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**REVISÃO**

# Comparison between training protocols with blood flow restriction in clinical musculoskeletal rehabilitation: protocol of a systematic review

## *Comparação entre os protocolos de treinamento com restrição do fluxo sanguíneo na reabilitação clínica musculoesquelética: protocolo de uma revisão sistemática*

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## Abstract

*Introduction*: The training with blood flow restriction (RFS) is increasingly used in the clinical rehabilitation of musculoskeletal disorders, but there is still much uncertainty about which parameters is ideal to use regarding the restriction pressure, combination with other therapies and which groups of patients can benefit most from the technique. *Objective*: To compare the effectiveness and safety of different methodologies for the use of RFS in the rehabilitation of musculoskeletal disorders. *Methods*: A systematic review will be performed through independent searches by two reviewers of studies indexed to Medline, SPORTDiscus, Central, Lilacs, CINAHL, Embase, J-STAGE and PEDro; in addition to sources of gray literature and in the bibliographic references of the studies included in the review. The study protocol was registered on the Prospero Platform (CRD422021233488). Randomized parallel-group clinical trials that tested the efficacy or safety of RFS training in individuals aged 18 years or older for at least three weeks will be considered. Details will be extracted on the application of RFS and

outcomes of pain, muscle strength and adverse events, considered as primary outcomes; in addition to functional capacity, discomfort, overall physical capacity and quality of life, composing the secondary outcomes. The risk of bias of the studies will be assessed using the PEDro scale and any disagreement during the process of selection, extraction and evaluation of the risk of bias will be decided by a third reviewer. *Expected results*: Expose the information available in the literature and provide clear guidance to clinicians and researchers on the prescriptions and recommendations of this technique.
**Keywords**: musculoskeletal rehabilitation; restriction of blood flow.

## Resumo

*Introdução*: O treino com restrição de fluxo sanguíneo (RFS) é cada vez mais utilizado na reabilitação clínica das disfunções músculo-esqueléticas, mas ainda existe muita incerteza sobre que parâmetros ideais para serem utilizados quanto à pressão de restrição, combinação com outras terapias e quais os grupos de pacientes que mais podem se beneficiar da técnica. *Objetivo*: Comparar a eficácia e a segurança de diferentes metodologias de utilização do RFS na reabilitação de disfunções musculoesqueléticas. *Métodos*: Será realizada uma revisão sistemática por meio de buscas independentes por meio de dois revisores de estudos indexados ao Medline, SPORTDiscus, Central, Lilacs, Cinahl, Embase, J-STAGE e PEDro; além de fontes da literatura cinza e nas referências bibliográficas dos estudos incluídos na revisão. O protocolo do estudo foi registrado na Plataforma PROSPERO (CRD422021233488). Serão considerados ensaios clínicos randomizados de grupos paralelos que testaram a eficácia ou segurança do treinamento RFS com indivíduos com 18 anos ou mais por pelo menos três semanas. Serão extraídos detalhes sobre a alicação do RFS e desfechos de dor, força muscular e eventos adversos, considerados como desfechos primários; além da capacidade funcional, desconforto, capacidade física geral e qualidade de vida, compondo os desfechos secundários. O risco de viés dos estudos será avaliado por meio da escala PEDro e qualquer discordância durante o processo de seleção, extração e avaliação do risco de viés será decidida por um terceiro revisor. *Resultados esperados*: Expor as informações disponíveis na literatura e fornecer orientações claras aos clínicos e pesquisadores sobre as prescrições e recomendações desta técnica.
**Palavras-chave**: reabilitação musculoesquelética; restrição do fluxo sanguíneo.

## Introduction

The regular practice of physical exercise is an indispensable resource for health promotion at the individual and collective level, being a tool for prevention and rehabilitation in various health conditions [1]. For the benefits of physical exercise to be optimized, it must be practiced under minimum parameters of frequency and intensity [2]. The World Health Organization (WHO) recommends that individuals with chronic diseases practice weekly at least 75 minutes or 150 minutes of moderate or intense aerobic activity, respectively [3]. In addition, the incorporation of muscle strengthening exercises with intensity between 60-70% of one maximum repetition (1RM) is recommended, as it offers additional benefits [3,4].

However, for some groups of patients, the use of conventional physical exercises presents limitations, because the minimum recommended training parameters are above the physical capacities of the patients, and alternatives are necessary for the benefits of physical activity to be enjoyed by these populations [5]. In this sense, training with blood flow restriction (BFR) has been a viable solution because it demands a high physical intensity even with low loads and less joint stress, which is the training condition desired for the clinical rehabilitation of patients with musculoskeletal disorders (MSD) [6,7].

The BFR training consists of placing a partially inflated cuff or tourniquet in the proximal region of a muscle group in which blood flow is desired, with the objective of evoking in a shorter time local and systemic physiological responses with low loads similar to those offered by moderate and high intensity training for a prolonged time [8].

In previous systematic reviews, BFR has been shown to be effective in the clinical rehabilitation of patients with MSD in terms of muscle strength, pain and muscle volume [9-11]. However, the high heterogeneity of BFR use in the studies raised prevents a concise recommendation on appropriate parameters that achieve the desirable therapeutic effects with the technique [12,13].

The most common clinical form of BFR use is the combination with resistance or aerobic exercises of low intensity, but it can be combined with high and moderate intensity training, or even used at rest [8]. In addition, the choice of blood flow restriction pressure (BFRP) is quite heterogeneous and can be based on formulas, percentages of occlusion pressure of each individual, diastolic pressure or absolute values [12].

Systematic reviews on the use of BFR in the rehabilitation of MSD are conducted focusing on lower limb pathologies, such as knee osteoarthrosis, patellofemoral pain syndrome and anterior cruciate ligament injury [14]. In addition, the studies included in the available reviews use protocols based exclusively on resistance exercises, excluding interventions that combine with aerobic exercise [7,9-11,13].

Thus, the current available literature does not provide an overview of the effectiveness of BFR in the rehabilitation of patients with MSD, in addition to grouping different methodologies for the use of BFR in the same analyses. Therefore, the aim of this study is to compare the methods of using BFR in the clinical rehabilitation of MSD, regardless of the site of the lesion and considering the characteristics of the therapeutic approaches employed.

## Methods

*Type of study*

This is a protocol of systematic review of the literature to compare the efficacy and safety of different BFR training methodologies in patients diagnosed with MSD. All stages of the study will be conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

*Ethical and local aspects of research*

The review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) platform (CRD422021233488). This study will be conducted at the Federal University of Amapá (UNIFAP), in the Post-Graduate Program in Health Sciences.

*Search strategy*

Searches will be performed in the following databases: Medline, SPORTDiscus, Central, Lilacs, Cinahl, Embase, J-STAGE and PEDro. In addition to searches in gray literature in bases such as OpenGrey and ProQuest. Search terms and keywords will be tailored to each database as appropriate. In addition, searches will be carried out in the bibliographic references of all articles included, in order to identify possible sources eligible for review.

There will be no language restriction, sources that are not in Portuguese, Spanish and English, will be forwarded to professional translation services. In cases where the absence of relevant data is identified, authors will be contacted to request additional information.

**Chart I** – *Search strategies of the systematic review*

| Database | Search strategies |
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| PubMed | 1. "musculoskeletal diseases"[MeSH] OR "musculoskeletal pain"[MeSH] OR “musculoskeletal system"[MeSH] OR "leg injuries"[MeSH] OR "arm injuries"[MeSH] OR "upper extremity"[MeSH] OR "lower extremity"[MeSH] OR "connective tissue diseases"[MeSH] OR “soft tissue injuries"[MeSH] OR "rheumatology"[MeSH] OR "orthopedics"[MeSH] OR "back pain"[MeSH] OR "neck pain"[MeSH] OR "athletic injuries"[MeSH] OR "back injuries"[MeSH] OR "joint dislocations"[MeSH] OR “fractures, bone"[MeSH] OR "fractures, cartilage"[MeSH] OR "hand injuries"[MeSH] OR "hip injuries"[MeSH] OR "sprains and strains"[MeSH] OR "tendon injuries"[MeSH] OR "ligaments"[MeSH] OR "bone diseases"[MeSH] OR arthritis OR chondrocalcinosis OR fibromyal* OR fibrositis OR fibrositides OR low back OR lupus OR osteitis OR osteoarthrit* OR osteoarthrop* OR osteochondr* OR hyperostos* OR osteonecros* OR osteoporos* OR periarthriti* OR rheumati* OR bone OR ligament* OR fracture OR tendon* OR muscle* OR “musculoskeletal injur*” OR menisc* OR “knee pain” OR fascia<br>2. blood flow restrict* OR blood-flow restrict* OR kaatsu OR "therapeutic occlusion"[MeSH] OR “occlu* training” OR “restrict* blood” OR “vascular restrict*” OR “vascular occlu*” OR “limb occlu*” OR “blood rest*” OR “blood occlu*” OR “arterial occlu*” OR “arterial restrict*” OR “venous restrict*” OR “occlu* pressure*” OR “hypoxia* training” OR “ischemi* training” OR “ischemi* strength*” OR “hypoxia* strength*” OR “ischemi* hypertroph*” OR “hypoxia* hypertroph*”<br>3. “rehabilitation”[Mesh] OR rehab* OR “physical therapy modalities”[Mesh] OR “rehabilitation centers”[Mesh] OR “physical and rehabilitation medicine”[Mesh] OR “rehabilitation research”[Mesh] OR “telerehabilitation”[Mesh] OR telerehab* OR physiot* OR “exercise”[Mesh] OR exercise* OR physical OR functional readapt* OR activit* OR kinesiotherapy OR “exercise movement techniques”[Mesh] OR training OR “resistance training”[Mesh] OR strength* OR weight bearing OR stretch* OR physical fitness OR exertion OR sport* OR therapeutic exercise OR resistance training OR aerobic exercises OR weightlifting OR treadmill* OR run OR walk* OR jogg* OR sprint* OR rowing OR bicycl* OR cycl* OR gym OR enduranc* OR run OR activity* OR isometric* isokinetic<br>4. (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab])<br>5. "animals"[Mesh] NOT "humans"[Mesh]<br>#1 AND #2 AND #3 AND #4 NOT #5<br>Result:4.019 |

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| Embase | 1. 'musculoskeletal disease'/exp OR 'rheumatology'/exp OR 'orthopedics'/exp OR 'musculoskeletal pain'/exp OR 'soft tissue injury'/exp OR 'limb injury'/exp OR 'upper limb'/exp OR 'lower limb'/exp OR 'connective tissue disease'/exp OR 'musculoskeletal system'/exp OR 'leg injury'/exp OR 'upper limb'/exp OR 'backache'/exp OR 'neck pain'/exp OR 'knee disease'/exp OR 'sport injury'/exp OR 'arthropathy'/exp OR 'dislocation'/exp OR 'fracture'/exp OR 'hand disease'/exp OR 'hip disease'/exp OR 'chondropathy'/exp OR 'muscle disease'/exp OR 'bone disease'/exp OR 'sprain'/exp OR 'ligament and tendon injury'/exp OR arthritis OR chondrocalcinosis OR fibromyal* OR fibrositis OR fibrositides OR hyperostos* OR 'low back' OR lupus OR osteitis OR osteoarthrit* OR osteoarthrop* OR osteochondr* OR osteonecros* OR osteoporos* OR periarthriti* OR rheumati* OR 'knee pain' OR fracture OR ligament* OR tendon* OR muscle* OR musculoskeletal OR menisc* OR fascia OR bone OR injur*<br>2. 'blood flow restriction'/exp OR 'blood-flow restr*' OR kaatsu OR 'therapeutic occlusion' OR 'occlu* training' OR 'restrict* blood' OR 'vascular restrict*' OR 'vascular occlu*' OR 'limb occlu*' OR 'blood rest*' OR 'blood occlu*' OR 'arterial occlu*' OR 'arterial restrict*' OR 'venous restrict*' OR 'occlu* pressure*' OR 'hypoxia* training' OR 'ischemi* training' OR 'ischemi* strength*' OR 'hypoxia* strength*' OR 'ischemi* hypertroph*' OR 'hypoxia* hypertroph*'<br>3. 'rehabilitation'/exp OR rehab* OR 'functional readaptation' OR 'medical rehabilitation' OR readaption OR readjustment OR 'rehabilitation engineering' OR 'rehabilitation potential' OR 'rehabilitation process' OR 'rehabilitation program' OR 'rehabilitation programme' OR telerehab* OR 'rehabilitative treatment' OR 'sport'/exp OR 'rehabilitation care'/exp OR 'physiotherapy'/exp OR 'kinesiotherapy'/exp OR 'dancing'/exp OR 'exercise'/exp OR 'walking'/exp OR 'physical activity'/exp OR 'resistance training'/exp OR sport* OR walk* OR swim* OR aquatic OR danc* OR running OR jogging OR aerobic* OR pilates OR exercis* OR gym* OR isometric* OR therap* OR training* OR physical OR strength OR resistance OR activity* OR fitness* OR 'weight-bearing' OR run OR isokinetic OR physiot*<br>4. 'clinical trial'/de OR 'randomized controlled trial'/de OR 'randomization'/de OR 'single blind procedure'/de OR 'double blind procedure'/de OR 'crossover procedure'/de OR 'placebo'/de OR 'prospective study'/de OR 'randomi?ed controlled' NEXT/1 trial* OR rct OR 'randomly allocated' OR 'allocated randomly' OR 'random allocation' OR allocated NEAR/2 random OR single NEXT/1 blind* OR double NEXT/1 blind* OR (treble OR triple) NEAR/1 blind* OR placebo*<br>5. ('animal'/exp) NOT ('human'/exp)<br>#1 AND #2 AND #3 AND #4 NOT #5<br>#6 AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)<br>Result:408 |

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| PEDro | 1. blood flow restri* AND [Filter]: Clinical trial<br>Result: 46<br>2. blood flow restriction AND [Filter]: Clinical trial<br>Result: 38<br>3. kaatsu AND [Filter]: Clinical trial<br>Result: 3<br>4. restrict* blood AND [Filter]: Clinical trial<br>Result: 128<br>5. therapeutic occlusion AND [Filter]: Clinical trial<br>Result: 2<br>6. occlu* training AND [Filter]: Clinical trial<br>Result: 61<br>7. vascular restrict* AND [Filter]: Clinical trial<br>Result: 13<br>8. vascular occlu* AND [Filter]: Clinical trial<br>Result: 27<br>9. limb occlu* AND [Filter]: Clinical trial<br>Result: 9<br>10. arterial occlu* AND [Filter]: Clinical trial<br>Result: 42<br>11. blood occlu* AND [Filter]: Clinical trial<br>Result: 48<br>12. arterial restrict* AND [Filter]: Clinical trial<br>Result: 19<br>13. venous restrict* AND [Filter]: Clinical trial<br>Result: 13<br>14. occlu* pressure* AND [Filter]: Clinical trial<br>Result: 55<br>15. hypoxia* training AND [Filter]: Clinical trial<br>Result: 18<br>16. ischemi* training AND [Filter]: Clinical trial<br>Result: 169<br>17. ischemi* strength* AND [Filter]: Clinical trial<br>Result: 47<br>18. hypoxia* strength* AND [Filter]: Clinical trial<br>Result: 3<br>19. ischemi* hypertrophy* AND [Filter]: Clinical trial<br>Result: 1<br>20. hypoxia* hypertrophy* AND [Filter]: Clinical trial<br>Result: 0 |

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| CENTRAL | 1. MeSH descriptor: [Musculoskeletal Diseases] explode all trees<br>2. MeSH descriptor: [Musculoskeletal Pain] explode all trees<br>3. MeSH descriptor: [Musculoskeletal System] explode all trees<br>4. MeSH descriptor: [Leg Injuries] explode all trees<br>5. MeSH descriptor: [Arm Injuries] explode all trees<br>6. MeSH descriptor: [Upper Extremity] explode all trees<br>7. MeSH descriptor: [Lower Extremity] explode all trees<br>8. MeSH descriptor: [Soft Tissue Injuries] explode all trees<br>9. MeSH descriptor: [Connective Tissue Diseases] explode all trees<br>10. MeSH descriptor: [Rheumatology] explode all trees<br>11. MeSH descriptor: [Orthopedics] explode all trees<br>12. arthritis OR chondrocalcinosis OR fibromyal* OR fibrositis OR fibrositides OR hyperostos* OR low back OR lupus OR osteitis OR osteoarthrit* OR osteoarthrop* OR osteochondr* OR osteonecros* OR osteoporos* OR periarthriti* OR rheumati* OR “knee pain” OR fracture OR ligament* OR injur* OR tendon* OR muscle* OR musculoskeletal OR menisc* OR fascia OR bone<br>13. MeSH descriptor: [Back Pain] explode all trees<br>14. MeSH descriptor: [Neck Pain] explode all trees<br>15. MeSH descriptor: [Athletic Injuries] explode all trees<br>16. MeSH descriptor: [Back Injuries] explode all trees<br>17. MeSH descriptor: [Joint Dislocations] explode all trees<br>18. MeSH descriptor: [Fractures, Bone] explode all trees<br>19. MeSH descriptor: [Fractures, Cartilage] explode all trees<br>20. MeSH descriptor: [Hand Injuries] explode all trees<br>21. MeSH descriptor: [Hip Injuries] explode all trees<br>22. MeSH descriptor: [Knee Injuries] explode all trees<br>23. MeSH descriptor: [Ankle Injuries] explode all trees<br>24. MeSH descriptor: [Sprains and Strains] explode all trees<br>25. MeSH descriptor: [Tendon Injuries] explode all trees<br>26. MeSH descriptor: [Ligaments] explode all trees<br>27. MeSH descriptor: [Bone Diseases] explode all trees<br>28. blood flow restriction OR "blood-flow restrict*" OR kaatsu OR "occlu* training" OR "restrict* blood" OR "vascular restrict*" OR "vascular occlu*" OR "limb occlu*" OR "blood rest*" OR "blood occlu*" OR "arterial occlu*" OR "arterial restrict*" OR "venous restrict*" OR "occlu* pressure*" OR "hypoxia* training" OR "ischemi* training" OR "ischemi* strength*" OR "hypoxia* strength*" OR "ischemi* hypertroph*" OR "hypoxia* hypertroph*"<br>29. MeSH descriptor: [Therapeutic Occlusion] explode all trees |

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| | 30. rehab* OR telerehab* OR physiot* OR exercise* OR physical OR functional readapt* OR activit* OR kinesiotherapy OR training OR strength* OR weight bearing OR stretch* OR fitness OR exertion OR sport* OR therapeutic exercise OR resistance training OR aerobic exercises OR weightlifting OR treadmill* OR run OR walk* OR jogg* OR sprint* OR rowing OR bicycl* OR cycl* OR gym OR enduranc* OR run OR activity* OR isometric* OR isokinetic<br>31. MeSH descriptor: [Rehabilitation] explode all trees<br>32. MeSH descriptor: [Physical Therapy Modalities] explode all trees<br>33. MeSH descriptor: [Rehabilitation Centers] explode all trees<br>34. MeSH descriptor: [Physical and Rehabilitation Medicine] explode all trees<br>35. MeSH descriptor: [Rehabilitation Research] explode all trees<br>36. MeSH descriptor: [Telerehabilitation] explode all trees<br>37. MeSH descriptor: [Exercise] explode all trees<br>38. MeSH descriptor: [Exercise Movement Techniques] explode all trees<br>39. MeSH descriptor: [Resistance Training] explode all trees<br>40. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #25 OR #26 OR #27<br>41. #28 OR #29<br>42. #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39<br>43. #40 AND #41 AND #42 [Limits in Trials]<br>Result:479 |

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| CINAHL | 1. (MH “musculoskeletal diseases”) OR (MH “musculoskeletal system”) OR (MH “leg injuries”) OR (MH “arm injuries”) OR (MH “upper extremity”) OR (MH “lower extremity”) OR (MH “connective tissue diseases”) OR (MH “soft tissue injuries”) OR (MH “rheumatology”) OR (MH “orthopedics”) OR arthritis OR chondrocalcinosis OR fibromyal* OR fibrositis OR fibrositides OR hyperostos* OR low back OR lupus OR osteitis OR osteoarthrit* OR osteoarthrop* OR osteochondr* OR osteonecros* OR osteoporos* OR periarthriti* OR rheumati* OR (MH “back pain”) OR (MH “neck pain”) OR (MH “athletic injuries”) OR (MH “back injuries”) OR (MH “hand injuries”) OR (MH “hip injuries”) OR (MH “tendon injuries”) OR (MH “ligaments”) OR “joint dislocations” OR fracture OR sprain* OR strain* OR “knee pain” OR ligament* OR injur* OR tendon* OR muscle* OR musculoskeletal OR menisc* OR fascia OR bone<br>2. blood flow restriction OR blood-flow restrict* OR kaatsu OR "therapeutic occlusion" OR occlu* training OR restrict* blood OR vascular restrict* OR vascular occlu* OR limb occlu* OR blood rest* OR blood occlu* OR arterial occlu* OR arterial restrict* OR venous restrict* OR occlu* pressure* OR hypoxia* training OR ischemi* training OR ischemi* strength* OR hypoxia* strength* OR ischemi* hypertroph* OR hypoxia* hypertroph*<br>3. (MH “rehabilitation”) OR (MH “rehabilitation centers”) OR (MH “telerehabilitation”) OR (MH “exercise”) OR (MH “resistance training”) OR rehab* OR telerehab* OR physical therap* OR physiot* OR exercise* OR physical OR functional readapt* OR activit* OR kinesiotherapy OR training OR strength* OR “weight bearing” OR stretch* OR physical fitness OR exertion OR sport* OR therapeutic exercise OR resistance training OR aerobic exercises OR weightlifting OR treadmill* OR run OR walk* OR jogg* OR sprint* OR rowing OR bicycl* OR cycl* OR gym OR enduranc* OR run OR activity* OR isometric* OR isokinetic<br>4. MH randomized controlled trials OR MH double-blind studies OR MH single-blind studies OR MH random assignment OR MH pretest-posttest design OR MH cluster sample OR TI (randomised OR randomized) OR AB (random*) OR TI (trial) OR MH (placebos) OR PT (randomized controlled trial) OR AB (control W5 group) OR MH (crossover design) OR MH (comparative studies) OR AB (cluster W3 RCT) OR MH (sample size) AND AB (assigned OR allocated OR control)<br>5. MH animals+ OR MH (animal studies) OR TI (animal model*)<br>6. MH (human)<br>7. S5 NOT S6<br>S1 AND S2 AND S3 AND S4 NOT S7<br>Result:556 |

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| **SPORTDiscus** | 1. (SU 'musculoskeletal diseases') OR (SU “musculoskeletal system”) OR (SU “leg injuries”) OR (SU “arm injuries”) OR (SU “connective tissue diseases”) OR (SU “soft tissue injuries”) OR (SU “rheumatology”) OR (SU “orthopedics”) OR (SU “neck pain”) OR (SU “joint dislocations”) OR (SU “bone fractures”) OR (SU “hip injuries”) OR (SU “ligaments”) OR (SU “bone disease”) OR "musculoskeletal pain" OR "upper extremity" OR "lower extremity" OR arthritis OR chondrocalcinosis OR fibromyal* OR fibrositis OR fibrositides OR hyperostos* OR low back OR lupus OR osteitis OR osteoarthrit* OR osteoarthrop* OR osteochondr* OR osteonecros* OR osteoporos* OR periarthriti* OR rheumati* OR “back pain” OR “back injuries” OR cartilage fractures OR "hand injuries" OR sprain* OR strain* OR tendon* OR "knee pain" OR ligament* OR injur* OR menisc* OR muscle* OR musculoskeletal OR fascia OR bone<br>2. blood flow restriction OR blood-flow restrict* OR kaatsu OR "therapeutic occlusion" OR occlu* training OR restrict* blood OR vascular restrict* OR vascular occlu* OR limb occlu* OR blood rest* OR blood occlu* OR arterial occlu* OR arterial restrict* OR venous restrict* OR occlu* pressure* OR hypoxia* training OR ischemi* training OR ischemi* strength* OR hypoxia* strength* OR ischemi* hypertroph* OR hypoxia* hypertroph*<br>3. (SU “rehabilitation”) OR (SU “rehabilitation centers”) OR (SU “rehabilitation research”) OR (SU “resistance training”) OR (SU “exercise”) OR rehab* OR telerehab* OR physiot* OR exercise* OR physical OR functional readapt* OR activit* OR kinesiotherapy OR training OR strength* OR weight bearing OR stretch* OR physical fitness OR exertion OR sport* OR therapeutic exercise OR resistance training OR aerobic exercises OR weightlifting OR treadmill* OR run OR walk* OR jogg* OR sprint* OR rowing OR bicycl* OR cycl* OR gym OR enduranc* OR run OR activity* OR isometric* OR isokinetic<br>4. SU randomized controlled trials OR SU double-blind studies OR SU single-blind studies OR SU random assignment OR SU pretest-posttest design OR SU cluster sample OR TI (randomised OR randomized) OR AB (random*) OR TI (trial) OR SU (placebos) OR (randomized controlled trial) OR AB (control W5 group) OR SU (crossover design) OR SU (comparative studies) OR AB (cluster W3 RCT) OR SU (sample size) AND AB (assigned OR allocated OR control)<br>S1 AND S2 AND S3 AND S4<br>Result:560 |
| **LILACS** | (blood flow restriction) OR (blood-flow restrict*) OR (kaatsu) OR (mh:(Therapeutic Occlusion)) OR (“occlu* training”) OR (“restrict* blood”) OR (“vascular restrict*”) OR (“vascular occlu*”) OR (“limb occlu*”) OR (“blood rest*”) OR (“blood occlu*”) OR (“arterial occlu*”) OR (“arterial restrict*”) OR (“venous restrict*”) OR (“occlu* pressure*”) OR ("hypoxia* training") OR ("ischemi* training") OR ("ischemi* strength*") OR ("hypoxia* strength*") OR ("ischemi* hypertroph*") OR ("hypoxia* hypertroph*")<br>Result:105 |
| **J-STAGE** | “blood flow restriction”<br>114<br>kaatsu<br>84<br>Result:198 |

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| **CLINICALTRIALS** | blood flow restriction AND [Filter]: Interventional<br>197<br>kaatsu AND [Filter]: Interventional<br>9<br>"therapeutic occlusion" AND [Filter]: Interventional<br>1<br>"occlusion training" AND [Filter]: Interventional<br>9<br>"blood restriction" AND [Filter]: Interventional<br>2<br>"vascular restriction" AND [Filter]: Interventional<br>0<br>"vascular occlusion" AND [Filter]: Interventional<br>102<br>"limb occlusion" AND [Filter]: Interventional<br>40<br>"blood occlusion" AND [Filter]: Interventional<br>4<br>“arterial restriction” AND [Filter]: Interventional<br>0<br>“venous restriction” AND [Filter]: Interventional<br>0<br>"occlusion pressure" AND [Filter]: Interventional<br>76<br>"hypoxia training" AND [Filter]: Interventional<br>1<br>“ischemic training” AND [Filter]: Interventional<br>2<br>“ischemic strengt" AND [Filter]: Interventional<br>0<br>“hypoxia strength” AND [Filter]: Interventional<br>0<br>“ischemic hypertrophy” AND [Filter]: Interventional<br>0<br>“hypoxia hypertrophy” AND [Filter]: Interventional<br>0<br>Result:443 |
| **Open Grey** | blood flow rest* OR kaatsu OR "therapeutic occlusion" OR "occlu* training" OR "restrict* blood" OR "vascular restrict*" OR "vascular occlu*" OR "limb occlu*" OR "blood rest*" OR "blood occlu*" OR "arterial occlu*" OR "arterial restrict*" OR "venous restrict*" OR "occlu* pressure*" OR "hypoxia* training" OR "ischemi* training" OR "ischemi* strength*" OR "hypoxia* strength*" OR "ischemi* hypertroph*" OR "hypoxia* hypertroph<br>Result:77 |
| **Proquest** | "blood flow restriction"<br>677<br>kaatsu<br>183<br>Result:860 |
| **Total: 8.444** | |

*Types of studies included*

Randomized clinical trials that tested the efficacy or safety of RFS training compared to a control group for a minimum of three weeks will be included.

*Types of participants*

The studies should have as population of interest adults (≥ 18 years) with MSD, defined by the WHO (2003) as a set of more than 150 diseases that affect the locomotor system of individuals, ranging from acute conditions of restricted duration, such as sprains, fractures and strains, to lifelong conditions that can lead to limitations and continuous disabilities, such as rheumatoid arthritis, fibromyalgia and osteoarthrosis.

*Primary outcomes*

- Pain: Measured by patient-reported pain assessment instruments (e.g., visual analog scale, numerical pain scale, or any other validated instrument).
- Muscle strength: Measured by an objective assessment (e.g., isokinetic dynamometer, manual, or any other validated instrument).
- Adverse events: Defined by the WHO [3] as an incident that results in harm to the patient, including lesions of biological tissues, functional limitations or any deleterious effect resulting from the intervention.

*Secondary outcomes*

- Discomfort: Measure of discomfort resulting from the use of RFS evaluated by validated instruments, such as the visual analog scale.
- Functional capacity: It refers to the ability to perform tasks and activities that the individual considers necessary or desirable for his life, and should be measured by instruments validated for the specific condition of the patient (for example, Lequesne Functional Questionnaire, Roland Morris Disability Questionnaire, among others).
- Overall physical capacity: Related to physical performance evaluated experimentally under conditions planned by validated instruments (e.g., Sit and Stand Up Test, 6-minute Walk Test, among others).
- Quality of life: According to the WHO (1995) quality of life is "the individual's perception of his insertion in life, in the context of the culture and value systems in which he lives and in relation to his goals, expectations, standards and concerns". It is a broad concept, affected in a complex way by physical health, psychological, mental, emotional state,

level of independence, social relationships and other life circumstances. Measures of validated instruments will be considered, such as SF-36, WHOQOL-100, among others.

*Selection of studies*

First, the titles and abstracts will be compared by two authors independently with a checklist of the pre-specified inclusion and exclusion criteria. The abstracts of the studies considered eligible, and those for which it is not possible to state whether the inclusion criteria were met, will be forwarded to the full-text screening stage.

The full texts of all potentially eligible articles will then be checked and compared with the inclusion and exclusion criteria checklist, again, by two reviewers independently, as described above. If at any stage of the process the two reviewers are not convinced as to the eligibility of any particular study, or there are discrepancies about the eligibility judgments, a third reviewer will be consulted and eligibility decided by consensus. Each step of the study selection process will be documented in a flowchart, following the PRISMA format and recommendation as shown in (Figure 1).

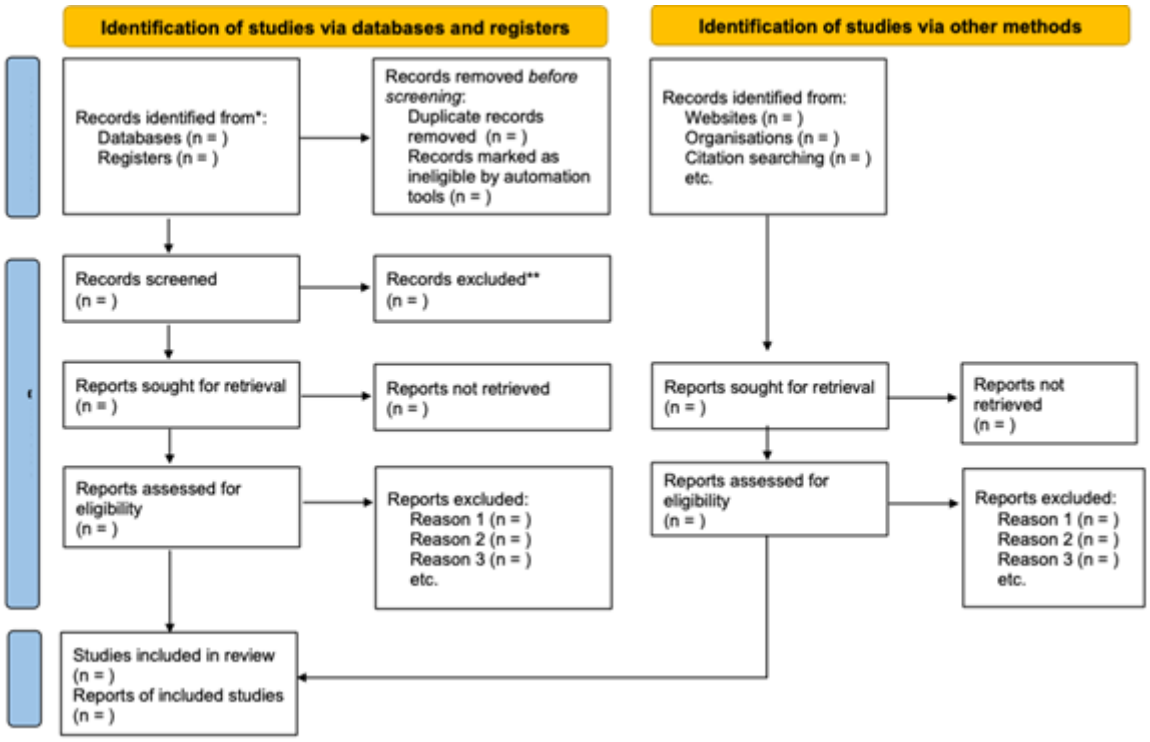


**Figure 1** – *Systematic review flowchart*

*Data extraction and management*

Data from the included studies will be extracted using a standardized form in PICO format (population, intervention, comparison, outcomes, and study design). Specifically, we plan to collect details about RFS application, study design characteristics, and information about participants. Age, gender, diagnostic criteria and severity of disease at baseline of the groups, details on the number of participants selected, randomized, analyzed, excluded and lost at follow-up.

On the use of the RFS will be collected information about the combination with other therapies, characteristics of the equipment used, region of application of the technique, frequency, time, intensity, interval, methodology for determining the restriction pressure and strategies to ensure the pressure selected during the intervention.

In addition, information on the method of randomization and concealment of allocation, blinding, use of stratification, incomplete outcome data, selective reporting, use of intention-to-treat analysis, duration of the study, outcome measures (continuous and dichotomous), reported time points, funding for the trial, and notable conflicts of interest of the trial authors.

Data eligible for subgroup analysis (percentage of blood flow restriction training restriction, training intensity, and number of joints affected) will also be collected in this phase. The extracted information will be manually entered into the Review Manager (RevMan) for synthesis and analysis.

*Assessment of the risk of bias*

The PEDro scale will be used to assess the risk of bias in the included studies. If available, the scores provided in the database platform (pedro.org.au) will be used. In unavailable cases, the PEDro scale will be applied by two independent authors. For discordant scores, a third reviewer will decide the outcome.

Trials with a score ≥ 6 will be considered as 'low risk' of bias; on the other hand, trials with a score < 6 will be considered as 'high risk' of bias [15].

*Strategy for data synthesis*

The statistical, methodological and clinical heterogeneity of the studies will be evaluated. The last two will be based on the methodology of application of the RFS and the characteristics of the population. Statistical heterogeneity will be assessed using the $I^2$ statistic, as defined by Higgins *et al.* in the Cochrane Handbook [16], being categorized as follows:

1. 0% to 40%: may not be important;
2. 30% to 60%: may represent moderate heterogeneity;
3. 50% to 90%: may represent substantial heterogeneity;
4. 75% to 100%: substantial heterogeneity.

In cases of substantial statistical heterogeneity, sensitivity analysis will be performed in order to detect studies that considerably increase the heterogeneity of the analysis. In addition, sensitivity analyses are planned after the exclusion of trials identified as at high risk of bias, with the aim of exploring the impact of risk classification of bias on the effects of interventions.

The results will be grouped and represented in forest plots only if the studies are sufficiently homogeneous, which will be analyzed through a pooled quantitative synthesis using a random effects model [16]. If it is not possible or appropriate to combine the results due to heterogeneity, the results will be presented narratively. If applicable, subgroup analyses will be conducted for the percentage of RFS (≤ 50% or ≥ 70%), training intensity (low-moderate or high) and for the number of joints affected (monoarticular or multiarticular).

Two reviewers will independently assess the quality of the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE), and disagreements will be resolved by a third reviewer. Finally, publication bias will be through the evaluation of funnel plots when 10 or more studies are included in a meta-analysis.

## Expected results

This study aims to conduct a systematic review to investigate the effectiveness of RFS in the rehabilitation of patients with MSD. We hope that the results will update the information available in the literature and provide clear guidance to clinicians and researchers on the prescriptions and recommendations of this technique, aiming to achieve the desirable therapeutic effects through blood flow restriction. However, it is important to highlight that there are common limitations in systematic review studies, such as the availability and quality of the included studies, the heterogeneity of the results and possible publication biases. These limitations should be considered when interpreting the results and applying the conclusions in clinical practice.

**Conflict of interests**
The authors have no conflicts of interest to declare.

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**Author contributions**
*Conception review*: Jardim RAC, Iosimuta NCR, Pinto ACPN and Matos AP; *Identification of studies and extraction of data*: Jardim RAC and Alves INL; *Statistical analysis and data interpretation*: Jardim RAC, Iosimuta NCR; *Manuscript writing*: Jardim RAC, Alves INL, Iosimuta NCR. *All the authors critically revised the manuscript*.

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