Blood Flow Restriction Therapy

An Evidence-Based Approach to Postoperative Rehabilitation

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Abstract

» Blood flow restriction therapy (BFRT) involves the application of a pneumatic tourniquet cuff to the proximal portion of the arm or leg. This restricts arterial blood flow while occluding venous return, which creates a hypoxic environment that induces many physiologic adaptations.

» BFRT is especially useful in postoperative rehabilitation because it produces muscular hypertrophy and strength gains without the need for heavy-load exercises that are contraindicated after surgery.

» Low-load resistance training with BFRT may be preferable to low-load or high-load training alone because it leads to comparable increases in strength and hypertrophy, without inducing muscular edema or increasing pain.

Muscular weakness and accompanying atrophy are prevalent after knee surgery, which negatively affects knee function. Thus, strength training is an integral part of postsurgical musculoskeletal rehabilitation. Traditionally, heavy-load exercises at ≥70% of an individual's 1-repetition maximum (1RM) have been necessary to elicit muscular hypertrophy and strength gains (Fig. 1)[1–3]. Recent research has shown that low-load resistance training (LL-RT; ≤60% 1RM)[4] to failure produces similar muscular hypertrophy and strength gains to heavy-load resistance training (HL-RT, >60% 1RM)[4,5]. Using LL-RT may be beneficial in the early recovery process when HL-RT would not be feasible.

Progressively over the past 15 to 20 years, LL-RT has incorporated blood flow restriction therapy (BFRT) to produce substantial muscular hypertrophy and strength gains without heavy-load exercises[6–11]. BFRT works by restricting arterial blow flow and occluding venous return, creating a pooling effect in working muscles. BFRT resistance levels typically start at 20% to 30% of 1RM and progressively increase to enhance the morphological and strength responses. BFRT is a good postoperative treatment option because it can stimulate muscular growth without substantially increasing pain or injury[6–10]. BFRT can be used in postoperative rehabilitation after many procedures, such as anterior cruciate ligament (ACL) reconstruction, medial patellofemoral ligament reconstruction, or articular cartilage procedures. BFRT is particularly indicated in the rehabilitation of patients with postoperative protected weight-bearing status, muscular inhibition, substantial postoperative pain, and/or a desire return to preoperative levels of muscular strength[12]. The purpose of this article was to review the potential mechanisms of BFRT, the physiologic adaptations after BFRT, optimal BFRT application, and its benefits and risks compared with traditional strength training for postoperative rehabilitation.

Blood Flow Restriction Therapy

BFRT involves inflating a pneumatic tourniquet cuff applied to the most proximal region of the arm or leg. As the cuff inflates, a corresponding decrease in distal arterial flow occurs and venous flow is

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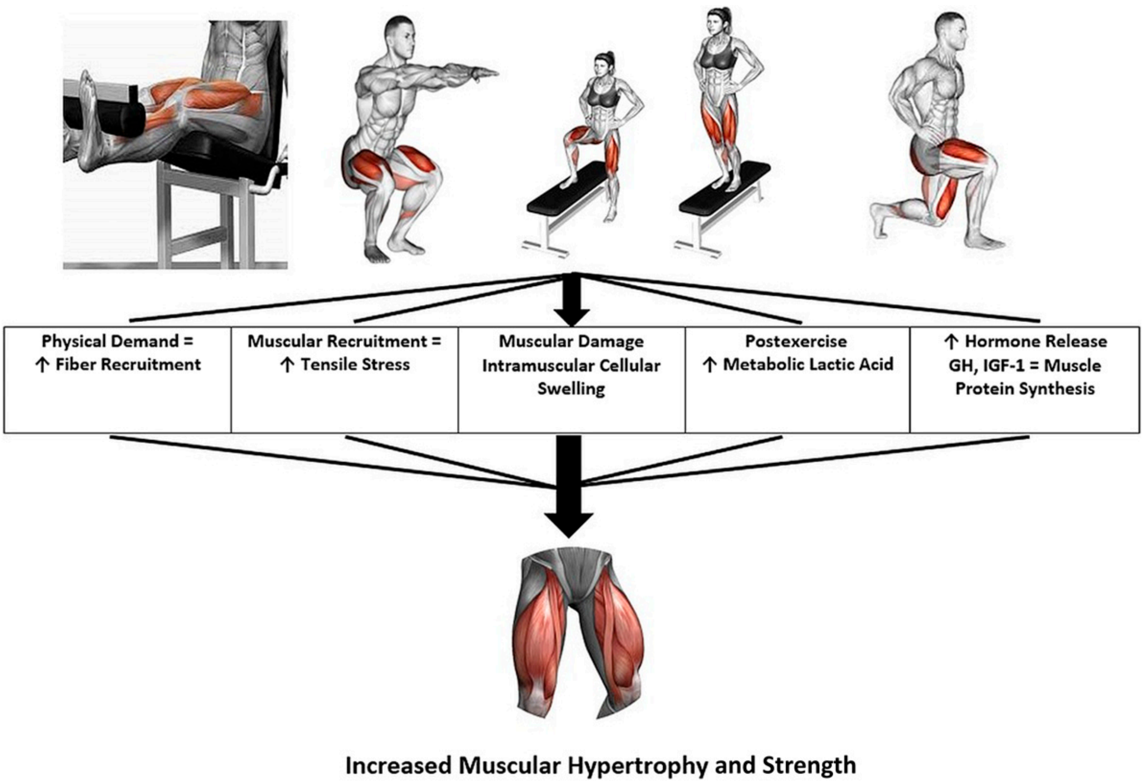

Fig. 1

Normal mechanisms of traditional strength training. GH = growth hormone, and IGF-1 = insulin-like growth factor.

occluded, which creates capillary pooling, muscular hypoxia, increased accumulation of metabolites, and activation of anabolic processes.[9]

Potential Mechanisms

While adaptive increases in muscular hypertrophy and strength have been well-documented using BFRT, the definitive mechanisms producing these results are multifactorial. One of the primary mechanisms that drives adaptive changes is hypoxia. The diminished arterial flow creates a hypoxic environment, leading to the accumulation of metabolites[13]. Decreased oxygen with limited venous return leads to muscle cell swelling, intramuscular anabolic signaling, increased muscle fiber excitability and recruitment, and subsequent accumulation of lactate (Fig. 2)[13,14]. This hypoxia stimulates myogenic stem-cell proliferation, leading to the addition of myonuclei and myofiber hypertrophy within the exercised muscle.[15,16]

Hormones also play an integral role in the anabolic response to resistance exercises. Plasma concentrations of growth hormone (GH), norepinephrine, and lipid peroxide increase after BFRT[17]. Local ischemia and the accumulation of lactate and H^+ ions may stimulate afferent neural activity resulting in enhanced GH release[13]. GH concentration reaches approximately 290 times higher than the resting level 15 minutes after BFRT exercise[17]. In addition, insulin-like growth factor (IGF-1) increases after BFRT exercises similar to that of high-intensity exercise[13,18] but does not seem to stimulate a testosterone response[19]. IGF-1 has a catalyst effect on mechano growth factor, which activates satellite cells and mediates their proliferation (Fig. 3)[3]. Low-load BFRT (LL-BFRT) seems to primarily trigger GH production, but its direct effect on strength gains is not fully understood.[13,17]

Intramuscular cellular swelling increases protein synthesis and decreases proteolysis within muscle fibers[20,21]. Cellular swelling may trigger the proliferation of satellite cells, facilitating their fusion to muscle fibers and leading to hypertrophy[13,21]. The BFRT-induced capillary pooling acutely increases the influx of water into the muscle cell[22]. This cellular swelling triggers anabolic signaling, which activates mammalian target of rapamycin (mTOR) and mitogen-activated protein-kinase pathways (Fig. 4)[22]. When the mTOR pathway is activated, it signals muscle protein synthesis, resulting in skeletal muscle hypertrophy[13,22]. BFRT's causative influx of water into cells and mTOR signaling may explain the attenuation of atrophy and weakness that is seen with the utilization of BFRT even in the absence of exercise.[23–25]

Mechanical stimulation of muscle fibers during muscular contractions and stretching stimulates intramuscular signaling pathways independent of hormones and growth factors (Fig. 5)[26]. Mechanical-induced tension disturbs the integrity of the muscle causing a mechanochemically transduced molecular and cellular response in the myofibrils and satellite cells[3]. Localized muscle

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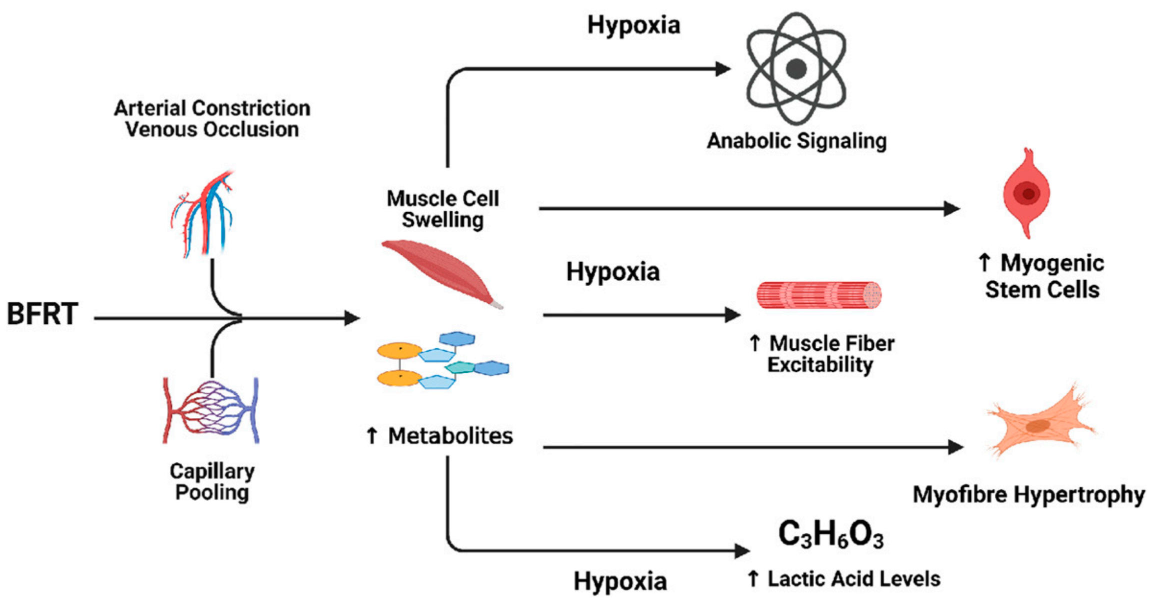

Fig. 2
Hypoxia mechanism. BFRT = blood flow restriction therapy.

tissue damage to the contractile elements or cytoskeleton is another theorized mechanism that may generate hypertrophic response[3]. These mechanical disruptions activate the mTOR pathway, initiating muscle protein synthesis[13]. In 1 study, patients performed knee extensions to failure; those in the BFRT group had enhanced mTOR signaling compared with the nonoccluded control group[27]. Contrary to mTOR's positive effects for hypertrophy, myostatin acts as an inhibitor of muscle growth[13]. BFRT has a suppressive effect on myostatin mRNA expression[13,15]. These intramuscular signaling actions accompanying LL-BFRT play a role in producing a proliferation of myogenic stem cells.[13]

BFRT also positively affects electromyograph (EMG) muscle activation during low-load exercises[17,28,29]. Takarada et al. reported a 1.8 times greater EMG muscular activation when using BFRT as compared with the control group, although there were no differences between groups regarding force production or mechanical work[17]. This enhanced muscle activation with LL-BFRT may be related to hypoxia; low-threshold type I motor units readily fatigue and require activation of type II glycolytic motor units to maintain force production[13]. When the low-load exercise focus was performed to failure, there was no increase in EMG activation between BFRT and control groups[27,30]. An increase in motor unit activation seems to correlate with the degree of metabolic stress associated with the exercise[28]. In addition, the hypertrophy and strength gains associated with BFRT may be due to the increased recruitment of type II motor units.[13]

Adaptive Changes

A meta-analysis was performed to identify which training variables produce the greatest strength and muscle hypertrophy outcomes.[31] The most important variables for strength increase are duration of training, total repetitions, frequency of training at 2 to 3 days per week, rest between sets, and performing isotonic exercises at an intensity of 15% to 30% of 1RM[31]. When comparing vigorous-intensity versus low-intensity BFRT with cycling, BFRT led to an increase in lean leg mass over time, whereas vigorous-intensity training produced no effect[32]. BFRT produces an adaptive increase in strength when performing either aerobic or resistance BFRT exercises[33]. When exercise was combined with BFRT, the muscle cross-sectional area (CSA) increased by 0.4 cm^2; this was a statistically significant

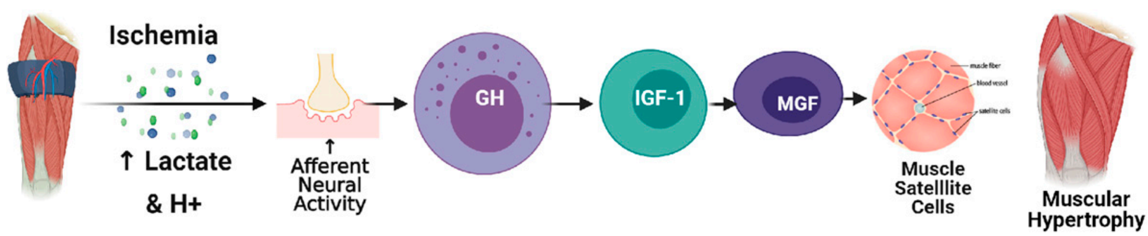

Fig. 3
Hormonal mechanism. GH = growth hormone, IGF-1 = insulin-like growth factor, and MGF = mechanogrowth factor.

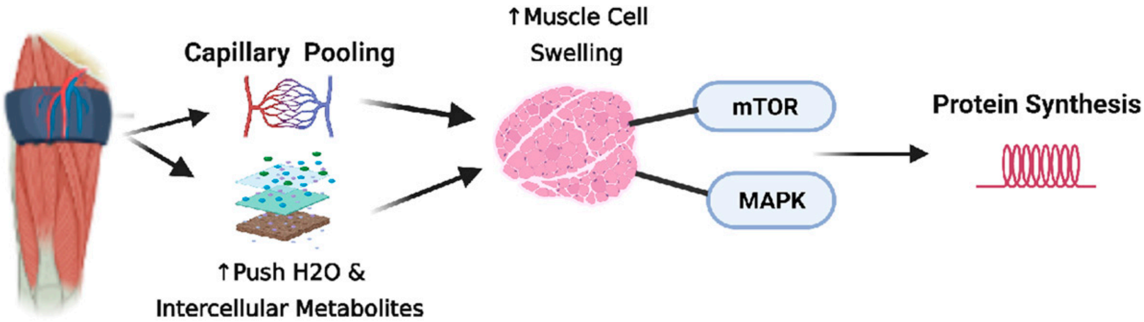

Fig. 4

Intramuscular swelling mechanism. mTOR = mammalian target of rapamycin, and MAPK = mitogen-activated protein-kinase pathways.

increase compared with the control group ($p = 0.001$)[33]. In a study of BFRT in women with knee osteoarthritis (OA), significant increases in quadriceps CSA were observed in the BFRT group compared with a low-load control group ($p = 0.02$); no significant difference was observed when compared with the high-load control ($p > 0.05$)[34]. A recent review also showed increases in strength in patients who underwent BFRT training compared with controls[35]. Overall, BFRT can increase muscular CSA, lean muscle mass, muscular hypertrophy, and overall strength.[9]

Immobilization leads to an acceleration of thigh muscular atrophy, which is a common concern after surgery. In a study of 14-day limb unloading in healthy patients (a control group [no BFRT], BFRT no exercise group, and a BFRT with neuromuscular electrical stimulation [NMES] group), the BFRT-NMES group showed no loss of lean thigh muscle mass and demonstrated a gain in muscle thickness[36]. Kakehi et al. immobilized subjects with a cast for 14 days and examined thigh muscle CSA before and after immobilization[37]. The BFRT group demonstrated a smaller decrease of thigh CSA compared with the control group[37]. After 30 days of limb suspension, the LL-BFRT group experienced insignificant losses in knee extensor CSA (1.2%) and strength (2.0%), whereas the limb suspension–only group demonstrated significant reductions in CSA (7.4%, $p = 0.04$) and strength (21%, $p = 0.02$)[38]. Thus, BFRT may attenuate thigh muscle atrophy.

Patient Perceptions of Exertion and Pain

Pain and effort level are 2 key factors that may affect a patient's attitude, motivation, and compliance with rehabilitation. Ratings of perceived exertion (RPE) allow a patient's perception of the exercise training load to be graded. For BFRT to be truly effective, it must also be psychologically well tolerated. BFRT increases RPE compared with non-BFRT control groups[27], but when comparing BFRT with high-intensity training (HIT), the RPE was the greatest

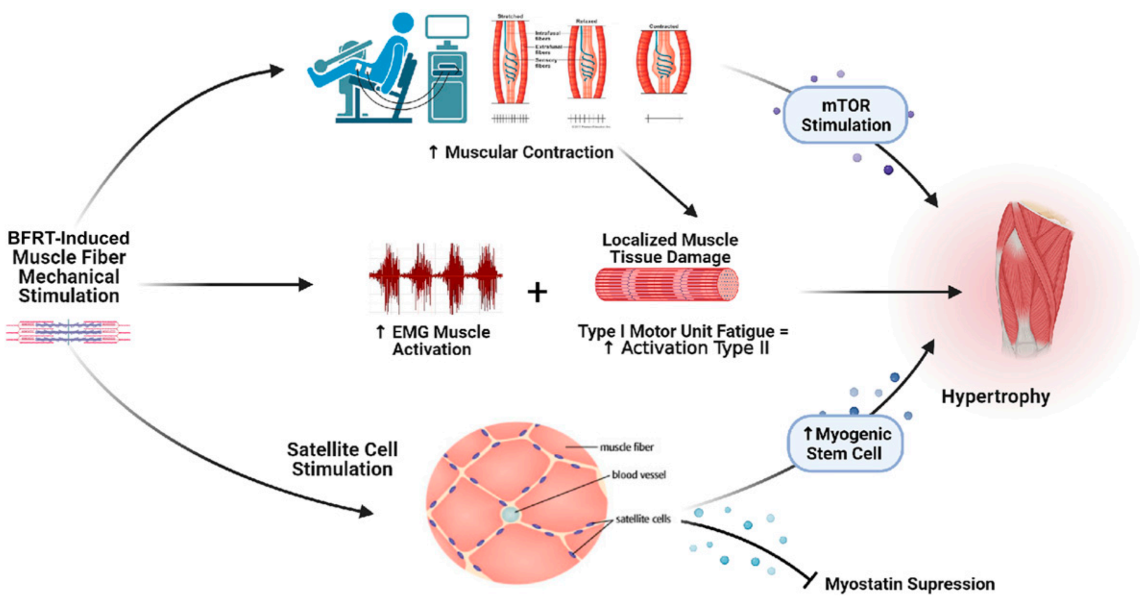

Fig. 5

Mechanical muscle fiber stimulation. BFRT = blood flow restriction therapy, EMG: electromyograph, and mTOR = mammalian target of rapamycin.

with HIT[39]. Notably, there were no differences in pain ratings between groups[39]. When comparing HL-RT, high-pressure intermittent BFRT, and low-pressure continuous BFRT, RPE was highest for HL-RT and high-pressure intermittent BFRT[39]. However, RPE for all 3 of these training modalities was higher than LL-RT[39]. Nonmuscular failure BFRT increases RPE and pain response, but to a lesser extent than HL-RT and LL-RT to muscular failure.[40]

Researchers compared the magnitude of exercise-induced hypoalgesia in a randomized crossover design trial using LL-RT (30% of 1RM), HL-RT (70% 1RM), and LL-BFRT (30% 1RM) at a 40% and 80% atrial occlusion pressure[41]. Subjects' pressure pain thresholds (PPT) were assessed before, at 5 minutes, and at 24 hours after exercise. Hypoalgesia effects were observed with HL-RT and both BFRT trials, and postexercise plasma beta-endorphin concentrations were elevated with the BFRT trials[41]. This elevation in endogenous opioid production observed with BFRT likely reduced pain sensitivity[41]. LL-BFRT is equally effective for improving function and muscle hypertrophy as compared with high-load quadriceps strengthening[6]. LL-BFRT also elicits decreased knee pain by 22 mm on a 0 to 100-mm visual analog scale[6]. In a double-blind, randomized study, BFRT was effective in the treatment of patellofemoral pain; it produced a 93% greater reduction in pain with activities of daily living than the standard of care group[42]. When comparing BFRT and traditional resistance training, patients in the BFRT group experienced a significant reduction of anterior knee pain ($p < 0.001$) when performing the single-leg step-down test, shallow and deep single-leg squats[43]. Following a national, randomized clinical trial investigating the effect of BFRT versus HL-RT for rehabilitation after ACL reconstruction, researchers concluded that BFRT improved muscular hypertrophy and strength to a similar degree as HL-RT[44]. However, BFRT also demonstrated greater reductions in pain and knee effusions[44]. This highlights that BFRT is an especially useful postoperative rehabilitation tool because it increases strength while also attenuating pain.D

Potential Risks

The potential risks associated with BFRT include blood clots; acute pain during training and secondary to delayed-onset muscle soreness; and nerve, blood vessel, or muscle damage. Although BFRT attenuates pain, especially compared with HL-RT, some pain may still be present acutely during and after training. One RCT investigating BFRT reported that 4 patients dropped out of the control group because of pain during high-intensity (HI) RT[45], demonstrating that some level of acute pain and discomfort may be present during any form of rehabilitative exercise and is not a risk of BFRT alone. In addition, research shows no evidence of increased blood clot risk with LL-BFRT. LL-BFRT can actually stimulate anticlotting fibrinolytic enzymes after a training session[11,46–49]. In addition, there is no evidence of decreased nerve conduction velocity, vessel damage, or an increase of muscular creatine kinase or myoglobin that would indicate significant muscular, nerve, or blood vessel damage after LL-BFRT exercises.[13,14,49,50]

Although the risks associated with BFRT are small, there are still some possible contraindications to the use of BFRT, including unstable hypertension, venous thromboembolism, hypercoagulable states, varicose veins, pregnancy, and hemophilia, among others.[51] These contraindications should continue to be studied and modified as more information about the safety of BFRT becomes available.

BFRT Application

Cuff width, pressure, duration of use, and continuous versus intermittent pressure play an important role in the effectiveness of BFRT. Enhancing the adaptive responses of BFRT is dependent on both the BFRT stimulus and the exercises performed. BFRT is traditionally performed with a physical therapist or other trained clinician, but 1 case report described successful increases in lean leg mass and strength after total knee arthroplasty with the use of an 8-week at-home BFRT training program[52]. This demonstrates that, with proper monitoring, both in-clinic and at-home BFRT may be safe, effective rehabilitation methods. The following sections highlight each variable that should be considered to optimize BFRT training outcomes.

Cuff Width

A range of systems and cuff sizes are available for BFRT (Table I). The required pressure to occlude the limb is largely determined by cuff width. Wider cuffs (up to 18 cm)[53] decrease vessel radius over a larger portion of the vessel. Thus, a lower pressure is needed to reach limb occlusion pressure (LOP) when using a wider versus a narrower (as small as 3 cm) cuff[50,54-|-56]. Researchers reported that the mean LOP for a wide cuff (13.5 cm) was 144 mm Hg and 235 mm Hg for a narrow cuff (5.0 cm); 37% of subjects still had arterial inflow at 300 mm Hg when using the narrow cuff[54]. Using wider cuffs allows for the LOP to be achieved at lower pressures and can thus aid in decreasing discomfort with BFRT[53]. In addition, larger limb circumferences require higher occlusion pressures to reach the same percentage of occlusion as compared with smaller limbs[54]. Furthermore, narrow cuffs have been associated with an increased risk for vessel, muscle, and nerve damage[49]. These points demonstrate that it is favorable to use a wider cuff when possible.

Cuff Pressure

Many early researchers studying BFRT applied a single, arbitrary pressure for all patients[55]. Using an arbitrary pressure in all patients with different limb circumferences will likely produce different BFRT stimuli and can increase discomfort[56]. To account for individual differences, LOP should ideally be

TABLE I Comparison of Common BFRT Systems

Device	KAATSU	BStrong®	Smart-Cuffs®	Delfi®
Cuff width	5 cm	5 to 7 cm	10 to 12 cm	11.5 cm
Doppler LOP capability	No	No	Yes	Yes
Inflation technique	Automatic machine	Handheld pump and sphygmomanometer	Handheld pump and sphygmomanometer	Automatic machine
Detachable hose-free movement	Yes	Yes	Yes	No
FDA listed	No	No	Yes	Yes
Cost	$1,900-$8,500/unit	$1,000.00/clinical set	$1,000.00/clinical set	$5,000.00/unit

determined for each individual using handheld Doppler or Doppler ultrasound[57], and training with BFRT should be expressed and documented as a percentage of the LOP. Examining RPE and ratings of discomfort with 6 pressures ranging from 40% to 90% LOP performed at 30% 1RM revealed that patients undergoing BFRT at the highest pressures completed less repetitions as the exercise moved from sets 2 to 4[58]. When total training volume was equalized, lower pressures produced decreased RPE and pain ratings as compared with higher pressures at 60% to 80% occlusion pressures[59]. LL-BFRT at 40% LOP may be sufficient to increase muscle size, endurance, peak strength, and total exercise volume while also decreasing discomfort as compared with 90% LOP[60]. Assessing knee extension exercises (30% 1RM) at 0%, 60%, 80%, and 100% LOP occlusion showed that the tissue saturation index decreased as pressure increased, except from 80% to 100%[61]. In addition, there was no difference in EMG quadriceps activity from 60% to 80% or 100% LOP[61]. Robust changes in tissue oxygenation and quadriceps EMG activity were produced with 60% occlusion while minimizing the risks and discomfort associated with higher pressures[61]. Higher cuff pressures seem to increase ratings of discomfort and decrease total exercise volume and may increase the risk for an adverse event. To decrease feelings of discomfort while providing an effective anabolic training stimulus, the training pressure should be between 40% and 80% LOP while performing LL-BFRT.[58,60–62] A 40 to 50% LOP is commonly used with upper extremity BFRT and 60% to 80% LOP with lower extremity.[50,63]

Exercise Load, Volume, Rest Periods, Duration, and Frequency

Although it may vary based on the patient and surgery performed, BFRT can be started as early as the third postoperative day and can be used throughout all phases of rehabilitation.[64] BFRT is most effective when combined with LL-RT. Training between 20% and 40% 1RM provides an ample stimulus to induce substantial muscular hypertrophy and strength gains[33,49,50,60,65]. The most commonly reported and frequently used set and repetition combination involves 75 repetitions performed over 4 sets; the first set consists of 30 repetitions, and the subsequent 3 sets each consist of 15 repetitions[31,33,49,50]. The combined effect of the resistance load and total work created by the number of repetitions leads to mechanical muscle fiber stimulation. Interset rest periods are normally short in duration, typically ranging from 30 to 60 seconds[28,31,50]. These brief interset rest periods enhance the intramuscular swelling mechanism[22,50,63]. Typically, the cuff remains inflated during these short rest periods, but it has been shown that similar muscle activation can be achieved with continuous or intermittent pressure during rest if a high cuff pressure is applied.[50]

Traditionally, resistance exercise is performed 3 to 5 times per week over an 8- to 12-week training period to produce muscular hypertrophy and adaptive strength gains[1,4,56]. In a recent systematic review investigating BFRT's treatment effect on knee pathology, the authors concluded that a minimum of 12 treatment sessions were required to produce measurable strength gains[66]. To produce anabolic changes with BFRT, a training frequency of 2 to 3 times per week over a minimum of 6 weeks, with an optimal duration of 9 to 10 weeks, is recommended[31,33,50]. As with all training and rehabilitation programs, BFRT should be periodized to ensure patient engagement, progressive difficulty, and optimum anabolic muscular stimulation.

Researchers found that the most important variables to increase strength were a 9- to 10-week training period (mean effect size= 1.38), 60 to 70 total repetitions per exercise (1.37), a frequency of 2 to 3 days per week (1.25), 30-second set rest periods (1.22), isotonic exercises (1.08), and intensity of 15%-30% of 1RM (1.08)[31]. When examining how to best generate adaptive hypertrophy, the positive mean effect size for each variable was isotonic exercises (1.08), training between 15% and 30% of 1RM load (1.08), training at a frequency of 2 to 3 days per week (0.48), training ≤ 4 weeks (0.48), and completing a minimum of 45 repetitions per exercise (0.44) with 30-second set rest periods (0.44)[31]. Table II presents the summary recommendations regarding

TABLE II BFRT Summary Recommendations for Training Variables

Variables	Best Evidence
Cuff placement	Proximally, ensure no gaps that the cuff overlaps[62]
Cuff size	Wide cuffs ≥ 10 cm width[49,54–56,62]
Cuff pressure and restriction form	40-50% LOP for upper extremity; 60-80% LOP for lower extremity[50,63]
	Intermittent pressure:↓ discomfort and equal RPE ratings vs continuous BFRT[62,65,66,68–71]
	Continuous pressure: ↑ RPE, ↑ pain/discomfort ratings[62,65,66,68–71]
Volume	45-75 repetitions per exercise[31,33,49,50]
	4 sets (repetitions/set): 30 × 15 × 15 × 15[49,50]
	Cycling or walking: 5-20 min/exercise at ≤50% max heart rate[32,33,50]
Training load and stimulus	Train at 20%-40% 1RM[31,33,49,50,62]
	Isolated and multijoint isotonic exercises performed in open and closed chain[6,38,41–44,46,50]
Interset rest	30 seconds are optimum[4,31,65]
Frequency and duration	Clinical rehabilitation 2 to 3 times per week for 8-10 weeks[31,33,50]
Exercise stimulus	Isolated BFRT only – attenuates loss of muscle mass and strength[37,38]
	BFRT + NMES – no loss of lean thigh muscle mass and ↑ thigh muscle thickness[36]
	Low-load BFRT – ↑ RPE, ↓ pain, substantial ↑ muscular hypertrophy & strength[6,31,35,41–44,50]
	BFRT + walking/cycling – maintain or moderate ↑ muscle mass & strength[32,33]

BFRT= blood flow restriction therapy, LOP= limb occlusion pressure, RPE= ratings of perceived exertion, 1RM= 1-repetition maximum, NMES=neuromuscular electrical stimulation. Adapted from: Scott BR, Loenneke JP, Slattery KM, Dascombe BJ. Exercise with blood flow restriction: an updated evidence-based approach for enhanced muscular development. Sports Med. 2015 Mar; 45(3):313 to 325.

training variables when implementing BFRT in postoperative rehabilitation.

Continuous versus Intermittent BFRT

Both continuous BFRT (cBFRT) and intermittent BFRT (iBFRT) produce muscular hypertrophy and strength gains when compared with controls; however, there is no consensus if one produces enhanced results over the other[31,50,62,66–70]. One of the primary reported side effects with cBFRT is acute pain and discomfort during exercise[69,70]. Three studies have investigated the perceptual responses and effects of continuous versus intermittent BFRT. In a study comparing iBFRT with cBFRT and high-intensity exercises, the RPE was lower for iBFRT[67]. Fitschen et al. compared cBFRT, iBFRT, and control (no BFRT) during leg extensions to failure[69]. cBFRT resulted in significantly ($p < 0.05$) greater pain ratings compared with iBFRT and control, and both BFRT groups performed fewer total repetitions than the control ($p < 0.001$)[69]. The authors concluded that iBFRT produced similar muscular fatigue as cBFRT but with less pain[69]. Freitas et al. compared low-intensity (LI) resistance training, HI resistance training, iBFRT, and cBFRT during bilateral leg press and knee extension exercises, measuring RPE and ratings of discomfort before and after each set[70]. Both BFRT conditions produced significantly greater ($p < 0.05$) RPE scores than the LI group but were significantly lower ($p < 0.05$) than HI[70]. Ratings of discomfort displayed no significant difference between the 2 BFRT groups during the first 2 sets of the leg press; however, the cBFRT evoked greater ratings during the last 2 sets. There were no significant differences between conditions when performing knee extension exercises[70]. Both the BFRT conditions produced similar perceptual responses; discomfort ratings were greater than LI but less than HI.[70]

Multiple researchers have investigated the hemodynamic effects of BFRT. One group of researchers compared blood lactate levels, double product (DP heart rate times systolic blood pressure) and RPE between those performing cBFRT, iBFRT, and HI exercises[67]. Each of the 3 exercise groups produced increases in lactate and DP at the end of the training session and an elevated HR during each exercise[67]. There was a greater percentage of change in both the lactate and DP levels for cBFRT compared with the iBFRT group[67]. Other researchers measured creatine kinase and lactate dehydrogenase (markers of muscle damage), protein carbonyl, thiobarbituric acid–reactive substance, and uric acid (markers of oxidative stress) before and after 4 training sessions of cBFRT and iBFRT[68]. Neither cBFRT nor iBFRT showed acute muscle damage or elevated oxidative stress markers[68]. Muscle activity was assessed during each set of LI, HI, cBFRT, and iBFRT while performing leg press and knee extension exercises. Measurements of blood lactate, muscle swelling, and plasma volume (%ΔPV) were also measured[71]. There were no significant differences in EMG activity across the cBFRT, iBFRT, and LI protocols at any time point, but all were significantly lower than HI. There were also no significant differences in lactate concentration, %Δ PV, or muscle swelling across LI, cBFRT, and iBFRT conditions; HI elicited significantly greater responses for all physiological markers[71]. These authors concluded that cBFRT and iBFRT produce the same acute physiological responses[71]. These results suggest that iBFRT may be the better option in moderating perceived pain and discomfort levels while eliciting similar RPE and physiological responses as cBFRT.

BFRT versus Traditional Strength Training

Multiple debates exist on the best training paradigm to maximize the adaptive responses to resistance exercise. Training with resistance loads ≤50% 1 RM promotes substantial increases in muscle strength and hypertrophy but is less effective than HL-RT[72]. Furthermore, a meta-analysis comparing changes in strength and hypertrophy lasting ≥ 6 weeks between LL-RT and HL-RT found that maximal strength benefits are obtained with HL-RT, while muscle hypertrophy is equally achieved from either LL-RT or HL-RT. However, HL-RT is often contraindicated postoperatively, and thus, BFRT may be a safe and useful adjunct to postoperative rehabilitation.

Fatela et al. investigated the acute quadriceps response to LL-RT, HL-RT, and LL-BFRT, measuring both pre-exercise and postexercise maximum voluntary contraction quadriceps peak torque[73]. Postexercise quadriceps torque decreased for both HL-RT (−9.5%) and LL-BFRT (−7.8%), but not with LL-RT[73]. The authors concluded that LL-BFRT enhances an acute magnitude response in muscular activation and fatigue, but not to the extent of HL-RT[73]. Shiromaru et al. examined whether early increases in quadriceps CSA were due to hypertrophy or edema after HL-RT and LL-BFRT[74]. MRI measurements were taken at baseline and after 3 and 6 weeks of training. Quadriceps CSA significantly increased at 3 weeks for both HL-RT and LL-BFRT ($p < 0.05$), but only HL-RT showed muscular edema[74]. HL-RT produced a significant reduction in range of motion and increased muscle soreness ratings (both $p < 0.05$), whereas LL-BFRT had no significant changes in these measures[74]. These results highlight that early increases of quadriceps CSA with LL-BFRT occur without edema, but increases with HL-RT are caused by edema and hypertrophy.[74]

Two recent systematic reviews and meta-analyses compared changes in muscular strength and hypertrophy between LL-BFRT and HL-RT[7,75]. One meta-analysis of studies that measured both pretraining and post-training assessments of muscular strength and hypertrophy found a mean muscle strength gain of 14.36±1.53% and significantly higher strength gains (+7.36%, effect size difference 0.63±0.09; 95% CI 0.43-0.80) for those in the HL-RT group compared with the LL-BFRT group[76]. The mean percentage gain in muscle mass was 7.22±0.58%, and between-group comparisons showed no significant gain (+0.74%) for HL-RT muscle mass as compared with LL-BFRT[76]. Grønfeldt et al. examined 16 studies and included a total pooled data of 153 HL-RT participants and 157 LL-BFRT participants[7]. Both HL-RT and LL-BFRT were equally effective in producing strength and hypertrophy gains[7]. The mean effect size across outcomes was 0.644 for LL-BFRT and 0.799 for HL-RT[7]. Wortman et al. examined the effect of BFRT for 250 athletes (age 19.8-25.9 years)[75]. Multiple studies included in this review showed that LL-BFRT produced significant strength gains, increased muscle

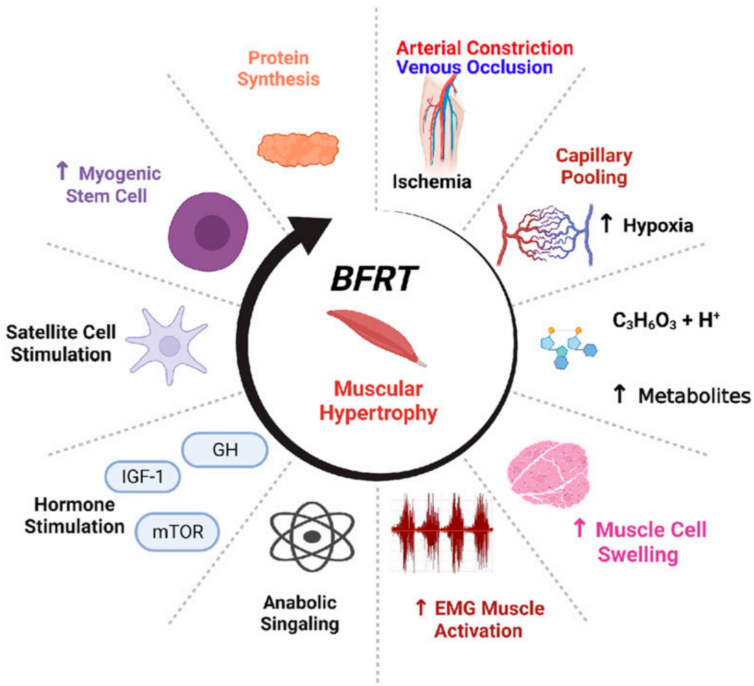

Fig. 6

Cellular changes associated with BFRT. BFRT = blood flow restriction therapy, EMG = electromyograph, IGF-1 = insulin-like growth factor-1, GH = growth hormone, and mTOR = mammalian target of rapamycin.

mass, and improvements in sport-specific measurements ($p < 0.05$)[75]. Researchers also concluded that LL-BFRT enhances muscle hypertrophy and strength in well-trained athletes and does not cause muscle damage[8]. These results demonstrate that LL-BFRT is an effective strength training stimulus.[7,8,34,76]

Key Clinical Points

BFRT induces positive physiological changes in muscular strength and mass. It artificially reduces blood flow to working muscles, creating a hypoxic environment. This hypoxia leads to the accumulation of metabolites, intramuscular swelling, and various cellular changes that play a role in increasing muscle fiber recruitment (Fig. 6).

BFRT is an effective strengthening stimulus for musculoskeletal rehabilitation that attenuates postoperative atrophy. BFRT is especially useful in patients who are non–weight-bearing postoperatively; it provides a safe and efficient way to simulate higher load training to prevent substantial atrophy. BFRT leads to moderate increases in muscle mass and strength when used with walking or cycling, and LL-BFRT is an effective training stimulus that increases muscular strength and hypertrophy to a similar extent as HL-RT. BFRT is a safe addition to traditional therapy, and its uses in rehabilitation should continue to be studied.

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