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# **Acute and chronic effects of blood flow restriction training in physically active patients with anterior cruciate ligament reconstruction: A systematic review**

## **ABSTRACT**

Context: Muscle atrophy and loss of knee function are common findings following anterior cruciate ligament (ACL) reconstruction. Rehabilitation through blood flow restriction (BFR) has gained clinical relevance when combined with low loads to improve these disorders in recent years.

Objective: To evaluate the rehabilitation effectiveness of ACL reconstruction with the use of BFR on pain, functionality, strength and muscle mass in physically active people.

Data sources: A search of PubMed, Web of Science, and MEDLINE was performed on March 31<sup>st</sup> 2023 following the PRISMA 2020 guidelines.

Study selection: Randomized clinical trials with active adults who underwent ACL surgery were included. They had to compare conventional treatments with the use of BFR, reporting values of pain, functionality, strength, or cross-sectional area (CSA). Articles whose participants presented concomitant injuries and whose intervention combined the use of BFR with treatments other than resistance training were excluded.

Study design: Systematic review.

Level of evidence: Level 2.

Data extraction: Study design, population, cuff pressure and main outcomes including strength, quadriceps CSA, pain, and functionality.

Results: Six studies out of a total of three hundred eighty-nine were included (152 participants; 90 males and 62 females). These included studies showed no differences on CSA or strength when comparing BFR training to high loads exercise. BFR has demonstrated improvements in knee functionality and pain compared with other interventions such as immobilization or high loads training.

26 Conclusions: The use of low loads combined with BFR improves pain, strength, functionality,  
27 and CSA. In addition, knee pain reduction and functionality are greater with BFR compared to  
28 the use of high loads or immobilization.

29

30 **Keywords:** blood flow restriction, occlusive training, kaatsu, anterior cruciate ligament,  
31 rehabilitation.

32

## INTRODUCTION

Anterior cruciate ligament (ACL) reconstruction is one of the most common surgeries<sup>48,49</sup>, especially in athletes involved in sports that require pivoting, jumping or changing of direction<sup>1,9</sup>. After surgery, the knee shows atrophy that is related to weakness and deficits in quadriceps or hamstrings muscle activation, as well as biomechanical and tissue quality alterations, a decreased torque ratio, and limb asymmetry<sup>7,15,42,51</sup>. In addition, ACL surgery is associated with a high risk of recurrence and contralateral injury, leading to serious psychological problems such as fear of recurrence or lack of confidence in the affected limb<sup>17,18,39,52</sup>. Furthermore, ACL injury as well as incorrect rehabilitation could result in the development of early osteoarthritis<sup>2,13</sup>.

The aim of rehabilitation is focused on restoring a structure to its original levels of strength and function after surgery, but it seems that it is an arduous process that can take up to 12 months to be completed<sup>14,15</sup>. However, in younger more active athletes, return to sport seems challenging until two years after surgery<sup>38</sup>. It has been established that rehabilitation programs should start from immobilization and progression without weight bearing, to an early return to range of motion (ROM) with an early achievement of full knee extension, immediate mobilization, full weight bearing, and then to introduce resistance training based on progression criteria before on-field training<sup>6,23,28</sup>. The American College of Sports Medicine recommends the use of loads greater than 60% of the repetition maximum (1RM) for hypertrophy<sup>3</sup>, but it has been observed that the use of vigorous loads may increase the risk of graft laxity and even re-rupture<sup>27,36</sup>. In addition, it has been demonstrated that the overuse of high loads in ACL reconstruction rehabilitation programs could result in pain and inflammation due to the great mechanical tension<sup>10,26</sup>.

Consequently, blood flow restriction (BFR) training has emerged as an alternative to high load training as the use of low loads (20-30% of 1RM) with the application of BFR could result in similar muscle improvements<sup>16</sup>. Consequently, in ACL surgery patients these types of loads are usually better tolerated and could be essential for those subjects with bone edema and/or associated meniscal injuries<sup>25</sup>. BFR is a technique based on the application of a wrapping device on the proximal part of the worked limb, which exerts a pressure that restricts venous return while

maintaining partial arterial flow ( $\approx 100$  mmHg), in order to induce tissue hypoxia in the area due to decreased blood flow during exercise <sup>16,34</sup>. This controlled ischemia induces muscle hypertrophy, mainly due to the levels of metabolic stress and muscle tension <sup>35,54</sup>, stimulating anabolic growth factors, as well as cell inflammation and hormone production in a systemic and localized manner <sup>31,46</sup>. In addition, it may stimulate the recruitment of fast-twitch muscle fibres and the production of reactive oxygen species <sup>24,44</sup>.

The use of BFR training has also been studied in healthy subjects and similar values have been observed in maximum strength increases and muscle mass compared to non-BFR low load resistance training <sup>33</sup>. In athletes, its use has been proposed as adjuvant training to improve sports performance, even for those subjects at risk of injury, or those who do not tolerate conventional strength training with high loads <sup>19,45,53</sup>. Given the increasing use of BFR both in training and rehabilitation of patients with ACL surgery, the aim of this study was to evaluate its effectiveness on functionality, pain, muscle CSA, and strength in physically active patients aged 18-35 years.

## **MATERIALS AND METHODS**

### *STUDY DESIGN*

The following systematic review was designed following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 <sup>41</sup> to ensure its methodological quality.

### *ELIGIBILITY CRITERIA*

Articles were considered eligible for the present systematic review based on the criteria developed following the PICOS framework (population, intervention, comparison, outcomes, and type of study) <sup>4</sup>. Eligibility criteria is presented on Table 1.

### *SEARCH STRATEGY*

PubMed, Web of Science (WOS) and MEDLINE databases were searched on March 31<sup>st</sup> 2023. The search strategy used was: ("blood flow restriction" OR BFR OR kaatsu OR occlusion OR "restriction of blood flow") AND ("anterior cruciate ligament" OR ACL OR ACLR OR "multi-ligament" OR meniscus) AND (injur\* OR tear OR repair OR reconstruction OR surgery). In addition, reference lists from the included studies were screened to detect potential studies to include.

#### *STUDY SELECTION*

The author was responsible for the search, collection and selection of articles using Rayyan software. First, duplicate articles were eliminated, and the titles and abstracts were reviewed, to discard those articles that did not meet the eligibility criteria, as well as those for which it was not possible to obtain the full text. A second filter was then performed by reading the full text for the same purpose.

#### *DATA EXTRACTION*

Data extraction was carried out using a standardized form to record on an Microsoft Excel sheet (i) author, journal, and year of publication, (ii) country of study publication, (iii) sample characteristics (sample size, gender, and age), (iv) characteristics of the BFR protocol (i.e., cuff pressure and resistance training variables), (v) conventional treatment protocol characteristics (resistance training variables), and (vi) outcomes (strength, quadriceps CSA, pain, and functionality). In the absence of any of the data, an attempt was made to contact the authors to obtain the necessary information. A qualitative adverse-effects analysis was conducted to evaluate the potential negative health effects of BFR and/or the dangers of implementing it incorrectly.

#### *QUALITY ASSESSMENT AND RISK OF BIAS*

The methodological quality and risk of bias of the studies used for this systematic review was assessed using the PEDro Scale <sup>37</sup>, which studies the internal validity of the trial and its statistical information using 10 criteria. This scale has an eleventh criterion related to the external validity of the article, for this reason this last criterion is not used to calculate the final score of the trial.

Two authors independently assessed each item and a third author settled the dispute if necessary. The methodological quality and risk of bias of the selected studies was classified as follows:  $\geq 7$ , high; 5–6, moderate;  $< 5$ , low <sup>47</sup>.

## RESULTS

### *STUDY SELECTION*

Figure 1 illustrates the results obtained from the different databases and the screening process. The search yielded a total of 389 studies, of which sixteen articles were considered eligible after removing duplicates and reading the titles and abstracts of the screened records. Finally, six trials were included in the review that met all the eligibility criteria previously described.

### *CHARACTERISTICS OF THE INCLUDED STUDIES*

Four out of six included trials used treatment with high loads (70% of 1RM) as a control group <sup>5,20,22,23</sup>. Another article uses an active treatment with load progression <sup>40</sup>, while the last of these uses the hospital protocol based on immobilization with placebo blood restriction <sup>50</sup>. Four of the articles have used an automatic blood restriction pressure calculation system <sup>5,20,22,23</sup>, while the remaining two have used the recommended pressure based on existing evidence on the technique <sup>40,50</sup>. Only one study showed acute responses after a resistance exercise session with and without the use of BFR <sup>20</sup>.

A total of 152 patients (90 men and 62 women) have been studied in the registries included in the review, 80 of whom have been treated with BFR. Two studies are reports of the same study but describe different types of results <sup>22,23</sup>. All participants are active subjects with recent ACL surgery with similar characteristics, except in two of the trials: One assessed healthy subjects without ACL injury in one of the control groups, whereas the other control group was constituted by ACL injured subjects <sup>20</sup>. The second showed significant differences in body mass index (BMI) values, being higher in the blood flow restriction group ( $p < 0.05$ ) <sup>5</sup>.

None of the included studies reported adverse effects related to the use of BFR training. Nonetheless, it is important to highlight that patients with cardiovascular disorders must be aware of the contraindications of the use of BFR <sup>5</sup>.

#### *QUALITY ASSESSMENT AND RISK OF BIAS*

The PEDro Scale <sup>37</sup> was used to assess the internal validity of each of the trials and their statistical information. None of the included studies showed low methodological quality and high risk of bias. The records showed sufficient internal validity (criteria 2-9), while two of the trials had low external validity (criteria 1) given their low applicability and generalizability in the absence of specification of the eligibility criteria <sup>40,50</sup>. All articles showed sufficient statistical information (criteria 10-11) to make their results interpretable (Table 2).

#### *RESULTS OF INDIVIDUAL STUDIES*

Table 3 shows the summary of the findings of each of the studies included in the systematic review.

##### *Muscle strength*

Muscle strength was evaluated in 3 studies by estimation of 1RM <sup>5</sup>, 10RM <sup>23</sup> isokinetic strength assessment <sup>5,23,40</sup>. Two studies compared the use of the BFR combined with low loads (30% of 1RM) and the use of high loads (70% of 1RM) <sup>5,20,23</sup>. Although all groups obtained significant improvements after treatment, none of them showed significant differences between the experimental and control groups. Ohta et al. <sup>40</sup> combined a circuit training with a progression of low loads, in which the experimental group combined it from the second week with the use of BFR. Both groups significantly improved their strength values of the flexor and extensor muscles. The group that supplemented the exercise with the BFR showed significant improvements compared to the control group ( $p<0.05$ ).

##### *Cross sectional area*



Two trials studied muscle atrophy following surgery, measured by CSA of the knee musculature<sup>40,50</sup>. The use of the BFR was associated with a higher CSA ratio of the operated/contralateral knee extensors ( $p=0.04$ )<sup>40</sup>, as well as a lower CSA decrease of the knee flexor and extensor musculature ( $p<0.05$ )<sup>50</sup>.

### *Pain*

Pain was reported in three studies. Two of them used the Borg numerical scale and both reported knee pain improvements with the use of BFR compared to the use of high loads (70% of 1RM)<sup>20,22</sup>. Specifically, Hughes et al.<sup>22</sup>, observed significant improvements both during the session ( $p<0.05$ ,  $d=2.5$ ) and 24 hours post-session ( $p<0.01$ ,  $d=3.1$ ) compared to the control group. Hughes et al.<sup>20</sup> showed acute responses 2-3 weeks after surgery, demonstrating that low load BFR (30% RM and 80% LOP) produced significantly greater muscle pain than non-BFR high loads (70% RM) resistance exercise in injured subjects or the same BFR protocol in non-operated subjects. Regarding knee pain, low load BFR resulted in significantly lower levels than non-BFR high loads training after surgery. The third trial used the pain score from the Knee Injury and Osteoarthritis Outcome Score (KOOS) scale with 0 representing extreme pain and 100 no pain<sup>23</sup>. The BFR group significantly increased the score compared to the control group ( $67\pm 10\%$  vs.  $39\pm 14\%$ ,  $p<0.01$ ).

### *Function*

Hughes et al.<sup>23</sup> assessed joint functionality using the International Knee Documentation Committee (IKDC), the KOOS, the Lower Extremity Function Scale (LEFS), and the Lysholm scale. After 8 weeks of training, the group that used the BFR obtained higher values in all the measures of the different tools ( $p<0.01$ ), demonstrating higher functionality.

## **DISCUSSION**

The use of BFR as rehabilitation for ACL reconstruction was shown to be generally effective without any adverse events reported. The findings in this systematic review showed that when combined with low loads (30% 1RM), gains in muscle CSA as well as strength of the knee flexor and extensor musculature are not significantly different from rehabilitation with the use of high loads (70% of 1RM). Even so, the values of knee pain reduction and functionality are significantly higher with the use of BFR compared to the use of high loads or immobilization.

In line with our findings, a systematic review with meta-analysis showed that low load using BFR produces greater muscle strength responses compared to low load in clinical musculoskeletal rehabilitation. Contrary to the results included in this review, it seems that the magnitude of the results is lower when compared to high loads. For this reason, the authors propose the use of active rehabilitation with the use of BFR as a progressive return to the use of high loads <sup>21</sup>, so as not to put graft laxity at risk and even cause re-rupture <sup>27,36</sup>. Regarding this last aspect, it has been shown that there is no increased risk of compromising the graft when the return to activity is accelerated <sup>29</sup>. On the other hand, the study conducted by Koc et al. <sup>30</sup> found no significant differences in graft laxity between the use or not of the BFR. Even so, the authors point out that more trials are needed to evaluate graft laxity in rehabilitation with BFR and low loads, compared to the use of high loads. In addition, it is important to consider that the included patients were mostly adults at risk of sarcopenia without knee surgery, who could better tolerate post-session pain using high loads than ACL patients in early stages as previously demonstrated <sup>20</sup>.

It is known that both pain and joint edema can cause quadriceps dysfunction, altering its strength and/or activation <sup>43</sup>. One of the articles included in this review reported a significant improvement in pain and joint effusion in the experimental group compared to the control group <sup>23</sup>. This finding, added to the hypoalgesia effect of exercise itself could explain the improvements in increased muscle strength as well as knee function <sup>21,30</sup>.

Another hypothesis argues that alterations in muscle morphology and nerve conduction following ACL injury perpetuate quadriceps weakness, which compromises movement patterns, decreases functional performance, increases the risk of re-injury, and contributes to articular cartilage

degeneration<sup>8,11</sup>. Although more research is still needed to understand the exact mechanisms of action, the use of BFR has demonstrated the ability to promote muscle hypertrophy and reduce post-surgical atrophy<sup>11,21</sup>. Takarada et al.<sup>50</sup> studied the CSA of the knee musculature in immobilization without any active work and obtained a significant decrease in extensor atrophy compared to those who used a placebo BFR. Recent research has shown that high occlusion pressures are not required to maximize muscle gains from exercise, and that low pressures are better tolerated as they cause less muscle soreness<sup>12,32</sup>. However, it appears that not using a BFR protocol with personalized pressure for each subject could vary the effect size<sup>30</sup>.

This systematic review exhibits three main limitations that should be highlighted: 1) Due to the heterogeneity of the intervention protocols, the lack of consensus on the measurement of cuff pressure and cuff size, as well as the differences between rehabilitation protocols, makes it difficult to generalize the results obtained, 2) In five of the registries, the study subjects were not blinded and in none of the cases were the therapists blinded, which reduces the internal validity of the trials. 3) Three out of the six studies<sup>20,22,23</sup> are from the same research laboratory, substantially raising the risk of bias.

## CONCLUSION

This systematic review highlights BFR for ACL reconstruction rehabilitation. Low loads combined with BFR improves pain, muscle strength, function, and CSA. It also reduces atrophy when immobilizing the limb. There were significant improvements in pain and function compared to the use of high loads, with similar improvements in muscle strength. This finding leads us to consider the use of BFR combined with low loads (30% of 1RM) as an initial treatment.

## REFERENCES

1. Acevedo RJ, Rivera-Vega A, Miranda G, Micheo W. Anterior Cruciate Ligament Injury. *Curr Sports Med Rep*. 2014;13:186-191.
2. Ajuied A, Wong F, Smith C, et al. Anterior cruciate ligament injury and radiologic progression of knee osteoarthritis: a systematic review and meta-analysis. *Am J Sports Med*. 2014;42:2242-2252. PMID: 24214929
3. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc*. 2009;41:687-708. PMID: 19204579
4. Amir-Behghadami M, Janati A. Population, Intervention, Comparison, Outcomes and Study (PICOS) design as a framework to formulate eligibility criteria in systematic reviews. *Emergency Medicine Journal*. 2020;37:387-387.
5. Bembien MG, Mitcheltree KM, Larson RD, et al. Can Blood Flow Restricted Exercise Improve Ham:Quad Ratios Better Than Traditional Training? *Int J Exerc Sci*. 2019;12:1080. PMID: 31523351
6. Beynnon BD, Uh BS, Johnson RJ, et al. Rehabilitation after anterior cruciate ligament reconstruction: a prospective, randomized, double-blind comparison of programs administered over 2 different time intervals. *Am J Sports Med*. 2005;33:347-359. PMID: 15716250
7. Birchmeier T, Lisee C, Geers B, Kuenze C. Reactive Strength Index and Knee Extension Strength Characteristics Are Predictive of Single-Leg Hop Performance After Anterior Cruciate Ligament Reconstruction. *J Strength Cond Res*. 2019;33:1201-1207. PMID: 30844991
8. Birchmeier T, Lisee C, Kane K, Brazier B, Triplett A, Kuenze C. Quadriceps Muscle Size Following ACL Injury and Reconstruction: A Systematic Review. *J Orthop Res*. 2020;38:598-608. PMID: 31608490

- 259 9. Boden BP, Dean GS, Feagin JA, Garrett WE. Mechanisms of Anterior Cruciate Ligament  
260 Injury. *Orthopedics*. 2000;23:573-578.
- 261 10. Cerqueira MS, de Brito Vieira WH. Effects of blood flow restriction exercise with very  
262 low load and low volume in patients with knee osteoarthritis: protocol for a randomized  
263 trial. *Trials*. 2019;20:135.
- 264 11. Charles D, White R, Reyes C, Palmer D. A Systematic Review of the Effects of Blood  
265 Flow Restriction Training on Quadriceps Muscle Atrophy and Circumference Post ACL  
266 Reconstruction. *Int J Sports Phys Ther*. 2020;15:882-891. PMID: 33344004
- 267 12. Counts BR, Dankel SJ, Barnett BE, et al. Influence of relative blood flow restriction  
268 pressure on muscle activation and muscle adaptation. *Muscle Nerve*. 2016;53:438-445.  
269 PMID: 26137897
- 270 13. Culvenor AG, Collins NJ, Guermazi A, et al. Early knee osteoarthritis is evident one year  
271 following anterior cruciate ligament reconstruction: a magnetic resonance imaging  
272 evaluation. *Arthritis Rheumatol*. 2015;67:946-955. PMID: 25692959
- 273 14. Curran MT, Bedi A, Kujawa M, Palmieri-Smith R. A Cross-sectional Examination of  
274 Quadriceps Strength, Biomechanical Function, and Functional Performance From 9 to 24  
275 Months After Anterior Cruciate Ligament Reconstruction. *Am J Sports Med*.  
276 2020;48:2438-2446. PMID: 32693626
- 277 15. Curran MT, Lepley LK, Palmieri-Smith RM. Continued Improvements in Quadriceps  
278 Strength and Biomechanical Symmetry of the Knee After Postoperative Anterior Cruciate  
279 Ligament Reconstruction Rehabilitation: Is It Time to Reconsider the 6-Month Return-to-  
280 Activity Criteria? *J Athl Train*. 2018;53:535-544. PMID: 29975571
- 281 16. Cuyul-Vásquez I, Leiva-Sepúlveda A, Catalán-Medalla O, Araya-Quintanilla F,  
282 Gutiérrez-Espinoza H. The addition of blood flow restriction to resistance exercise in

individuals with knee pain: a systematic review and meta-analysis. *Braz J Phys Ther.* 2020;24. PMID: 32198025

17. Czuppon S, Racette BA, Klein SE, Harris-Hayes M. Variables associated with return to sport following anterior cruciate ligament reconstruction: a systematic review. *Br J Sports Med.* 2014;48:356-364. PMID: 24124040

18. Faleide AGH, Magnussen LH, Strand T, et al. The Role of Psychological Readiness in Return to Sport Assessment After Anterior Cruciate Ligament Reconstruction. *Am J Sports Med.* 2021;49:1236-1243. PMID: 33656938

19. Grønfeldt BM, Lindberg Nielsen J, Mieritz RM, Lund H, Aagaard P. Effect of blood-flow restricted vs heavy-load strength training on muscle strength: Systematic review and meta-analysis. *Scand J Med Sci Sports.* 2020;30:837-848. PMID: 32031709

20. 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. PMID: 30014968

21. Hughes L, Paton B, Rosenblatt B, Gissane C, Patterson SD. Blood flow restriction training in clinical musculoskeletal rehabilitation: a systematic review and meta-analysis. *Br J Sports Med.* 2017;51:1003-1011. PMID: 28259850

22. Hughes L, Patterson SD, Haddad F, et al. Examination of the comfort and pain experienced with blood flow restriction training during post-surgery rehabilitation of anterior cruciate ligament reconstruction patients: A UK National Health Service trial. *Phys Ther Sport.* 2019;39:90-98. PMID: 31288213

23. Hughes L, Rosenblatt B, Haddad F, et al. Comparing the Effectiveness of Blood Flow Restriction and Traditional Heavy Load Resistance Training in the Post-Surgery Rehabilitation of Anterior Cruciate Ligament Reconstruction Patients: A UK National

Health Service Randomised Controlled Trial. *Sports Med.* 2019;49:1787-1805. PMID: 31301034

24. Hwang PS, Willoughby DS. Mechanisms Behind Blood Flow-Restricted Training and its Effect Toward Muscle Growth. *J Strength Cond Res.* 2019;33 Suppl 1:S167-S179. PMID: 30011262

25. Jakobsen TL, Thorborg K, Fisker J, Kallemose T, Bandholm T. Blood flow restriction added to usual care exercise in patients with early weight bearing restrictions after cartilage or meniscus repair in the knee joint: a feasibility study. *J Exp Orthop.* 2022;9:101. PMID: 36192606

26. Jan M-H, Lin J-J, Liao J-J, Lin Y-F, Lin D-H. Investigation of Clinical Effects of High- and Low-Resistance Training for Patients With Knee Osteoarthritis: A Randomized Controlled Trial. *Phys Ther.* 2008;88:427-436.

27. Janssen RPA, Scheffler SU. Intra-articular remodelling of hamstring tendon grafts after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2014;22:2102-2108. PMID: 23982759

28. Jenkins SM, Guzman A, Gardner BB, et al. Rehabilitation After Anterior Cruciate Ligament Injury: Review of Current Literature and Recommendations. Accessed February 20, 2023. <https://doi.org/10.1007/s12178-022-09752-9>

29. Kim JG, Kim WS, Kim SG, Lee DH. Accelerated Versus Non-accelerated Rehabilitation After Primary Anterior Cruciate Ligament Reconstruction Using Hamstring Autografts: A Systematic Review and Meta-analysis of Comparative Studies. *Indian J Orthop.* 2021;55:405-415. PMID: 33927819

30. Koc BB, Truyens A, Heymans MJLF, Jansen EJP, Schotanus MGM. Effect of Low-Load Blood Flow Restriction Training After Anterior Cruciate Ligament Reconstruction: A Systematic Review. *Int J Sports Phys Ther.* 2022;17:334-346. PMID: 35391871

31. Layne AS, Larkin-Kaiser K, MacNeil RG, et al. Effects of blood-flow restriction on biomarkers of myogenesis in response to resistance exercise. *Applied Physiology, Nutrition, and Metabolism*. 2017;42:89-92.
32. Loenneke JP, Kim D, Fahs CA, et al. Effects of exercise with and without different degrees of blood flow restriction on torque and muscle activation. *Muscle Nerve*. 2015;51:713-721. PMID: 25187395
33. Loenneke JP, Wilson JM, Marín PJ, Zourdos MC, Bembien MG. Low intensity blood flow restriction training: a meta-analysis. *Eur J Appl Physiol*. 2012;112:1849-1859. PMID: 21922259
34. Loenneke JP, Wilson JM, Wilson GJ, Pujol TJ, Bembien MG. Potential safety issues with blood flow restriction training. *Scand J Med Sci Sports*. 2011;21:510-518. PMID: 21410544
35. May AK, Russell AP, Della Gatta PA, Warmington SA. Muscle Adaptations to Heavy-Load and Blood Flow Restriction Resistance Training Methods. *Front Physiol*. 2022;13.
36. Ménétrey J, Duthon VB, Laumonier T, Fritschy D. “Biological failure” of the anterior cruciate ligament graft. *Knee Surg Sports Traumatol Arthrosc*. 2008;16:224-231. PMID: 18183368
37. de Morton NA. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. *Aust J Physiother*. 2009;55:129-133. PMID: 19463084
38. Nagelli C V., Hewett TE. Should Return to Sport be Delayed Until 2 Years After Anterior Cruciate Ligament Reconstruction? Biological and Functional Considerations. *Sports Medicine*. 2017;47:221-232.
39. O’Connor RF, King E, Richter C, Webster KE, Falvey ÉC. No Relationship Between Strength and Power Scores and Anterior Cruciate Ligament Return to Sport After Injury



- Scale 9 Months After Anterior Cruciate Ligament Reconstruction. *Am J Sports Med.* 2020;48:78-84. PMID: 31877093
40. Ohta H, Kurosawa H, Ikeda H, Iwase Y, Satou N, Nakamura S. Low-load resistance muscular training with moderate restriction of blood flow after anterior cruciate ligament reconstruction. *Acta Orthop Scand.* 2003;74:62-68. PMID: 12635796
41. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Rev Esp Cardiol (Engl Ed).* 2021;74:790-799. PMID: 34446261
42. Palmieri-Smith RM, Lepley LK. Quadriceps Strength Asymmetry After Anterior Cruciate Ligament Reconstruction Alters Knee Joint Biomechanics and Functional Performance at Time of Return to Activity. *Am J Sports Med.* 2015;43:1662-1669. PMID: 25883169
43. Palmieri-Smith RM, Villwock M, Downie B, Hecht G, Zernicke R. Pain and effusion and quadriceps activation and strength. *J Athl Train.* 2013;48:186-191. PMID: 23672382
44. Pearson SJ, Hussain SR. A review on the mechanisms of blood-flow restriction resistance training-induced muscle hypertrophy. *Sports Med.* 2015;45:187-200. PMID: 25249278
45. Pignanelli C, Christiansen D, Burr JF. Blood flow restriction training and the high-performance athlete: science to application. *J Appl Physiol (1985).* 2021;130:1163-1170. PMID: 33600282
46. de Queiros VS, Rolnick N, de Alcântara Varela PW, Cabral BG de AT, Silva Dantas PM. Physiological adaptations and myocellular stress in short-term, high-frequency blood flow restriction training: A scoping review. *PLoS One.* 2022;17:e0279811.
47. Ribeiro de Ávila V, Bento T, Gomes W, Leitão J, Fortuna de Sousa N. Functional Outcomes and Quality of Life After Ankle Fracture Surgically Treated: A Systematic Review. *J Sport Rehabil.* 2018;27:274-283.

48. Sanders TL, Maradit Kremers H, Bryan AJ, et al. Incidence of Anterior Cruciate Ligament Tears and Reconstruction: A 21-Year Population-Based Study. *Am J Sports Med*. 2016;44:1502-1507. PMID: 26920430
49. Siegel L, Vandenakker-Albanese C, Siegel D. Anterior Cruciate Ligament Injuries. *Clinical Journal of Sport Medicine*. 2012;22:349-355.
50. Takarada Y, Takazawa H, Ishii N. Applications of vascular occlusion diminish disuse atrophy of knee extensor muscles. *Med Sci Sports Exerc*. 2000;32:2035-2039. PMID: 11128848
51. Thomas AC, Wojtys EM, Brandon C, Palmieri-Smith RM. Muscle atrophy contributes to quadriceps weakness after anterior cruciate ligament reconstruction. *J Sci Med Sport*. 2016;19:7-11. PMID: 25683732
52. Wiggins AJ, Grandhi RK, Schneider DK, Stanfield D, Webster KE, Myer GD. Risk of Secondary Injury in Younger Athletes After Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis. *Am J Sports Med*. 2016;44:1861-1876. PMID: 26772611
53. Wortman RJ, Brown SM, Savage-Elliott I, Finley ZJ, Mulcahey MK. Blood Flow Restriction Training for Athletes: A Systematic Review. *Am J Sports Med*. 2021;49:1938-1944. PMID: 33196300
54. Wortman RJ, Brown SM, Savage-Elliott I, Finley ZJ, Mulcahey MK. Blood Flow Restriction Training for Athletes: A Systematic Review. *Am J Sports Med*. 2021;49:1938-1944.

## TABLES

Table 1. Eligibility criteria

Category	Inclusion criteria	Exclusion criteria
Patients	Participants were 18-35 years old and were physically active before undergoing surgery of ACL.	Participants with other health problems such as cardiovascular or mental disorders. Participants with other type of injuries not localized in the knee.
	Rehabilitation programs after ACL reconstruction with the use of BFR resistance training.	Studies without standardized rehabilitation protocols.
Comparisons	Control groups that performed conventional rehabilitation without the use of BFR.	Studies that applied different rehabilitation protocols, all of them including the use of BFR.
Outcomes	Studies that reported values of pain, knee functionality, muscle strength and/or quadriceps CSA.	Lack of baseline (i.e., contralateral non-injured limb or the injured limb prior to surgery) measures.
Study design	Randomized controlled trials	Studies with other study design such as observational studies, meta-analyses or case reports.

*ACL: Anterior cruciate ligament; BFR = blood flow restriction*

Table 2. Quality and risk of bias, PEDro Scale.

	Specified eligibility criteria	Random allocation	Concealed allocation	Homogeneous groups	Blinded subjects	Blinded therapists	Blinded assessors	Less than 15% of dropouts	Intention-to-treat analysis	Statistical comparisons	Point measures and measures of variability	TOTAL	QUALITATIVE ASSESSMENT
<b>Hughes et al. (2019a)</b> <sup>23</sup>	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7	High
<b>Hughes et al. (2019b)</b> <sup>22</sup>	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7	High
<b>Bemben et al. (2019)</b> <sup>5</sup>	Yes	Yes	Yes	No	No	No	Yes	Yes	No	Yes	Yes	6	Moderate
<b>Hughes et al. (2018)</b> <sup>20</sup>	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7	High
<b>Ohta et al. (2003)</b> <sup>40</sup>	No	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	6	Moderate
<b>Takarada et al. (2000)</b> <sup>50</sup>	No	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	8	High

Table 3. Summary of studies included in the review

Author (year)	Type of study	Characteristics of the sample	Intervention	Cuff pressure	Duration of intervention	Outcomes
<b>Hughes et al. (2019a)</b> <sup>23</sup>	Randomised clinical trial.	EG: n = 12 (7 m, 5 f), age 29±7 years, BMI 25.40±3.86 kg/m <sup>2</sup> .  CG: n = 12 (10 m, 2 f), age 29±7 years, BMI 26.41±4.35 kg/m <sup>2</sup> .	8 weeks, 2 x/week  Activation:  5 min bike + unilateral low weight press.  Intervention:  Unilateral press (30s break between sets)  EG = 4 series (30, 15, 15, 15 reps)  30% 1RM + BFR.  CG = 3x10 (70% 1RM).	Personalised  automatic  pressure  80% LOP	8 weeks, 16 sessions	10RM:  ↑EG and ↑CG (p<0,01)  EG = CG (p=0,22)  IKDC, LEFS and KOOS:  ↑EG and ↑CG (p<0,01)  EG > CG (p<0,01)  Pain (KOOS scale):  ↑EG and ↑CG (p<0,01)  EG > CG (p<0,01)
<b>Hughes et al. (2019b)</b> <sup>22</sup>	Randomised clinical trial.	EG: n = 12 (7 m, 5 f), age 29±7 years, BMI 25,40±3,86 kg/m <sup>2</sup> .	8 weeks, 2 x/week  Activation:	Personalised  automatic  pressure	8 weeks, 16 sessions	Knee pain during session:  ↓EG and ↓CG (p<0,05)  EG < CG (p<0,05)

			5 min bike + unilateral low weight	80% LOP			Knee pain post 24h:
		CG: n = 12 (10 m, 2 f), age	press.				↓EG and ↓CG (p<0,05)
		29±7 years, BMI 26,41±4,35	Intervention:				EG < CG (p<0,01)
		kg/m <sup>2</sup> .	Unilateral press (30s break between				Muscle pain:
			sets)				↓EG and ↓CG (p<0,05)
			EG = 4 series (30, 15, 15, 15 reps)				EG > CG (p<0,05)
			30% 1RM + BFR.				
			CG = 3x10 (70% 1RM).				
<b>Bemben et al. (2019)</b> <sup>5</sup>	Randomised clinical trial.	EG: n = 6 f; age 21,67±0,82 years, BMI 24,32±1,70 kg/m <sup>2</sup> .	6 weeks, 2 x/week	Personalised automatic pressure	6 weeks, 18 sessions	18 1RM:	
			Chest press, lat pulldown, biceps curl, leg press, quadriceps extension and hamstring curl. Rest 1 min between	50% LOP			↑EG and ↑CG (p<0,001)
			sets.				EG = CG (p>0,05)
		CG: n = 8 f, age 21,63±0,74 years, BMI 21,39±2,10 kg/m <sup>2</sup> .	CG = 3x10 (70% 1RM).				Torque:
							↑EG and ↑CG (p<0,009)
							EG = CG (p>0,05)

			EG = 3x10 (70% 1RM) and hamstring curl 4 sets (30,15,15,15 reps) 30%1RM + BFR.		
<b>Hughes et al. (2018)</b>	Randomised clinical trial.	CG1: n = 10 (10 m, 0 f), age 28±5 years, BMI 25,25±3,20 kg/m <sup>2</sup> , uninjured.	Acute responses. Activation: 5 min bike + unilateral low weight press.	Personalised automatic pressure 80% LOP	Muscle pain: EG > CG1 (p<0,05) EG > CG2 (p<0,01) Knee pain: EG < CG2 (p<0,01) RPE: EG = CG2 (p>0,05)
		EG: n = 10 (6 m, 4 f), age 29±5 years, BMI 25,69±4,16 kg/m <sup>2</sup> . 2-3 weeks post-surgery.	Intervention: Unilateral press (30s break between sets) CG1: 4 sets (30,15,15,15 reps) 30%1RM + BFR.		
		CG2: n = 10 (7 m, 3 f), age 31±7 years, BMI 23,51±3,38 kg/m <sup>2</sup> . 2-3 weeks post-surgery.	EG: 4 sets (30,15,15,15 reps) 30%1RM + BFR. CG2: 3x10 (70%1RM).		

<b>Ohta et al. (2003)</b> <sup>40</sup>	Randomised clinical trial.	EG: n = 22 (13 m, 9 f), age 28±9,7 years, weight 65±14 kg.  CG: n = 22 (12 m, 10 f), age 30±9,7 years, weight 63±8,8 kg.	16 weeks  Straight leg raises + hip abduction:  Week 1-8: 2 x 20x5". 6x/week  (progressive load 0-2kg)  Adduction with ball:  Week 1-12: 2 x 20x5". 6x/week.  ½ Squat:  Week 5-16: 2 x 20x6". 6x/week.  (progressive load 0-14kg).  Step-up:  Week 5-16: 3 x 20x25cm.  6x/week. (progressive load 0-14kg)  Banded knee extension:  Week 9-12: 1x20. 6x/week.	180 mm Hg with 16 weeks  hand-pumped  tourniquet	Muscular torque knee extensor muscle  (operated/healthy ratio):  CC60: EG > CG (p<0,001)  CC180: EG > CG (p=0,004)  IM60: EG > CG (p<0,001)  Muscular torque knee flexor muscle (operated/healthy ratio):  CC60: EG > CG (p=0,05)  CC180: EG > CG (p=0,04)  IM60: EG > CG (p=0,02)  CSA (operated/healthy ratio):  Extensor muscle group:  EG > CG (p=0,04)
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			Week 13-16: 2x20. 6x/week.				Flexor + adductor muscle
			Walking squat:				group:
			Week 13-16: 3x60 steps. 6x/week.				EG = CG (p>0,05)
			EG: idem exercises + BFR (from week 2).				
<b>Takarada et al. (2000)</b> <sup>50</sup>	Randomised clinical trial.	EG: n = 8 (4 males, 4 females), age 22,4±2,1 years, body mass 67,8±2 kg (males) and 49,8±0,7 kg (females), height 169,8±0,7 cm (males) and 157,8±1,3 cm (females).  CG: n = 8 (4 males, 4 females), age 23±2,5 years, body mass 71±5,8 kg (males) and 53,4±1,6 kg (females),	2 weeks EG: intermittent occlusion 5 sets 5 min + 3 min rest. 2x/day. CG: placebo occlusion.	200-260 mm Hg	2 weeks	CSA extensor muscle group: ↓EG and ↓CG (p<0,05) EG < CG (p=0,046) CSA flexor muscle group: ↓EG and ↓CG (p<0,05) EG = CG (p=0,69)	

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height 173,4±1 cm (males)

and 158,5±1,1 cm (females)

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EG, experimental group; CG, control group; m, male; f, female; BMI, body mass index; 1RM, repetition maximum; BFR, blood flow restriction; LOP, Limb Occlusion Pressure; IKDC, The International Knee Documentation Committee; LEFS, The Lower Extremity Function Scale; KOOS, Knee Injury and Osteoarthritis Outcome Score; RPE, rate of perceived exertion; CC, concentric contraction in isokinetic test; CSA, cross sectional area; ↑, increase; ↓, decrease.

## **FIGURE LEGENDS**

Figure 1. Flow diagram of literature search according to the PRISMA statement