Blood Flow Restriction Training Can Improve Peak Torque Strength in Chronic Atrophic Postoperative Quadriceps and Hamstrings Muscles

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Purpose: To report a prospective study of patients who underwent blood flow restriction training (BFRT) for marked quadriceps or hamstring muscle deficits after failure to respond to traditional rehabilitation after knee surgery. **Methods:** The BFRT protocol consisted of 4 low resistance exercises (30% of 1 repetition maximum): leg press, knee extension, mini-squats, and hamstring curls with 60% to 80% limb arterial occlusion pressure. Knee peak isometric muscle torque (60° flexion) was measured on an isokinetic dynamometer. **Results:** Twenty-seven patients (18 females, 9 males; mean age, 40.1 years) with severe quadriceps and/or hamstrings deficits were enrolled from April 2017 to January 2020. They had undergone a mean of 5.3 ± 3.5 months of outpatient therapy and 22 ± 10 supervised therapy visits and did not respond to traditional rehabilitation. Prior surgery included anterior cruciate ligament reconstruction, partial or total knee replacements, meniscus repairs, and others. All patients completed 9 BFRT sessions, and 14 patients completed 18 sessions. The mean quadriceps and hamstrings torque deficits before BFRT were 43% ± 16% and 38% ± 14%, respectively. After 9 BFRT sessions, statistically significant improvements were found in muscle peak torque deficits for the quadriceps ($P = .003$) and hamstring ($P = .02$), with continued improvements after 18 sessions ($P = .004$ and $P = .002$, respectively). After 18 BFRT sessions, the peak quadriceps and hamstring peak torques increased > 20% in 86% and 76% of the patients, respectively. The failure rate of achieving this improvement in peak quadriceps and hamstring torque after 18 BFRT sessions was 14% and 24%, respectively. **Conclusions:** BFRT produced statistically significant improvements in peak quadriceps and hamstring torque measurements after 9 and 18 sessions in a majority of patients with severe quadriceps and hamstring strength deficits that had failed to respond to many months of standard and monitored postoperative rehabilitation. **Level of Evidence:** Level IV therapeutic case series.

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There is a subset of patients who undergo major knee surgical procedures and who develop a persistent and troublesome postoperative weakness and atrophy of the knee joint musculature with limitations in ambulation, activities of daily living, and return to occupations or athletics.[1-8] Marked lower limb muscle atrophy and prolonged dysfunction may occur even with modern postoperative rehabilitation programs that use early knee motion, weightbearing, electrical muscle stimulation, and open- and closed-kinetic chain exercises. Residual quadriceps weakness may persist many months or years after major operations such as anterior cruciate ligament (ACL) reconstruction, preventing return to athletic activities.[7,9-14]

Current recommendations to achieve muscle hypertrophy include using resistance training loads of 60% to 70% of 1 repetition maximum (1-RM).[15] These higher loads are commonly not tolerable in postoperative patients because of pain, soft tissue swelling, and damage to joint structures. Blood flow restriction training (BFRT) with low-resistance loads (30% of 1-RM) has been advocated early in the postoperative phase to lessen muscle atrophy. Partial vascular occlusion is achieved with an extremity tourniquet and is combined with weightbearing, nonweightbearing, and resistance

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machine exercises.[16,17] BFRT has been shown to be better tolerated than high-resistance training after surgery, because patients can perform effective low-resistance strengthening with reduced knee pain and swelling symptoms.[18-20] Positive effects of BFRT on muscle strength and volume have been reported in small cohorts after ACL reconstruction,[21-23] knee arthroscopy,[24] and total knee arthroplasty.[25] Hughes et al.[26] compared high-load resistance training alone to BFRT therapy within 2 weeks of ACL reconstruction (n = 12 each group) and reported BFRT produced similar or greater improvements in function parameters, with reduced knee pain and joint effusion, and recommended that BFRT be introduced in the early rehabilitation phase.

There is inconclusive evidence on BFRT because of limited studies, small patient populations, varying BFRT protocols, and lack of statistical power to support conclusions.[22-24,27,28] A recent systematic review of BFRT for lower extremity muscle weakness of studies published between 1974 to 2017 found that only 9 of 534 published articles met the inclusion criteria with objective data related to knee surgery or arthritis.[16] Authors reported statistically significant improvements in 6 of the 7 studies that determined quadriceps strength and BFRT was reported as safe with no serious complications reported. Minniti et al.[20] reported a systematic review on the safety of BFRT for a variety of musculoskeletal disorders, with 19 of 322 studies meeting the eligibility criteria. These authors concluded that BFRT was a safe strengthening approach with rare adverse events, although further research was recommended to screen for adverse events as BFRT becomes a more widespread modality.

The mechanisms responsible for BFRT strength gains involve inducing different forms of muscle metabolic stress and have been discussed in detail elsewhere.[17,29-31] There is limited evidence to determine whether BFRT is effective as a rescue type treatment in patients who are many months after surgery and who have severe and chronic quadriceps and hamstring strength deficits after failing a closely supervised and lengthy postoperative therapy program.

The purpose of this study was to report the effect of BFRT for marked quadriceps or hamstring muscle deficits after failure to respond to many months of standard supervised rehabilitation after knee surgery. The hypothesis was that at least 50% of the patients would achieve a >10% increase in quadriceps and hamstrings peak torques after 9 BFRT sessions and 20% or greater increase in peak torques after 18 BFRT sessions.

Methods

Study Design

The enrollment period of this study was from April 2017 to January 2020. The inclusionary criteria for BFRT were (1) postoperative 20% or greater difference from the contralateral extremity in isometric quadriceps or hamstrings strength or 2 cm or greater thigh muscle atrophy to the contralateral extremity and (2) agreement to complete at least 9 training sessions. The exclusionary criteria were (1) pregnancy, (2) history of varicose veins, (3) history of deep venous thrombosis or pulmonary embolism, (4) use of oral contraceptives, (5) history of myocardial infarction, stroke, unstable cardiac disease, and use of heart medications, (6) hypertension (>140/90), and (7) cardiac disorders of any type including tachycardia (>100 beats/min).[19]

This is a prospective study of patients who had undergone knee surgery and were then enrolled in a postoperative rehabilitation program to regain knee muscle strength and function. The patients were identified by the surgeon and physical therapist as having persistent strength deficits and a failure to respond to a standard open- and closed-kinetic chain outpatient program that was monitored by postoperative isokinetic torque objective measurements. The patients represented a heterogenous group, with the prior knee surgeries and patient demographics listed in Table 1. All patients were informed of the purposes, risks, and potential discomforts with BFRT training before providing written consent. This study conformed to guidelines outlined in the Declaration of Helsinki and was approved by our hospital institutional review board and registered at clinicaltrials.gov NCT04357184.

BFRT Protocol

All patients underwent 2 or 3 training sessions per week for a total of 9 sessions (Table 1).[29,32] Further BFRT training was recommended and occurred on the basis of the patient's discretion, time constraints, and overall ability to continue. Fourteen patients underwent a second round of BFRT training for a total of 18 sessions. The patients completed training under the direct supervision of a research assistant in our clinic. The exercises performed are shown in Figure 1 and consisted of leg press, knee extension, mini-squats, and hamstring curls with 60% to 80% limb arterial occlusion pressure.

A commercially available cuff (Smart Cuffs, Strongsville, OH) was used in this study. During the first session, a research assistant positioned the cuff on the involved leg only and instructed the patient on application. Patients were instructed to place the cuff around their upper thigh as close to the inguinal area as comfortable snug against the skin. In patients who had adipose tissue, the cuff was instructed to be tight. Pressure was determined using an ultrasound doppler in either the supine or 45° inclined position. Patients were instructed to inflate the cuff, and limb occlusion pressure was measured until no there were no Doppler arterial pulses, indicating

Table 1. Patient Demographics, Preoperative and Operative Variables

Patient Variable	Data
Gender	
Female	18
Male	9
Knee	
Right	17
Left	10
Age, yr	40.1 ± 18.4
Height, cm	167.7 ± 9.8
Weight, kg	74.8 ± 18.6
Body mass index, kg/m^2	26.3 ± 4.8
Days training begun after surgery	241 ± 232
Referred after surgery elsewhere	7 (25%)
Supervised rehabilitation visits before BFRT	22 ± 10
Months home therapy program before BFRT	5.3 ± 3.5
BFRT done for:	
Quadriceps and hamstrings strength deficits	16
Quadriceps deficit only	10
Hamstrings deficit only	1
No. BFRT sessions completed:	
9 sessions	27
18 sessions	14
Operation	
ACL reconstruction, isolated	2
ACL reconstruction with meniscus repair or partial meniscectomy	7
TKA, primary	6
TKA, revision	2
Medial unicompartmental knee arthroplasty	1
Distal femoral osteotomy	1
Arthroscopy, multiple releases	2
MPFL revision reconstruction	1
Arthroscopy, lateral release	1
Posterolateral ligament reconstruction	1
Arthroscopy, medial meniscus repair, partial lateral meniscectomy	1
Osteochondral autograft transfer femoral condyle	1
Arthroscopy, fat pad resection	1

Data are reported as mean ± standard deviation or number.
ACL, anterior cruciate ligament; BFRT, blood flow restriction training; MPFL, medial patellofemoral ligament; TKA, total knee arthroplasty.

complete arterial occlusion. The limb muscles remained in a relaxed state during this process.

The cuff pressures during the exercises were individualized and set between 60% to 80% of the complete arterial occlusion pressure to provide a maximum and minimum threshold for BFRT. Patient complaints of cuff thigh pain, muscle pain and fatigue, and overall comfort during the exercises were used as a general guide for the cuff pressure setting within this threshold. The 1-RM was determined for each patient as described elsewhere,[33,34] and the loading for the resistive exercises was standardized to 25% to 35% of 1-RM.

The research assistant asked each patient to rate the muscle burn for each exercise, with the goal of achieving a 7 on a 0 to 10 scale to ensure muscle exhaustion. Muscle burn was defined as tired and fatigued to differentiate it from muscle pain. On the scale, 0 indicated no effort and 10, unmanageable pain. Patients who had muscle pain at 80% dropped the cuff pressure by 10 mm Hg until muscle burn was achieved. Patients who had lower pressure used slightly higher weights to achieve muscle burn. In patients who began to reach heavier weights (no more than 10% increase in weight at a time), the pressure was adjusted by 10 mm Hg. No patient dropped below the 60% threshold. If a patient came close to the threshold, the weight was increased no more than 10% to provide an increased burn. The patients' cuff pressure was retaken, and the 60% to 80% range was reset, along with the 1-RM to ensure proper weight was used.

The exercises and rest periods are shown in Table 2. The cuff was inflated for the duration of each of the 4 exercises. Although there was no reliable manner to monitor the pressure during the exercise, it was periodically checked between repetitions to ensure it was maintained. After the fourth set of repetitions for each exercise, the cuff was deflated for 2 minutes. A 5 cm—wide cuff was used in the initial months of the study and changed to a 10 cm—wide cuff because of better tolerance and less pressure required to achieve partial occlusion.[35] After 9 training sessions, the 1-RM and cuff pressure were determined and reset if required. In addition, all patients were prescribed a home exercise program. The program varied according to each patient's individual requirements and consisted of body weight open- and closed-kinetic chain exercises usually 3 days a week and was not tracked for this study.

Quadriceps and Hamstring Strength Testing Parameters

All patients were tested on a Biodex System 3 (Biodex Medical Systems, Inc., Shirley, NY) before the first training session and then after 9 sessions. Patients who then continued training were tested after the 18th BFRT session. After a 10-minute warm-up on a stationary bicycle, the patients were positioned in the dynamometer chair with the knee at 60° of flexion and secured per the manufacturer's instructions. Peak quadriceps and hamstrings isometric torque was measured bilaterally from 3 repetitions, each of 10 seconds' duration. The repetitions alternated between knee extension and knee flexion and included a 15-second rest period between repetitions. Peak torque was measured in foot pounds and normalized to the patients' body weight (lbs). The average of the 3 repetitions was calculated and the deficit between legs determined. Verbal encouragement was provided for every test.

Table 2. Blood Flow Restriction Training Exercise Protocol

Exercise	Repetitions	Rest	Repetitions	Rest	Repetitions	Rest	Repetitions	Rest
#1 Leg press machine, 30% 1-RM	30	1 min	15	1 min	15	1 min	15	2 min, cuff deflated
#2 Hamstring curl machine, 30% 1-RM	30	1 min	15	1 min	15	1 min	15	2 min, cuff deflated
#3 Leg extension machine, 30% 1-RM	30	1 min	15	1 min	15	1 min	15	2 min, cuff deflated
#4 Mini-squat	30	1 min	15	1 min	15	1 min	15	2 min, cuff deflated

1-RM, 1 repetition maximum; min, minute

Thigh Circumference Measurements

Standard thigh circumference measurements were taken 5 cm and 15 cm above the superior pole of the patella with a standard tape measuring device in patients who underwent training at our facility.

Patient Satisfaction

The level of satisfaction was rated on a 0 to 10 scale, with 10 indicating the highest satisfaction possible. Patients were asked if they believed BFRT was more effective than the traditional rehabilitation program they had participated in and could respond significantly better, somewhat better, or no better.

Statistical Analysis

Descriptive data are presented as means ± SD. Paired Student *t*-tests were used to evaluate changes from before training to after training for average peak torque

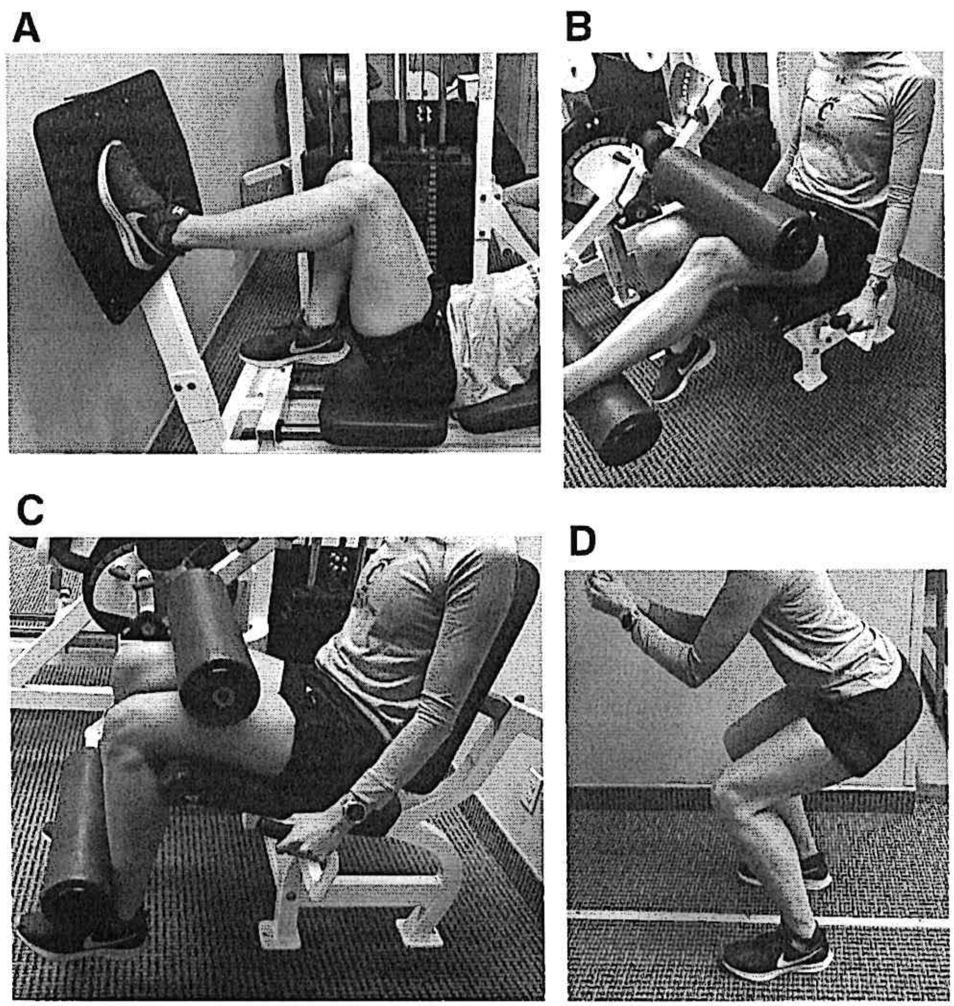

Fig 1. BFRT using (a) leg press machine, (b) hamstring curl machine, (c) knee extension machine, and (d) mini-squat.

Table 3A. Improvements in Quadriceps Muscle Strength and Deficits

	Effect 9 BFRT Sessions			Effect 18 BFRT Sessions		
	Pre-train (n=26)	Post-train (n=26)	*P* *ES*	Pre-train (n = 14)	Post-train (n = 14)	*P* *ES*
Quadriceps peak torque, involved side	71 ± 39	84 ± 47	<.0001 0.31	64 ± 39	85 ± 51	.004 0.35
Quadriceps peak torque noninvolved side	122 ± 58	132 ± 62	.003 0.16	117 ± 63	131 ± 63	.02 0.22
Quadriceps deficit (%)	43 ± 16	36 ± 19	.003 0.35	48 ± 17	38 ± 22	**.004** **0.52**

Data are presented as mean ± standard deviation. Bold indicates significant effect according to both *P* and ES values.
BFRT, blood flow restriction training; ES, effect size; NS, not significant.

values and strength deficits for the cohort. The results were also analyzed according to the percent change (improvement) from pretraining values for peak torques and strength deficits and were distributed into 4 categories: (1) ≥ 30%, (2) 20% to 29%, (3) 11% to 19%, and (4) ≤ 10%. The χ^2 and Fisher's exact test were used to determine significant differences for these data. The level of significance was set at *P* <.05. Effect sizes (ES) were calculated and interpreted according to Cohen,[36] where >0.8 was considered large, 0.8 to 0.5 moderate, and <0.5 small.[37] A significant effect required both *P* < .05 and ES > 0.50. Post-hoc power analysis compared the mean muscle strength percentage strength gains from a recent meta-analysis (14% ± 1.5%)[38] with the results of our study. With 27 patients in our study, we achieved a power of 95% at an alpha level of 0.05 to detect a meaningful difference in both quadriceps and hamstrings strength gains. Statistical studies also used Minitab 18 Statistical Software 2010 (Minitab, Inc., State College, PA).

Results

Participants

Twenty-seven patients were enrolled and completed this study from April 2017 to January 2020. Twenty patients (74%) enrolled were surgical patients of the senior author who underwent supervised rehabilitation with a team approach of experienced therapists at our center. The remaining 7 of 27 patients (26%) were referred for treatment after outside surgery and development of chronic muscle atrophy after an average of 9.2 months of therapy outside of our center. The patients began BFRT a mean of 241 ± 232 days (range, 92 to 1122) after surgery. Before training, they had undergone a mean of 22 ± 10 (range, 0 to 37) supervised rehabilitation visits and a home exercise program for an average of 5.3 ± 3.5 months (range, 2 to 18 months) that failed to resolve atrophy after a variety of operative procedures. All patients but 1 had a quadriceps deficit ≥20%, and 12 had a hamstrings deficit of ≥20%. All completed at least 9 BFRT sessions. A total of 18 sessions were completed by 14 patients with quadriceps deficits and 9 patients with hamstring deficits.

Effect BFRT on Quadriceps and Hamstrings Strength

Before training began, the mean quadriceps deficit (in 26 knees) was 43% ± 16% (range, 20%-76%, Table 3). The quadriceps deficits ranged from 20% to 40% in 13 knees; from 41% to 60% in 10 knees; and >60% in 3 knees. Although significant improvements were found in quadriceps peak torques (Fig. 2) and deficits (Fig. 3) after 9 training sessions (*P* < .0001 and *P* = .003, respectively), the ES were small (0.31 and 0.35, respectively). After 18 training sessions, the mean

Table 3B. Improvements in Hamstrings Muscle Strength and Deficits

	Effect 9 BFRT Sessions			Effect 18 BFRT Sessions		
	Pre-train (n = 12)	Post-train (n = 12)	*P* *ES*	Pre-train (n = 8)	Post-train (n = 8)	*P* *ES*
Hamstrings peak torque involved side	35 ± 19	44 ± 22	.002 0.45	33 ± 17	44 ± 19	**.0005** **0.66**
Hamstrings peak torque noninvolved side	55 ± 27	58 ± 28	NS 0.08	56 ± 27	58 ± 22	NS 0.11
Hamstrings deficit (%)	38 ± 14	22 ± 26	**.02** **0.78**	43 ± 15	25 ± 13	**0002** **1.31**

Data are presented as mean ± standard deviation. Bold indicates significant effect according to both *P* and ES values.
BFRT, blood flow restriction training; ES, effect size; NS, not significant.

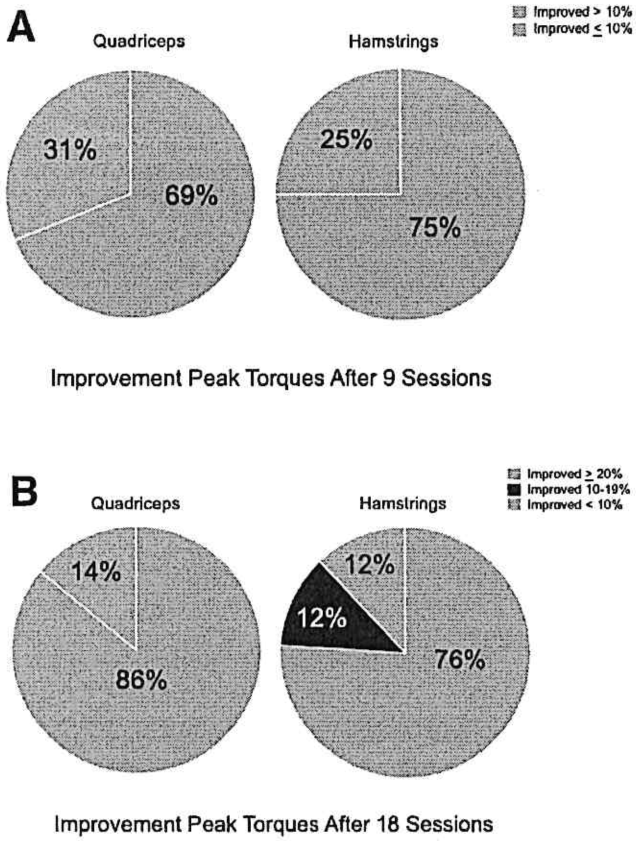

Fig 2. The percent improvement of quadriceps and hamstring peak torques are shown after 9 (A) and 18 (B) BFRT sessions.

quadriceps deficit (in 14 patients) significantly decreased (P = .004, ES 0.52). Mean peak torques decreased; however, ES were small (P = .004, ES 0.35).

Before BFRT, the mean hamstrings deficit (in 12 knees) was 38% ± 14% (range, 20%-66%). The hamstring deficits ranged from 20% to 40% in 8 knees; from 41% to 60% in 3 knees; and >60% in 1 knee. Statistically significant improvements occurred after 9 and 18 sessions (in 8 patients) for hamstrings peak torques and deficits. After 18 training sessions, the mean hamstrings deficit decreased from 43% ± 15% before training to 25% ± 13% (P = .002, ES 1.31).

The study hypothesis was proven because more than 50% of the cohort had >10% increase in quadriceps and hamstring peak torques after 9 BFRT sessions, and 20% or greater of the cohort had these improvements after 18 sessions. Thigh circumference measurements shown in Table 4 showed minimal changes.

Patient Satisfaction

The mean satisfaction score, obtained in 19 patients, was 8.9 ± 1.5 points (range, 4 to 10). Sixty-three percent believed the BFRT program produced significantly better results than their previous traditional rehabilitation program, and the remainder indicated it produced somewhat better results. There were no complications. One patient complained of muscle soreness after exercise.

Discussion

The most important finding of this study was the statistically significant improvements in quadriceps and hamstring peak torques and deficits after 9 BFRT sessions and continued improvements after 18 BFRT sessions. These improvements occurred in patients who had participated in a closely supervised postoperative therapy program for an average of 5.3 months after knee surgery in which the surgeon and therapist noted no or limited improvement in quadriceps and hamstring strength. The mean quadriceps deficit in 26 patients before training was 43% (range, 20%-76%), and the mean hamstring deficit in 12 patients was 38% (range, 20%-66%). These muscle strength deficits prevented training with heavy resistance weights and other standard rehabilitation exercises normally used to promote increases in muscle mass and strength. Most of these patients underwent postoperative therapy after surgery at our center by the senior author, following well-established and published knee surgery protocols. From a clinical standpoint, it is sometimes surprising to

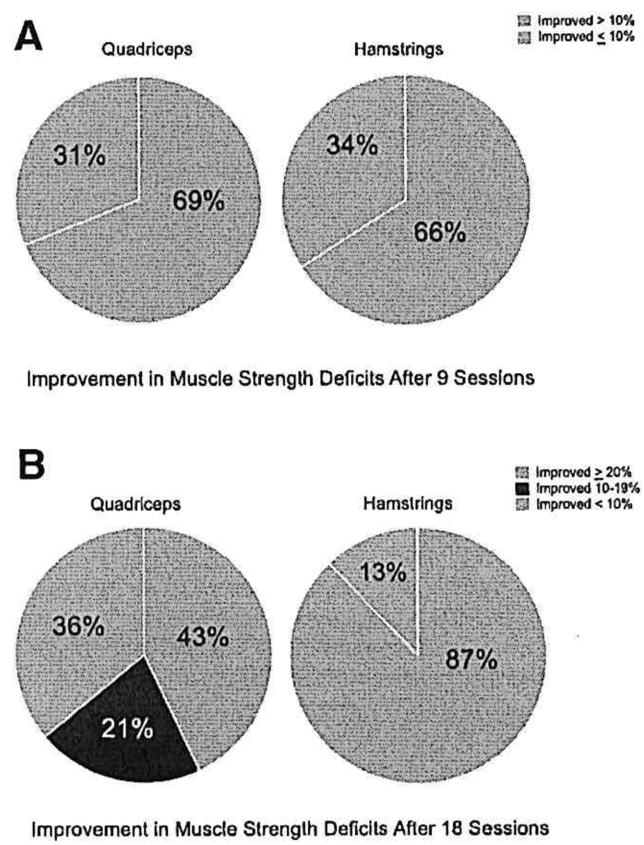

Fig 3. The percent improvement of quadriceps and hamstring muscle strength deficits are shown after (A) and 18 (B) BFRT sessions.

Table 4. Thigh Circumference Measurements

Measurement From Superior Pole of Patella	Preoperative (cm)	Post 9 Sessions (cm)	Change Post 9 Sessions (cm)	Post 18 Sessions (cm)	Change Post 18 Sessions (cm)
15 cm	49.8 ± 6.1 (n = 20)	49.3 ± 6.1 (n = 17)	0.5 ± 1.7 *P* = NS ES = 0.08	51.2 ± 7.8 (n = 8)	0.9 ± 2.5 *P* = NS ES = 0.11
5 cm	42.5 ± 5.1 (n = 20)	42.4 ± 5.1 (n = 17)	0.6 ± 1.0 *P* = .03 ES = 0.11	42.7 ± 6.8 (n = 8)	0.6 ± 2.1 *P* = NS ES = 0.10

NOTE: Data are presented as mean ± standard deviation.
ES, effect size; NS, not significant.

see the severe extent of muscle weakness that may occur in some patients after knee surgery in an early postoperative period, because of a combination of postoperative pain, knee swelling, and overall inability to participate in standard open and closed chain standard knee exercises. For example, 11 of 26 patients of the senior author were enrolled at 3 months after surgery with an average quadriceps deficit of 46.6% and hamstring deficit of 32.5%. The BFRT provided low-resistance exercises with diminished knee symptoms to interrupt the downward therapy course that was occurring in these patients.

Our hypothesis was proven after both 9 and 18 BFRT sessions as statistically significant increases in quadriceps and hamstring peak torque were measured. After 9 sessions, a >10% increase in muscle strength occurred in quadriceps and hamstring peak torques in 69% and 75% of the patients, respectively. After 18 training BFRT sessions, a ≥20% increase in quadriceps and hamstring peak torques was measured in 86% and 76% of the patients, respectively. The failure rate to respond after 18 BFRT sessions (<20% improvement) in peak quadriceps and hamstring torques was 14% and 24%, respectively.

Authors have published on the application of BFRT early in the postoperative period with recommendations that the low-resistance BFRT is an important therapy modality to be considered in the overall therapy protocol.[26,39] It is not known whether BFRT has a beneficial effect in patients who have already developed marked muscle atrophy and strength deficits because only 2 studies with a limited number of patients have been published to our knowledge. Hylden et al.[40] reported on 7 active duty Service members with chronic quadriceps and hamstrings weakness who were >3 months after surgery in which traditional therapy and resistance training failed to improve strength. The BFRT protocol involved training 3 days a week for 2 weeks for a total of 6 sessions. The authors reported improvements for flexion and extension for peak torque that ranged from 13% to 38%, for average power that ranged from 42% to 81%, and total work that ranged from 35% to 55%. Kilgas et al.[21] conducted a study of 9 patients a mean of 5 years after ACL reconstruction and reported that knee extensor strength increased by 20% ± 14% with a BFRT program for 25 minutes, 5 times a week for 4 weeks consisting of single-leg knee extension, bodyweight half-squats, and walking activities at 50% limb occlusion pressure.

The extrapolation of the results of the current study, and overall promising results of BFRT in other studies has led to the adoption at our Center of a BFRT program after all major knee operative procedures beginning at 3 weeks after surgery. Some patients after their initial BFRT instruction choose to perform a home-based program; however, we prefer that training be conducted under the direct supervision of the therapy staff because this study showed the necessity for close supervision and adjustments with regard to cuff pressures and load resistance for each exercise to achieve the level 7 muscle burn. Patients are educated on the BFRT protocol and the associated limb discoloration and muscle discomfort with the cuff inflation that may initially produce anxiety. Therapists and athletic trainers in busy clinics require adequate patient scheduling so an appropriate amount of time is available because BFRT is initially time consuming; however, it has proven to be a beneficial modality to offer to postoperative patients. There are physiological adaptations produced by BFRT, and studies have provided important patient recommendations regarding cuff width, exercises, and cuff pressures.[19,29,35,41]

Blood flow to the upper or lower extremity and tissue perfusion decreases (non-linear manner) with increasing limb occlusion pressures (LOP). Kilgas et al.[42] showed that at 60% to 80% LOP, the blood flow decreased in the upper extremity approximately 20% and 45%, respectively, during rest and during exercise even with increased blood flow induced by active muscle contractions that was referred to as an exercise-induced hyperemic response. After exercise, blood flow levels returned to those similar to pre-exercise levels. Singer et al.[43] showed in the lower extremity that a 60% to 80% LOP decreased femoral arterial blood flow by 34% and 45%, respectively. Maintaining the LOP after exercise continues metabolic stress, and pressures above 80% did not result in decreases in oxyhemoglobin and increases in deoxyhemoglobin levels that reflect overall metabolic stress. This data facilitates recommendations on safe BFRT guidelines. A range of 60% to 80% LOP allows continued blood flow perfusion in a safe and tolerable manner, avoiding higher pressures that are uncomfortable and not necessary to produce overall muscle metabolic stress. A potential problem with BFR training is that the tourniquet easily compresses venous structures to markedly restrict venous return. The continued arterial blood inflow with a tourniquet at 60% to 80% LOP increases overall extremity blood volume[44,45] with venous engorgement, and therefore a shortened time period of LOP remains as a safety factor.

Recent publications on BFRT have evaluated the safety and adverse events of BFRT and concluded the addition of BFRT as a modality is a safe strengthening approach and no more likely for an adverse event in comparison to standard exercises.[16,17,20,29] Isolated BFRT rare case reports of upper extremity vein thrombosis, rhabdomyolysis, and increased cardiac stress have not been reported in published knee BFRT studies.[20] There are published patient exclusion criteria, as adopted in this study, to exclude patients with medical disorders including renal, cardiac, neurologic, blood disorders including clotting and sickle cell disorders, extremity venous abnormalities, immune, and cancer-related diseases. Clinicians need to be aware of pre-existing or risk factors before recommending BFRT. Published studies report on the advantage and application of BFRT and the low-resistance exercises in patients with postoperative restrictions or pain with high resistance exercises, prolonged weightbearing restrictions, recurrent knee swelling with strengthening exercises, persistent muscle atrophy not responding to standard therapy protocols, and decreasing muscle atrophy in the initial knee surgery postoperative phase.[16,17,20,24,29,38] The most frequent patient complaints are delayed muscle soreness and fatigue, and close supervision is necessary during the BFRT sessions on monitoring cuff pressures, exercises, and patient safety. BFRT represents an interim modality as a bridge to later higher resistance and strengthening protocols that are eventually necessary for final muscle strengthening and return of lower limb function. There still exists a paucity of well-controlled studies, inconsistent BFRT protocols, and studies with appropriate power that prevent conclusions with regard to optimal BFRT protocols and research on intensity, duration, and safety is needed in different patient populations. Added training is necessary for the physician and therapist, and recommended BFRT protocols and patient guidelines have been published.[32,35,46,47]

Recent reviews of cardiovascular risk during BFRT that have suggested that training may evoke increased blood pressure that may add 5 to 10 mm Hg to the usual blood pressure response during resistance training.[48-50] Authors have cautioned that this increase may trigger major cardiovascular events in patients with elevated risks, such as those middle-aged or elderly or with hypertensive or coronary artery disease. Specifically, reductions in blood flow to exercising muscle engage the exercise pressor reflex (EPR), a reflex that contributes to the autonomic cardiovascular response to exercise. The EPR generates increases in sympathetic nerve activity in diseases such as hypertension, heart failure, and peripheral artery disease. This could result in cardiac arrhythmia, myocardial infarction, stroke, or sudden cardiac death and the concern expressed in these review articles was generated by BFRT in elderly patients and in cardiac rehabilitation. The extent of this risk in normal healthy patients has not been determined.

Limitations

There are limitations to this study that include small patient numbers, the heterogenous enrollment of patients at different time periods from surgery and postoperative rehabilitation, varying operative procedures, and the amount of time postoperatively BFRT was initiated. A selection bias may exist as the recommendations for inclusion in the study by the therapist and surgeon was based on a lack of response for many postoperative months to standard therapy protocols; however, inclusion in the study required documentation of at least a 20% or greater deficit in muscle strength and in the majority of patients, this muscle deficit was 2 times this amount. Furthermore, a majority of the patients were under treatment by experienced therapists at our center using well-established and published postoperative therapy protocols. It was not possible to establish a control patient group because no published study has provided an alternative protocol for patients with chronic muscle atrophy not responding to well monitored and structured standard postoperative open and closed-chain rehabilitation protocols. The patients provided their own internal control in the lack of a response to their therapy program and necessity for an alternative BFRT modality. The study protocol did not include patient-reported outcome subjective evaluation scales as these outcome measures depend on other variables such as the success of the surgical procedure and patient expectations and the study focus was solely on an objective increase of the change in muscle strength isokinetic measurements with the BFRT program. We did not obtain magnetic resonance imaging or ultrasound cross-sectional area measurements or muscle biopsies. In this study, a blood pressure cuff was used that lacked a more sophisticated design to monitor and maintain the same percent occlusion pressures during the different exercises due to expense issues with treating multiple patients. The blood pressure was initially measured with the patient in the supine position and not in the exercise position in which pressure gradients may change. The use of the contralateral limb as a control would be problematic if also affected with disuse muscle atrophy.

Conclusions

BFRT produced statistically significant improvements in peak quadriceps and hamstring torque measurements after 9 and 18 sessions in a majority of patients with severe quadriceps and hamstring strength deficits that had failed to respond to many months of standard and monitored postoperative rehabilitation.

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References

1. Huber R, Viecelli C, Bizzini M, et al. Knee extensor and flexor strength before and after anterior cruciate ligament reconstruction in a large sample of patients: Influence of graft type. *Phys Sportsmed* 2019;47:85-90.
2. Chung KS, Ha JK, Yeom CH, et al. Are muscle strength and function of the uninjured lower limb weakened after anterior cruciate ligament injury? Two-year follow-up after reconstruction. *Am J Sports Med* 2015;43:3013-3021.
3. Larsen JB, Farup J, Lind M, Dalgas U. Muscle strength and functional performance is markedly impaired at the recommended time point for sport return after anterior cruciate ligament reconstruction in recreational athletes. *Hum Mov Sci* 2015;39:73-87.
4. Hsiao SF, Chou PH, Hsu HC, Lue YJ. Changes of muscle mechanics associated with anterior cruciate ligament deficiency and reconstruction. *J Strength Cond Res* 2014;28: 390-400.
5. Schache MB, McClelland JA, Webster KE. Lower limb strength following total knee arthroplasty: A systematic review. *Knee* 2014;21:12-20.
6. Moon YW, Kim HJ, Ahn HS, Lee DH. Serial Changes of quadriceps and hamstring muscle strength following total knee arthroplasty: A meta-analysis. *PLoS One* 2016;11: e0148193.
7. Tourville TW, Jarrell KM, Naud S, Slauterbeck JR, Johnson RJ, Beynnon BD. Relationship between isokinetic strength and tibiofemoral joint space width changes after anterior cruciate ligament reconstruction. *Am J Sports Med* 2014;42:302-311.
8. Risberg MA, Oiestad BE, Gunderson R, et al. Changes in knee osteoarthritis, symptoms, and function after anterior cruciate ligament reconstruction: A 20-year prospective follow-up study. *Am J Sports Med* 2016;44:1215-1224.
9. de Jong SN, van Caspel DR, van Haeff MJ, Saris DB. Functional assessment and muscle strength before and after reconstruction of chronic anterior cruciate ligament lesions. *Arthroscopy* 2007;23:28 e21-23.
10. Oiestad BE, Holm I, Engebretsen L, Aune AK, Gunderson R, Risberg MA. The prevalence of patellofemoral osteoarthritis 12 years after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2013;21:942-949.
11. Karanikas K, Arampatzis A, Bruggemann GP. Motor task and muscle strength followed different adaptation patterns after anterior cruciate ligament reconstruction. *Eur J Phys Rehabil Med* 2009;45:37-45.
12. Konishi Y, Oda T, Tsukazaki S, Kinugasa R, Hirose N, Fukubayashi T. Relationship between quadriceps femoris muscle volume and muscle torque after anterior cruciate ligament rupture. *Knee Surg Sports Traumatol Arthrosc* 2011;19:641-645.
13. Konishi Y, Oda T, Tsukazaki S, Kinugasa R, Fukubayashi T. Relationship between quadriceps femoris muscle volume and muscle torque at least 18 months after anterior cruciate ligament reconstruction. *Scand J Med Sci Sports* 2012;22:791-796.
14. Pietrosimone BG, Lepley AS, Ericksen HM, Gribble PA, Levine J. Quadriceps strength and corticospinal excitability as predictors of disability after anterior cruciate ligament reconstruction. *J Sport Rehabil* 2013;22:1-6.
15. American College of Sports M. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 2009;41: 687-708.
16. Barber-Westin S, Noyes FR. Blood flow-restricted training for lower extremity muscle weakness due to knee pathology: A systematic review. *Sports Health* 2019;11:69-83.
17. Hughes L, Paton B, Rosenblatt B, Gissane C, Patterson SD. Blood flow restriction training in clinical musculoskeletal rehabilitation: a systematic review and meta-analysis. *Br J Sports Med* 2017;51:1003-1011.
18. Loenneke JP, Thiebaud RS, Abe T. Does blood flow restriction result in skeletal muscle damage? A critical review of available evidence. *Scand J Med Sci Sports* 2014;24: e415-e422.
19. Mattocks KT, Jessee MB, Mouser JG, et al. The application of blood flow restriction: Lessons from the laboratory. *Curr Sports Med Rep* 2018;17:129-134.
20. Minniti MC, Statkevich AP, Kelly RL, et al. The safety of blood flow restriction training as a therapeutic intervention for patients with musculoskeletal disorders: A systematic review. *Am J Sports Med* 2020;48:1773-1785.
21. Kilgas MA, Lytle LLM, Drum SN, Elmer SJ. Exercise with blood flow restriction to improve quadriceps function long after ACL reconstruction. *Int J Sports Med* 2019;40: 650-656.
22. Ohta H, Kurosawa H, Ikeda H, Iwase Y, Satou N, Nakamura S. Low-load resistance muscular training with moderate restriction of blood flow after anterior cruciate ligament reconstruction. *Acta Orthop Scand* 2003;74:62-68.
23. Takarada Y, Takazawa H, Sato Y, Takebayashi S, Tanaka Y, Ishii N. Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. *J Appl Physiol (1985)* 2000;88:2097-2106.
24. Tennent DJ, Hylden CM, Johnson AE, Burns TC, Wilken JM, Owens JG. Blood flow restriction training after knee arthroscopy: A randomized controlled pilot study. *Clin J Sport Med* 2017;27:245-252.

25. Gaunder CL, Hawkinson MP, Tennent DJ, Tubb CC. Occlusion training: Pilot study for postoperative lower extremity rehabilitation following primary total knee arthroplasty. *US Army Med Dep J* 2017;2-17:39-43.
26. Hughes L, Rosenblatt B, Haddad F, et al. Comparing the effectiveness of blood flow restriction and traditional heavy load resistance training in the post-surgery rehabilitation of anterior cruciate ligament reconstruction patients: A UK National Health Service Randomised Controlled Trial. *Sports Med* 2019;49:1787-1805.
27. Iversen E, Rostad V, Larmo A. Intermittent blood flow restriction does not reduce atrophy following anterior cruciate ligament reconstruction. *J Sport Health Sci* 2016;5:115-118.
28. Giles L, Webster KE, McClelland J, Cook JL. Quadriceps strengthening with and without blood flow restriction in the treatment of patellofemoral pain: A double-blind randomised trial. *Br J Sports Med* 2017;51:1688-1694.
29. DePhillipo NN, Kennedy MI, Aman ZS, Bernhardson AS, O'Brien LT, LaPrade RF. The role of blood flow restriction therapy following knee surgery: Expert opinion. *Arthroscopy* 2018;34:2506-2510.
30. Franz A, Behringer M, Nosaka K, et al. Mechanisms underpinning protection against eccentric exercise-induced muscle damage by ischemic preconditioning. *Med Hypotheses* 2017;98:21-27.
31. Wilkinson BG, Donnenwerth JJ, Peterson AR. Use of blood flow restriction training for postoperative rehabilitation. *Curr Sports Med Rep* 2019;18:224-228.
32. DePhillipo NN, Kennedy MI, Aman ZS, Bernhardson AS, O'Brien L, LaPrade RF. Blood flow restriction therapy after knee surgery: indications, safety considerations, and postoperative protocol. *Arthrosc Tech* 2018;7:e1037-e1043.
33. Kraemer WJ, Patton JF, Gordon SE, et al. Compatibility of high-intensity strength and endurance training on hormonal and skeletal muscle adaptations. *J Appl Physiol* 1995;78:976-989.
34. Reiman MP, Manske RC. *Functional Testing in Human Performance*. Champaign, IL: Human Kinetics, 2009.
35. Patterson SD, Hughes L, Warmington S, et al. Blood flow restriction exercise position stand: Considerations of methodology, application and safety. *Front Physiol* 2019;10:533.
36. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. New York: Academic Press, 1977.
37. Batterham AM, Hopkins WG. Making meaningful inferences about magnitudes. *Sportscience* 2005;9:6-13.
38. Lixandrao ME, Ugrinowitsch C, Berton R, et al. Magnitude of Muscle Strength and Mass Adaptations Between High-Load Resistance Training Versus Low-Load Resistance Training Associated with Blood-Flow Restriction: A Systematic Review and Meta-Analysis. *Sports medicine (Auckland, N.Z.)* 2018;48:361-378.
39. Curran MT, Lepley LK, Palmieri-Smith RM. Continued improvements in quadriceps strength and biomechanical symmetry of the knee after postoperative anterior cruciate ligament reconstruction rehabilitation: Is it time to reconsider the 6-month return-to-activity criteria? *J Athl Train* 2018;53:535-544.
40. Hylden C, Burns T, Stinner D, Owens J. Blood flow restriction rehabilitation for extremity weakness: A case series. *J Spec Oper Med* 2015;15:50-56.
41. Vopat BG, Vopat LM, Bechtold MM, Hodge KA. Blood flow restriction therapy: Where we are and where we are going. *J Am Acad Orthop Surg* 2020;28:e493-e500.
42. Kilgas MA, McDaniel J, Stavres J, Pollock BS, Singer TJ, Elmer SJ. Limb blood flow and tissue perfusion during exercise with blood flow restriction. *Eur J Appl Physiol* 2019;119:377-387.
43. Singer TJ, Stavres J, Elmer SJ, et al. Knee extension with blood flow restriction: Impact of cuff pressure on hemodynamics. *Eur J Appl Physiol* 2020;120:79-90.
44. Aebi MR, Willis SJ, Girard O, Borrani F, Millet GP. Active preconditioning with blood flow restriction or/and systemic hypoxic exposure does not improve repeated sprint cycling performance. *Front Physiol* 2019;10:1393.
45. Willis SJ, Alvarez L, Borrani F, Millet GP. Oxygenation time course and neuromuscular fatigue during repeated cycling sprints with bilateral blood flow restriction. *Physiol Rep* 2018;6:e13872.
46. Scott BR, Loenneke JP, Slattery KM, Dascombe BJ. Blood flow restricted exercise for athletes: A review of available evidence. *J Sci Med Sport* 2016;19:360-367.
47. Hughes L, Patterson SD, Haddad F, et al. Examination of the comfort and pain experienced with blood flow restriction training during post-surgery rehabilitation of anterior cruciate ligament reconstruction patients: A UK National Health Service trial. *Phys Ther Sport* 2019;39:90-98.
48. Cristina-Oliveira M, Meireles K, Spranger MD, O'Leary DS, Roschel H, Pecanha T. Clinical safety of blood flow-restricted training? A comprehensive review of altered muscle metaboreflex in cardiovascular disease during ischemic exercise. *Am J Physiol Heart Circ Physiol* 2020;318:H90-H109.
49. Spranger MD, Krishnan AC, Levy PD, O'Leary DS, Smith SA. Blood flow restriction training and the exercise pressor reflex: a call for concern. *Am J Physiol Heart Circ Physiol* 2015;309:H1440-H1452.
50. Loenneke JP, Wilson JM, Wilson GJ, Pujol TJ, Bemben MG. Potential safety issues with blood flow restriction training. *Scand J Med Sci Sports* 2011;21:510-518.