CRITICALLY APPRAISED TOPIC

FOCUSED CLINICAL QUESTION

Does a 71-year-old male with knee osteoarthritis demonstrate more improved strength and overall function with participation in blood flow restriction therapy in comparison to participation in resistance strength training?

AUTHOR

Prepared by	Madison Bell	**Date**	11/27/2020
Email address	madison_bell@med.unc.edu		

CLINICAL SCENARIO

The patient is a 71-year-old male that presented to outpatient ortho PT with a referral for lower extremity strengthening. Upon evaluation, patient expressed having a recent diagnosis of osteoarthritis (OA) in both of his knees that has been causing daily pain and thus a significant decline in his functional mobility. Patient demonstrated weakness (MMT of 4/5 or 4-/5) with hip abduction, hip extension, knee extension, and knee flexion. Patient was able to complete exercises prescribed (mini squats, static lunges holding onto a wall, and standing hip abduction and extension), but was hesitant to add weight or resistance to such exercises due to fear of increasing pain.

This patient presentation of being unable to or having a fear of participating in strength training was something I commonly saw in the clinic in the geriatric population. Patients would reach a plateau and *could* continue to get stronger but were unable to use resistance/weights for a plethora of reasons and were therefore not reaching their full capabilities with strength training and functional mobility. Thus, this led me to the idea of assessing the research on the safety and efficacy of the application of blood flow restriction (BFR) therapy specifically in the geriatric population. Lack of motivation is not necessarily the issue for continuing to want to get stronger but it is more an issue of trying to find a creative pain-free strength training alternative. Clinical practice is always evolving, and BFR could be a new treatment idea to add to the toolbox for the geriatric population, specifically those presenting with lower extremity OA.

SUMMARY OF SEARCH

[Best evidence appraised and key findings]

Eight articles were found that met inclusion/exclusion criteria, including 2 systematic reviews, 5 randomized control trials, and 1 case study.

- When individualized to the patient, BFR can be a safe, feasible, and effective treatment approach to increase knee strength and function while simultaneously not increasing knee pain for older adults with osteoarthritis.
- For those with osteoarthritis, BFR is found to be more effective than low-load resistance training for increasing muscle strength and is equally as effective as high-load resistance training while minimizing the mechanical stress placed on the joint.
- Overall, there is limited available evidence that is specifically comparing BFR with traditional strength training according to the outcomes of strength, pain, and function and further research is warranted to determine the efficacy and effectiveness of this treatment approach for this patient population.

CLINICAL BOTTOM LINE *(a concise statement that responds directly to your clinical question)*

There is evidence suggesting that a 71-year-old male with knee osteoarthritis that is limiting his function due to pain could safely benefit from blood flow restriction therapy with less increases in pain and adequate strength gains compared to traditional loaded resistance training, although the efficacy and effectiveness of this intervention still needs additional research of high methodological quality. It would be imperative to consider any precautions or contraindications of this patient's PMH before initiating the intervention of BFR as well as individualization of cuff parameters appropriately.

This critically appraised topic has been individually prepared as part of a course requirement and has been peer-reviewed by one other independent course instructor

SEARCH STRATEGY

Terms used to guide the search strategy			
Patient/Client Group	**I**ntervention (or Assessment)	**C**omparison	**O**utcome(s)
Geriatric Elderly Older adult Lower extremity osteoarthritis	Blood flow restriction BFR Occlusion training	Resistance strength training Weight training	Strength Patient-reported function

Final search strategy (history):

1. geriatric OR elderly OR older adult
2. osteoarthritis OR arthritis
3. blood flow restriction OR occlusion training
4. resistance training OR strength training OR weight training
5. strength
6. function
7. #1 AND #2 AND #3 AND #4 AND #5 AND #6
8. #1 AND #2 AND #3 AND #4 AND (#5 OR #6)
9. #1 AND #2 AND #3 AND (#5 OR #6)
10. #1 AND #2 AND #3 AND #4
11. #1 AND #2 AND #3
12. #1 AND #3
13. #2 AND#3

Databases and Sites Searched	**Number of results**	**Limits applied, revised number of results (if applicable)**
PubMed	**3537**	**301 (Filters: RCT, systematic review, meta-analysis)**
Web of Science	**200**	**NA**
Embase	**1353**	**147 (Filters: RCT, systematic review, meta-analysis)**
CINAHL	**33**	**NA**

INCLUSION and EXCLUSION CRITERIA

Inclusion Criteria
• Older adult population • Diagnosis of osteoarthritis • Standardized patient-reported measures of both pain and level of function • Blood flow restriction therapy • PTs administering the BFR are certified in doing so
Exclusion Criteria
• Not English • Patient population includes higher-level athletes • Textbook

RESULTS OF SEARCH

Summary of articles retrieved that met inclusion and exclusion criteria

Author (Year)	Risk of bias (quality score)*	Level of Evidence**	Relevance	Study design
Ferlito (2020)[1]	**AMSTAR - 9/11**	**1a**	**High**	**Systematic review & meta-analysis**
Harper (2019)[2]	**PEDro - 7/11**	**1b**	**High**	**RCT (pilot)**
Ferraz (2018)[3]	**PEDro - 6/11**	**1b**	**Moderate**	**RCT**
Bryk (2016)[4]	**PEDro - 6/11**	**1b**	**High**	**RCT**
Karabulut (2009)[5]	**PEDro - 4/11**	**1b**	**Moderate**	**RCT**
Lima-Soares (2019)[6]	**JBI Critical Appraisal Checklist for Case Reports – 6/8**	**5**	**Moderate**	**Case report**
Serrano (2019)[7]	**AMSTAR - 6/11**	**3 (includes study with level 3 evidence)**	**Low**	**Systematic review**
Tennent (2017)[8]	**PEDro - 7/11**	**1b**	**Low**	**RCT (pilot)**

*Indicate tool name and score

**Use Portney & Watkins Table 16.1 (2009); if downgraded, indicate reason why

BEST EVIDENCE

The following 2 studies were identified as the 'best' evidence and selected for critical appraisal. Rationale for selecting these studies were:

Harper SA, Roberts LM, Layne AS, et al. Blood-Flow Restriction Resistance Exercise for Older Adults with Knee Osteoarthritis: A Pilot Randomized Clinical Trial. *J Clin Med*. 2019;8(2). doi:10.3390/jcm8020265

- → Includes all the criteria of the clinical question (geriatric, lower extremity OA, BFR therapy).
- → Uses strength, function, and quality of life measures to assess change.
- → Level 1 evidence and good methodological quality according to the PEDro scale.

Ferlito JV, Pecce SAP, Oselame L, De Marchi T. The blood flow restriction training effect in knee osteoarthritis people: a systematic review and meta-analysis. *Clin Rehabil*. August 2020:269215520943650. doi:10.1177/0269215520943650

- → Includes all the criteria of the clinical question (geriatric, lower extremity OA, BFR therapy).
- → Uses strength, pain, and function measures to assess change.
- → Level 1 evidence and excellent methodological quality according to the AMSTAR scale.

SUMMARY OF BEST EVIDENCE

(1) Description and appraisal of (Blood-Flow Restriction Resistance Exercise for Older Adults with Knee Osteoarthritis: A Pilot Randomized Clinical Trial) by (Harper et al, 2019)[2]

Aim/Objective of the Study/Systematic Review:
The objectives of this pilot RCT include assessing both the safety and efficacy of using BFR in the older adults with knee OA population, as well as assessing the feasibility of completing a fully-powered RCT for comparing the effects of BFR to moderate-intensity resistance training (MIRT) in the population of older adults with knee OA.
Study Design

[e.g., systematic review, cohort, randomised controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]

Note: For systematic review, use headings 'search strategy', 'selection criteria', 'methods' etc. For qualitative studies, identify data collection/analyses methods.

This study is a two-arm randomized, single-masked pilot trial. There was a safety team consisting of the main investigator, physician, other staff, and a Data and Safety Monitoring Board that solely monitored the patient's safety throughout the trial. The staff that administered the assessments were masked to the intervention assignment as indicated by the Consolidated Standards of Reporting Trials Group. To address contamination bias, the intervention and assessments were completed in different locations and the different intervention groups were completed at different times. The statistical analysis was completed by someone who was masked to the intervention assignments throughout the study. Linear mixed models were used to assess change over time for each outcome. Group-by-time interaction was used to assess changes from baseline according to the intervention at week 6 and week 12. Estimated mean differences with 95% CIs were used without detection of statical differences due the setup of the pilot study. At week 12, for the participants that completed 80% or more of the exercise classes, a secondary efficacy analysis was completed.

Setting

[e.g., locations such as hospital, community; rural; metropolitan; country]

Department of Orthopaedics & Rehabilitation, University of Florida in Gainesville, Florida.

Participants

[N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]

Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article.

35 participants all equal to over the age of 60 with a diagnosis of knee OA participated in the trial. Recruitment consisted of mailing, newspaper advertisement, and various techniques used in the community. Eligibility criteria included "(1) ≥60 years of age, (2) objective functional limitations, (3) no participation in regular resistance training, and (4) symptomatic knee OA" (p.2). Those that had a peripheral vascular disease, systolic BP of > 160 or < 100 mmHg, resting diastolic BP of > 100 mmHg, other contraindications to use of a tourniquet, or other medical conditions that presented contraindications to exercise training were excluded from participation. The sample was randomized into either the BFR intervention group (n=16) or the MIRT intervention group (n=19).

At baseline, key characteristics of these groups were similar including age, sex, race, ethnicity, BMI, BP, gait speed, WOMAC pain subscale, peak torque extension, leg press 1RM, leg extension 1RM, leg curl 1RM, and calf flexion 1RM. However, there was a significantly higher self-reported knee pain using the visual analog scale at baseline in the MIRT group.

There were 2 participants that dropped out of the study, one from each intervention group. Additionally, 3 participants in each group stopped participating in the intervention but stayed in the trial as a whole. Overall adherence to the interventions were 81.4% for the BFR group and 83.0% for the MIRT group.

Intervention Investigated

[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided]

Control

Supervised lower-body resistance training 3x/week that consists of a warm-up, strength training, stretching, and balance exercises. Resistance was provided with standard isotonic equipment from Life Fitness. 1RM was calculated at baseline to determine appropriate weights for the leg press, leg extension, calf flexion, and leg curl and this was reassessed at week 3, 6, 9, and 12. The Borg scale was used to assess RPE during each exercise session.

The exercise protocol for the MIRT group was aligned with the recommendations for older adults with OA and included performing the leg press, leg extension, leg curl, and calf flexion at 60% 1RM.

Blood tests were used for safety reasons to monitor adverse effects at baseline, as well as at week 6 and 12.

Experimental

Supervised lower-body resistance training 3x/week that consists of a warm-up, strength training, stretching, and balance exercises. Resistance was provided with standard isotonic equipment from Life Fitness. 1RM was calculated at baseline to determine appropriate weights for the leg press, leg extension, calf flexion, and leg curl and this was reassessed at week 3, 6, 9, and 12. The Borg scale was used to assess RPE during each exercise session.

The low-load BFR group performed the leg press, leg extension, leg curl, and calf flexion at 20% 1RM with compression from the cuffs provided at both proximal thighs throughout the lower extremity strengthening exercises. In between exercises, the cuff was deflated before being inflated again before the next exercise. The following equation was used to determine appropriate cuff inflation: [pressure mm Hg = 0.5 (SBP) + 2(thigh circumference) + 5] (p.4). All exercises were performed to fatigue.

Blood tests were used for safety reasons to monitor adverse effects at baseline, as well as at week 6 and 12.

Outcome Measures

[Give details of each measure, maximum possible score and range for each measure, administered by whom, where]

Assessments were administered by an investigator separate to the investigator administering the interventions.

- Unilateral isokinetic strength of the knee extensors of the limb with knee OA assessed via a dynamometer (if both knees exhibit OA, then the knee with a higher self-report pain was tested).
- Unilateral knee extensor peak torque (Nm) at 60, 90, and 120 degrees/second.
- Walking speed assessed via 10 laps of 40 meters (400 meters total) walking at the participant's usual pace.
- Pain after assessment of walking speed via the visual analog scale (1-10, with 10 being the worst pain).
- Lower-extremity function assessed via the Short Physical Performance Battery (SPPB). This assessment includes ability to stand side-by-side, semi-tandem, and tandem; fastest 3- or 4-meter walk; and timed 5x sit-to-stand. Scores range from 0-12, with 12 being highest lower extremity function.
- Self-assessed physical function via the Late Life Function and Disability Instrument (LLFDI). This includes a self-assessment of ability to complete a wide range of tasks, as well as the frequency able to complete and any associated limitations. Scores from the 16 tasks are scored from 0-100 – a higher score is indicative a higher self-perceived level of function.
- Knee-related pain assessed via the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). This measure has established validity and sensitivity specific to the effects of treatment in those with lower limb OA and associated pain. The participants self-assess their knee pain and its influence on completing an activity with a rating of difficulty from 0-4 (0 = none; 1 = mild, 2 = moderate, 3 = severe, 4 = extreme).
- Serum concentrations of N-terminal peptide of procollagen type III, tumor necrosis-like inducer of apoptosis, and insulin-like growth factor assessed via an enzyme-linked immunosorbent assays kit.

Main Findings

[Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable. You may summarize results in a table but you must explain the results with some narrative.]

Exercise training volume and 1RM: "Overall, pre- to post-training changes in 1RM for the four training exercises were as follows (mean and 95% CI): leg press 72.29 (40.47, 105.11) lbs, leg extension 41.34 (27.50, 55.19) lbs, calf flexion 75.16 (45.64, 104.68) lbs, and leg curl 17.67 (7.61, 27.72) lbs. Differences in post-training changes in 1RM between groups were as follows (BFR relative to MIRT): leg press −50.81 (−117.22, 15.60) lbs, leg extension −26.60 (−54.94, 1.74) lbs, calf flexion −30.66 (−91.05, 29.73) lbs, and leg curl −16.46 (−36.05, 3.13) lbs" (p.6)

<u>Intent-to-treat analysis (according to week 12 for all measures):</u>

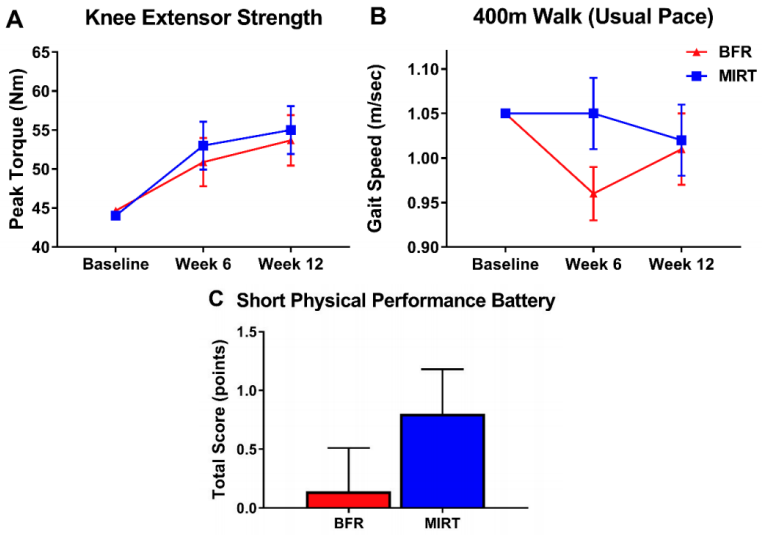
Knee extensor peak torque: Pre- to post-training change was 9.96 (5,76, 14,16) Nm across both groups. Between groups mean, BFR relative to MIRT was –1.87 (-10.96, 7.23) Nm.

Knee extensor strength: Positive effects for both groups at 60, 90, and 120 degrees/second.

400m walk gait speed: Mean change was −0.03 (−0.08, 0.01) m/s. Between groups change was −0.01 (−0.11, 0.09) m/s.

SPPB: Across both groups, change was 0.47 (−0.03, 0.97) points. Between groups, mean change was −0.66 (−1.74, 0.42) points.

Efficacy analysis for mean knee extensor strength, 400 m walk, and SPPB (p. 7):

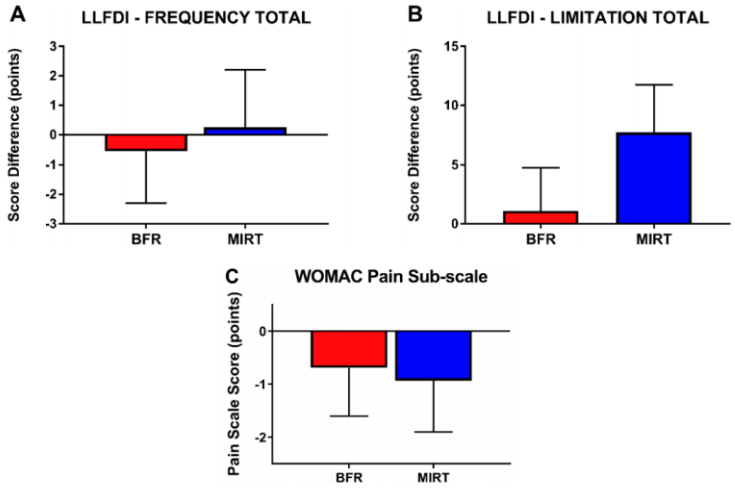


Values displayed are estimated marginal mean +/- SEM.

LLFDI: For Frequency Total, both groups change from pre to post training was −0.14 (−2.23, 1.94) points and between groups change was −0.79 (−6.76, 5.17) points. For Limitation Total, both groups change from pre to post training was 4.36 (0.06, 8.72) points and between group change was 6.60 (−18.99, 5.79) points.

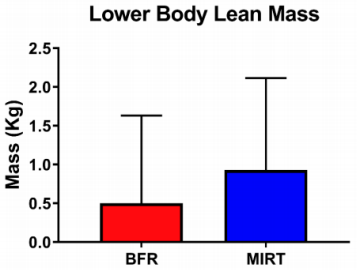
WOMAC: Across groups, the pain subscale change was −0.81 (−2.04, 0.42) points and between group change was 0.24 (−2.51, 2.98) points.

Efficacy analysis for LLFDI Frequency Total, LLFDI Limitation Total, and WOMAC Pain sub-scale (p.7):



Values displayed are estimated marginal mean +/- SEM.

Total lean mass and total body fat: Change from pre to post training for total lean mass was 0.40 (−0.61, 1.40) kg and between groups change was −1.10 (−3.44, 1.24) kg. Changes from pre to post training for total body fat percentage was −1.02 (−0.13, −1.91) % and between groups was 1.12 (-0.90, 3.14) %. Change from pre to post training for lower body lean mass specifically was 0.71 (1.07, 0.36) kg and between groups change was -0.44 (−1.26, 0.39) kg (pictured below, p.8)

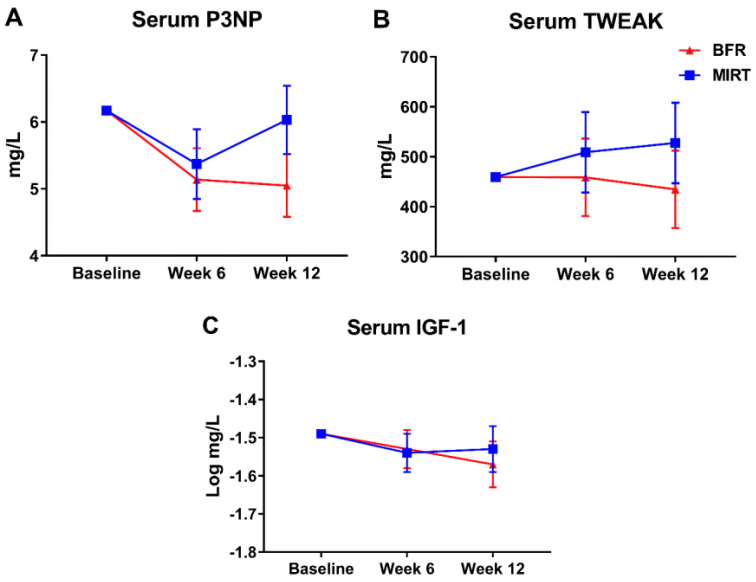


Values displayed are estimated marginal mean +/- SEM.

Biomarkers:

Across groups, the mean change for serum P3NP was −0.63 (−1.28, 0.02) mg/dL and between groups change was 0.98 (−2.39, 0.44) mg/dL. Across groups, the mean change for serum TWEAK was 21.70 (−90.16, 133.56) mg/dL and between groups was −92.70 (−306.14, 120.74) mg/dL. Across groups, the mean change for serum IGF-1 was 92.70 (−306.14, 120.74) mg/dL and between groups was 0.04 (−0.19, 0.11) mg/dL.

Efficacy analysis for the biomarkers (p. 8):



Values displayed are estimated marginal mean +/- SEM.

Original Authors' Conclusions

[Paraphrase as required. If providing a direct quote, add page number]

The authors concluded that overall, BFR is a safe and feasible approach to strength training in older adults with knee OA and may be associated with less increases in knee pain when compared to MIRT. Thus, a fully-powered RCT is warranted to further compare the effects of BFR and MIRT. Additionally, the serum biomarkers assessed in this study were able to explain differences between the BFR and MIRT groups and this should be remembered when creating the fully-powered RCT.

Critical Appraisal

Validity

[Summarize the internal and external validity of the study. Highlight key strengths and weaknesses. Comment on the overall evidence quality provided by this study.]

PEDro scale: 7/11

Eligibility criteria: Yes; Random allocation: Yes; Concealed allocation: No; Baseline comparability: Yes; Blind subjects: No; Blind therapists: No; Blind assessors: Yes; Adequate follow-up: No; Intention-to-treat analysis: Yes; Between-group comparisons: Yes; Point estimates and variability: Yes.

Strengths: Since eligibility criteria has been identified, this enhances the overall external validity. The random allocation of subjects ensures that the control and intervention groups are in fact comparable. The groups were similar at baseline enhancing the randomization process. The assessors were blinded and therefore the effects presented in the results can be interpreted without added bias from the assessor. Intention-to-treat analyses were ran for all desired outcomes to help eliminate unwanted systematic bias. Between groups statistical analyses were completed for all desired outcomes to demonstrate appropriate assessment of effects being attributed to chance or not. Additionally, the treatment effect estimates were measured to assess the difference between control and intervention outcomes.

Weaknesses: The lack of concealed allocation indicates that the decisions made about participants to include could have been influenced by the investigator knowing if they were going to be in the intervention group or not which could lead to systematic bias in the study. Lack of concealment could be associated with a less significant effect size. Although most indicators were similar at baseline across participants, those in the

MIRT group did have a higher mean pain level to start compared to those in the BFR group, which could lead to discrepancies in the results. Neither the subjects or the therapists were blinded, which could increase the risk of placebo effects for self-report measures. However, strength measures were objective to help eliminate such risk. While outcomes were gathered for all of the remaining participants at the end of the study, this only totalled to <85% of the starting participants, thus introducing further potential biases.

Including random allocation, baseline comparability, blinding of assessors, and intention-to-treat analyses are all factors that enhance this study's internal validity. However, lack of concealed allocation, blinding of the subjects and therapists, and < 85% of subjects reporting key outcomes, takes away from the overall level of internal validity. External validity is enhanced with the reporting of the eligibility criteria to provide information on the appropriate population for these results to be applied to, but the placebo and Hawthorne effects must be taken into consideration. Overall, the quality of the validity of this study is good and results can be interpreted taking into consideration the strengths and weaknesses discussed above.

Interpretation of Results

[This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.]

The main objective of this study was first to determine if BFR is a safe and feasible option for the older adult population with knee OA. Due to lack of information provided surrounding the one "adverse event" in the BFR group, it's hard to make a full conclusion from solely this study about the safety of this intervention and therefore precautions/contraindications should always be assessed prior to initiation of this intervention. In regards to feasibility, it appears that patients were accepting of the intervention, but again, this would need to be determined on an individual basis before initiation. Preliminary results of this pilot study show that the BFR intervention may be a less painful yet still effective strength training option for this population and a fully-powered RCT should assess the effects of BFR versus MIRT in order to draw adequate conclusions.

Applicability of Study Results

[Describe the relevance and applicability of the study to your clinical question and scenario. Consider the practicality and feasibility of the intervention in your discussion of the evidence applicability.]

This pilot study's main objective was to determine the safety of BFR, which is not directly relevant to the clinical question, however, is an extremely important consideration when choosing this intervention for a patient. The preliminary results that are more relevant to the clinical question (BFR vs. MIRT) are promising for choosing BFR as a less painful approach to strength training. The findings of this study are applicable to the clinical question surrounding the factors of safety and feasibility of administration.

(2) Description and appraisal of (The blood flow restriction training effect in knee osteoarthritis people: a systematic review and meta-analysis) by (Ferlito et al, 2020)[1]

Aim/Objective of the Study/Systematic Review:

The aim of this systematic review and meta-analysis was to assess and synthesize the evidence presented in randomized trials on the effects of blood flow restriction (BFR) compared to using high load and low load training, as well as assess and synthesize the variety of applications of BFR specifically in those with knee osteoarthritis.

Study Design

[e.g., systematic review, cohort, randomised controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]

Note: For systematic review, use headings 'search strategy', 'selection criteria', 'methods' etc. For qualitative studies, identify data collection/analyses methods.

Ferlito et al. is a systematic review and meta-analysis of randomized control trials.

Search strategy: The data sources that were searched for this systematic review include CENTRAL, PEDro, PubMed, and BVS (which includes Lilacs, Medline, and SciELO). This review used the PRISMA-P guidelines for the search and selectin of randomized trials which included the following main keywords: therapeutic occlusion, resistance training, knee osteoarthritis, blood flow restriction, and kaatsu training.

Selection criteria: Two independent reviewers assessed data based on the main outcomes presented (strength, function, and pain) and according to inclusion/exclusion criteria. Additionally, exercise application

and prescription was extracted. One of the authors performed the meta-analysis using RevMan Review Management Software for studies that included a comparison of BFR to low or high load strength training.

- Inclusion criteria: RCT, participants had a diagnosis of OA, intervention of BFR/kaatsu, measure of strength and pain, measure of function and quality of life, comparison of BFR versus high or low load strength training
- Exclusion criteria: Systematic review and meta-analysis, integrative review, case study, observational study, participants that had another existing knee pathology in addition to OA

Data collection: The authors gathered information from each article that includes the study design, number of participants, mean age, sex, BMI, period of training, exercises, exercise intensities, exercise protocols, exercise frequency, cuff protocol, outcome measures, results, methodological quality, and the conclusions/discussions. Meta-analysis was completed using data from 3 of the 5 studies included assessing the comparison of BFR versus high load strength training using the 2 variables of knee muscle strength and knee function.

Quality assessment: The PEDro rating scale was used to evaluate the methodological quality of each eligible RCT included (all included RCTs demonstrated a score of greater than or equal to 6/11), as well as assessment of the statistical description of the study.

Setting

[e.g., locations such as hospital, community; rural; metropolitan; country]

Authors are physiotherapists at the Department of Physiotherapy of University Center in Bento Gonçalves, Rio Grande do Sul, Brazil.

Participants

[N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]

Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article.

This systematic review included a total of 5 articles that were all RCTs. PEDro scores were classified as "good" for each RCT (> or = 6/11). The number of participants in each study ranged from 27 to 48. The mean age of participants in each study ranged from 55.4 to 68.2 years old. One study included both sexes as participants, one study included only male participants, and three studies included only female participants. For this systematic review, a total of 190 participants were assessed across the RCTs with a mean age of 59.89 years old (+/- 7.47 years) and was largely composed of females.

Intervention Investigated

[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided]

Control

The comparison group for each study was either low load (20-30% 1RM) or high load (60-80% 1RM) strength training without the application of BFR.

Experimental

All studies assessed the use of BFR in combination with low load strength training (20-30% 1RM) administered by a trained physiotherapist. The duration of intervention ranged from 4 to 12 weeks. The exercise frequency ranged from 2-3x/week. Only 3 of the 5 studies reported the type and size of the inflator device/cuff used. Inflated pressure of the cuff during exercise ranged from 100-200 mmHg. Exercise protocols were reported for 4 of the 5 studies. Types of exercises were different for each study, although the leg press was included in 4 of the 5 studies. Other exercises included seated knee extension, calf raises, hamstring curl, isometric bridging, and sensory-motor training.

Outcome Measures

[Give details of each measure, maximum possible score and range for each measure, administered by whom, where]

Strength, pain, and function were measured in each of the five studies, but the outcome measures used to assess such varied across studies.

Functional measures: Timed Up and Go, Timed Position Test, Stair Climb Power, WOMAC, Lequesne, Late Life Function and Disability Index, Short Physical Performance Battery, and gait speed.

Pain: WOMAC Pain Subscale, KOOS pain, Numeric Pain Rating Scale

Strength: Bilateral isotonic leg press, isokinetic knee extensor, 1RM of seated leg press, 40% of 1RM of seated leg press, isometric voluntary contraction, and 1RM of knee extension.

Muscle size (assessed in 2 of 5 studies): Muscle CSA

Main Findings

[Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable. Use a table to summarize results if possible.]

The meta-analysis of the effects of BFR versus high load resistance training on knee strength demonstrated no significant different between BFR versus high load training (n=124, SMD=0.00, 95% CI, -0.54-0.54, I^2 =0%, *P*=1.00). The meta-analysis of the effects of BFR versus high load resistance training on knee function demonstrated higher significant increases in knee function with high load training (n=245, SMD=-0.20, 95% CI, -0.45-0.06, I^2=0%, *P*=0.13). Descriptive analysis shows significant positive effects from BFR compared to high load training, found with the measurements of quadriceps strength and pain during exercise. The studies that used knee pain as an outcome measure had high levels of heterogeneity (I^2>80%), so the results of such were only descriptively reported. There was no significant difference in knee pain between BFR and low load training (n=81, MD=-1.70, 95% CI, -8.65-5.24, I^2=13%, *P*=0.63). Two of the five studies assessed knee function and increases were found for both BFR and low load training (n=116, SMD=0.01, 95% CI, -0.42-0.44, I^2=25%, *P*=0.95). There was not a meta-analysis performed on the data from the three studies that assessed muscle strength from BFR versus low load training due to lack of homogeneity (I^2>90%). Descriptive analysis showed significant positive effects from BFR compared to low load training with the measurements of 1RM of knee extension, 1 RM of leg press, 40% 1RM of leg press, isokinetic knee extensor torque, and quadriceps volume. One of the five studies assessed muscle volume and found a significant effect of BFR compared to low load training (n=40, MD=1.66, 95% CI, 0.93-2.38, *P*<0.00001).

Original Authors' Conclusions

[Paraphrase as required. If providing a direct quote, add page number]

The authors do recommend the use of BFR training in patients with knee osteoarthritis due to its ability to produce responses that compare to high load resistance training for the outcomes of muscle strength, muscle volume, knee pain, and knee function. Additionally, using BFR training resulted in more of an increase in muscle volume and strength compared to using low load training alone. This is beneficial because low load training alone is not as effective in increasing muscle volume compared to BFR. Meta-analysis heterogeneity is likely explained by the "diversity in the BFR application and used exercise protocols" (p.9) such as differences in cuff size and pressure used. Due to the oftentimes challenging or contraindicated exercises associated with high load training, BFR can be a safer, effective, and less painful alternative by placing less mechanical stress on the joints when administered by a trained professional and individualized appropriately. Authors recommend future studies to further assess the effectiveness of individualizing BFR to patients as well as appropriate progression of exercises with long-term follow-up.

Critical Appraisal

Validity

[Summarize the internal and external validity of the study. Highlight key strengths and weaknesses. Comment on the overall evidence quality provided by this study.]

AMSTAR score: 9/11

A priori design provided: yes; two independent data extractors: yes; comprehensive search: yes; status of publication: yes; list of studies: no; characteristics of studies: yes; quality assessment: yes; quality assessment used in conclusions: yes; appropriate methods to combine studies: yes; publication bias assessed: no; conflict of interest stated: yes.

Strengths:

- **Selection criteria:** Specific inclusion/exclusion criteria identified to address decreasing heterogeneity of subjects. Heterogeneity of training protocol appropriately discussed in the review.
- **Discussion of results:** The authors provide adequate discussion of the outcomes they found for the associated interventions, demonstrating adequate internal validity. The authors also integrate evidence from other similar reviews and studies that support their findings. Additionally, they provide clinical findings and applicability of results.

- **Discussion of limitations:** The authors discuss several limitations including low number of studies included, lack of homogeneity, no long-term follow-up, and non-blinding of participants and therapists in all of the included studies.
- **Quality of selected studies:** The authors used the PEDro scale to assess each RCT's methodological quality and all studies included were rated as "good" or better (6/11 or higher).
- **Search strategy:** Specific key words used and searched across multiple databases, and all studies used were very recent (within the past 5 years).

Weaknesses:

- **Presentation of data:** Some of the tables presented lack organization and key data and only present whether an intervention had a positive or negative effect (or no effect) instead of including data in the tables on how the authors got to that conclusion.
- **Publication bias:** No statement about inclusion or exclusion of grey literature.
- **Selection bias:** While the authors did search multiple databases, they did not include citations for the articles that they excluded from the study.
- **Internal validity:** Due to different exercise and cuff protocols being used in the studies, this limits the conclusions drawn about which protocol is most effective.
- **External validity:** Due to heterogeneity of results of this review, the generalizability is limited.

Interpretation of Results

[This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.]

This systematic review does provide up-to-date evidence for the comparable strength and functional effects of BFR with low-load training to high-load training alone, and BFR specifically demonstrates a greater increase in muscle volume (CSA) than low-load training alone. While high-load training can produce larger strength gains than BFR, this is oftentimes not a viable option in those with osteoarthritis due to high mechanical load at the joint causing increased pain. Due to heterogeneity of the intervention protocols across the studies, only descriptive data could be gathered for some of the outcomes. Therefore, it's difficult to draw adequate conclusions about the implementation of specific parameters of BFR in the OA population. However, the authors discussed the importance of individualizing parameters of the cuff when implementing this technique in practice. The overwhelming clinically significant result I gathered from this review is that BFR training can produce strength and functional gains in people with knee OA without a large increase in pain and is thus a viable option to consider when creating a treatment plan for this population.

Applicability of Study Results

[Describe the relevance and applicability of the study to your clinical question and scenario. Consider the practicality and feasibility of the intervention in your discussion of the evidence applicability.]

Relevance & Applicability: This systematic review and meta-analysis presents relevant and applicable results according to the clinical question. The search strategy was administered across multiple databases and included PRISMA-P guidelines for the search and selection of randomized trials which included relevant main keywords for the CAT's population, intervention, comparison, and outcome such as therapeutic occlusion, resistance training, knee osteoarthritis, blood flow restriction, and kaatsu training. This review assessed most of the inclusion criteria of the CAT including a diagnosis of osteoarthritis; standardized measures of pain, strength, and function; and BFR administered by a trained PT/physiotherapist. Most of the patients of the included studies would also be considered as older adults, however, not all of them were 65 and older. The quality of the RCTs included were all rated by the PEDro scale as "good" or higher, making the results adequately applicable. The authors presented the protocols used for exercises and the cuffs very clearly for each RCT. While this made for heterogenous data, it does provide multiple efficient approaches to consider.

Practicality & Feasibility: Administering BFR training is within the PT's scope of practice but should receive the appropriate training for such.[9] A common limitation to its use is the initial cost of the BFR equipment. Adverse effects of using BFR in this population were not discussed in this review but should always be considered by the PT on an individual patient basis. As stated previously, there were no identical BFR protocols presented in the RCTs making it unclear which is most appropriate. Therefore, further research is indicated to provide clear evidence on the different and most appropriate protocols. The outcome measures used provide a wide variety of outcomes (pain, strength, function) to assess in patients using BFR that affect multiple domains of their life including physically and mentally. If the PT is confident in their knowledge of the physiological concepts of BFR, becomes trained in appropriate use of the equipment, and is able to purchase the appropriate equipment, this technique can be a feasible approach to strength training in people with OA.

SYNTHESIS AND CLINICAL IMPLICATIONS

[Synthesize the results, quality/validity, and applicability of the two studies reviewed for the CAT. Future implications for research should be addressed briefly. Limit: 1 page.]

The combined results gathered in this systematic review and RCT suggest that BFR is a safe and feasible treatment intervention for older adults with osteoarthritis when a trained therapist administers the appropriate intervention with individualized exercise and cuff parameters. Often times, patients with OA are either hesitant or unable to complete high load strength training due to increased pain caused by increased mechanical load on the joints. Additionally, low load strength training alone may not be enough resistance to produce adequate strength gains. Therefore, BFR combined with low load strength training may be a viable option for producing comparable strength and functional effects (to high load training) while simultaneously not increasing pain, and furthermore for producing greater increases in muscle volume and strength when compared to low load training alone.

These findings provide pertinent clinical implications for patients with OA that have the potential to continue to get stronger but are limited secondary to pain. Being able to provide our patients with a safe opportunity to gain strength and therefore function is very clinically relevant and applicable. It is within a PT's scope of practice to deliver BFR training once having received proper training and is a unique intervention to store in our toolbox.[9] Additional research has found that BFR is an effective post-surgical intervention for strength and functional gains that leads to an increased quality of life in older adults.[7] Oftentimes, patients with OA undergo total joint replacements, and BFR can thus be a post-surgical intervention for this population as well.

As discussed previously, due to the heterogeneity of the BFR and exercise protocols used, it's unclear as to which is most effective for this population. Both articles presented with good methodological quality but their limitations discussed previously should still be considered when interpreting the results. Future high methodological quality research should thus focus on the efficacy and effectiveness of individualized application of BFR and the associated parameters of such. Additionally, the current research does not present with any long-term follow-up results. Future research should aim to assess long-term strength and functional gains with long-term use of BFR as well as maintenance of gains after discontinuing BFR intervention. BFR is an established intervention for a plethora of patient populations, and thus more research is warranted to continue to assess appropriate efficacious and effective parameters for the geriatric population, specifically those with OA, in order to provide this population with a less painful alternative that still allows them to gain strength, function, and overall quality of life.

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