Blood Flow Restriction Therapy and Its Use for Rehabilitation and Return to Sport: Physiology, Application, and Guidelines for Implementation

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Abstract: Blood flow restriction (BFR) is an expanding rehabilitation modality that uses a tourniquet to reduce arterial inflow and occlude venous outflow in the setting of resistance training or exercise. Initially, this technique was seen as a way to stimulate muscular development, but improved understanding of its physiologic benefits and mechanism of action has allowed for innovative clinical applications. BFR represents a way to decrease stress placed on the joints without compromising improvements in strength, whereas for postoperative, injured, or load-compromised individuals BFR represents a way to accelerate recovery and prevent atrophy. There is also growing evidence to suggest that it augments cardiovascular fitness and attenuates pain. The purpose of this review is to highlight the physiology and evidence behind the various applications of BFR, with a focus on postoperative rehabilitation. While much remains to be learned, it is clear that blood flow restriction therapy stimulates muscle hypertrophy via a synergistic response to metabolic stress and mechanical tension, with supplemental benefits on cardiovascular fitness and pain. New forms of BFR and expanding applications in postoperative patients and athletes hold promise for expedited recovery. Continued adherence to rehabilitation guidelines and exploration of BFRs physiology and various applications will help optimize its effect and prescription. **Level of Evidence:** V, expert opinion.

Blood flow restriction (BFR) therapy, a controlled form of vascular occlusion combined with resistance training or exercise, has seen tremendous growth in recent years. Initially, this modality of rehabilitation gained notoriety for its use in wounded service-members with volumetric muscle loss and limb-salvage scenarios, but it has expanded across a number of applications, including regular strength training, postoperative rehabilitation, and atrophy prevention. Other novel forms being applied clinically also include BFR with aerobic exercise, passive application (i.e., BFR in the absence of exercise), and neuromuscular stimulation. As awareness of BFR has grown so too has the knowledge behind its physiologic mechanism of action. This has uncovered multiple benefits beyond that of muscular growth, including improvement in muscular endurance, cardiovascular fitness, pain, and bone density.[1-3] The purpose of this review is to highlight the physiology and evidence behind the various applications of BFR, with a focus on postoperative rehabilitation. Consideration also will be given to guidelines for safe implementation.

Physiology/Mechanism of Action

Before exploring the applications and practical guidelines for implementing BFR, it is important to understand its mechanism of action. A number of mechanisms have been theorized, but currently it is believed that metabolic stress from vascular occlusion and mechanical tension from resistance training or exercise lead to synergistic increases in muscle hypertrophy and strength.[4-9] At a cellular level, metabolites, hormonal differences, cell-to-cell signaling, cellular swelling, and intracellular signaling pathways have all been implicated.[5,6,10-13] Metabolites, which accumulate during exercise and are known mediators of muscular

Fig 1. Blood flow restriction with resistance training, aerobic exercise, passive application, and neuromuscular stimulation.

hypertrophy, are amplified by BFR's relative ischemic and hypoxic conditions. They are believed to induce earlier, peripherally mediated fatigue, resulting in greater motor unit recruitment, as suggested by the fact that BFR under low loads has similar recruitment to that of high load resistance training.[7,14,15] In addition, type II fast-twitch muscle fibers, which are normally only preferentially recruited at greater intensity, are activated at lower loads under BFR conditions, providing rationale for the increased muscle hypertrophy in low-load BFR in comparison with similar low-load exercise alone.[16-18] However, greater motor unit recruitment is not limited to muscles distal to the area of occlusion. In both upper- and lower-extremity BFR, more proximal muscle groups (gluteus maximus, shoulder [deltoid/rotator cuff], and pectoralis major) have been shown to have greater levels of recruitment as compared with controls.[19-23] This is hypothesized to occur in response to the early fatigue of synchronous muscle groups distal to the occlusion site and has important implications in BFR's use after procedures or injuries where a tourniquet cannot be applied proximally.

The supraphysiologic benefits of exercise with BFR also may be partially explained by the proliferation of satellite cells, multipotent cells within muscle connective tissue responsible for muscle growth and regeneration. Although satellite cells initially were thought to only be activated in the setting of high-resistance training, their proliferation is increased even under low loads with BFR, with associated increases in muscle protein synthesis, myonuclei content, myofiber size, and muscle strength.[16,24,25]

The physiologic adaptations noted during and after BFR also have been found to be mediated by several notable cell signaling pathways. Stimulation of protein translation via the mechanistic target of rapamycin pathway, which is important in muscle protein synthesis and hypertrophy,[26-28] appears to play a fundamental role in the effects of BFR,[11,12] whereas myostatin, a negative regulator of muscle growth and promoter of muscle fibrosis, has been shown to be downregulated after BFR.[13,29,30] Although the exact contribution of each mechanistic pathway may not yet be completely understood, the available evidence offers important insight which will help guide further research to optimize rehabilitation efforts.

Applications

In its earliest applications, BFR was used to stimulate muscular growth, but as word of its potential has disseminated so too have the applications and indications for its use. Current forms include BFR with low-load resistance training, aerobic exercise, passive

BFR, and neuromuscular stimulation (Fig 1). These various modalities have been studied across a variety of demographic subgroups including athletes and non-athletes, healthy and injured, preoperative and postoperative, young and old.

By far the most common form of BFR is with resistance exercise (BRF-RE), with multiple systematic reviews and meta-analyses demonstrating its benefits.[31-34] From these studies it is clear that low-load BFR-RE is superior in multiple respects, including building muscle strength and size, to that of isolated low load resistance training and comparable to that of high load resistance training alone. However, although low-load BFR-RE may not necessarily be superior to that of high-load resistance training in terms of muscle strength, the ability to train at a greater frequency with less mechanical stress on the joints allows for broad application, in postoperative, injured, and cardiac rehabilitation patients, in season athletes and elderly individuals.

In the interest of providing concise, practical recommendations for producing muscle hypertrophy with BFR-RE, 20% to 40% of 1 repetition maximums are recommended in concert with BFR cuff pressures set between 40% and 80% of limb occlusion pressure (LOP).[35] Four sets of repetitions (30, 15, 15, 15) has been most commonly used in practice and produces the beneficial adaptions noted in BFR. Generally, rest between sets of 30 to 60 seconds is recommended, with concern that longer periods and intermittent BFR (relieving the cuff pressure between sets) may limit the stress for adaption.[35] Two to three BFR sessions per week are recommended, in line with recommendations for skeletal muscle hypertrophy in standard resistance training of 2 to 4 times per week. A more aggressive regimen, including twice-daily BFR training, may be a reasonable option to accelerate recovery in the early rehabilitation period following an injury or surgery.[35]

A hallmark of returning patients to activity or sports is improvement and maintenance of their aerobic fitness. The postoperative period can severely diminish aerobic capacity and in hospitalized or elderly individuals this component of physical health can be the crux of functional recovery. The study of BFR with aerobic exercise (BFR-AE) has been more limited compared with resistance training, but markers of aerobic fitness, including absolute and relative oxygen consumption (VO_2), along with exercise time to exhaustion, have all been shown to increase more compared to control training groups.[1,36] In addition, low-intensity exercise in combination with BFR has shown similar substantial improvements in VO_2 and strength even in already highly trained athletes.[37-39] While it is often felt that a threshold of 50% VO_2 should be reached to improve aerobic capacity, a clinical protocol for BFR-AE of 40% VO_2 maximum (or walking at approximately 2-4 miles per hour) for as little as 15 to 20 minutes may be able to achieve similar effects over 2 to 6 weeks.[36,39,40] These effects are believed to be mediated by a decrease in venous return, which is compensated for by increases in heart rate, resulting in adjustments to the effective window for aerobic adaptation. While not necessarily the main focus of BFR-AE, improvements in strength, muscle size, glycogen composition, capillary fiber density, and functional measures, such as timed-up and-go and chair sit-to-stand, also have been noted across various studies.[36,39-42]

Although the benefits of BFR and exercise are felt to be most beneficial in tandem, BFR's positive effect has been shown to be present in the absence of exercise as well. For individuals in the postoperative period, immobilized, casted or hospitalized, BFR alone represents a potential solution to prevent disuse atrophy. A systematic review of 3 studies in non−weight-bearing or immobilized individuals (1 following anterior cruciate ligament reconstruction [ACLR] and 2 for short-leg cast immobilization and non−weight-bearing in healthy individuals) showed BFR attenuated reductions in knee torque and prevented disuse atrophy. However, the conclusions from the review itself were limited due to high risk of bias of each study.[43] One other study looking at intensive care patients in comas undergoing BFR with passive mobilization, using the contralateral limb as a control, showed BFR was an effective way to reduce muscle wasting from the thigh. However, across the studies looking at BFR alone and with passive motion, large ranges of pressure have been applied without relative reference numbers such as LOP, limiting standardization and generalizability of the findings. Nevertheless, it appears that high pressures (70%-100% LOP) provide a stronger stimulus to prevent atrophy, while the most common protocol in these scenarios is 5 minutes of BFR, followed by 3 minutes of reperfusion, for 3 to 4 cycles, once or twice a day for 1 to 8 weeks.[35]

Another budding area of interest includes the use of BFR with neuromuscular stimulation. Neuromuscular stimulation often is used in the early postoperative period and as maintenance/preventative therapy in training rooms for collegiate and professional athletes. Early evidence suggests the effect of this therapy, which provides unloaded, isometric contractions, may be enhanced by BFR.[33,44] With further study, this could prove useful as an adjunct in the early recovery period following knee surgery where quadriceps control is often a limiting factor in rehabilitation progression.

Postoperative Rehabilitation

The rapid onset and significant burden of atrophy following surgery and/or immobilization is well documented, as are the detrimental effects of atrophy on recovery, overall function, and reinjury.[45-47] With

immobilization alone, healthy, nonsurgical patients had a 7% decrease in quadriceps muscle at 7 days, with atrophy after knee surgery being comparatively greater, up to 33% at 3 weeks.[48-50] The benefits of low load (or no load) BFR are perfectly suited for this population given improved skeletal muscle maintenance, less associated muscle damage postexercise,[51] hypoalgesia,[52] and decreased mechanical stress on the joints.

BFR is being investigated after both upper- and lower-extremity surgery, but most notably significant interest has been paid to ACLR. Multiple randomized controlled trials with varying postoperative protocols have observed somewhat differing results, but it appears that low-load BFR applied within the first few weeks after surgery is effective at improving muscular size and strength over standard rehabilitation.[53] More recent studies have also shown improvements in knee-specific patient-reported outcomes, as well as reduced knee pain and effusions, compared with standard rehabilitation.[54,55] Although the majority of research has focused on mitigating muscle loss acutely, BFR also has shown benefit in more chronic postoperative deficits. In individuals with severe chronic thigh weakness after knee surgery the majority made significant increases in strength after just 9 BFR sessions.[56] In addition, one study found that patients on average 5 years out from ACLR with mild persistent quadriceps deficits were able to benefit from BFR.[57] A scoping review of the literature pointed out that while most of these studies contain measures of muscle volume and/or strength, these measures are of limited value in assessing benefits to functionality.[58] One other notable limitation of the current literature is that there are few studies of BFR in ACLR that use autografts derived from the extensor mechanism, whether quadriceps tendon or patellar tendon. This is particularly relevant as the quadriceps muscle is likely more prone to atrophy in these scenarios, which may potentiate the benefit of BFR.

While prescription of BFR after ACLR has been shown to be effective, BFR may also be warranted in instances of prolonged non−weight-bearing/immobilization (meniscal repair, meniscal transplant, articular cartilage procedures, osteotomy), multiligamentous reconstructions or in those individuals with prolonged and refractory atrophy. Evidence of BFR's benefit for muscle groups proximal to the site of occlusion also has expanded its potential use for shoulder and hip procedures, but before advocating for routine prescription from arthroscopy to arthroplasty, further evidence of clinical benefit is needed.[19-21,59]

Safety Considerations

While remarkable to see the influence of scientific evidence on athletic performance, some caution is warranted given the risks associated with inappropriate BFR usage. This is especially true, given uncertainty regarding its effectiveness in scenarios in which pressure is applied via less-precise methods than pneumatic tourniquets with calibrated pressures. Temporary paresthesias, bruising, and delayed-onset muscle soreness all may result after routine BFR use, but serious adverse events, including rhabdomyolysis, prolonged pain, and syncopal events, can result from inappropriate utilization, over exertion, or in individuals who are not healthy enough for moderate or intense physical activity.[60] Lastly, while blood clots were often cited as a risk in early studies and discussion of BFR, there is no evidence to support an increased risk of thromboembolic events.[61] In fact, the opposite may even be true, with BFR offering a protective effect against such events, given its stimulation of the fibrinolytic system. These points notwithstanding, implementation of BFR, within consensus guidelines, does not appear to increase the risk of adverse events any more than standard exercise modalities.

Conclusions

BFR therapy stimulates muscle hypertrophy via a synergistic response to metabolic stress and mechanical tension, with supplemental benefits on cardiovascular fitness and pain. New forms of BFR and expanding applications in postoperative patients and athletes hold promise for expedited recovery. Continued adherence to rehabilitation guidelines and exploration of BFRs physiology and various applications will help optimize its effect and prescription.

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