of 50% occlusion pressure. Vechin and Libardi’s average pressure was 67-71 mmHg, which are the lowest pressures in the literature surveyed. In a survey of 25 articles, 19 reported pressures rather than % occluded, with a mean of 155.5 mmHg.

 **Literature Consensus on Occlusion Pressure: 50% occluded minimum or 150 mmHg.**

Percentage 1RM for LL-BFR

 While Low Load is considered a key principle for concurrent training with BFR, there is also some variability in how this manifests in the literature. However, typical low load as it is defined, and as it appears is 20-30% 1 RM. Libardi, and Vechin all utilized 1 RM Test to determine a participants 1 RM prior to intervention, and retested participants halfway through their program to increase load as necessary. Both of the Cook studies relied upon 1RM predictions, based upon a the Haff and Triplett equation for determining 1 RM.

 **Literature Consensus on 1RM Percentage LL-BFR:: 20-30%**

Frequency and Duration of Protocol

 The majority of studies in the literature last anywhere from 8-16 weeks, for 2-5 sessions per week. Given that muscle hypertrophy requires a minimum of 8 weeks to appear, any protocol monitoring hypertrophy must be a duration of 8 weeks or longer. When it comes to programming and intervention with patients, explaining the timeline of expected gains is key to managing patient expectations, and patient maintaining buy-in. Current research suggests that strength gains prior to these 8 weeks are neurological gains, reflecting changes in recruitment and increased efficiency of existing musculature. Interestingly enough, Cook’s 2017 paper found that the LL-BFR group did not experience these neurological gains until the second half the study, suggesting that BFR delays neurological gains.4 This suggests that any BFR protocol must be at least 6 weeks, and may see delayed results. As the Cook study only measured results at 6 and 12 weeks, it is unclear at what point the neurological gains appeared, but only that they appeared within a 6-12 week window. Therefore, to be certain in hypertrophic and neurological gains, it is recommended that BFR program last 8-12 weeks at minimum.

 Frequency varies in the literature. However, in a 2017 systematic review of 12 studies, with a weekly frequency that varied from 2-3x a week, and each of these studies found a statistically positive effect of LL-BFR on strength outcomes. Based upon these 12 studies, Cardoso et al recommended that BFR protocols met with a frequency of at least 2-3 per week to achieve and maintain benefits.22 However, simply because this is the most popular frequency does not necessarily mean it is the most ideal, but that it is the most attainable. Research attempting to differentiate between different training volumes and frequencies has not yet been performed.

 **Literature Consensus on Minimum Duration of Protocol: 8-12 weeks, 2-3x week.**

Observations Concerning Maximum Voluntary Contraction

 Maximum Voluntary Contraction is a measure of the maximal force that can be exerted by a muscle, typically assessed with an isokinetic dynamometer with three trials that are averaged. In both Cook papers, MVC gains were less in the BFR group when compared to the HL (+11.0, +11.2 vs 23.1%,19.3). Even more interesting is that these MVC values differed at 6, and 12 weeks. At 6 weeks, the HL group demonstrated a 20% increase in MVC, while the BFR group demonstrated -0.4% MVC.4,24 This suggests that BFR may have an impact on the neural component of strength. Natsume et al, while not performing a resistance training program, found that MVC following BFR intervention demonstrated a 5.2% decrease in the 20 minutes immediately after, indicating that BFR may acutely decrease MVC while also having chronic effects.13

 Utilizing the Cook date, it’s observable that MVC gains did progress in the second 6 weeks, rising from a negative value to approximately 11%. While most neural gains typically happen early in strength gains, where improved recruitment manifests as improved weight lifted, Cook’s data suggests that neural gains may be delayed.

 Yasuda et al also assessed impact of BFR on MVC, utilizing resistance band loading rather than resistance training, making the amount of load difficult to assess.25,26 Participants performed a similar protocol, utilizing band intensities theoretically correlating to 20-30% 1RM, and also underwent MVC testing. They found that MVC values of the knee extensors increased 13.7% (p value of 0.028) in the BFR group compared to pre-protocol values, making the data somewhat compelling. However, they did not perform MVC testing as 6 weeks, making it impossible to know if there was a similar pattern. This is particularly compelling, as both Cook and Yasuda had identical frequency and duration; 2x, for 12 weeks, and both found MVC increases ~10%.4,24–26

 What differs between Cook and Yasuda’s work is the MVC of the HL group. Cook found that MVC was markedly increased in the high load intensity, while Yasuda found no such gains. However, Yasuda’s data for the HL group was not statistically significant (p = 0.196), making it inappropriate to compare. Luckily for this paper, the impact of HL resistance band training on MVC is not within the scope of this topic.

 Clinically, this data has two key implications. Strength gains may be delayed when utilizing a BFR training load, as neural and hypertrophy gains will be back-loaded to appear in the 6-12 weeks after beginning training. Patients should be counseled that gains may not be as visibile or noticeable during those first 6 weeks, and assured that slower gains are normal. Secondly, individuals undergoing BFR have reduced MVC, and therefore reduced ability to contract and support themselves following a perturbation or loss of balance. Immediately following intervention, participants may be less stable, and are therefore at higher risk for falls. This may mean that participants be cautioned against performing dynamic activities following intervention, or even participate in a cool down program to potentially allow MVC recovery. Further evidence is required to understand the difference in MVC values between groups.

Only three articles included in this assessment reported MVC values, indicating that these conclusions require more

Risks and Precautions with Blood Restriction in Older Adults

Considerations in Reviewing the Literature

Falls Risk

 Falling is considered one of the greatest threats to the elderly; individuals who fall are at risk for fractures, hospitalizations, and may never return to their previous full function, decreasing their quality of life and increasing the support required by the healthcare system.27 Falling is thought to increase with age, due to changes in the nervous system such as decreased proprioception, as well as physiological changes, including decreased maximum power capacity.2 Muscle power, the ability to respond with maximum strength in a short period of time, is thought to be a key skill for the ability to respond to perturbations, and prevent a fall.28 What’s more, once an individual has fallen, their risk for recurrent falls increases; falling is a compounding problem that taxes the older adult and the healthcare system.27 Resistance training has been demonstrated the capacity to increase muscle strength, as well as the rate of force production (power) by on average, 8% in older adults, even with a spectrum of sessions per week, repetitions, and intensity. Resistance training, even in small doses, has statistically significant impacts on power production, suggesting it has the capacity to reduce falls risk.29 In particular, high load resistance training is thought to reap the most benefits in terms of power. However, there are some concerns in prescribing high load resistance training to older adults, namely the increased risk of injury using high weights, a lack of familiarity with exercise, and increased frailty with old age. Thus, there has been a search for an exercise regime that provides the benefits of high load resistance training with fewer risks; blood flow restriction when combined with low load resistance training has been suggested to meet this particular niche. However, while BFR has demonstrated strength and hypertrophy gains, it’s the consensus of the literature on BFR’s impact on falls risk is still unclear.

 A systematic review from 2020 sought to answer this particular niche question. It included studies with participants over the age of 60, with interventions lasting longer than 4 weeks, and an intervention group of BFR training with low load resistance training, and a control group. A total of 8 studies were included in the review, with a total of 234 participants assessed.27 Two the studies reported a statistically significant improvement in the 30 second-sit-to-stand in the experimental group, with an increase of 2.6 (±3.4) to 4.0 (±0.9) in number of reps performed at the end of intervention.

 Ultimately, none of the studies included rates of falls, or falls risk. They included secondary outcomes, such as LE strength, physical performance, LE functioning, and one report balanced. Other studies did include functional outcome measures, incudling the TUG and the 30STS which are measures of strength. Ozaki and Clarkson both indicated statistically significant changes in TUG times following 6 weeks of walking intervention by 0.5 sec each. However, participants were completing TUGs in well under 12 seconds, the cut off to indicate falling.14,16 MDC changes for the TUG in Parkison groups and Alheimer’s patients are 3.5 and 4.09 seconds respectively, and while these are not the populations of interest, they provide a guiding rule to suggest that these decreases in TUG time may not be clinically significant.

 Indirectly, one could make conclusions about the role of BFR and its strength inducing benefits as a precursor to providing older adults with the necessary power and training to respond to perturbations to reduce falls, but there is currently no direct evidence supporting BFR-LL as a modality to be used to reduce falls risk.

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Gaps in Research

-Well, high load is totally possible in older adults

-Example of post-surgical evidence

Expected Length

-2 hours-3 hours to really read a paper, and put into an evidence table.

180 hours total, so 60 papers to read.

10-12 key articles,

2-3 for peripheral, like falls risk.

Data Table

-Occlusion Pressures Used

-Frequency and Duration of Exercise

-Age

-Hypertrophy

-Strength

-Length of Study

* Falls Risk: Potential increase in falls risk immediately after a session (reduced MVC right after?)