Blood Flow Restriction Therapy Versus Standard Care for Reducing Quadriceps Atrophy After Anterior Cruciate Ligament Reconstruction

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Clinical Scenario: Quadriceps atrophy and weakness are common after anterior cruciate ligament reconstruction (ACLR). Blood flow restriction (BFR) therapy, alone or in combination with exercise, has shown some promise in promoting muscular hypertrophy. This review was conducted to ascertain the extent to which current evidence supports the use of BFR for reducing quadriceps atrophy following ACLR in comparison with standard care. **Clinical Question:** Is BFR more effective than standard care for reducing quadriceps atrophy after ACLR? **Summary of Key Findings:** The literature was searched for studies that directly compared BFR treatment to standard care in patients with ACLR. Three level I randomized control trial studies retrieved from the literature search met the inclusion criteria. **Clinical Bottom Line:** Reviewed data suggest that a short duration (13 d) of moderate-pressure BFR combined with low-resistance muscular training does not appear to measurably affect quadriceps cross-sectional area. However, a relatively long duration (15 wk) of moderate-pressure BFR combined with low-resistance muscular training may increase quadriceps cross-sectional area to a greater extent than low-resistance muscular training alone. The results of the third randomized control trial suggest that employing BFR while immobilized in the early postoperative period may reduce quadriceps atrophy following ACLR. Additional data are needed to establish if the benefits of BFR on quadriceps atrophy after ACLR outweigh the inherent risks and costs. **Strength of Recommendation:** All evidence for this review was level 1 (randomized control trial) based on the Centre for Evidence-Based Medicine criteria. However, the findings were inconsistent across the 3 studies regarding the effects of BFR on quadriceps atrophy resulting in a grade “B” strength of recommendation.

Keywords: knee-extensor strength, postoperative rehabilitation, vascular occlusion

Clinical Scenario

Quadriceps atrophy and weakness are common after anterior cruciate ligament reconstruction (ACLR).^{1,2} Blood flow restriction (BFR) therapy, alone or in combination with exercise, has shown some promise in promoting muscular hypertrophy.¹⁻³ This review was conducted to ascertain the extent to which current evidence supports the use of BFR to reduce quadriceps muscle atrophy following ACLR in comparison with standard care.

Focused Clinical Question

Is BFR more effective than standard care for reducing quadriceps atrophy after ACLR?

Summary of Search, “Best Evidence” Appraised, and Key Findings

- The literature was searched for studies that directly compared BFR to standard care in patients with ACLR.
- Three level 1 randomized clinical trial (RCT) studies were retrieved.^{1,2,4}

- One RCT showed greater improvements in quadriceps cross-sectional area (CSA) after 15 weeks of low-resistance muscular training with moderate-pressure BFR (180 mm Hg) compared with low-resistance muscular training alone.²
- A second study found that 13 days of low-resistance muscular training with moderate-pressure (130–180 mm Hg) BFR resulted in no difference in quadriceps CSA reduction versus low-resistance muscular training alone.⁴
- The third study reported that 10 days of moderate-pressure (180–260 mm Hg) intermittent BFR while immobilized in a knee brace from the third to 14th postoperative days (standard care at the study site) resulted in less quadriceps CSA reduction than sham BFR with knee immobilization.¹

Clinical Bottom Line

Reviewed data suggest that a short duration (13 d) of moderate-pressure BFR combined with low-resistance muscular training does not appear to measurably affect quadriceps CSA.⁴ However, a relatively long duration (15 wk) of moderate-pressure BFR combined with low-resistance muscular training may increase quadriceps CSA to a greater extent than low-resistance muscular training alone.² The results of the third RCT suggest that employing BFR while immobilized in the early postoperative period may reduce quadriceps atrophy following ACLR.¹ Additional data are needed to establish if the benefits of BFR on quadriceps atrophy after ACLR outweigh the inherent risks and costs.

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Strength of Recommendation

All 3 reviewed studies were level 1 RCTs.^{1,2,4} However, the findings were inconsistent across the 3 studies regarding the effects of BFR on quadriceps atrophy resulting in a grade “B” strength of recommendation.^{1,2,4}

Search Strategy

Terms Used to Guide Search Strategy

- **Patient/Client Group:** anterior cruciate ligament reconstruction
- **Intervention:** blood flow restriction training OR occlusive training OR vascular restriction rehabilitation AND (therapeutic or treatment)
- **Comparison:** traditional rehabilitation (strengthening OR resistance)
- **Outcome(s):** cross-sectional area of knee extensors OR atrophy OR knee extensor torque

Sources of Evidence Searched

- PubMed
- CINAHL Plus
- SPORTDiscus
- MEDLINE
- EBSCOhost
- Cochrane Database of Systematic Reviews
- Additional resources obtained via manual search of reference lists

Inclusion and Exclusion Criteria

Inclusion Criteria

- Patients who underwent ACLR
- Studies that compared BFR training to standard care
- Limited to humans
- Limited to English language
- Limited to 2000–2018 publication dates

Exclusion Criteria

- Case studies
- Studies involving participants who had other pathologies of the knee in addition to ACLR

Results of Search

An extensive search of the literature yielded many articles; however, only 3 studies met the eligibility requirements and were considered for review.^{1,2,4} These studies are summarized in Table 1. Two studies were RCTs that examined the effect of BFR with exercise versus low-resistance exercise alone after ACLR.^{2,4} One study was an RCT that examined the effect of BFR while immobilized in a knee brace compared with a sham treatment, where the cuff was applied but not inflated during knee brace immobilization.¹

Best Evidence

The studies identified in Table 1 are the best available evidence found for this review. All 3 articles were level 1 evidence RCTs based on Centre for Evidence-Based Medicine (2011).⁵

Implications for Practice, Education, and Future Research

The objective of this review was to determine if there is evidential support for BFR to reduce quadriceps atrophy following ACLR. The 3 studies identified as the best available evidence to answer this question were high-quality RCTs, but their outcomes were mixed. Two studies reported a significant reduction in quadriceps atrophy in comparison with their control groups, whereas the third study found no between-group differences in atrophic changes.^{1,2,4} This disparity in outcomes may be due to a variety of factors including but not limited to, cuff size, occlusive pressure, individual treatment session duration, and length of the intervention period. For instance, Iversen et al⁴ used occlusive inflation pressures ranging from 130 to 180 mm Hg, whereas Takarada et al¹ used occlusive pressures ranging from 180 to 260 mm Hg. Ohta et al² used an occlusive inflation pressure of 180 mm Hg exclusively. Both Takarada et al¹ and Ohta et al² reported benefits with BFR suggesting that higher inflation pressures may be required to significantly affect muscle CSA. The tourniquet cuff size also varied between studies. Iversen et al⁴ used a 14-cm pneumatic cuff, whereas Takarada et al¹ used a 9-cm cuff for their study. Ohta et al² did not report the dimensions of the tourniquet cuff used in their study.

The length of the individual treatment sessions varied somewhat between the studies as did the intervention period duration. Ohta et al² used BFR for as long as each participant could endure during the exercise sessions with no specific inflation duration time per day, whereas subjects in both the Iversen et al⁴ and Takarada et al¹ studies had BFR for 50 minutes per day. Given these differences and the disparity in outcomes between these studies, it is difficult to make recommendations regarding the optimal duration of individual BFR treatment sessions for retarding quadriceps atrophy after ACLR.

The length of the intervention period also varied between studies. Ohta et al² studied the effects of a 15-week intervention period, whereas the intervention period in the Iversen et al⁴ and Takarada et al¹ investigations were 13 and 10 days, respectively. Ohta et al² and Iversen et al⁴ both used BFR with low-resistance exercise, although only Ohta et al² reported a benefit with BFR suggesting that a relatively lengthy training period may be required for the beneficial effects of BFR on quadriceps CSA to manifest when combined with low-resistance muscular training. There is need for additional data on the impact of treatment session duration (eg, 30, 60 min) and intervention period duration (eg, 3, 4, 6, 12, and 14 w) with BFR after ACLR.

It is important to note that the studies in this review evaluated quadriceps CSA via magnetic resonance imaging (MRI) at different times relative to surgery. Iversen et al⁴ analyzed MRI data of quadriceps CSA 2 days prior to surgery and 16 days after surgery, whereas Ohta et al² used MRI data at an unspecified time before surgery and at 16 weeks after surgery. By contrast, Takarada et al¹ assessed quadriceps CSA via MRI on the third postoperative day and 12 days later. As baseline quadriceps CSA measurements were taken at disparate time points in these studies, it is difficult to make comparisons. In addition, the anatomic location of quadriceps CSA

Table 1 Characteristics of Included Studies

	Study 1 Ohta et al (2003)	Study 2 Iversen et al (2014)	Study 3 Takarada et al (2000)
Study design	RCT	RCT	RCT
Participants	44 recreational patients (M = 25, F = 19; mean age = 29 y; range = 18–52) who underwent ACLR using a semitendinosus tendon autograft were followed for 16 wk postoperatively. Subjects were randomly assigned to intervention group (n = 22; M = 12, F = 10; traditional rehabilitation with BFR) or to the control group (n = 22; M = 13, F = 9; traditional rehabilitation without BFR). No significant differences were found between groups before intervention (age, sex distribution, body weight, preoperative range of motion, anterior instability preoperatively)	24 physically active patients (M = 14, F = 10; mean age = 27 y; range = 18–40 y) who had ACLR using hamstring tendon graft were followed for 16 d postoperatively. Subjects were randomly assigned to intervention group (n = 12; M = 7, F = 5; traditional rehabilitation with BFR) or to the control group (n = 12; M = 7, F = 5; traditional rehabilitation without BFR). No significant differences between groups before intervention (age, height, weight, IKDC score, and time from injury to surgery)	16 postoperative patients with ACL repair (M = 8, F = 8; mean age = 23 y; range = 20–25 y) who underwent ACLR using no specified graft were followed for 14 d postoperatively. Subjects were randomly assigned to intervention group (n = 8; M = 4, F = 4; BFR) or to the control group (n = 8; M = 4, F = 4; usual program recovery of immobilization without BFR). No significant differences were found between groups before intervention (age, height, and weight) but type of ACL grafts used was not examined
Intervention(s) investigated	Starting 8 d postoperatively, all subjects were asked to perform a rehabilitation exercise regimen 6x/week from weeks 2–16 and to record what they completed in a training notebook. The BFR group performed all exercises using an air tourniquet on the proximal thigh inflated to 180 mm Hg. Tourniquet cuff dimensions were not reported. Total inflation time could not be calculated from the study data. The exercises consisted of straight leg raises, hip joint abduction, hip joint adduction, half squats, step-ups, resisted knee flexion with elastic tubing, and knee-bending walking exercises. Subjects were asked to perform 20 repetitions of each exercise, 2–3x/day. The control group followed the same exercise regimen without BFR without any cuff applied	Starting on the second postoperative day, all subjects were asked to perform daily rehabilitation exercises and to record what they completed each day along with occlusion pressures if applicable. The BFR group performed all exercises using a 14-cm-wide pneumatic occlusion cuff on the proximal thigh while sitting reclined 45°. The cuff was inflated to the target occlusive pressure for 5 min and followed by removal of pressure for 3 min, 2x/d, 5x/session, from days 2 to 14. Total inflation time was 50 min. The occlusive pressure was initially 130 mm Hg and gradually increased by 10 mm Hg every other day to a final pressure of 180 mm Hg. During the occlusion intervals, subjects completed exercises consisting of quadriceps setting progressing to knee extensions over a knee roll and straight leg raises. Subjects were asked to perform 20 repetitions of each exercise 2x/day. The control group followed the same exercise regimen without BFR without any cuff applied	Starting on the fourth postoperative day, subjects were given BFR or sham BFR treatments. All subjects were immobilized with a knee brace for the entirety of the study. No exercises were prescribed for either group. The BFR group wore a 9-cm-wide pneumatic occlusion cuff on the proximal thigh and placed 100 mm distally to hip joint, while sitting with their upper body reclined 45°. The cuff was inflated to the target occlusive pressure for 5 min and followed by removal of pressure for 3 min 5x, 2x/day, between days 3 and 14 postoperatively. Total inflation time was 50 min. The occlusive pressure was initially 180 mm Hg and gradually increased by 10 mm Hg based on the degree of postoperative recovery of each patient. Final pressures ranged between 200 and 260 mm Hg by the end of the study. The sham group used the same cuff placement for the same duration without cuff inflation
Outcome measure(s)	CSA of knee-extensor muscle group was measured prior to surgery and 16 wk after surgery, 15 cm proximal to the upper margin of the patella (distal to the occlusion cuff location during the intervention period) using T1 MRI in an axial plane with subjects supine. Single muscle fiber diameter biopsies were collected during surgery (pre-BFR) and 16 wk postoperatively. Knee-extensor muscular torques were measured using an isokinetic myodynamometer during concentric contractions at 60°/s and 180°/s	CSA of knee-extensor muscle group was measured 2 d prior to surgery and 16 d after surgery at 40% and 50% of the femur length (measured distal to proximal from the lateral joint line of the knee) using T1 MRI in an axial plane with subjects supine	CSA of knee-extensor muscle group was measured 3 d after surgery and 14 d after surgery at 2 images/ portions near the midpoint of the femur (distal to the occluded site) using T1 MRI in an axial plane with subjects supine

(continued)

Table 1 (continued)

	Study 1 Ohta et al (2003)	Study 2 Iversen et al (2014)	Study 3 Takarada et al (2000)
Main findings	After the 15-wk intervention period, the BFR group showed significant differences in knee-extensor CSA ratio (knee-extensors CSA:femur CSA) ($P = .04$) and knee-extensor muscle torque ($P < .001-.004$) compared with the control. There was a moderate clinically meaningful difference between groups for CSA of knee extensors (Cohen's $d = 0.78$). There was no significant difference in preoperative /postoperative ratios of single fiber diameters	After the 13-d intervention period, there were no significant between-group differences in change of CSA of knee extensors ($P = .63$) compared with the control group. There was a moderate clinically meaningful difference between groups for CSA of knee extensors (Cohen's $d = 0.67$)	After the 10-d intervention period, the BFR group showed a significantly smaller decrease in knee-extensor CSA ($P = .046$) compared with the control. There was no significant difference found for change in CSA of knee flexors ($P = .69$) compared with control. There was a high clinically meaningful difference between groups for CSA of knee extensors (Cohen's $d = 2.1$)
Level of evidence	1	1	1
Conclusion	15 wk of low-resistance muscular training with moderate-pressure BFR (180 mm Hg) resulted in greater improvements in knee-extensor CSA and knee-extensor torque compared with muscular training alone in patients with ACLR	13 d of low-resistance muscular training plus moderate-pressure (130–180 mm Hg) intermittent BFR resulted in no difference in knee-extensor muscle CSA reduction compared with low-load resistance muscular training alone in patients with ACLR	10 d of moderate-pressure (180–260 mm Hg), intermittent BFR while immobilized in a knee brace resulted in less knee-extensor muscle CSA reduction than sham BFR (cuff applied but not inflated) with knee brace immobilization in patients with ACLR

Abbreviations: ACLR, anterior cruciate ligament reconstruction; BFR, blood flow restriction; CSA, cross-sectional area; F, female; IKDC, International Knee Documentation Committee; M, male; RCT, randomized control trial; MRI, magnetic resonance imaging; T1, T1 weighted MRI imaging.

measurements varied between all 3 studies. Iversen et al⁴ measured quadriceps CSA at 40% and 50% of the length of the femur (starting at the distal end), whereas Takarada et al¹ measured 2 sections near the midportion of the femur and distal to where BFR was applied. Ohta et al² expressed MRI results as a ratio of quadriceps CSA to the CSA of the femur, whereas Iversen et al and Takarada et al reported MRI results as the anatomical CSA of the quadriceps alone, further adding to the difficulty of making comparisons between the studies. Future researchers should consider measuring muscle volume rather than CSA as the former may be more accurate for evaluating muscle size.⁴

Future researchers should also consider measuring muscular torque or force output before and after BFR. Only 1 study in this review evaluated knee-extensor and knee-flexor torques.² Ohta et al² reported significant improvements in both knee torques in the BFR group when compared with the non-BFR treatment group.² The consistent inclusion of torque or force measurements would add a clinically meaningful variable to future research on the effectiveness of BFR therapy.

The mechanisms whereby mechanical tension and metabolic stress from BFR influence muscle CSA are not fully understood at this time.³ Restricting blood flow induces local hypoxia, which in turn is thought to cause blood pooling and the accumulation of metabolic subproducts leading to specific nervous and hormonal responses. These responses can result in increased plasma concentration of adrenaline and growth hormone and may reveal the underlying atrophy-attenuating effect from BFR.¹ In addition, when exercising muscle is exposed to a hypoxic environment, as was the case in 2 of the reviewed studies, the type I muscle fibers that require large amounts of oxygen for contraction cannot adequately function resulting in preferential activation of type 2 muscle fibers.⁶ Rehabilitation following ACLR traditionally involves moderate- to high-intensity (>50–60% 1-repetition maximum) strengthening exercises to facilitate muscle growth.³ However, preferential recruitment of type 2 muscle fibers during BFR may reduce postoperative muscle atrophy with low-resistance exercise to a similar extent as high-resistance exercises.³ It is theorized that exercise performed during BFR promotes fast-twitch type 2 muscle fiber recruitment and increased stimulation of muscle growth factors.³ Increased recruitment has been shown to cause stronger muscle contractions leading to ischemia followed by reactive hyperemia.⁷ However, Ohta et al² found no significant differences between type 1 and type 2 fiber ratios preintervention and postintervention via muscle biopsies.² Furthermore, there was no preferential increase in diameter for either fiber type.² Future studies that help elucidate how an occlusive stimulus can aid muscle hypertrophy will help in determining the optimal parameters for BFR after ACLR.

The possibility of short- and long-term side effects from BFR merits further investigation. Participants in the study by Ohta et al² reported a dull pain/discomfort from the tourniquet after roughly 12 minutes of BFR.² The authors of the other 2 reviewed studies did not report adverse effects from the BFR treatment protocols.

In healthy individuals, the impact of BFR on the cardiovascular system, muscle damage, oxidative stress, and nerve conduction velocity is similar to regular exercise.⁸ However, serious side effects have been reported with BFR in healthy populations including venous thrombosis, rhabdomyolysis, and pulmonary emboli.⁹ Additional data are needed on the short- and long-term effects of BFR in patient populations. Clearly, the safety and efficacy of BFR need to be well established before widespread utilization should be considered.

Acknowledgment

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