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IJSPT

SYSTEMATIC REVIEW

A SYSTEMATIC REVIEW OF THE EFFECTS OF BLOOD FLOW RESTRICTION TRAINING ON QUADRICEPS MUSCLE ATROPHY AND CIRCUMFERENCE POST ACL RECONSTRUCTION

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ABSTRACT

Background: ACL reconstruction often results in an extended period of muscle atrophy and weakness. Blood flow restriction (BFR) training is a technique that has been shown to decrease muscle atrophy in a variety of populations.

Purpose: The purpose of this systematic review was to analyze the research presented on the effect of blood flow restriction training on quadriceps muscle atrophy and circumference post ACL reconstruction.

Study Design: Systematic Review

Methods: Articles were reviewed using the databases Google Scholar, PubMed, and EBSCO. Keywords included blood flow restriction training, ACL reconstruction, and quadriceps.

Inclusion criteria included: English language, peer-reviewed journals; randomized control trials; and articles including blood flow restriction and measurement of quadriceps atrophy and circumference post ACL reconstruction. Exclusion criteria included non-English language publications; studies without a control group; and articles without sufficient data to evaluate the methodology. Four studies met the selection criteria and were assessed using the GRADE scale, which analyzes the strength of a study based on study limitations, precision, consistency, directness, and publication bias. After a GRADE designation was assigned, the following information was extracted from and compared across the studies: participant demographics, cuff used, graft used during ACL reconstruction, tool used to assess muscle atrophy, protocol used, and conclusions.

Results: Three out of four studies showed some amount of an increase in femoral muscle cross sectional area after the use of BFR combined with low-intensity resistance training (LIRT). The strength of all four studies was moderate when assessed using the GRADE scale.

Conclusion: This review of the available evidence yields promising results regarding the use of BFR and LIRT in the remediation of femoral muscle atrophy after an ACL reconstruction. Further research is necessary before BFR can be recommended for use in clinical settings.

Level of evidence: 3a

Key Words: Anterior cruciate ligament reconstruction, blood flow restriction, quadriceps muscle atrophy.

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INTRODUCTION

Lower extremity muscle atrophy and loss of mass is common after surgery, often due to the need for a period of joint unloading and limited weight bearing.[1-3] For example, after arthroscopic knee surgery, the decrease in quadriceps muscle volume is as high as 33% [4,5] and atrophy can occur in as little as two weeks.[3,6,7] Anterior cruciate ligament (ACL) injuries are among the most common lower extremity injuries in sports and often require surgical reconstruction.[8-10] Regaining femoral muscle mass and strength after ACL reconstruction can be particularly difficult.[11-13] Compared to the contralateral limb, discrepancies in knee extensor strength can be as high as 30% on the surgical side six months after surgery.[14] The difference in quadriceps cross sectional area (CSA) between the contralateral and surgical side is as much as 18% after six years.[13,15,16]

Quadriceps dysfunction has the potential to create abnormal motor patterns, impacting activities of daily living and increasing the risk for re-injury.[3] For example, altered single limb vertical jumping and landing techniques are documented during sporting activities and restoration of quadriceps function is often needed in order for return to sports without restriction.[15,17]

Various interventions are available to remediate persistent quadriceps atrophy after ACL reconstruction, including neuromuscular electrical stimulation (NMES) and exercise. The goal of NMES is to minimize quadriceps atrophy,[18] increase the intensity of a contraction during exercise,[19] and improve strength.[20] The rationale for incorporating NMES to reestablish quadriceps strength and muscle recruitment is to address muscle inhibition secondary to pain and joint effusion.[18,21] NMES begins as early as the third day post-operatively[21] and continues as long as twelve weeks after surgery.[22] While there is limited evidence for the use of NMES as a stand-alone intervention,[23] volitional exercise combined with NMES may be more effective at improving quadriceps strength.[24] Lower extremity strengthening exercises are also a common component of rehabilitation protocols post ACL reconstruction.[25] Open and closed kinetic chain exercises are frequently used to restore quadriceps strength and both appear safe in the early portion of a rehabilitation program.[26]

Blood flow restriction (BFR) training is a relatively new technique for either the prevention of muscle atrophy or possibly the inducement of muscle hypertrophy.[27,28] The procedure involves placing an inflatable cuff or tourniquet on the proximal end of an extremity while progressively increasing the internal pressure to the point of limiting arterial blood flow influx and the venous efflux.[29] Advocates of BFR claim it can be combined with low-intensity resistance training (LIRT) to achieve comparable muscle adaptations seen with higher intensity resistance training (HIRT).[28-30] The ability to train at a lower intensity with diminished stress, load, or pain on the tibiofemoral or patellofemoral joints could contribute to improved functional outcomes.

During bouts of HIRT, the byproduct lactate is released and accumulates in muscle tissue, increasing the amount of available growth hormones (GH). This hormone release also occurs when BFR is applied with LIRT despite the mechanical load being much lower.[31-33] Growth hormone production is also associated with an increase in collagen synthesis. GH stimulates the insulin-like growth factor (IGF-1), which utilizes satellite cells and combines them with muscle fibers to create new myocytes. This is what allows BFR training to potentially promote repair and hypertrophy.[34-37]

Blood flow restriction training may remediate the muscle impairments seen post ACL reconstruction by affecting muscle fiber recruitment, stem cell proliferation, and metabolic stresses. These effects are beneficial for healing and potentially improving recovery and functional outcomes.[38] Therefore, the purpose of this systematic review was to analyze the research presented on the effect of blood flow restriction training on quadriceps muscle atrophy and circumference post ACL reconstruction

METHODS

Literature Search Strategy

The available evidence was reviewed through September 2019 using the databases Google Scholar, PubMed, and EBSCO. Keywords included blood flow restriction training, ACL reconstruction, and quadriceps.

Selection Criteria

Inclusion criteria included: English language, peer-reviewed journals; randomized control trials; and articles including blood flow restriction and measurement of quadriceps atrophy and circumference post ACL reconstruction. Exclusion criteria included non-English language publications; studies without a control group; and articles without sufficient data to evaluate the methodology.

The titles and abstracts from the initial database search were screened by one author (DC) for relevance on the topic. Then all four authors reviewed the potential full-text articles together using the above-mentioned criteria to arrive at a consensus. The senior author (DC) appraised the final list to ensure agreement among authors. The review included four articles with publication dates ranging from 2000 to 2019 and the search strategy is depicted in Figure 1.

The included studies were evaluated using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) scale to examine the quality of evidence. The GRADE scale assesses five domains: the presence of limitations, imprecision of measurements, inconsistency of outcomes, indirectness of interventions, and publication bias. An overall designation of "high," "moderate", "low", or "insufficient" are assigned to each article based on the strength of ratings of the five domains. The general rule when downgrading or upgrading a GRADE rating is to move down or up one category per issue. For example, if the initial rating for the outcome of a randomized controlled trial was "high", it could change to "moderate" if there was high risk for bias. It

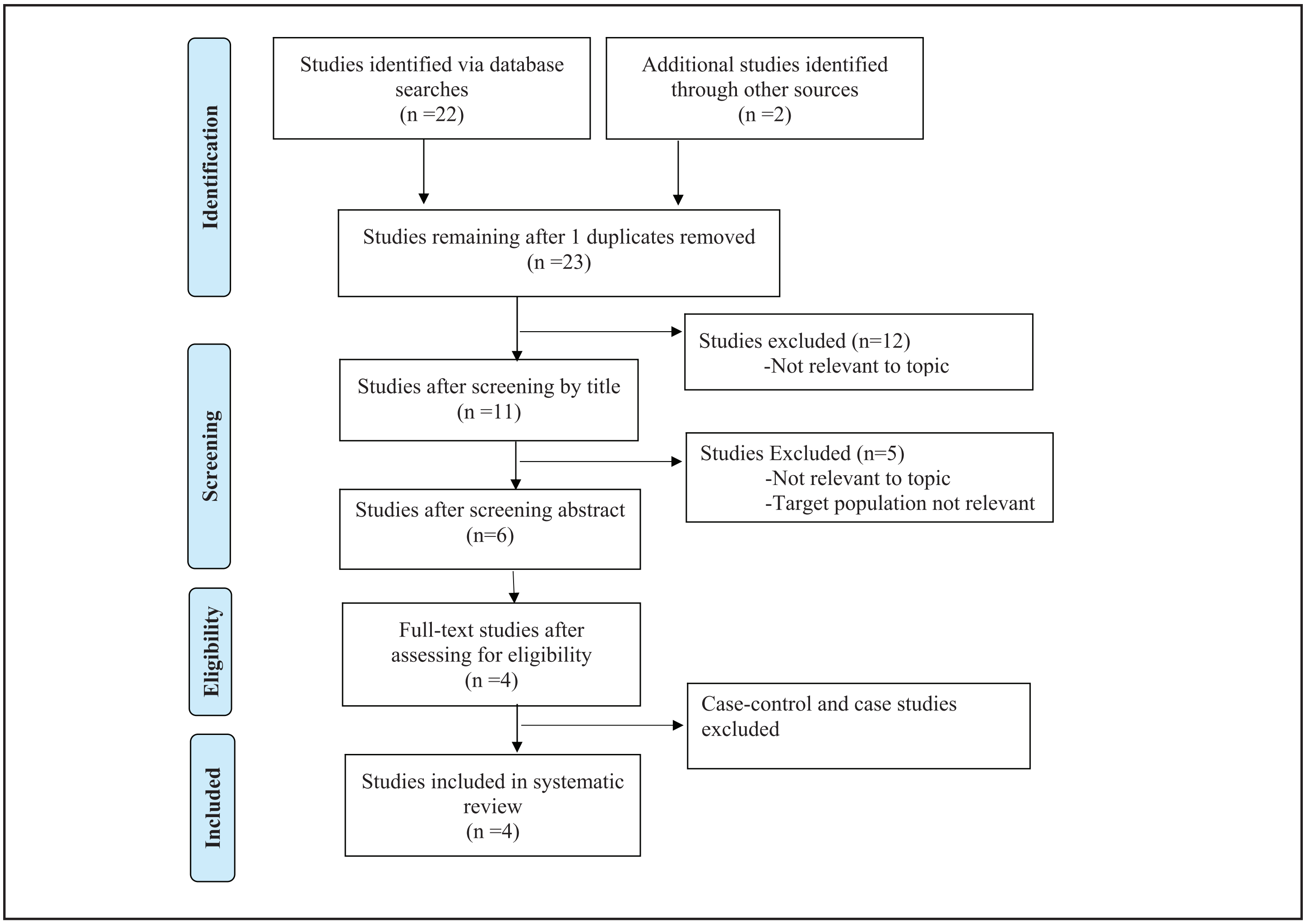

Figure 1. *Literature Search Strategy Results.*

could further change to "low" if there was significant heterogeneity between groups in the study. A definition of each rating is provided in Table 1, an explanation of the five criteria using for the rating system is provided in Table 2, and the results of the GRADE evaluation for each article are represented in Table 3.[39,40] After a GRADE designation was assigned, the following information was extracted from and compared across the studies: participant demographics, cuff used, graft used during ACL reconstruction, tool used to assess muscle atrophy, protocol used, and conclusions.

RESULTS

GRADE Scale Results

The four included studies were randomized control trials (RTCs), each having a quality of "moderate" according to the GRADE scale. Overall three of four studies showed a decrease in post-surgical muscle atrophy with the use of BFR combined with LIRT. One study did not result in an acute increase in quadriceps cross sectional area when measured 16 days after surgery.

Participant Demographics

The number of participants in the reviewed studies ranged from 14 to 44 with males used as subjects slightly more than females. Also, there was no significant difference between experimental and control groups with regard to age, height or weight in all studies. Patient demographics are presented in Table 4.

Cuff and Graft

Systems of blood flow restriction were not standardized across all studies. The various occlusion devices

Table 1. *GRADE Quality of Evidence Ratings.*

Rating	Definition
High	Additional research is not likely to alter the confidence in the estimate of the effect.
Moderate	Additional research is likely to influence the confidence in the estimate of the effect and may change the estimate.
Low	Additional research is very likely to have an important influence on the confidence in the estimate of the effect and is likely to change the estimate.
Insufficient	Any estimate of effect is very uncertain.

Table 2. *GRADE Criteria Definitions.*

Criteria	Definitions
Study Limitations	Lack of subject blinding, lack of clear randomization, large subject attrition, or stopping a trial early are examples of study limitations.
Precision	Imprecision occurs when there is a large confidence interval which may skew the results and quality of the data.
Consistency	Inconsistency occurs when there is unexplained and significant variability in the results that differed from previous studies.
Directness	Indirectness occurs when there is an indirect comparison of two populations, outcomes, or interventions. The validity of the conclusions may not be transferable to both groups.
Publication Bias	Publication bias occurs when studies with unfavorable results remain unpublished while studies with positive findings are published at a higher rate.

Table 3. *GRADE Scale Results.*

Author	Study Limitations	Precision	Consistency	Directness	Publication Bias	Overall
Takarada 2000	Medium	Imprecise	Consistent	Direct	Undetected	Moderate
Ohta 2003	Low	Imprecise	Consistent	Direct	Undetected	Moderate
Iversen 2014	Medium	Imprecise	Consistent	Direct	Undetected	Moderate
Lambert 2019	Medium	Imprecise	Consistent	Direct	Undetected	Moderate

Table 4. *Participant Demographics.*

Author	Number of Participants	Age Range	Gender Breakdown	Mean Weight ± SD (kg)
Takarada 2000	16	22.4 ± 2.1 experimental, 23 ± 2.5 control	8 males, 8 females	Experimental: male 67.8 ± 2.0 female 49.8 ± 0.7; Control: male 71.0 ± 5.8 female 53.4 ± 1.6
Ohta 2003	44	18-52	25 males, 19 female	65 ± 14 experimental 63 ± 8.8 control
Iversen 2014	24	18-40	14 males, 10 females	76.9 ± 12.1 experimental 77.6 ± 9.6 control
Lambert 2019	14	23±7	8 males, 6 females	75±14

included an unspecified pneumatic occlusion cuff, an unspecified air tourniquet, and the Delfi personalized occlusion cuff. Pneumatic occlusion devices involve inflating a blood pressure cuff to a pre-designated pressure on a resting muscle. The Delfi Personalized Tourniquet System automatically adjusts its pressure to maintain a percentage of the pre-designated percentage of occlusion. This pressure will adjust depending on the change in girth of the exercising muscle. Information related to cuff type is depicted in Table 5.

Measurements, Protocol, and Study Conclusions

Initiation of BFR ranged from two days to two weeks post-operative and graft types included a hamstring tendon autograft,[2,28] a patella tendon autograft,[45] while one study did not specify.[30] With regards to rehabilitation protocols, there were significant variations among the studies. Some performed BFR exercises multiple times a day[2,30,45] while others were only once per day.[28] There was also variation in the number of reported exercises performed each session while some studies did not specify at all. One study did not combine any form of exercise with the application of BFR, but there was still a statistically significant reduction in atrophy of the quadriceps.[30] Three studies used MRI[2,28,30] to measure changes in CSA while one study used a Dual-Energy X-ray Absorptiometry (DEXA)[45] scan to measure lean muscle mass. Table 6 summarizes each study's protocol and results.

In general, the studies leaned towards significant differences between groups that utilized BFR and LIRT and those that did not. Takarada had individuals three days' post-op apply an occlusion cuff for two sessions a day without exercise. Each session consisted of five minutes on and three minutes off for a

Table 5. *Cuff Use and Graft Type.*

Author	Type of Cuff	Pressure Used	Initiation of BFR	Type of Graft
Takarada 2000	Pneumatic occlusion cuff (brand not specified)	180 (start) - 238 mmHg (end mean)	3rd day post-operatively	Undisclosed
Ohta 2003	Air tourniquet (brand not specified)	180 mm Hg	2 weeks post-operatively	Hamstring tendon autograft
Iversen 2014	Delfi low pressure pneumatic occlusion cuff	130 (start) - 180 mmHg (end)	2nd day post-operatively	Hamstring tendon autograft
Lambert 2019	Delfi personalized tourniquet system	80% limb occlusion pressure	10 days post-operatively	Patella tendon autograft

total of five repetitions. The protocol was performed until the14th day post-op and then quadriceps CSA was compared to a control group who did not use an occlusion cuff after surgery. While both groups had quadriceps atrophy on day 14, the amount of atrophy in the experimental group was 1.6% compared to 2.2% in the control group.[30] Ohta had two groups exercise six times per week using the same protocol for 16 weeks after ACL reconstruction. The experimental group exercised with BFR while control group did not. After 16 weeks, MRI revealed a statistically significant increase in knee extensor CSA in the group that exercised using BFR.[28] Lambert had a BFR group and control group perform the same exercise protocol for 12 weeks after ACL reconstruction. Bone mineral density, bone mass, and lean muscle mass were measured with a DEXA scan pre-operatively and at 6 and 12 weeks post-operative. The control group had a significant decrease in thigh lean mass at 12 weeks compared to the BFR group.[45] The only study that did not show a difference between the control and BFR group was by Iversen.[2] In their study, the experimental group performing low load quadriceps exercises with an occlusion cuff for five minutes followed by removal of the cuff for three minutes. This was repeated for five repetitions, 2x/a day. The control group performed the same exercises without occlusion stimulus. Quadriceps CSA was assessed using an MRI two days before surgery and 16 days post-operatively. Although both groups saw a statistically significant difference in quadriceps CSA, there was no significant difference between groups.

DISCUSSION

While the initial results regarding the use of BFR look promising, the physiological underpinnings of BFR on reducing muscle atrophy are still not fully understood. One possible explanation is that resistance training in a BFR-induced anaerobic environment causes the release of GH, IGF-1 and satellite cells due to the buildup of lactate in the exercising muscle.[30,34] GH and IGF-1 work together to produce new myocytes with the satellite cells and the release of these hormones occurs whether the level of resistance intensity is high or low with the inclusion of blood flow restriction. However, while GH and IGF-1 stimulate new muscle cells, they do not cause the protein synthesis needed for muscle hypertrophy to occur. So while BFR and LIRT have shown the capability to decrease atrophy and promote hypertrophy, the exact mechanism for how this occurs remains an area for future research.[41-44]

Differences in the methodology of the study by Iversen may account for the reason positive results were not uniformly found across all included articles in this review.[2] For example, the level of post-op muscle atrophy in Iversen's study was distinctly smaller than in the other studies. Starting from a greater level of muscle function meant participants had less impairments to overcome. Additionally, the Iversen study used a wider cuff compared to other studies and also did not individually adjust the restrictive pressure to each individual, which likely did not effectively limit arterial inflow and venous

Table 6. *Protocol and Study Results.*

Author/ Study Design	Muscle Girth Change	Measurement Tool	Protocol	Study Length	Conclusions
Takarada 2000 Randomized Control Trial	Both the control and experimental groups had quadriceps atrophy on day 14. However, the amount of atrophy in the experimental group was 1.6% compared to 2.2% in the control group.	MRI measured cross-sectional area on 3rd and 14th day post-op.	2 sessions daily of vascular occlusive without exercise. Each session consisted of 5 minutes on and 3 minutes off for 5 repetitions. Protocol performed 3rd to 14th days post-op.	11 days post-operative	Vascular occlusive therapy without exercise can acutely diminish post-operative disuse atrophy of knee extensors.
Ohta 2003 Randomized Control Trial	MRI revealed a statistically significant increase in knee extensor cross sectional area (CSA) in the experimental group. Biopsy revealed a small but statistically insignificant reduction in the control group.	Biopsy and MRI measured CSA preoperatively and at 1 and 16-weeks postoperatively.	Patients received 6 exercise sessions per week. Experimental group exercised with BFR while control group did not. Both groups followed the same training schedule.	Weeks 1-16 post-operative	Training with moderate restriction of blood flow is an effective intervention after ACL reconstruction to prevent knee extensor atrophy.
Iversen 2014 Randomized Control Trial	Both the experimental and control groups saw a statistically significant difference in quadriceps CSA 16 days after surgery. There was no significant difference between groups.	MRI 2 days before surgery and 16 days post-operatively measured thigh CSA.	The experimental group received an occlusion stimulus for 5 min. while performing low load quadriceps exercises followed by removal of occlusion for 3 minutes. This was repeated for 5 repetitions, 2x/ day. The control group performed the same exercises without occlusion stimulus.	16 days post-operative	BFR did not result in an acute increase in quadriceps CSA 16 days after ACL reconstruction.

Table 6. *Protocol and Study Results. (continued)*

Lambert 2019 Randomized Control Trial	The control group had a significant decrease in thigh lean mass at 12 weeks compared to the BFR group.	DEXA taken pre-operatively and at 6, 12 weeks' post-operative. Bone mineral density, bone mass, and lean muscle mass were measured with a DEXA taken pre-operatively and at 6,12 weeks post-operative	Both groups performed quadriceps setting isometrics, bilateral concentric/ eccentric leg presses, and concentric/ eccentric hamstring curls. Exercises were performed for 4 sets (30-15-15-15 repetitions) with 30 sec. of rest between sets.	Weeks 1-12 post-operative	Lean muscle mass remained decreased in the control group after 12 weeks compared to the BFR group.

outflow in the exercising muscle group. Improperly fitted cuffs are shown to be the biggest factor for ineffective arterial occlusion and needs to be taken into account when interpreting the results of this particular study. Finally, the timeframe for initiation of BFR training may have affected interpretation of results. Participants in the Iversen study did not begin the use of an occlusion cuff until 10 days after surgery while participants in the other three studies began exercise with an occlusion cuff an average of two days after surgery. It is possible if the participants in the Iversen study began BFR training sooner, they may have had similar reductions in muscle atrophy.

Diminished strength and increased muscle atrophy are common impairments after ACL reconstruction and typically 4-6 months are required for the graft to mature to the point it is able to tolerate loading.[11,12] During this period of recovery, a high-load rehabilitation program is ill-advised due to the risk of rupturing the reconstructed ligament.[10] Multiple reports have demonstrated the correlation between early recovery of quadriceps strength after surgery and the improvement in knee function.[13,14,16] BFR can be combined with exercise traditionally performed throughout ACL rehabilitation, whether isometric, concentric, eccentric, open chain or closed chain, to decrease stress on the knee by using only 20-30% of the patient's 1RM and has been shown to increase femoral muscle girth, knee extensor strength, and maintaining bone mineral density in the affected limb.[45] These physiological changes have the potential to limit the aforementioned quadriceps dysfunction, which may impact functional abilities such as gait or activities that require rapid change of direction. The addition of BFR causes similar muscular adaptations as higher load programs, but with less potential threat to the reconstructed ligament. This could mean earlier joint loading and recovery of strength. Future studies should investigate whether the addition of BFR to traditional ACL rehabilitation protocols leads to earlier return to unrestricted activities or athletic competition.

Limitations

The majority of the articles evaluated according to the GRADE scale were of moderate strength. This highlights the fact there are a limited number of high-quality studies in this area. The difference in methodologies between the four randomized control trials lead to differences between the authors' methods including study duration, exercise parameters, and outcomes measures such as extremity girth or strength. This inconsistency between methods potentially leads to the lack of ability to apply the reported results. Future BFR research should focus on studies with increased sample sizes, consistent

BFR and exercise parameters, clearly defined outcome measures, and an appropriately defined length of study allowing for adaptations within the musculature to occur.

CONCLUSION

The application of an occlusion cuff and blood flow restriction training combined with low intensity resistance training may have a positive effect on remediating the loss the femoral muscle cross sectional area after an ACL reconstruction. BFR most likely causes an increase in growth hormone levels and collagen synthesis, thereby stimulating the production of new myocytes. However, there is a need for further research to fully understand the physiological effects of both BFR alone and BFR combined with LIRT. More randomized control trials with larger sample sizes and long-term results should be completed before BFR can be recommended and clinicians incorporate this intervention as part of their standard of care post ACL reconstruction.

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