Received: 15th January 2022
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Blood Flow Restriction Resistance Training in Tendon Rehabilitation: A scoping review on intervention parameters, physiological effects, and outcomes

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Please cite as: Burton I & McCormack A. (2022). Blood Flow Restriction Resistance Training in Tendon Rehabilitation: A scoping review on intervention parameters, physiological effects, and outcomes

Acknowledgements: None declared

Authorship contributions: IB conceptualised the work and developed the methods, search strategy and framework for the review. IB and AM contributed to the development of the research questions and the study design. All authors developed the first and subsequent drafts of the manuscript and reviewed and approved the manuscript.

Funding: None declared

Conflicts of interest/Competing interests: None declared.

Data availability statement: All data relevant to the study are included in the article or uploaded as supplementary information.

ABSTRACT

Objective: To identify current evidence on blood flow restriction training (BFRT) in tendon injuries and healthy tendons, evaluating physiological tendon effects, intervention parameters and outcomes.

Methods: This scoping review was reported in accordance with the PRISMA Extension for Scoping Reviews (PRISMA-ScR). Databases searched included MEDLINE, CINAHL, AMED, EMBase, SPORTDiscus, Cochrane library (Controlled trials, Systematic reviews), and five trial registries. Two independent reviewers screened studies at title/abstract and full text. Following screening, data was extracted and charted, and presented as figures and tables alongside a narrative synthesis. Any study design conducted on adults, investigating the effects of BFRT on healthy tendons or tendon pathology were included. Data were extracted on physiological tendon effects, and intervention parameters and outcomes with BFRT.

Results: 13 studies were included, 3 on tendinopathy, 2 on tendon ruptures and 8 on healthy Achilles, patellar, supraspinatus and vastus lateralis tendons. A variety of outcomes were assessed, including pain, function, strength, and tendon morphological and mechanical properties, particularly changes in tendon thickness. BFRT intervention parameters were heterogeneously prescribed.

Conclusion: Despite a dearth of studies to date on the effects of BFRT on healthy tendons and in tendon pathologies, preliminary evidence for beneficial effects of BFRT on tendons and clinical outcomes is encouraging. As BFRT is a relatively novel method, definitive conclusions, and recommendations on BFRT in tendon rehabilitation cannot be made at present, which should be addressed in future research, due to the potential therapeutic benefits highlighted in this review.

Keywords: Blood flow restriction; Tendinopathy; Resistance training; Exercise; Physiotherapy; Tendon

INTRODUCTION

Tendinopathy is a disease entity which can cause significant pain and functional limitations for individuals and collectively places a tremendous burden on society through high healthcare costs.[1,2] In chronic tendinopathy, tendons experience morphological changes and can present with increased tendon thickness, fibril disorganization, and neovascularization caused by repetitive tendon microtrauma.[3,4] Tendinopathy prevalence has been shown to be higher in athletes due to frequent jumping, landing, running and change of direction movements.[5] Collectively, tendinopathies can account for up to 30% of all musculoskeletal conditions requiring medical attention, with up to 22% of elite athletes having patellar tendinopathy at least once during their sporting careers.[6-8] Complete and partial tendon ruptures are also common in both athletes and the general population with the Achilles tendon having the highest prevalence of ruptures.[9] Like tendinopathy, tendon ruptures can also cause significant pain, disability and functional limitations and are associated with significant societal and healthcare costs, whether treated surgically or conservatively, with there being a lack of consensus on optimal treatment methods.[10]

Resistance training has long been considered the treatment of choice in the rehabilitation of chronic tendinopathies, with both eccentric and heavy slow resistance training (HSRT) demonstrating positive clinical effects, for both improving symptoms and tendon structure.[11,12] Progressive resistance training is also considered an essential element of rehabilitation following tendon rupture to counteract muscle atrophy and stimulate tendon repair, whether treated conservatively or surgically.[13] The application of progressive tendon loads during rehabilitation is essential to not compromise tendon healing, with the precise dosage parameters of resistance training loading a critical consideration.[14] Prolonged time under tension with traditional heavy loads during the early phase of tendon rehabilitation could be counterproductive and compromise tendon healing.[15,16] Blood flow restriction training (BFRT) is a method of resistance training which utilises pneumatic cuffs or straps around a limb to partially restrict arterial blood flow, while simultaneously occluding venous outflow until the cessation of cuff pressure.[17] BFRT also known as occlusion, hypoxic or Kaatsu training has become increasingly popular over the last decade as a method for enhancing strength gains in healthy populations such as athletes and more recently as a rehabilitation tool in those with musculoskeletal pathologies.[18-20] For example, BFRT has been found to be an efficacious method for increasing strength gains and muscle hypertrophy in rehabilitation following surgery for anterior cruciate ligament (ACL) rupture.[21,22] The physiological benefits associated with BFRT, include beneficial adaptations to the cardiovascular, endocrine, and musculoskeletal systems with psychosocial benefits also reported such as mood and performance improvement.[23-31]

Whilst traditional eccentric or HSRT utilises heavy training loads of up to 70% of 1 repetition maximum (1-RM), low intensity BFRT typically uses loads in the range of 20-40% of 1RM, which may be more tolerable for patients not able to tolerate high muscle-tendon training loads, while still preventing muscle atrophy and promoting hypertrophy.[32-35] Interventional studies have found superior or similar clinical outcomes with low-load BFRT (LL-BFRT) compared to conventional high-load resistance training (HL-RT) in knee rehabilitation for ACL reconstruction, patellofemoral pain, and knee osteoarthritis.[36-42] BFRT has been shown to cause exercise-induced hypoalgesia through endogenous opioid and endocannabinoid mechanisms, so could therefore be a useful pain management tool in early musculoskeletal rehabilitation, particularly in the presence of an acute pain response.[43-46] Recent evidence suggests that LL-BFRT may be a superior method for augmenting muscular adaptations in early musculoskeletal rehabilitation, which has been found to be comparably effective for inducing muscular hypertrophy and only minimally inferior for increasing muscular strength compared to HL-RT.[47-53] The mechanisms of action of BFRT in muscular adaptation is thought to be related to increased inflammation and metabolic stress which augments plasma growth hormone and blood lactate levels.[54-56] Due to a paucity of research, it is unclear what effects BFRT may have on tendons, but the induced ischemic muscular milieu may facilitate morphological and mechanical tendon properties through enhanced collagen metabolism and tendon remodelling.[57,58] Despite these potential beneficial physiological mechanisms of BFRT on tendon healing, the method of training has received a dearth of attention in tendon rehabilitation, despite the clinical benefits found for other musculoskeletal conditions and the knowledge of resistance training being the most evidence-based treatment available for tendinopathies. Therefore, the objective of this scoping review is to evaluate current research on the use of BFRT for treating tendon injuries. The scoping review will be guided by addressing the following review questions on specific aspects of BFRT interventions within tendon rehabilitation:1. What outcomes have been reported for BFRT in healthy tendons and rehabilitation for tendon injuries and which outcome measures have been used? 2. What BFRT intervention and cuff parameters have been used in published studies? 3. What physiological mechanisms explaining effects of BFRT on tendons and tendon injuries have been investigated in published studies?

METHODS

Due to the exploratory nature of the research questions a scoping review was conducted as they are recommended for mapping key concepts, evidence gaps and types of evidence within a particular field and can help guide future research and the possibility of conducting systematic reviews on the topic.[59] The scoping review is reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-analysis extension for Scoping reviews known as the PRISMA-ScR.[59] This scoping review aimed to evaluate current BFRT interventions in healthy tendons and the rehabilitation of tendon injuries for the first time in the literature. The results will allow dissemination of the parameters of research BFRT interventions to clinical practitioners through peer-reviewed journal publication, allowing increased likelihood of implementation in clinical practice. The review will also outline future research and exercise reporting needs within BFRT interventions in tendon rehabilitation.

Eligibility criteria

The inclusion criteria for the scoping review were guided by a modified PICO (PCoCo) as recommended for scoping reviews.[59] Studies including adults aged eighteen years or older with no history of tendon pathology or a diagnosis of a tendon injury for any time duration were considered. Tendon injuries included both acute partial or full tendon tears or ruptures and any chronic tendon injuries diagnosed as any tendinopathy. Any tendon condition characterised by common tendinopathy symptoms, including full thickness tendon rupture were considered for inclusion. Studies including participants with other concurrent injuries or medical conditions not tendon related were excluded. The concept of interest was BFRT for healthy tendons or for the treatment of any tendon related injury, including any type or format such as BFRT performed with bodyweight or external resistance. The BFRT intervention could be used as a first or second-line intervention and may be delivered in isolation or combined with other treatments. BFRT may be delivered across a range of settings by health or exercise professionals. BFRT interventions could be delivered in a supervised or unsupervised manner, using any methods for training progression and monitoring. The context considered for inclusion included any setting in which BFRT interventions have been provided. This scoping review considered both experimental and quasi-experimental study designs including randomized controlled trials and non-randomized controlled. In addition, prospective and retrospective cohort studies, case series and case reports were considered for inclusion. Unpublished studies, reviews or reports were not considered for inclusion.

Search strategy

The search was carried out using a uniform search strategy across all databases (Appendix 1) and it included key words from two main concepts: Blood Flow Restriction ('Kaatsu', 'Occlusion training'), and Tendon ('tendon', 'tendinopathy', 'tendon rupture'). The Boolean operators "Or" and "And" were used to link the key words from each concept and to link the concepts themselves, respectively. A 3-step search strategy was implemented in this scoping review. It incorporated the following: 1) a limited search of MEDLINE and CINAHL using initial keywords as, followed by analysis of the text words in the title/abstract and those used to describe articles to develop a full search strategy; 2) The full search strategy was adapted to each database and applied to MEDLINE, CINAHL, AMED, EMBase, SPORTDiscus, and the Cochrane library (Controlled trials, Systematic reviews). The following trial registries were also searched: ClinicalTrials.gov, ISRCTN, The

Research Registry, EU-CTR (European Union Clinical Trials Registry), ANZCTR (Australia and New Zealand Clinical Trials Registry). Databases were searched from inception to January 1st, 2022 (Search performed on January 1st, 2022). The search for relevant grey literature included Open Grey, MedNar, Cochrane central register of controlled trials (CENTRAL), EThOS, CORE, and Google Scholar. 3) For each article located in steps 1 and 2, a search of cited and citing articles using Scopus and hand-searching where necessary, was conducted. Studies published in a language other than English were only considered if a translation was available as translation services are not available to the authors.

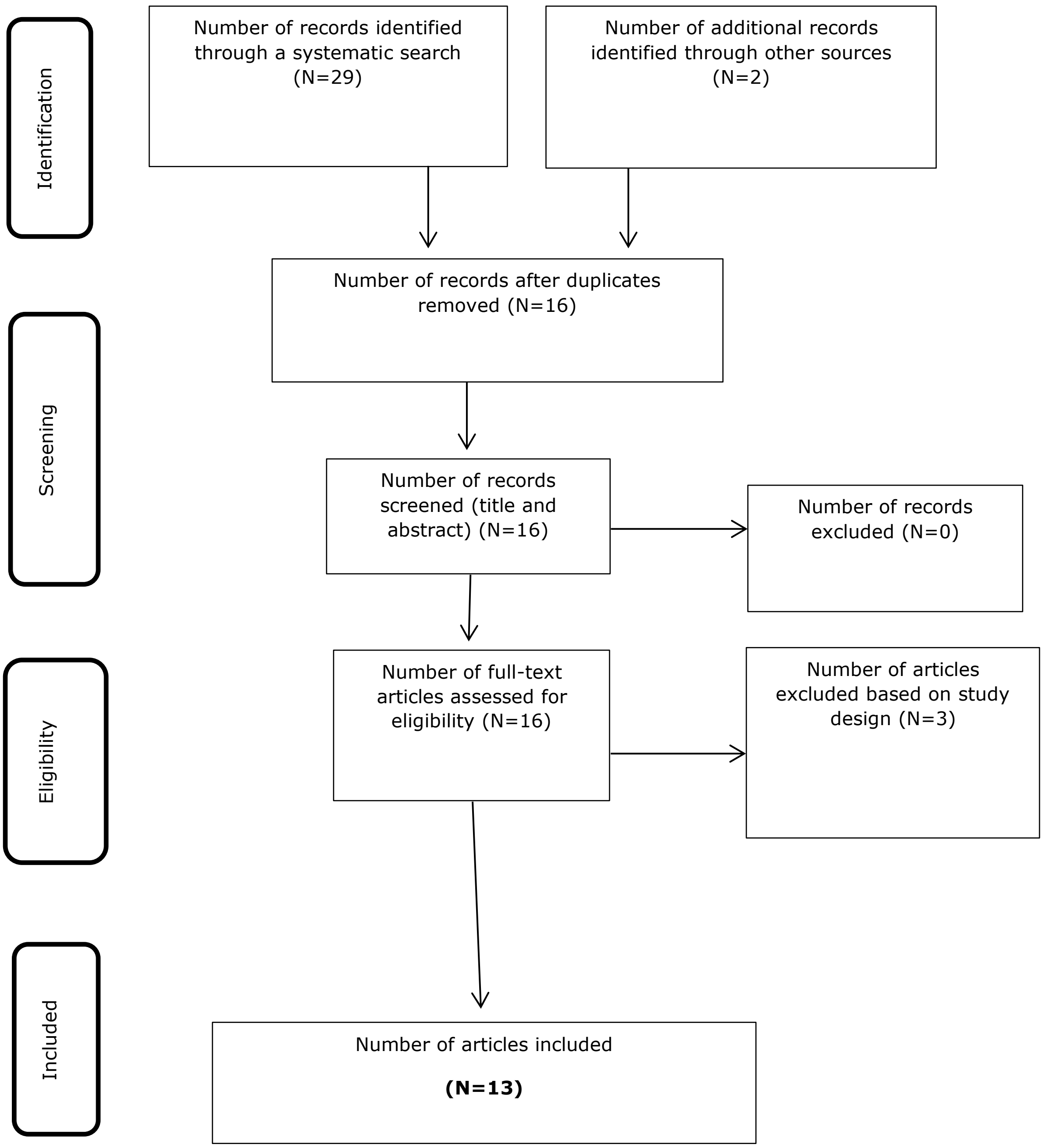
Study selection

Following the search, all identified citations were collated and uploaded into RefWorks and duplicates removed. Titles and abstracts were then screened by two independent reviewers for assessment against the inclusion criteria for the review. Potentially relevant studies were retrieved in full, and their citation details imported into Covidence (Veritas Health Innovation, Melbourne, Australia). Two independent reviewers assessed the full text of selected citations in detail against the inclusion criteria. Any disagreements that arose between the reviewers at each stage of the study selection process were resolved through discussion or by input from a third reviewer. The results of the search are reported in accordance with the PRISMA-ScR.[59] In accordance with guidance on conducting scoping reviews, critical appraisal was not conducted.[59]

Data extraction

Data were extracted from sources included in the scoping review by one reviewer, with independent data extraction by a second reviewer for at least 10% of studies. The data extracted included specific details regarding the population, concept, context, study methods and key findings relevant to the review questions. The data extracted included dimensions such as study type, purpose, population & sample size, methods, details of the BFRT intervention, specific exercises and outcome measures used. Details of the BFRT interventions included type, dosage, cuff parameters, and methods used to progress and adjust the training stimulus. Data were also be extracted on any physiological mechanisms which have been investigated to explain the effects of BFRT on tendons. The extracted data are presented in Table 1 with a narrative synthesis accompanying the tabulated results.

FIGURE 1: PRISMA study flow diagram



RESULTS

Included study characteristics

The literature search yielded 29 articles, of which 13 met the inclusion criteria and were included in the review, which is summarised in the PRISMA flow chart (FIGURE 1), with an overview of the characteristics of the included studies provided in Table 1. Five studies investigated the effects of BFRT on tendon pathologies, three on patellar tendinopathy, including one case series[60] and two case reports.[61-62] Two case reports investigated BFRT with tendon ruptures, one on biceps tendon rupture[63] and one on Achilles tendon rupture.[64] Eight studies investigated the effects of BFRT on healthy tendons, five on the Achilles tendon, including four RCTs[65-68] and one cross-sectional study,[69] one RCT on the patellar tendon,[70] one RCT on the supraspinatus tendon,[71] and one cohort study on the vastus lateralis tendon.[72] The sample sizes of included studies ranged from one to 56, with only 12 participants in total for tendon pathologies out of a total of 292 participants, with most included participants having healthy tendons. All included studies investigated the effects of a LL-BFRT intervention, five in isolation[60-64] four compared with LL-RT,[66,68,69,71] three compared with HL-RT,[65,70,72] and one with both LL-RT and HL-RT.[67] The duration of BFRT interventions ranged from a single session to 14 weeks. The most common exercises used for the BFRT interventions were, plantarflexion calf raises (8), leg press (4), and knee extension (2).

Outcome measures

Four studies assessed pain as an outcome measure with BFRT, two with VAS scales and two with NRS-P scales. Patient reported function scales were assessed in three studies, with two using the Victorian Institute of Sport Assessment Patellar (VISA-P) for patellar tendinopathy and one using both the Disabilities of the Arm, Shoulder and Hand (DASH) and Mayo Elbow Performance Index score for biceps tendon rupture. Seven studies assessed strength as an outcome, with five using dynamometry, one using 1-RM testing and one using an isokinetic Biodex system. Eight studies used ultrasound (US) to assess tendon mechanical and morphological properties, with tendon thickness the most assessed tendon outcome, measured in five studies, with four studies also assessing tendon stiffness. Muscle properties were assessed in four studies, with three studies using US to assess muscle volume or cross-sectional area and one using magnetic resonance imaging (MRI). One study used thermograms to assess Achilles tendon skin temperature. One study assessed power using an isokinetic Biodex system. One study used MRI to assess tendon signal intensity (hypoechogenicity).

Outcomes

The five studies that investigated the effects of a BFRT intervention on a tendon pathology, all found clinical improvements in pain, function, and muscle strength for included patients, with athletic patients being able to return to sport. The eight studies that investigated BFRT on populations with healthy tendons, all found beneficial physiological effects on tendon morphology and mechanical properties, including beneficial changes in tendon stiffness, thickness, vascularity, signal intensity and skin temperature. However, two studies did not find changes in tendon stiffness following BFRT. Several studies also found increases in muscle volume and cross-sectional area which was associated with increases in muscular strength and decreased pain levels.

Training parameters

All included studies applied a BFRT cuff to either the proximal or distal affected limb, however there were wide variances in the type and size of cuffs used, with cuff width ranging from 7-15cm. Occlusion pressure was calculated as either absolute pressure ranging from 80-180 mm Hg, or a percentage of arterial occlusion ranging from 30-80%. There were wide variances in the sets and repetitions of prescribed exercises, with the commonly recommended BFRT protocol of 4 sets of 30,15,15, and 15 repetitions being implemented in seven studies. The number of sets across studies ranged from 3-6, with repetitions ranging from 5-30, with one study using muscular failure instead of predefined repetitions. Training frequency ranged from 2-7 times per week, with training intensity most commonly at 30% of 1-RM, as applied in nine studies. Most studies did not report how the training stimulus was progressed, with two studies progressively increasing occlusion pressure, one increasing percentage of 1-RM (20-35%), and two studies reported using small increases in external weight. Rest time between exercises was 30 seconds in seven studies and one minute in two studies, with four studies reporting three minutes rest between different exercises, with three of these studies deflating cuff pressure between exercises.

DISCUSSION

The main findings of this scoping review were that despite the dearth of studies available on the effects of BFRT on tendons, studies do indicate that BFRT can produce beneficial effects on tendons. Preliminary evidence from case series and case reports indicates that BFRT may be helpful for improving clinical outcomes such as pain in function in rehabilitation of tendinopathy and tendon ruptures, however no RCTs have been conducted in these populations. The evidence for beneficial changes in healthy tendons is more robust due to several RCTs on the topic, showing beneficial physiological effects on tendon morphology and mechanical properties, including beneficial changes in tendon stiffness, thickness, vascularity, signal intensity (hypoechogenicity) and skin temperature. Although it is unclear if these beneficial effects found in healthy tendons would also occur with pathological tendons, the preliminary evidence suggesting clinical improvement with BFRT in tendon pathology, is suggestive of potential comparable physiological benefits in tendon pathology. There is a clear need for further interventional studies of BFRT in tendinopathy and tendon rupture rehabilitation, with high quality large scale RCTs required to reach definitive conclusions and recommendations for BFRT in tendon pathology. However, there is a clear scientific rationale for the potential of clinical improvements in tendon pathology with BFRT as evidenced by the beneficial effects seen in healthy tendons, and the improvement of clinical outcomes with BFRT in other musculoskeletal disorders. Given the increased research interest and clinical use of BFRT in musculoskeletal rehabilitation for non-tendon pathologies, the dearth of available studies applying BFRT to tendon pathologies could be considered somewhat surprising. This is particularly relevant considering resistance training is considered the gold-standard first-line treatment intervention for tendinopathies, particularly Achilles and patellar tendinopathy, due to a plethora of evidence showing the clinical efficacy of resistance training such as eccentric and heavy slow resistance training.[73] Perhaps the belief that resistance training in tendinopathy must include high loads has been a limiting factor in the application of LL-BFRT and could explain why it is an underutilized tool in tendon rehabilitation. Despite their being clear evidence that heavier loads are required for altering tendon morphology and mechanical properties,[14] training with heavy loads would not be possible for some populations and may even be contraindicated, such as in acute tendinopathy and early tendon rupture rehabilitation.

The evidence from RCTs comparing LL-BFRT with HL-RT, suggests comparable outcomes for improving muscle and tendon properties,[65,70] with these changes possibly serving as the mechanisms to explain the clinical benefit seen with BFRT in the case reports in tendinopathy and tendon rupture rehabilitation. It could be postulated that the potency of the muscular and tendinous milieu induced by the BFRT stimulus under low load conditions, is potent enough to counteract the requirements of heavy loads to stimulate tendon adaptations sufficiently to derive clinical improvements. However, this theory will remain unproven until the existence of high-quality intervention research. The first RCT investigating the effects of LL-BFRT compared to HL-RT in patellar tendinopathy has been registered in Denmark, by the authors who conducted the positive case series included in this review.[60] This trial will be the first step in determining if a shift is required in the tendinopathy rehabilitation field, from the belief that HL-RT is a prerequisite for improving outcomes in tendinopathy, to a possible future where both HL-RT and LL-BFRT are both viable rehabilitation methods, giving clinicians and patients more options and choice during rehabilitation. This may be particularly relevant for non-athletic patients who are unaccustomed to training with heavy loads, sedentary elderly patients, or those who may have contraindications to heavy training and those with an acute painful or reactive tendinopathy or recent tendon rupture, who would be unable to tolerate the loads required with HL-RT. In the rehabilitation of ACL ruptures, LL-BFRT has been found to be a beneficial training method for increasing muscular adaptations in those who have difficultly performing HL-RT.[74] Furthermore, LL-BFRT has been shown to attenuate pain, increase strength and improve function in rehabilitation for hospital inpatients,[75] ACL rupture,[76] patellofemoral pain,[77] rheumatoid arthritis,[78] ankle fractures,[79] and knee osteoarthritis,[39] suggesting pain improvement may be possible with lower training loads in tendon injuries without subjecting all patients to HL-RT.

Included studies used low training intensities, with most programming training based on a percentage of an individual’s 1-RM, typically 30%, which is congruent with loads between 20-40% of 1RM which are typically recommended in the BFRT literature.[80] It is well established that LL-BFRT requires a higher volume of repetitions to derive physiological adaptations,[81] with the 30-15-15-15 program of 75 repetitions per set, completed with four sets typically recommended.[76] Whilst seven studies implemented this regime, the number of sets across studies ranged from 3-6, with repetitions ranging from 5-30, with one study using muscular failure instead of predefined repetitions. It is unclear if training to volitional muscular failure with BFRT is required to derive adaptations and may be unnecessary given previous BFRT evidence,[76] and the knowledge that muscular failure is not required for muscle hypertrophy, with overall training load volume considered more relevant for augmenting hypertrophy.[82-85] Details on rest periods and whether cuff pressure was maintained or deflated between sets and exercises varied across studies. However, previous research has shown that rest with an inflated or deflated cuff are viable options,[86] although longer rest periods may reduce metabolic stress and therefore limit potential adaptations compared to short rest periods.[76,87,88] Despite large variances in the BFRT arterial occlusion pressure of included studies which ranged from 30-80%, recommendations for occlusion pressure in the literature do range from 40-80%,[76,89] suggesting pressure should be individualised based on measures of arterial pressure and comfort levels.[90,91]

This review has several limitations, particularly the small number of studies included, with only five studies on tendon pathology, all being case series or case reports, highlighting the need for future high-quality studies with larger sample sizes, as there are no RCTs on BFRT in tendon pathology currently available. Future studies should also investigate the effects on specific subgroups known to be at increased risk for tendon injuries such as athletes. There was considerable heterogeneity of the BFRT parameters implemented in studies, with standardised methods and reporting of interventions required in future BFRT studies in tendon rehabilitation to enhance clinical translation of the research interventions. The longest follow-up times of included BFRT interventions were 14 weeks, with much longer follow up times required to assess the long-term adaptations and outcomes of BFRT on healthy and pathological tendons. Methods for monitoring and recording adherence to BFRT should also be emphasised in future studies as several included studies did not report the adherence level to BFRT, which may vary due to perceptual responses and comfort which may affect reported clinical outcomes.[92-95]

PERSPECTIVES

The superiority of LL-BFRT over standard LL-RT for muscular adaptations have been previously highlighted,[96-102] with findings from this review suggesting the same may be true for tendon adaptations. However, it remains unclear whether LL-BFRT or standard HL-RT is a superior method for inducing muscular adaptations, with some studies finding equal benefit for muscle strength gains[103-107] and others suggesting HL-RT is a superior method.[108] Some studies included in this review suggest that the tendon adaptations in the healthy Achilles and patellar tendon following LL-BFRT are comparable to those evoked by HL-RT, which is an encouraging finding for the field of tendon rehabilitation.[65,70] However, these comparable beneficial tendon adaptations found in the high-quality RCTs on healthy tendons need to be investigated in high-quality RCTs in tendon pathology before conclusions can be drawn and recommendations made. Such findings, if found to be comparable and translate in tendon pathology may require a paradigm shift in the tendinopathy rehabilitation field in relation to the prescription of resistance training interventions, particularly for select populations not able to tolerate the standard and proven HL-RT interventions.[109]

CONCLUSION

Despite a dearth of studies to date on the effects of BFRT on healthy tendons and in tendon pathologies such as tendinopathy, preliminary evidence for beneficial effects of BFRT on tendons and clinical outcomes is encouraging. As BFRT is a relatively novel method, particularly its application in musculoskeletal rehabilitation, definitive conclusions, and recommendations on BFRT in tendon rehabilitation cannot be made at present, which should be addressed in future research, due to the potential therapeutic benefits highlighted in this review. The addition of LL-BFRT as a viable rehabilitation method in tendinopathy rehabilitation would be complimentary to currently utilised HL-RT interventions and provide more rehabilitation options for patients unable to tolerate HL-RT during tendon rehabilitation.

Appendix 1: Search strategy

- Information sources and search strategy.

Databases: MEDLINE (PubMed), CINAHL, AMED, EMBase, SPORTDiscus CENTRAL of Cochrane Library

Search fields: Title, abstract, key words

Search terms (database subject headings)

1. - "Blood Flow Restriction" OR "Kaatsu" OR "Occlusion Training" 2 - "tendon" OR "tendinopathy" OR "tendon rupture"

3. 1 AND 2

Table 1: Characterises of included studies and BFRT intervention parameters

Author, Study design, population	Intervention, exercises, duration	Training parameters	Cuff parameters	Outcome measures	Mechanisms studied	Outcomes, results
Skovlund et al.[60] Case series, n=7, Patellar tendinopathy	Low-load BFRT: SL leg press, knee extension, 3 weeks	Sets: 6, Reps: 5-30, Freq: 3 x WK, Prog: increase volume based on pain response, Int: 10RM, (30% of 1RM). Maximum 105 reps per session	Polyester cuff (15cm wide) fitted at proximal thigh. Occlusion pressure: 120 mm Hg Cuff pressure released for 3Min between exercises.	Pain (NRS-P, SLDS), Function (VISA-P) Tendon vascularity (US), Knee extensor strength (MVC – static dynamometry)	Tendon vascularity (US doppler activity) diminished by 31% following 3 weeks (9 sessions). No changes in tendon thickness. Increase in knee extensor strength.	Intervention was effective for improving clinical outcomes. Pain with SLDS reduced by 50%. Adherence: 98%
Cuddeford et al.[62] Case report, n=1, Patellar tendinopathy	Low-load BFRT: SL leg press, SLDS, 12 weeks	Sets:4, Reps15-30; Freq 2 x WK: Prog: increase resistance (10lbs Inc), Int: 15-30RM (1RM testing)	Delfi tourniquet system fitted at proximal lower extremity. Occlusion pressure: 80% restriction of arterial inflow. 30 second rest between sets (cuff not removed)	Pain (VAS), Function (VISA-P), Tendon size (US, Hip & knee strength (handheld dynamometry, SL leg press 1RM)	Improvements in tendon thickness and resolution of hypoechoic region (US). Increased lower limb strength.	Patients improved clinical outcomes and returned to sports activity. Adherence: supervised.
Sata[61], Case report, n=1, Patellar tendinopathy	Low-load BFRT: straight leg raises, hip abduction & adduction, calf raise, toe raise, squat, crunch, back extension, basketball shooting, 3 weeks	Sets: 3, Reps; 15, Freq: 5-6 x WK, Prog: Int:15rm (30% of 1RM)	Kaatsu cuff fitted at proximal lower limb. Occlusion pressure range: 160-180 mmHg.	MRI (signal intensity). Thigh circumference	MRI signal intensity was reduced, and the thigh circumference was increased by 7 mm and 2 mm for the right and left sides.	Patient improved clinical outcomes and returned to playing basketball Adherence: NR
Wentzell[63], Case report, n=1, Biceps tendon rupture	Manual therapy, laser therapy, progressive strength training including Low-load BFRT: Isometric	Sets: 4, Reps: 30,15,15,15, Freq: 7 x WK, Prog: increase resistance (1.5-4lbs) difficulty	Blood pressure cuff fitted at proximal arm. Occlusion pressure: 80mmHg.	Pain (NPRS), Function (DASH, Mayo Elbow Performance Index score.	NR	Patient improved clinical outcomes & returned to preinjury activity (weightlifter) Adherence: NR

	forearm pronation & supination, elbow flexion & extension 14 weeks	& ROM, Int: 10-30% MVC				
Yow et al.[64] Case report, n=2, Achilles tendon rupture	Low-load BFRT: Leg press, calf press, 6 weeks	Sets: 4, Reps: 30,15,15,15, Freq:NR, Prog: NR, Int: 30% of 1RM	Delfi tourniquet system (14cm wide) fitted at proximal thigh. Occlusion pressure: 80%, 180 mm Hg.	Strength & power (isokinetic testing – Biodex system).	NR	Patients improved strength & power and returned to sports. Adherence: NR
Centner et al.[65] RCT, n=55, Healthy Achilles tendon	1.Low-load BFRT: standing & seated calf raises (20-35% 1RM) 2. High load RT (70-85% 1RM) 3. Non-exercise control, 14 weeks	Sets:3, Reps;6-12, Freq: 3 x WK, Prog: increase resistance (5% of 1rm every 4 WK, 20-35%), Int: 20-35% of 1RM Rest: 1 MIN between sets, 3 MIN between exercises	Pneumatic nylon tourniquet (12cm wide) fitted on proximal thigh. Occlusion pressure: 50% arterial occlusion. Pressure maintained during 1 MIN rest; cuff deflated during 3 MIN rest.	Tendon morphology, Mechanical & material properties (US), and muscle (US) cross-sectional area (CSA) and isometric strength (MVC – isokinetic dynamometer).	Both groups induced significant increases in tendon stiffness & CSA, which were comparable between groups. Gastrocnemius medialis muscle CSA and plantar flexor strength significantly increased in both Groups. No changes in control group.	Adaptive change in Achilles tendon properties following low-load BFRT appears comparable to that evoked by high-load RT. Adherence: supervised
Centner et al.[70] RCT, N=29, Healthy patellar tendon	1.Low-load BFRT: bilateral leg press & knee extension, standing & seated calf raises (20-35% 1RM) 2. High load RT (70-85% 1RM), 14 weeks	Sets: 4, Reps: 30,15,15,15, Freq: 3 x WK, Prog: increase resistance (5% of 1rm every 4 WK, 20-35%), Int: 20-35% of 1RM Rest: 1 MIN between sets, 3 MIN between exercises	Pneumatic nylon tourniquet (12cm wide) fitted on proximal thigh. Occlusion pressure: 50% arterial occlusion. Pressure maintained during 1 MIN rest; cuff deflated during 3 MIN rest.	Tendon morphology, mechanical & material properties (US & MRI), and muscle (MRI) cross-sectional area (CSA) and strength (dynamic 1RM).	Both groups induced significant increases in tendon stiffness & CSA, muscle mass & strength, which were comparable between groups. Groups, except knee extension 1RM was higher in BFRT group.	Both HL and LL-BFR cause substantial changes in patellar tendon properties and the magnitude of changes are not significantly different between conditions. Adherence: supervised
Chulvi-Medrano et al.[66] RCT, n=56,	1. LL BFRT: plantarflexion 2. LL RT, single session	Sets:3, Reps;15, Freq: single	High precision compression meter (57cm long x 9cm	Tendon thickness (US)	BFRT group had significantly greater decrease in tendon	Significant difference in tendon thickness between

Healthy Achilles tendon		session, Prog: NR, Int: 30% of 1RM Rest: 30 seconds between sets	wide) fitted on proximal thigh. Occlusion pressure: 30%.		thickness compared to LL RT, immediately and 24 hours after exercise.	groups, which may be associated with neurotendinous fluid movement in response to BFRT. Adherence: NR
Gavanda et al.[68] RCT, n=21, Healthy achilles tendon	1. LL BFRT: plantarflexion 2. LL RT, 6 weeks	Sets:4, Reps; to muscular failure, Freq: 2 x WK, Prog: occlusion pressure increased every 4 WKs, Int: 30% of 1RM, Rest: 30 seconds between sets	Twist lock (7cm wide) cuffs fitted below patella. Occlusion pressure: 60%.	Calf volume, gastrocnemius muscle thickness (US), maximal hopping test for leg stiffness, 1-RM smith machine calf raise, pain 9VAS)	No difference found in leg stiffness between groups: used to measure tendon adaptations.	Leg stiffness and calf volume did not change, VAS, 1RM and muscle thickness improved equally in both groups. Adherence: NR
Kubo 2006[72], Cohort, n=9, Healthy vastus lateralis tendon	1. LL BFRT (20% of 1RM): plantarflexion 2. HL RT (80% of 1RM), 12 weeks	Sets:4, Reps; 25, 18, 15, 12, Freq: 3 x WK, Prog: NR, Int: 20% of 1RM Rest: 30 seconds between sets	Elastic pneumatic belt fitted on proximal thigh. Occlusion pressure: 37.7%.	Maximal isometric knee extension torque (MVC - dynamometer) and muscle volume. Specific tension of vastus lateralis (VL) was calculated from MVC, muscle volume & muscle architecture measurements. Stiffness of tendon aponeurosis in VL (US) during isometric knee extension.	The BFRT protocol did not alter the stiffness of tendon-aponeurosis complex in knee extensors, while the HL protocol increased it significantly.	Both groups significantly increased MVC and muscle volume of quadriceps femoris. Specific tension of VL increased significantly 5.5% for HL, but not for LL. Tension and tendon properties were found to remain following LL BFRT, whereas they increased significantly after HL RT. Adherence: NR
Picon-martinez et al.[67] RCT, n=52, healthy achilles tendon	1. LL BFRT (30% 1RM): plantarflexion 2. LL RT (30% 1RM) 3. HL RT (75% 1RM), single session	Sets:4, Reps; 30, 15, 15, 15, Freq: single session, Prog NR, Int: 30% of 1RM, Rest: 30 seconds between sets	Pneumatic CUFF (9cm width) fitted under knee joint. Occlusion pressure: 30%.	Achilles tendon thickness (US): immediately, 60MIN and 24 hours after training.	Achilles tendon thickness was significantly reduced immediately after, 60 min and 24 hours post-LL BFRT	BFRT may be an effective strategy to stimulate a positive response in Achilles tendon thickness. Adherence: NR

					group and remained unchanged in the other groups.	
Brumitt et al.[71] RCT, n=46, healthy supraspinatus tendon	1. LL BFRT: side-lying external rotation 2. LL RT, 8 weeks	Sets:4, Reps; 30, 15, 15, 15, Freq: 2 x WK, Prog: NR, Int: 30% of 1RM Rest: 30 seconds between sets	Delfi tourniquet system fitted at proximal upper arm. Occlusion pressure: 50%,	Rotator cuff strength (dynamometry), supraspinatus tendon thickness (US)	Both groups increased supraspinatus tendon thickness, with no significant difference between groups.	BFRT did not augment rotator cuff strength gains or tendon thickness when compared to RT. Both groups significantly increased rotator cuff strength and tendon size. Adherence: supervised
Canfer et al.[69] Cross sectional, n=12, healthy achilles tendon	1. LL BFRT: bodyweight SL heel raise 2. LL RT	Sets:4, Reps; 30, 15, 15, 15, Freq: single session, Prog: NR, Int: 30% of 1RM Rest: 30 seconds between sets	Occlusion cuff (7 cm) fitted at distal lower leg. Occlusion pressure: 80%. Cuff only deflated after 4th set.	Thermograms to assess Achilles tendon skin temperature (Tskin)	A lower Tskin was seen following BFRT exercise at the tendon insertion, but not at the free tendon or the musculotendinous junction. A significant effect of time upon changes in Tskin were observed in both groups.	Region specific changes in Tskin were found, with greater and longer reductions at the Achilles insertion following BFRT. findings could have implications for the programming of BFRT on tendon health. Adherence: NR

Abbreviations: LL-BFRT: low-load blood flow restriction training, HL-RT: high load resistance training, RM: repetition maximum, Tskin: skin temperature, SL: single leg, US: ultrasound, MRI: magnetic resonance imaging, MIN: minute, NR: not reported, Int: intensity, Freq: frequency, Prog: Progression, RCT: randomised controlled trial, VL: vastus lateralis, MVC: maximum voluntary contraction, VAS: visual anologue scale, NRS-P: pain numeric rating scale, VISA-P: Victorian Institute of Sport Assessment Patellar, SLDS: single leg decline squat, n: number, WK: week, ROM: range of motion.

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