Perioperative Blood Flow Restriction Rehabilitation in Patients Undergoing ACL Reconstruction

A Systematic Review

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Background: Low-load blood flow restriction (BFR) training has attracted attention as a potentially effective method of perioperative clinical rehabilitation for patients undergoing orthopaedic procedures.

Purpose: To (1) compare the effectiveness of low-load BFR training in conjunction with a standard rehabilitation protocol, pre- and postoperatively, and non-BFR interventions in patients undergoing anterior cruciate ligament reconstruction (ACLR) and (2) evaluate protocols for implementing BFR perioperatively for patients undergoing ACLR.

Study Design: Systematic review; Level of evidence, 2.

Methods: A systematic review of the 3 medical literature databases was conducted to identify all level 1 and 2 clinical trials published since 1990 on BFR in patients undergoing ACLR. Patient demographics from included studies were pooled. Outcome data were documented, including muscle strength and size, and perceived pain and exertion. A descriptive analysis of outcomes from BFR and non-BFR interventions was performed.

Results: A total of 6 studies (154 patients; 66.2% male; mean ± SD age, 24.2 ± 3.68 years) were included. Of these, 2 studies examined low-load BFR as a preoperative intervention, 1 of which observed a significant increase in muscle isometric endurance ($P = .014$), surface electromyography of the vastus medialis ($P < .001$), and muscle blood flow to the vastus lateralis at final follow-up ($P < .001$) as compared with patients undergoing sham BFR. Four studies investigated low-load BFR as a postoperative intervention, and they observed significant benefits in muscle hypertrophy, as measured by cross-sectional area; strength, as measured by extensor torque; and subjective outcomes, as measured by subjective knee pain during session, over traditional low-load resistance training (all $P < .05$). BFR occlusion periods ranged from 3 to 5 minutes, with rest periods ranging from 45 seconds to 3 minutes.

Conclusion: This systematic review found evidence on the topic of BFR rehabilitation after ACLR to be sparse and heterogeneous likely because of the relatively recent onset of its popularity. While a few authors have demonstrated the potential strength and hypertrophy benefits of perioperative BFR, future investigations with standardized outcomes, long-term follow-up, and more robust sample sizes are required to draw more definitive conclusions.

Keywords: blood flow restriction; anterior cruciate ligament reconstruction; clinical rehabilitation; KAATSU

High-intensity resistance training can induce limb muscle hypertrophy and strength gains, which are desired outcomes in physical rehabilitation after surgery.² However, patients undergoing anterior cruciate ligament reconstruction (ACLR) cannot tolerate high-intensity training, defined as 60% to 85% of the 1 repetition maximum weight, in the immediate perioperative period.

Blood flow restriction (BFR) by the application of a pneumatic cuff to the lower extremity during low-intensity resistance training (approximately 20% of 1 repetition maximum weight) has been shown to significantly increase thigh muscle cross-sectional area, as well as carotid arterial and venous compliance, in healthy volunteers.¹,⁶¹ The anaerobic conditions of BFR induce an angiogenic stimulus through upregulation of vascular endothelial growth factors.
Furthermore, given the recent increased awareness of this therapy, there is a myriad of new research with heterogeneous indications and results. For the aforementioned reasons, the purposes of the present systematic review are to (1) compare the effectiveness of low-load BFR (LL-BFR) training in conjunction with a rehabilitation protocol, pre- and postoperatively, versus non-BFR interventions in patients undergoing ACLR and (2) evaluate protocols for implementing BFR perioperatively for patients undergoing ACLR.

METHODS

Search Strategy

This review was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A literature search was undertaken to identify studies evaluating BFR training as a rehabilitation or rehabilitation protocol after ACLR for the period between January 1, 1990, and May 14, 2019, within the MEDLINE, CINAHL, and EMBASE databases. The following search terms were used:

(((vascular occlusion OR blood flow restriction) OR blood flow occlusion) OR kaatsu) OR partial occlusion)) AND (((((anterior cruciate ligament reconstruction) OR ACLR) OR anterior cruciate ligament surgery) OR ACL surgery) OR anterior cruciate ligament)).

Resulting articles from the search underwent title and abstract screening, and studies investigating the utility of BFR before or after ACLR were selected. An additional search through the reference list of eligible articles was performed. Systematic review registration was performed in May 2019 with the PROSPERO International prospective register of systematic reviews.

Inclusion and Exclusion Criteria

Eligible studies were included after application of the following inclusion criteria: studies involving BFR as a rehabilitation or rehabilitation intervention in patients undergoing ACLR, English language in a scientific peer-reviewed journal, and level 1 or 2 evidence or qualification as a randomized controlled trial. Ongoing level 1 clinical trials without publication of complete data were not included.

Study Selection and Data Extraction

Studies eligible for inclusion were screened independently by 2 reviewers (Y.L. and C.K.). Duplicates and those not meeting the inclusion criteria were excluded. For the included studies, data extraction was inclusive of the following variables: (1) study design and population characteristics; (2) rehabilitation protocol, including device used, occlusion characteristics, exercise performed, and duration of BFR training; and (3) outcome measures, including muscle strength and size, perceived exertion and pain, and physical function. Data extraction was then performed with a custom spreadsheet. As almost all included studies evaluated different outcome measures, precluding a meta-analysis, we elected to proceed with a descriptive analysis of outcomes. Pooled demographic variables were calculated assuming independence of samples.

Study Quality and Reporting

Quality of the included studies was assessed with the Jadad score, which is a criterion for the evaluation and appraisal of randomized clinical trials. It is based on a composite score calculated from the following 3 metrics, with 1 point for an answer of yes and 0 points for an answer of no: (1) Is the study self-described as randomized? (2) Is the study self-described as double-blinded? (3) Does the study provide an adequate description of dropouts and withdrawals? After this initial assessment, secondary grading was performed on the basis of the following: an additional point was given if, for question 1, the method for randomization was described and was appropriate or, for question 2, the method of double-blinding was described and was appropriate. Conversely, a point was deducted if the methods for questions 1 and 2 were described and were inappropriate. Final scores for studies assessed may range from 0 to 5.
Additionally, an assessment of each study was performed with the modified Cochrane Risk of Bias tool,24 a method created and validated by the Cochrane Collaboration to determine the risk of bias in randomized trials. The tool focuses on the various domains of trial design, conduct, and reporting and proposes a judgment regarding the relevant risk of bias within each domain, graded as “high risk,” “low risk,” or “some concern.” The domains include random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting. If not enough information is provided in the methodology to make a judgment, the domain is listed as “not reported.”

Statistical Analysis

Age and body mass index of the study participants were extracted from the included studies and pooled with weighted means. All statistical analysis was performed with RStudio software (v 1.0.143; R Foundation for Statistical Computing).

RESULTS

The database search yielded 25 articles. After initial title and abstract screening, 15 articles regarded the topic in question and were assessed for eligibility. From this selection, 6 studies were of level 1 evidence per the PRISMA statement and were included in the analysis, as illustrated by Figure 1. An overview of study characteristics is provided in Table 1. The Jadad scores for the included studies ranged from 2 to 4, indicating average to rigorous study quality based on randomization and blinding protocols. Using Cochrane risk assessment we found 1 study26 was at high risk of bias in 1 category and 4 were at high risk in 2 categories (Table 2).

Study Populations

Of the 6 studies, 2 each were from Slovenia and Japan23,59,73,83 and 1 each from Norway and the United Kingdom.26,31 Two studied preoperative rehabilitation before ACLR after a chronic injury,23,83 while 4 studied26,31,59,73 postoperative rehabilitation. Sample sizes ranged from 16 to 44. All studies were randomized into 2 study arms with 1 exception, which was stratified into 3 study arms.26 Control arms in the trials were sham BFR in 3 studies23,73,83 nonrestricted activities in 2 studies31,59 and, for the study with 3 arms,26 BFR on healthy knees and nonrestricted activity. A total of 154 patients were enrolled in the 6 studies. Pooled demographics of the included studies are as follows: the mean ± SD age was 29.5 ± 7.7 years; body mass index was 24.2 ± 3.68 kg/m²; and 66.2% of the patients were male (Table 3).

BFR Protocol

Detailed BFR protocols are provided in Table 4. BFR was used in conjunction with specifically outlined LL resistance training and/or low- to moderate-intensity postoperative rehabilitation. Training load ranged from body weight to 30% of 1 repetition maximum. Constant occlusion pressure was applied in 4 studies,23,26,59,83 and escalating pressures were utilized in 2 studies.31,73 Occlusive pressures ranged from 130 to 238 mm Hg, while cuff width ranged from 9 to 14 cm. BFR was achieved with occlusion cuffs in 2 studies26,73 and tourniquets in 4 studies.23,31,59,83 Duration of BFR exercise regimen ranged from 1 day25 (to examine acute perceptual and hemodynamic responses) to 16 weeks, with frequency ranging from a single session over 48 hours to 6 sessions per week. One group reported on 2 daily BFR sessions.73 Exercise volume ranged from 75 to 100 repetitions per session; in 2 studies,23,83 volume was determined by number of
repetitions to volitional failure.\textsuperscript{23,83} BFR occlusion periods ranged from 3 to 5 minutes, with rest periods ranging from 45 seconds to 3 minutes.

Outcome Measures

Muscle strength was assessed through measurement of maximal volitional isometric contraction torque in 2 studies\textsuperscript{23,83} and by muscular torque ratio of the knee flexors to the knee extensors in 1 study.\textsuperscript{23,60,83} Additional measures of muscle strength and activation included surface electromyography (EMG) of the vastus medialis, EMG amplitude, time of sustained contraction, and blood flow to the vastus lateralis.\textsuperscript{83} Muscle size was assessed through measurement of the cross-sectional area and volume of the individual muscles, the extensor groups, and the flexor groups, as well

### TABLE 1
Overview of Study Characteristics\textsuperscript{a}

| Author (Year)       | Level of Evidence | No. Study Design                                                                 | Jadad Score | Study Arms (No.)          | Surgery Description     | Graft Type                                      |
|---------------------|-------------------|----------------------------------------------------------------------------------|-------------|---------------------------|-------------------------|------------------------------------------------|
| Zargi\textsuperscript{83} (2018) | 2                 | Pre-ACLR BFR (12) Pre-ACLR sham BFR (12)                                         | 4           | Pre-ACLR BFR (12) Pre-ACLR sham BFR (12) | Arthroscopic single bundle | Double-stranded ipsilateral semitendinosus-gracilis autograft |
| Hughes\textsuperscript{25} (2018) | 2                 | Uninjured BFR (10) Post-ACLR BFR, light resistance (10) Post-ACLR, heavy resistance (10) | 2           |                                          |                         | Hamstring tendon autograft                       |
| Grapar Zargi\textsuperscript{22} (2016) | 2                 | Pre-ACLR BFR (13) Pre-ACLR sham BFR (13)                                         | 4           |                                          | Arthroscopic single bundle | Double-stranded ipsilateral semitendinosus-gracilis autograft |
| Iversen\textsuperscript{30} (2016) | 1                 | Post-ACLR BFR (12) Post-ACLR nonrestricted activity (12)                          | 4           | Post-ACLR BFR (12) Post-ACLR nonrestricted activity (12) |                         | Hamstring tendon autograft                       |
| Ohta\textsuperscript{59} (2003)     | 1                 | Post-ACLR BFR (22) Post-ACLR nonrestricted activity (22)                          | 3           | Post-ACLR BFR (22) Post-ACLR nonrestricted activity (22) |                         | Semitendinosus autograft                        |
| Takarada\textsuperscript{73} (2000) | 1                 | Post-ACLR BFR (8) Post-ACLR sham BFR (8)                                          | 2           | Post-ACLR BFR (8) Post-ACLR sham BFR (8) |                         |                                                 |

\textsuperscript{a}Dashes signify not available. ACL, anterior cruciate ligament; ACLR, anterior cruciate ligament reconstruction; BFR, blood flow restriction.

### TABLE 2
Overview of Study Characteristics

| Author (Year)    | Random Sequence Generation | Allocation Concealment | Blinding of Participants and Personnel | Blinding of Outcome Assessment | Incomplete Outcome Data | Selective Reporting |
|------------------|----------------------------|------------------------|----------------------------------------|------------------------------|-------------------------|--------------------|
| Zargi\textsuperscript{83} (2018) | Low risk                  | Low risk               | Not reported                           | Low risk                    | Low risk                | Low risk           |
| Hughes\textsuperscript{25} (2018) | High risk                 | High risk              | Low risk                              | Low risk                    | Low risk                | Low risk           |
| Grapar Zargi\textsuperscript{22} (2016) | High risk                 | High risk              | Low risk                              | Low risk                    | Low risk                | Low risk           |
| Ohta\textsuperscript{59} (2003)     | High risk                 | High risk              | Not reported                          | Not reported                | Low risk                | Low risk           |
| Takarada\textsuperscript{73} (2000) | High risk                 | High risk              | Not reported                          | Not reported                | Low risk                | Low risk           |

### TABLE 3
Pooled Demographic Data of Included Studies

| Patients, No. | 154 |
|---------------|-----|
| Age, y, mean ± SD | 29.5 ± 7.7 |
| Male sex, %   | 66.2 |
| Body mass index (n = 110), mean ± SD | 24.2 ± 3.68 |

repetitions to volitional failure.\textsuperscript{23,83} BFR occlusion periods ranged from 3 to 5 minutes, with rest periods ranging from 45 seconds to 3 minutes.
### TABLE 4
Overview of Study Protocols<sup>a</sup>

| Author (Year) | Device Used | Occlusion Pressure/ Cuff Width | Exercises | Volume and Frequency | Duration |
|---------------|-------------|-------------------------------|-----------|----------------------|----------|
| Zargi<sup>25</sup> (2018) | Contoured pneumatic tourniquet cuff | Intervention: 150 mm Hg, 14 cm Sham: 20 mm Hg, 14 cm | Unilateral resisted knee extension in open kinetic chain on leg extension machine | Warm-up: 10-15 reps × 0.5 kg | 5 sessions over 8 d preop Last session performed within 48 h of surgery |
| Hughes<sup>25</sup> (2018) | Dual-purpose easy-fit variable contour nylon cuff | Intervention ACLR: 145 mm Hg, 11.5 cm Intervention uninjured: 138, 11.5 cm | Unilateral leg press | Warm-up: 5 min, unloaded cycling; 10 reps, unilateral leg press; 5-min rest | 1 session of familiarization and 1 session of BFR intervention over 2 d, starting at 22 d postop |
| Grapar Zargi<sup>22</sup> (2016) | Contoured pneumatic tourniquet cuff | Intervention: 150 mm Hg, 14 cm Sham: 20 mm Hg, 14 cm | Unilateral resisted knee extension in open kinetic chain on leg extension machine | Warm-up: 10-15 reps × 0.5 kg | 5 sessions over 10 d preop Last session performed within 48 h of surgery |
| Iversen<sup>30</sup> (2016) | Contoured pneumatic tourniquet cuff | Starting pressure set to 130 mm Hg, increased by 10 mm Hg daily from postop days 2 to 14 up to maximum pressure of 180 mm Hg or highest tolerable pressure; 14 cm | Isometric quadriceps contractions Progressing to leg extension over a knee roll Straight leg raises | Warm-up: NA | 2 sessions per day over 12 d, starting at day 2 postop, ending on day 14 postop; MRI on day 16 postop |
| Ohta<sup>59</sup> (2003) | Hand-pumped air tourniquet | 180 mm Hg | Straight leg raise Hip joint abduction Half squat Elastic tube exercise (bending knee from 45° to 100°) Knee bend walking exercise (walking in half squat for 60 steps) | Warm-up: NA | 6 sessions per week for 14 wk, starting at 2 wk postop, ending 16 wk postop |

(continued)
as the femoral muscle group en bloc; anatomic cross-sectional measurements were performed through magnetic resonance imaging. Subjective outcomes assessed included the levels of perceived pain and exertion. Physical function assessments included the single-leg anterior reach distance and tests of anterior instability. Two studies performed intergroup and temporal comparisons using factorial analysis of variance to assess for differences between BFR and sham, between pre- and postsurgery, and between operative and healthy legs, with post hoc Tukey test for pairwise comparisons where a significant main effect was determined. For the purposes of this review, only significant intergroup (BFR vs sham) differences are reported in Tables 5 and 6.

Descriptive Outcomes

With respect to BFR as a preoperative intervention, 1 study observed no significant differences in outcome measures, including postoperative changes in vastii or rectus volume. However, a second study by the same group observed that several outcome measures were significantly greater in the BFR group as compared with the sham BFR controls at 12-week follow-up, including muscle isometric endurance ($P = .014$), surface EMG amplitude of the vastus medialis ($P = .001$), and muscle blood flow to the vastus lateralis ($P < .001$).

With respect to BFR as a postoperative intervention, 2 of 3 studies observed significantly less muscle atrophy as measured by cross-sectional area of the knee extensor muscles when compared with controls ($P < .05$). Postoperative BFR was also associated with significantly greater cross-sectional area of the flexor and total quadriceps muscle group in 1 of 2 studies ($all P < .05$) and with significantly greater strength of the operative limb in the other study ($all P < .05$), as measured by muscular torque ratio of the injured extensor and flexor to their counterparts in the healthy limb. One study comparing subjective outcome measures by Hughes et al found that BFR was associated with significantly increased rates of perceived exertion and reduction of muscle pain during session but significantly decreased levels of knee pain during and after session, as compared with non-BFR ACLR rehabilitation ($all P < .05$) (Table 5). One study provided data regarding complications, where 2 patients in the LL-BFR group dropped out because of lower limb “dull pain” related to the tourniquet.

Study Quality and Reporting

The Jadad score was utilized to assess the quality of the trials included, with scores ranging from 2 to 4. All studies included were self-described as randomized and provided appropriate description of the randomization procedure. Four studies were double-blinded, while 3 provided descriptions of appropriate blinding methods. Only 1 study included a description of participants who dropped out or withdrew from the study.

Table 4 (continued)

| Author (Year) | Device Used | Occlusion Pressure/ Cuff Width | Exercises | Volume and Frequency | Duration |
|---------------|-------------|--------------------------------|-----------|----------------------|----------|
| Takarada et al (2000) | Pneumatic occlusion cuff | Initially 180 mm Hg, increased at 10 mm Hg intervals, maximum pressure at 238 mm Hg; 9 cm | Intervention and control groups performed low-intensity exercise described as the “usual program for recovery in the hospital with their injured knee kept immobilized by means of knee brace” | Warm-up: NA | 2 sessions per day for 11 d, starting at 3 d postop, ending 14 d postop |

Values are presented as mean ± SD where indicated. ACLR, anterior cruciate ligament reconstruction; bpm, beats per minute; BFR, blood flow restriction; MRI, magnetic resonance imaging; NA, not available; postop, postoperative; preop, preoperative; reps, repetitions; RM, repetition maximum; ROM, range of motion.
DISCUSSION

The main findings from this descriptive analysis were as follows: (1) literature surrounding the topic of BFR rehabilitation in patients with ACLR is limited and heterogeneous, and (2) some but not all of the available evidence suggests that BFR as a pre- or postoperative intervention is beneficial to muscle volume and strength/endurance, at least in the early postoperative period, when compared with nonrestricted postoperative activity. These observations are in line with existing literature that has demonstrated increases in muscle hypertrophy with BFR application in healthy and injured/postoperative populations. Additionally, comparison of acute subjective outcomes between LL-BFR and high-load conventional rehabilitation found increased ratings of perceived exertion.

| Author (Year) | Time Points of Follow-up | Treatment Group | Attrition, % | Outcome Measures |
|---------------|--------------------------|-----------------|-------------|-----------------|
| Zargi (2018)  | Preop, 4 wk postop, 12 wk postop | Control: pre-ACLR sham BFR | 0 | MVIC torque: T:C, P = .519 |
|               | Treatment: pre-ACLR BFR | | | Muscle isometric endurance (time of sustained contraction): T > C, P = .014 |
|               | | | | Surface EMG of vastus medialis: T > C, P = .001 |
|               | | | | Median frequency calculation of EMG amplitude: T:C, P = .730 |
|               | | | | Muscle blood flow in vastus lateralis: T > C, P < .001 |
|               | | | | Blood pressure: T:CNI-BFR, T:CACLR-HL, P < .05 |
|               | | | | RPE: T > CNI-BFR, P < .01, T:CACLR-HL, P > .05 |
|               | | | | Perceived muscle pain during session: T > CNI-BFR, P < .05, T > CACLR-HL, P < .01 |
|               | | | | Perceived knee pain during session: T < CACLR-HL, P < .05 |
|               | | | | Perceived knee pain 24 h postexercise: T < CACLR-HL, P < .01 |
| Hughes (2018) | Approximately 23 d after surgery for ACLR groups | Control: NI BFR and post-ACLR standard rehabilitation, heavy resistance | 0 | Vastii volume: T:C, P > .05 |
|               | Treatment: post-ACLR BFR, light resistance | | | Rectus femoris volume: T:C, P = .113 |
|               | | | | MVIC torque: T:C, P = .556 |
|               | | | | Single-leg anterior reach distance functional test: T:C, P > .05 |
|               | | | | CSA of quadriceps at 40% femur length: T:C, P > .05 |
|               | | | | CSA of quadriceps at 50% of femur length: T:C, P > .05 |
|               | | | | Mean change in anatomic CSA: T:C, P = .6265 |
| Iversen (2016) | Preop, 16 d postop | Control: post-ACLR nonrestricted activity | 0 | Muscular torque ratio of operative knee extensor/contralateral knee extensor: |
|               | Treatment: post-ACLR BFR | | | Measured at CC60: T > C, P < .001 |
|               | | | | Measured at CC180: T > C, P = .004 |
|               | | | | Muscle isometric endurance of femur length: T:C, P < .001 |
|               | | | | CSA ratio of operative knee extensor muscle group/contralateral knee extensor muscle group: T > C, P = .04 |
|               | | | | Single-fiber diameter ratio for type 1 and 2 fibers: T:C, P < .05 |
|               | | | | Range of motion (extension limit and flexion): T:C, P < .05 |
|               | | | | Anterior instability: T:C, P < .05 |
|               | | | | Total CSA (cm²) of the quadriceps femoris: T > C, P < .05 |
|               | | | | Extensor CSA: T > C, P < .05 |
|               | | | | Flexor CSA: T > C, P < .05 |
|               | | | | Femur CSA: T:C, P > .05 |
| Ohta (2003)   | Preop, 16 d postop | Control: post-ACLR nonrestricted activity | 4.5 | Muscle blood flow in vastus medialis: T:C, P = .001 |
|               | Treatment: post-ACLR BFR | | | Measured at CC60: T > C, P < .001 |
|               | | | | Measured at CC180: T > C, P = .004 |
| Takarada (2000) | Postop days 3 and 14 | Control: post-ACLR nonrestricted activity | 0 | Muscle blood flow in vastus medialis: T:C, P = .001 |
|               | Treatment: post-ACLR BFR | | | Measured at CC60: T > C, P < .001 |

“Bold indicates P < .05. ACLR, anterior cruciate ligament reconstruction; BFR, blood flow restriction; C, control; CC, concentric contraction; CSA, cross-sectional area; EMG, electromyography; HL, high load; IM, isometric; MVIC, maximal voluntary isometric contraction; NI, uninjured; postop, postoperative; preop, preoperative; RPE, rating of perceived exertion; T, treatment.”
### TABLE 6
Comparison of BFR and Non-BFR Outcomes

| Author (Year)          | BFR Outcome                                | Non-BFR Outcome                               | P Value          |
|------------------------|--------------------------------------------|------------------------------------------------|------------------|
| **Preop:**             |                                            |                                                |                  |
| Zargi83 (2018)         | Preop: MVIC, Nm: 210 ± 44                  | Preop: MVIC, Nm: 210 ± 44                     | Time-group interaction: MVIC, Nm: P = .519 |
|                        | Muscle isometric endurance, s: 145 ± 47   | Muscle isometric endurance, s: 95 ± 90        | Muscle isometric endurance: P = .014 |
|                        | Surface EMG amplitude: 0.274 ± 0.16        | Surface EMG amplitude: 0.224 ± 0.1            | Surface EMG amplitude: P = .001 |
|                        | EMG median frequency: 53.2 ± 11            | EMG median frequency: 49.9 ± 5.9              | EMG median frequency: P = .730 |
|                        | Muscle blood flow: 1.26 ± 0.3              | Muscle blood flow: 1.53 ± 0.4                 | Muscle blood flow: P < .001 |
| 4 wk postop:           | MVIC, Nm: NA                              | MVIC, Nm: NA                                  |                  |
|                        | Muscle isometric endurance, s: 153 ± 54    | Muscle isometric endurance, s: 95 ± 90        |                  |
|                        | Surface EMG amplitude: 0.391 ± 0.293       | Surface EMG amplitude: 0.187 ± 0.103          |                  |
|                        | EMG median frequency: 45.7 ± 10.1          | EMG median frequency: 41.7 ± 5.8              |                  |
|                        | Muscle blood flow: 1.92 ± 0.81             | Muscle blood flow: 0.97 ± 0.20                |                  |
| 12 wk postop:          | MVIC, Nm: 196 ± 48                         | MVIC, Nm: 181 ± 34                            |                  |
|                        | Muscle isometric endurance, s: 199 ± 71    | Muscle isometric endurance, s: 187 ± 94       |                  |
|                        | Surface EMG amplitude: 0.256 ± 0.160        | Surface EMG amplitude: 0.210 ± 0.086           |                  |
|                        | EMG median frequency: 45.9 ± 4.4           | EMG median frequency: 44.1 ± 3.7              |                  |
|                        | Muscle blood flow: 1.49 ± 0.75             | Muscle blood flow: 1.36 ± 0.32                |                  |
| **Preop:**             |                                            |                                                |                  |
| Hughes25 (2018)        | Preop: MVIC, Nm: 241 ± 74                  | Preop: MVIC, Nm: 241 ± 74                     |                  |
| ACLR group with BFR    | Perceived exertion, au: 18                 | Perceived exertion, au: 15.5                  | Between groups analysis at 22 d postop: |
| rehabilitation, 22 d   | Perceived muscle pain, au: 8               | Perceived muscle pain, au: 3                   | Perceived exertion, ACLR-BFR vs |
| postop:                | Perceived knee pain, au: 1.5               | Perceived knee pain, au: 2.5                   | NI-BFR: P < .01  |
| NI control with BFR    |                                            |                                                | Perceived exertion, ACLR-BFR vs |
| rehabilitation, 25 d   |                                            |                                                | ACLR-HL: P > .05 |
| postop:                |                                            |                                                | Perceived muscle pain, ACLR-BFR vs |
|                        | Perceived exertion, au: 14.5               | Perceived muscle pain, au: NI-BFR: P < .05    | ACLR-HL: P > .05 |
|                        | Perceived muscle pain, au: 5.5             | Perceived muscle pain, au: ACLR-BFR vs NI-BFR: | ACLR-HL: P < .01 |
|                        | Perceived knee pain, au: NA                | Perceived knee pain, au: ACLR-HL: P < .05     | ACLR-HL: P > .05 |
| **Preop:**             |                                            |                                                | ACLR-HL: P > .05 |
| Grapar Zargi22         | Preop: MVIC, Nm: 241 ± 74                  | Preop: MVIC, Nm: 191 ± 59                     | Time-group interactions |
| (2016)                 | Vastii muscle volume, cm³: 1670 ± 362      | Rectus femoris muscle volume, cm³: 1462.7 ± 382 | Perceived exertion: P < .01 |
|                        | Rectus femoris muscle volume, cm³: 225.4 ± 53.9 | Rectus femoris muscle volume, cm³: 170 ± 43.7 | Perceived muscle pain: P < .01 |
|                        | Anterior reach distance, cm: −0.5          | Anterior reach distance, cm: −4.0             | Perceived knee pain: P > .05 |
| 4 wk postop:           | MVIC, Nm: NA                              | MVIC, Nm: NA                                  | Difference between time points: MVIC, Nm: P = .025 |
|                        | Vastii muscle volume, cm³: 1325.9 ± 302.3  | Vastii muscle volume, cm³: 1210.3 ± 285.9     | Vastii muscle volume, cm³: P = .00 |
|                        | Rectus femoris muscle volume, cm³: 215.6 ± 45.4 | Rectus femoris muscle volume, cm³: 164.1 ± 46.6 | Rectus femoris muscle volume, cm³: P = .00 |
|                        | Anterior reach distance, cm: NA            | Anterior reach distance, cm: NA               | Anterior reach distance, cm: P > .05 |
| 12 wk postop:          | MVIC, Nm: 201 ± 47                         | MVIC, Nm: 172 ± 47                            | Difference between BFR and non-BFR: MVIC, Nm: P > .05 |
|                        | Vastii muscle volume, cm³: 1444.3 ± 265.6  | Vastii muscle volume, cm³: 1334.2 ± 337.2     | Vastii muscle volume, cm³: P > .05 |
|                        | Rectus femoris muscle volume, cm³: 216.3 ± 56.3 | Rectus femoris muscle volume, cm³: 171.4 ± 45.6 | Rectus femoris muscle volume, cm³: P > .05 |
|                        | Anterior reach distance, cm: −3.75         | Anterior reach distance, cm: −4.5             | Anterior reach distance, cm: P > .05 |

(continued)
Table 6 (continued)

| Author (Year) | BFR Outcome | Non-BFR Outcome | P Value |
|---------------|-------------|-----------------|---------|
| **Iversen**<sup>30</sup> (2016) | | | Time point analysis between preop and postop: |
| | Preop: CSA quadriceps at 40% femur length, cm<sup>2</sup>: 77.5 ± 2.5 | CSA quadriceps at 50% femur length, cm<sup>2</sup>: 87.0 ± 3.6 | CSA quadriceps at 40% femur length, cm<sup>2</sup>: 25.4 ± 3.2 | CSA quadriceps at 50% femur length, cm<sup>2</sup>: 42.8 ± 3.4 |
| | 16 d postop: CSA quadriceps at 40% femur length, cm<sup>2</sup>: 67.7 ± 2.7 | CSA quadriceps at 50% femur length, cm<sup>2</sup>: 73.9 ± 3.5 | Reduction in CSA quadriceps at 40% femur length, cm<sup>2</sup>: -9.7 ± 1.0 | Reduction in CSA quadriceps at 50% femur length, cm<sup>2</sup>: -11.5 ± 0.7 |
| | | | Mean change in CSA quadriceps from baseline to 16 d, cm<sup>2</sup>: -13.8 ± 1.1 | |
| **Obta**<sup>59</sup> (2003) | Preop: Extensor torque, CC60°: 84 ± 13 | Extensor torque, CC180°: 90 ± 9 | Extensor torque, IM60°: 94 ± 21 | Extensor torque, CC180°: 99 ± 16 |
| | Extensor torque, CC180°: 84 ± 14 | Extensor torque, IM60°: 90 ± 16 | Flexor torque, CC60°: 91 ± 18 | Flexor torque, CC180°: 94 ± 17 |
| | Flexor torque, CC60°: 92 ± 19 | Flexor torque, CC180°: 96 ± 19 | Extensor CSA<sup>+</sup>: injured:healthy: 91 ± 7 | Extensor CSA<sup>+</sup>: injured:healthy: 92 ± 11 |
| | Flexor + adductor CSA<sup>+</sup>: 99 ± 3 | Range of motion, extension (deg): 3.1 ± 5.8 | Range of motion, flexion (deg): 144 ± 15 | Range of motion, flexion (deg): 146 ± 7.7 |
| | | Anterior instability, mm°: 5.3 ± 5.3 | Anterior instability, mm°: 5.3 ± 1.6 | |
| | 16 wk postop: Extensor torque, CC60°: 76 ± 16 | Extensor torque, CC180°: 77 ± 13 | Extensor torque, IM60°: 84 ± 19 | Extensor torque, CC180°: 65 ± 13 |
| | Extensor torque, CC180°: 88 ± 15 | Extensor torque, IM60°: 63 ± 19 | Flexor torque, CC60°: 72 ± 11 | Flexor torque, CC180°: 74 ± 12 |
| | Flexor torque, CC180°: 84 ± 18 | Extensor torque, IM60°: 62 ± 14 | Extensor CSA<sup>+</sup>: preop:postop: 101 ± 11 | Extensor CSA<sup>+</sup>: preop:postop: 92 ± 12 |
| | Flexor + adductor CSA<sup>+</sup>: preop:postop: 105 ± 19 | Range of motion, extension (deg): 1.9 ± 3.7 | Type 1 muscle fiber diameter (μm): preop:postop: 103 ± 10 | Type 1 muscle fiber diameter (μm): preop:postop: 95 ± 11 |
| | Type 2 muscle fiber diameter (μm): preop:postop: 102 ± 8 | Range of motion, flexion (deg): 140 ± 5.9 | Type 2 muscle fiber diameter (μm): preop:postop: 97 ± 7 | Type 2 muscle fiber diameter (μm): preop:postop: 97 ± 7 |
| | | Range of motion, extension (deg): 3.1 ± 3.6 | Range of motion, flexion (deg): 143 ± 8.7 | Range of motion, extension (deg): 3.1 ± 3.6 |
| | Total CSA of thigh, cm<sup>2</sup>: 167.5 ± 5.1 | Extensor CSA, cm<sup>2</sup>: 54 ± 3 | Type 1 muscle fiber diameter (μm): preop:postop: 102 ± 8 | Type 1 muscle fiber diameter (μm): preop:postop: 97 ± 7 |
| **Takarada**<sup>73</sup> (2000) | 3 d postop: Total CSA of thigh, cm<sup>2</sup>: 167.5 ± 5.1 | Extensor CSA, cm<sup>2</sup>: 54 ± 3 | Type 2 muscle fiber diameter (μm): preop:postop: 102 ± 8 | Type 2 muscle fiber diameter (μm): preop:postop: 97 ± 7 |
| | Extensor CSA, cm<sup>2</sup>: 46.2 ± 2.6 | Flexor CSA, cm<sup>2</sup>: 49.1 ± 4.7 | Flexor + adductor CSA, cm<sup>2</sup>: 64.8 ± 5.4 | Flexor + adductor CSA, cm<sup>2</sup>: 44.8 ± 5.4 |
| | Femur CSA, cm<sup>2</sup>: 7 ± 0.3 | Flexor CSA, cm<sup>2</sup>: 46.2 ± 4.7 | Femur CSA, cm<sup>2</sup>: 64.8 ± 5.4 | Femur CSA, cm<sup>2</sup>: 44.8 ± 5.4 |
| | Total CSA of thigh, cm<sup>2</sup>: 156.3 ± 6.5 | Extensor CSA, cm<sup>2</sup>: 46.2 ± 2.6 | Flexor + adductor CSA, cm<sup>2</sup>: 64.8 ± 5.4 | Flexor + adductor CSA, cm<sup>2</sup>: 44.8 ± 5.4 |
| | Flexor CSA, cm<sup>2</sup>: 41.7 ± 2.2 | Flexor CSA, cm<sup>2</sup>: 46.2 ± 4.7 | Femur CSA, cm<sup>2</sup>: 64.8 ± 5.4 | Femur CSA, cm<sup>2</sup>: 44.8 ± 5.4 |
| | Femur CSA, cm<sup>2</sup>: 7 ± 0.2 | Femur CSA, cm<sup>2</sup>: 46.2 ± 4.7 | Femur CSA, cm<sup>2</sup>: 64.8 ± 5.4 | Femur CSA, cm<sup>2</sup>: 44.8 ± 5.4 |
| Between-group analysis at 16 wk: Extensor torque, CC60°: P < .05 | Extensor torque, CC180°: P < .001 | Flexor torque, IM60°: P < .004 | Flexor torque, CC180°: P < .001 |
| Between-group analysis at 14 d: Total CSA of thigh, cm<sup>2</sup>: P < .05 | Extensor CSA, cm<sup>2</sup>: P < .001 | Flexor CSA, cm<sup>2</sup>: P < .05 | Femur CSA, cm<sup>2</sup>: P < .001 |

<sup>a</sup>Values are presented as mean ± SD where indicated. Bold P values indicate P < .05. ACLR, anterior cruciate ligament reconstruction; BFR, blood flow restriction; CC, concentric contraction; CSA, cross-sectional area; EMG, electromyography; HL, high load; IM, isometric; MVIC, maximal voluntary isometric contraction; NA, not available; NI, uninjured; postop, postoperative; preop, preoperative; RPE, rating of perceived exertion.

<sup>b</sup>Muscular torque, concentric contraction at 60 deg/s, expressed as operated:healthy ratio.

<sup>c</sup>Muscular torque, concentric contraction at 180 deg/s, expressed as operated:healthy ratio.

<sup>d</sup>Muscular torque, isometric contraction at 60° of knee flexion, expressed as operated:healthy ratio.

*CSA expressed as ratio to femur on same image.

*Anterior instability measured with knee ligament arthrometer KT2000 at 133 N.
and reduced in- and postsession knee pain with LL-BFR. With comparable increases in muscle cross-sectional area between LL-BFR and heavy-load training, this new observation highlights the appeal of LL-BFR as a potentially effective alternative that can lead to reduced residual knee pain. Ultimately, definitive assessment of the effects of BFR in this population remains uncertain because of the quality of the present literature.

Of the 3 studies assessing strength as an outcome, the 1 with the longest training duration found a difference in muscular torque ratio between the operative knee extensor and the contralateral extensor in patients who underwent 84 sessions of LL-BFR, as opposed to unrestricted low-load training. This was likely due to the presence of a dose-dependent relationship between training and strength gain such that more sessions lead to greater differences. Evidence on other populations in the literature supports a difference in strength gains between LL-BFR and low-resistance training alone prescribed between 6 and 8 weeks of rehabilitation. In contrast, evidence on the effect of BFR on post-ACLR muscle atrophy is conflicting. Of the 2 studies reviewed, 1 found almost a 50% reduction in muscle atrophy with BFR, while the other found no difference in quadriceps cross-sectional area between the control and intervention groups. However, authors of the latter study acknowledged subtherapeutic training intensity as a possible reason for this difference and suggested the incorporation of neuromuscular electrostimulation into future research models to detect the effects of BFR on a more granular level.

The implementation of BFR has generally been indicated for patients with debilitating ongoing clinical rehabilitation, such as the elderly or surgical candidates or athletes involved in sports at a competitive level. While these 2 populations may ostensibly have distinct needs, their goals of rehabilitation attempted to predict the AOP as a percentage of the brachial systolic blood pressure. However, a more recent investigation identified thigh circumference as the greatest predictor of AOP. Additionally, considerations for setting initial pressures according to tourniquet material (nylon vs elastic) has been highlighted. Of note, none of the studies included in this systematic review completely employed these guidelines in their methods.

The current paradigm in training protocol is experiencing a similar transition toward individualized prescriptions to maximize gains. Studies in the literature have observed a domain-specific timeline for LL-BFR to demonstrate a significant advantage over non-BFR low-resistance training. Significant hypertrophy has been noted after as short as 6 days of training and can be effectively achieved by most protocols: rehabilitation trials for patients undergoing surgery typically last 2 to 6 weeks and as long as 20 weeks. Those for the elderly last longer, averaging 10 to 12 weeks. However, there is the observation that improvements in muscle strength require a longer duration of training. A comparative study demonstrated that while high-load resistance training (without BFR) yielded greater strength increases initially, results were equivalent to LL-BFR at 12 weeks of training. This implies that an appropriate period of familiarization may yield hormonal and neural adaptations to more effectively utilize occlusion training.

A comparison of pre- and postoperative BFR training in patients undergoing ACLR in this review found the strongest evidence of significant improvements in muscle hypertrophy and strength over standard rehabilitation protocols in candidates for postoperative BFR. Of the 2 studies on preoperative BFR, only 1 found a significant improvement over sham intervention in muscular endurance, activation, and perfusion. These outcomes were likely confounded by the significantly reduced training durations of preoperative BFR (5 sessions over 10 days). Additionally, both trials enrolled only patients with chronic ACL rupture, where there is a greater likelihood of functional adaptation after

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1References 2, 10, 14, 33, 40, 45, 49-52, 60, 62, 80.

2References 1, 13, 15, 20, 25, 39, 48, 57, 58, 70.
injury. An ongoing trial is examining 4 weeks of BFR pre-
habilitation as part of an overall perioperative protocol for
ACLR, providing further insight to the optimal timing of
BFR intervention.16 (Appendix Table A1). The strong evi-
dence for the increased benefit of combined pre- and post-
operative BFR rehabilitation after orthopaedic surgery,18,64
makes it imperative to continue evaluating BFR as a pre-
habilitation intervention.

There are several limitations to consider while interpret-
ing the results of this study. While significant differences in
short-term muscle strength and hypertrophy were demon-
strated in some of the studies, none provided follow-up data with
regard to changes in primary clinical outcomes or return to
sports. The heterogeneity in outcome variables precluded a
meta-analysis. Torque and cross-sectional areas are common outcome
measurements, are readily
obtained,2,5,8,10,11,73,81-83 and warrant inclusion in the
design of future trials. The study by Hughes et al16 examined
immediate subjective perspectives during and after
BFR performed only a single session. Their results may not
be generalizable to patients who are well-adapted to the
volume and intensity of BFR protocols. Overall, there was a
small number of patients in the collective cohort of studies
reviewed and poor reporting of adverse events. Long-term
follow-up data in these studies were sparse, and firm
recommendations regarding safety cannot be made.

CONCLUSION

The evidence for the benefits of BFR rehabilitation after
ACLR is sparse and heterogeneous possibly because of the
novel nature of the technique. Although several studies have
shown potential muscle strength and hypertrophy benefits in
patients undergoing perioperative BFR in the
setting of ACLR, future investigations with standardized
outcomes, long-term follow-up, and more robust sample
sizes are required to draw more definitive conclusions.

REFERENCES

1. Abe T, Kawamoto K, Yasuda T, Kearsn CF, Midoriwaka T, Sato Y. Eight
days KAATSU-resistance training improved sprint but not jump
performance in collegiate male track and field athletes. Int J KAATSU
Train Res. 2005;1(1):19-23.
2. Abe T, Loenneke JP, Fahs CA, Rossow LM, Bemben MG. Exercise intensity and
muscle hypertrophy in blood flow-restricted limbs and non-restricted muscles: a
brief review. Clin Physiol Funct Imaging. 2012;32(4):247-252.
3. Abe T, Mouser JG, Dankel SJ, et al. A method to standardize the
blood flow restriction pressure by an elastic cuff. Scand J Med Sci
Sports. 2019;39(3):329-335.
4. Abe T, Sakamaki M, Fujita S, et al. Effects of low-intensity walk
training with restricted leg blood flow on muscle strength and aerobic
capacity in older adults. J Geriatr Phys Ther. 2010;33(1):34-40.
5. AORN Recommended Practices Committee. Recommended prac-
tices for the use of the pneumatic tourniquet in the peroperative
practice setting. Aorn J. 2007;86(4):640-655.
6. Bezerra de Morais AT, Santos Cergueria M, Moreira Sales R, Rocha T,
Galvao de Moura Filho A. Upper limbs total occlusion pressure
assessment: Doppler ultrasound reproducibility and determination of
predictive variables. Clin Physiol Funct Imaging. 2017;37(4):
437-441.
7. Bond CIW, Hackney KJ, Brown SL, Noonan BC. Blood flow restriction
resistance exercise as a rehabilitation modality following orthopaedic
surgery: a review of venous thromboembolism risk. J Orthop Sports
Phys Ther. 2019;49(1):17-27.
8. Bowman EN, Elshaar R, Milligan H, et al. Proximal, distal, and con-
tralateral effects of blood flow restriction training on the lower extrem-
ities: a randomized controlled trial. Sports Health. 2019;11(2):
149-156.
9. Brown H, Binnie MJ, Dawson B, Bullock N, Scott BR, Peeling P. Factors
affecting occlusion pressure and ischemic preconditioning. Eur J Sport Sci. 2018;18(3):387-396.
10. Bryk FF, Dos Reis AC, Fingerhut D, et al. Exercises with partial vas-
cular occlusion in patients with knee osteoarthritis: a randomized
clinical trial. Knee Surg Sports Traumatol Arthrosc. 2016;24(5):
1580-1586.
11. Centner C, Wiegel P, Gollhofer A, König D. Effects of blood flow
restriction training on muscular strength and hypertrophy in older
individuals: a systematic review and meta-analysis. Sports Med. 2019;49(1):95-108.
12. Cook SB, LaRoche DP, Villa MR, Barile H, Manini TM. Blood flow
restricted resistance training in older adults at risk of mobility limita-
tions. Exp Gerontol. 2019;138:145.
13. Cugno M, Uziel L, Fabrizi I, Bottasso B, Maggioni F, Agostoni A. Fibrinolytic response in normal subjects to venous occlusion and
DDAVP infusion. Thromb Res. 1989;56(5):625-634.
14. Dankel SJ, Jesse MB, Abe T, Loenneke JP. The effects of blood flow
restriction on upper-body musculature located distal and proximal to
applied pressure. Sports Med. 2016;46(1):23-33.
15. El-Sayed MS, El-Sayed Ali Z, Ahmadizad S. Exercise and training
effects on blood haemostasis in health and disease: an update. Sports Med. 2004;34(3):181-200.
16. Erickson LN, Lucas KCH, Davis KA, et al. Effect of blood flow restric-
tion training on quadriceps muscle strength, morphology, physiology,
and knee biomechanics before and after anterior cruciate ligament
reconstruction: protocol for a randomized clinical trial. Phys Ther. 2019;99(8):1010-1019.
17. Fahl CA, Loenneke JP, Rossow LM, Tiebaud RS, Bemben MG. Meth-
odological considerations for blood flow restricted resistance exer-
cise. J Trainol. 2012;1(1):14-22.
18. Failla MJ, Logerstedt DS, Grindem H, et al. Does extended preoper-
ative rehabilitation influence outcomes 2 years after ACL reconstruc-
tion? A comparative effectiveness study between the MOON and
Delaware-Oslo ACL cohorts. Am J Sports Med. 2016;44(10):
2608-2614.
19. Ferguson RA, Hunt JEA, Lewis MP, et al. The acute angiogenic sig-
nalling response to low-load resistance exercise with blood flow
restriction. Eur J Sport Sci. 2018;18(3):397-406.
20. Fortin JF, Billaut F. Blood-flow restricted warm-up alters muscle
hemodynamics and oxygenation during repeated sprints in American
football players. Sports (Basel). 2019;7(5):121.
21. Fujita T, Brechue WF, Kurita K, Sato Y, Abe T. Increased muscle
volume and strength following six days of low-intensity resistance
training with restricted muscle blood flow. Int J KAATSU Train Res. 2008;4(1):1-8.
22. Giles L, Webster KE, McClelland J, Cook JL. Quadriceps strengthen-
ing with and without blood flow restriction in the treatment of patello-
emoral pain: a double-blind randomised trial. Br J Sports Med. 2017;
51(23):1688-1694.
23. Grapar Zargi T, Drobnic M, Jkoder J, Strazar K, Kacin A. The effects of
preconditioning with ischemic exercise on quadriceps femoris muscle
atrophy following anterior cruciate ligament reconstruction: a quasi-
randomized controlled trial. Eur J Phys Rehabil Med. 2016;52(2):
310-320.
24. Grindem H, Granan LP, Risberg MA, Engebretsen L, Snyder-Mackler L, Eitzen I. How does a combined preoperative and postoperative
rehabilitation programme influence the outcome of ACL reconstruc-
tion 2 years after surgery? A comparison between patients in the
Delaware-Oslo ACL Cohort and the Norwegian National Knee Liga-
ment Registry. Br J Sports Med. 2015;49(6):385-389.
25. Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:D5928.

26. Hughes L, Paton B, Haddad F, Rosenblatt B, Gissane C, Patterson SD. Comparison of the acute perceptual and blood pressure response to heavy load and light load blood flow restriction resistance exercise in anterior cruciate ligament reconstruction patients and non-injured populations. Phys Ther Sport. 2018;33:54-61.

27. 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(13):1003-1011.

28. Hunt JEA, Stodart C, Ferguson RA. The influence of participant characteristics on the relationship between cuff pressure and level of blood flow restriction. Eur J Appl Physiol. 2016;116(7):1421-1432.

29. Ingram JW, Dankel SJ, Buckner SL, et al. The influence of time on determining blood flow restriction pressure. J Sci Med Sport. 2017;20(8):777-780.

30. Ishii N, Madarame H, Odagiri K, Nagamuna M, Shihoda K. Circuit training without external load induces hypertrophy in lower-limb muscles when combined with moderate venous occlusion. Int J KAATSU Train Res. 2005;11(1):24-28.

31. 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(1):115-118.

32. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials. 1996;17(1):1-12.

33. Karabulut M, Bembem DA, Sherk VD, Anderson MA, Abe T, Bembem MG. Effects of high-intensity resistance training and low-intensity resistance training with vascular restriction on bone markers in older men. Eur J Appl Physiol. 2011;111(8):1659-1667.

34. Ladlow P, Coppel CJ, Dharm-Datta S, et al. The effects of low-intensity blood flow restricted exercise compared with conventional resistance training on the clinical outcomes of active UK military personnel following a 3-week in-patient rehabilitation programme: protocol for a randomized controlled feasibility study. Pilot Feasibility Stud. 2017;3:1-71.

35. Ladlow P, Coppack RJ, Dharm-Datta S, et al. Low-load resistance training with blood flow restriction improves clinical outcomes in musculoskeletal rehabilitation: a single-blind randomized controlled trial. Front Physiol. 2018;9:1269.

36. Lambert B, Hedt CA, Jack RA, et al. Blood flow restriction therapy preserves whole limb bone and muscle following ACL reconstruction. Orthop J Sports Med. 2019;7(3)(suppl 2):23259671198325900196.

37. Larkin KA, Macneil RG, Dirain M, Sandesara B, Manini TM, Buford TW. Blood flow restriction enhances post-resistance exercise angio-genic gene expression. Med Sci Sports Exerc. 2012;44(11):2077-2083.

38. Laswati H, Sugianto D, Poerwandari D, Pangkahilia JA, Kimura H. Low-intensity exercise with blood flow restriction increases muscle strength without altering hsCRP and fibrinogen levels in healthy subjects. Chin J Physiol. 2018;61(3):188-195.

39. Laurentino GC, Ugrinowitsch C, Roschel H, et al. Strength training with blood flow restriction diminishes myostatin gene expression. Med Sci Sports Exerc. 2012;44(3):406-412.

40. Lejkowski PM, Pajączkowski JA. Utilization of vascular restriction training in post-surgical knee rehabilitation: a case report and introduction to an under-reported training technique. J Can Chiropr Assoc. 2011;55(4):280-287.

41. Libardi CA, Chacon-Mikahil MPT, Cavaglieri CR, et al. Effect of concurrent training with blood flow restriction in the elderly. Int J KAATSU Train Res. 2015;36(5):395-399.

42. Lipker LA, Persinger CR, Michalko BS, Durall CJ. Blood flow restriction therapy versus standard care for reducing quadriceps atrophy after anterior cruciate ligament reconstruction. J Sport Rehabil. 2019;28(8):897-901.

43. Likandrao 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 Med. 2018;48(2):361-378.

44. Loenneke JP, Fahs CA, Rossov LM, et al. Blood flow restriction pressure recommendations: a tale of two cuffs. Front Physiol. 2013;4:249.

45. Loenneke JP, Fahs CA, Rossov LM, et al. Effects of cuff width on arterial occlusion: implications for blood flow restricted exercise. Eur J Appl Physiol. 2012;112(8):2903-2912.

46. Loenneke JP, Thiebaud RS, Abe T, Bembem MG. Blood flow restriction pressure recommendations: the hormesis hypothesis. Med Hypotheses. 2014;82(3):623-626.

47. Loenneke JP, Wilson JM, Wilson SJ, Pujol TJ, Bembem MG. Potential safety issues with blood flow restriction training, Scand J Med Sports. 2011;21(4):510-518.

48. Lowery RP, Joy JM, Loenneke JP, et al. Practical blood flow restriction training increases muscle hypertrophy during a periodized resistance training programme. Eur J Appl Physiol. 2014;134(4):317-321.

49. Luebbers PE, Fry AC, Kirley LM, Butler MS. The effects of a 7-week practical blood flow restriction program on well-trained collegiate athletes. J Strength Cond Res. 2014;28(8):2270-2280.

50. Manimmanakorn A, Hamlin MJ, Ross JJ, Taylor R, Manimmanakorn N. Effects of low-load resistance training combined with blood flow restriction or hypoxia on muscle function and performance in netball athletes. J Sci Med Sport. 2013;16(4):337-342.

51. Manimmanakorn A, Manimmanakorn N, Taylor R, et al. Effects of resistance training combined with vascular occlusion or hypoxia on neuromuscular function in athletes. Eur J Appl Physiol. 2013;113(7):1767-1774.

52. Martin-Hernandez J, Santos-Lozano A, Foster C, Lucia A. SyncpO episodes and blood flow restriction training. Clin J Sport Med. 2018;28(8):e89-e91.

53. Mattar MA, Gualano B, Perandini LA, et al. Safety and possible effects of low-intensity resistance training associated with partial blood flow restriction in polymyositis and dermatomyositis. Arthritis Res Ther. 2014;16(5):473.

54. Montgomery R, Paterson A, Williamson C, Florida-James G, Ross MD. Blood flow restriction exercise attenuates the exercise-induced endothelial progenitor cell response in healthy, young men. Front Physiol. 2019;10:447.

55. Mouser JG, Ade CJ, Black CD, Bembem DA, Bembem MG. Brachial blood flow under relative levels of blood flow restriction is decreased in a nonlinear fashion. Clin J Sport Med. 2018;28(8):425-430.

56. Nakajima T, Kurano M, Iida H, et al. Use and safety of KAATSU training: results of a national survey. Int J KAATSU Train Res. 2006;2(1):5-13.

57. Nascimento DDC, Petriz B, Oliveira SDC, et al. Effects of blood flow restriction exercise on hemostasis: a systematic review of randomized and non-randomized trials. Int J Gen Med. 2019;12:91-100.

58. Noto T, Hashimoto G, Takagi T, et al. Paget-Schroetter syndrome resulting from thoracic outlet syndrome and KAATSU training. Intern Med. 2017;56(19):2959-2961.

59. 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(4):62-68.

60. Ozaki H, Miyachi M, Nakajima T, Abe T. Effects of 10 weeks walk training with leg blood flow reduction on carotid arterial compliance and muscle size in the elderly adults. Angiology. 2010;62(1):81-86.

61. Ozaki H, Sakamaki M, Yasuda T, et al. Increases in thigh muscle volume and strength by walk training with leg blood flow reduction in older participants. J Gerontol A Biol Sci Med Sci. 2011;66(3):256-263.

62. Ozawa Y, Kato T, Shihoda H, Tsukuba K. Vision loss by central retinal vein occlusion after KAATSU training: a case report. Medicine. 2015; 94(36):e1515.
APPENDIX

TABLE A1
Protocols of Ongoing Level 1 Trials on Perioperative BFR in Patients Undergoing ACLR

| Author (Year) | Device Used | Exercises | Volume and Frequency | Duration |
|---------------|-------------|-----------|----------------------|----------|
| Erickson15 (2019) | Pressurized cuff to the proximal thigh that partially occludes blood flow as the patient exercises | Primary outcome measure: quadriceps strength (peak torque, rate of torque development) Secondary outcome measures: knee extensor movement, knee flexion excursion, knee flexion angle, quadriceps cross-sectional area, quadriceps muscle physiology | Not published in abstract | Presurgical blood flow restriction therapy 3×/wk for 4-5 mo up to surgery
| Lambert36 (2019) | Automated tourniquet around the proximal thigh outfitted with Doppler (Delfi) | Weeks 1-3: quadriceps contractions Weeks 3-12: bilateral leg press Weeks 4-6: hamstring curl Weeks 4-12: eccentric leg press Weeks 7-12: eccentric hamstring curl | All exercises performed at 20% predicted 1 repetition maximum of contralateral leg All exercises, 4 sets of 30-15-15-15 repetitions separated by 30-s rest BFR group performed exercises with cuff at 80% arterial limb occlusion | 12 wk of rehabilitation (2 sessions/wk) beginning at 10 d postsurgery Functional assessments performed at weeks 8 and 12 DEXA scan performed pre- and postoperatively at weeks 6 and 12 |

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4Oclusion pressure/cuff width was not published in either abstract. ACLR, anterior cruciate ligament reconstruction; BFR, blood flow restriction; DEXA, dual-energy x-ray absorptiometry.