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Low-Load Resistance Training With Blood Flow Restriction Is Effective for Managing Lateral Elbow Tendinopathy: A Randomized, Sham-Controlled Trial

ateral elbow tendinopathy (LET) is the most common pathology of the elbow with symptoms over the lateral humeral epicondyle during wrist movements and gripping. The prevalence of LET ranges from 1% to 3% in the general population, and up to 10% in tennis players and 29% in manual workers. Lateral elbow tendinopathy can cause a significant decline in quality of life with a substantial psychological and economic burden. Exercise with or

- without passive interventions is the first-line treatment option, resulting in small benefits for reducing pain and improving function compared to passive interventions alone. There is no substantial evidence that 1 type of loading is more beneficial than others for LET. 12,35,44,56
- Blood flow restriction (BFR) is a popular method of training, which involves lowload resistance training (LLRT) (20-40% of 1 repetition maximum [RM]) with partial restriction of the arterial blood flow by placing inflatable air cuffs at the most proximal part of the exercising limb. 41 Contemporary evidence supports LLRT with BRF (LLRT-BFR) as a useful alternative when high-intensity exercises are contraindicated or too painful. 11,20,26 Low-load resistance training with blood flow restriction improves muscle strength, 15,16,24,59 muscle growth, 25,66,67 and tendon adaptations 9,10 in healthy individuals, and produces hypoalgesia⁵⁴ in patients with knee pathologies compared to conventional high-load resistance training (>70% of 1 RM). However, the effects on upper limb musculoskeletal conditions are unclear.8
- Patients with LET have reduced grip strength and elbow function 6.57,58 due to pain and strength deficits. There is a bioplausible rationale for LLRT-BFR improving LET

- OBJECTIVE: To evaluate the effect of low-load resistance training with blood flow restriction (LLRT-BFR) when compared to LLRT with sham-BFR in patients with lateral elbow tendinopathy (LET).
- DESIGN: Randomized controlled trial.
- METHODS: Forty-six patients with LET were randomly assigned to a LLRT-BFR or a LLRT with sham-BFR treatment group. All patients received soft tissue massage, supervised exercises with BFR or sham intervention (twice a week for 6 weeks), advice, and a home exercise program. The primary outcome measures were pain intensity, patient-rated tennis elbow evaluation (PRTEE) score, pain-free grip strength, and global rating of change, measured at baseline, 6 weeks, and 12 weeks. Between-group differences were evaluated using mixed-effects models with participant-specific random effects for continuous data. Global rating of change was analyzed using logistic regression.
- RESULTS: Statistically significant between-group differences were found in favor of LLRT-BFR

- compared to LLRT with sham-BFR in pain intensity at 12-week follow-up (-1.54, 95% CI: -2.89 to -0.18; P=.026), pain-free grip strength ratio at 6-week follow-up (0.20, 95% CI: 0.06 to 0.34; P=.005), and PRTEE at 6- and 12-week follow-up (-11.92, 95% CI: -20.26 to -3.59; P=.006, and -15.23, 95% CI: -23.57 to -6.9; P<.001, respectively). At 6- and 12-weeks, patients in the LLRT-BFR group had greater odds of reporting complete recovery or significant improvement (OR = 6.0, OR = 4.09, respectively).
- **CONCLUSION:** Low-load resistance training with blood flow restriction produced significantly better results compared to the LLRT with sham-BFR for all primary outcomes. Considering the clinically significant between-group improvement in function (>11 points in PRTEE) and the better success rates in the LLRT-BFR group, this intervention may improve recovery in LET. *J Orthop Sports Phys Ther* 2022;52(12):803-825. Epub: 14 September 2022. doi:10.2519/jospt.2022.11211
- KEY WORDS: KAATSU training, lateral epycondylitis, tennis elbow, therapeutic exercise, rehabilitation

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symptoms (including via exercise-induced hypoalgesia, endogenous opioid, and endocannabinoid mechanisms of pain modulation). ^{20,31,37,38,54} We hypothesized that a loading program of the asymptomatic elbow flexors and extensors (of the limb with LET) with BFR application adhering to the best practice guidelines (30% of 1 RM, 30-15-15-15 reps) and a BFR progressive loading program with a pain monitoring approach of wrist flexors and extensors (3 sets of 10 reps) would trigger a pain modulation mechanism without risking patients to flare up because of the increased exercise volume.

The primary aim of this randomized sham-controlled trial was to compare the effect of a LLRT-BFR program to a LLRT program with sham-BFR in pain intensity, function, grip strength, and self-rated improvement in patients with LET. We also aimed to evaluate (secondary outcomes) if the application of BFR would induce significant changes in isometric elbow flexion and extension strength, or in elbow common extensor tendon (ECET) thickness compared to the sham-BFR application.

METHODS

Study Design

A prospective randomized sham-controlled design was implemented in a community setting (Attica, Greece). Participants were recruited from June 2020 to December 2021 via advertisements at the University of West Attica and from medical consultants' referrals. Two physiotherapists with 4 and 8 years of experience delivered both interventions in a private physiotherapy clinic. The trial was prospectively registered in ISRCTN (https://doi.org/10.1186/ISRCTN10724178).

Participants

Participants were eligible if they were between 18 and 60 years, and were diagnosed with LET with symptoms for more than 2 weeks. The diagnosis was based on the following criteria: pain on palpation over the lateral epicondyle; positive Cozen's, Maudsley's, and/or Mill's test;

decrease (>10%) in grip strength while the elbow is extended compared to when the elbow is flexed.³⁴ The exclusion criteria were shoulder tendinopathy on the same side, cervical radiculopathy, rheumatoid arthritis, neurological deficit, radial nerve entrapment, previous interventions (<6 months), or episodes of LET in the same elbow during the last 2 years. Patients with serious cardiovascular diseases, high blood pressure (>140/90), venous deficiency, breast surgery, upper quadrant orthopaedic surgeries during the last 6 months, history of deep venous thrombosis, body mass index (BMI)>30, Crohn's disease, and history of heart surgery or cancer were also excluded due to the application of BFR training.43,46

At the initial eligibility assessment, potential participants were examined by a musculoskeletal physiotherapist (MM) with 17 years of experience and gave written informed consent in compliance with the Declaration of Helsinki.³ Ethics approval was obtained from the Ethics Committee of the University of West Attica (ID: 36898/03-06-2020).

Randomization and Masking

A computer-generated randomization sequence at a 1:1 ratio was performed by a researcher who was not involved in data collection. Group allocation was concealed for all participants and study personnel (assessor and data analyst) throughout the study, except the administrative assistant who was responsible for contacting and allocating the participants to groups. Allocations were sealed in opaque, consecutively numbered envelopes by an administrative assistant not involved in recruitment. Due to the nature of the intervention, physiotherapists delivering the exercise program could not be blinded to the group allocation, but they were trained and instructed to ensure equal provision of motivation and treatment for both groups.

Interventions

The participants were randomized to either a LLRT-BFR group using 40%-50% of complete arterial occlusion pressure

or a LLRT-with-sham-BFR group using <20% of complete arterial occlusion pressure with the cuff minimally inflated to the point that was comfortably positioned on the proximal site of the limb. Blood flow restriction was conducted by using an automatic personalized tourniquet system (Mad-Up Pro, France).

All participants received a standardized intervention, including soft tissue massage, supervised exercises, advice and education, and a home exercise program delivered via an exercise instruction booklet.

Each session started with determining arterial occlusion pressure in the standard anatomical position.³⁶ The only difference between the groups was the application of BFR or sham-BFR during the supervised exercises. A detailed description of the interventions is presented in (APPENDIX TABLE 1).

A 2-stage training program was used. In the first stage, all exercises were performed with BFR or sham-BFR. Each session included 4 sets (30-15-15-15 repetitions) of elbow flexion and extension exercises (concentric-eccentric) at 30% of 1 RM using dumbbells. Then, wrist flexion, extension, and supination-pronation exercises followed using 3 sets of 10 repetitions with the minimum free weight based on a pain-monitoring approach (acceptable pain during the exercise: <2 out of 10 in a numeric pain-rating scale).64 Load was adjusted accordingly on a weekly basis by adding 0.5-1 kg as indicated be the pain during loading. Static stretching exercises (3 repetitions \times 30 seconds) of the wrist extensors and flexors were performed at the end of each session.56 The second stage started at least after 2 weeks of training and if patients did not report pain during or after exercises. Then, patients performed the first-stage training program (with BFR or sham-BFR) with the addition of exercises without BFR (wall push-ups, wrist extension-flexion using a rubber bar, hand grip using a soft ball, and standing rowing exercises). 17,64

A metronome was used to pace the exercise performance (2-second concentric

and 2-second eccentric phases) to ensure equal time under load between groups. A 30-second break and a 1-minute break were used between sets and exercises, respectively. The cuff was deflated between different exercises but not between sets. A home exercise program was instructed to be performed every second day (APPENDIX).

Physiotherapy sessions were conducted twice a week (30-45 minutes each) over a period of 6 weeks. A weekly diary for monitoring adherence to the home exercise program and cointerventions was used. Therapists recorded any adverse events (such as delayed onset muscle soreness, excessive pain during exercises, numbness, bruising, and tingling) reported by the patients following the intervention sessions.

Primary Outcomes

Before randomization, a blinded assessor (MM) recorded demographic characteristics (ie, age, duration of symptoms, BMI, previous symptoms, dominant side, and alleged cause), and primary and secondary outcomes at baseline and at 6-and 12-week follow-up.

The primary outcome measures were pain intensity, patient-rated tennis elbow evaluation (PRTEE) score, pain-free grip strength (PFGS), and global rating of change (GROC). Pain intensity was considered the worst level of pain over the last week and was measured on an 11-point numeric pain-rating scale with a minimum clinically important difference (MCID) of 2.1 points (>30% from the pooled weighted mean from the baseline scores).17,57 The Greek version of the PRTEE questionnaire was used as a condition-specific, validated tool to measure pain and disability.17,55 PRTEE score ranges between 0 and 100, with a score of 100 representing the worst imaginable pain with a very significant functional disability.49 The MCID for PRTEE score was set at 11 points. 48 Pain-free grip strength has been reported as a reliable measurement method in patients with LET (intraclass correlation coefficients [ICC] ranging from 0.86 to 0.96).²⁹ For the PFGS test, a Jamar hand dynamometer was used, calculating the mean value (kilograms) of 3 efforts, separated by 30-second rest intervals with participants lying in supine position and the elbow fully extended.^{17,53} The MCID of PFGS in patients with LET has been reported to be 7 kg⁵⁷ (18% change in PFGS ratio).³⁵ Pain-free grip strength measurements of the affected side were presented as a ratio of the maximum grip strength of the unaffected side.⁵⁸ Global rating of change was recorded on a 6-point Likert-scale ("much worse" to "completely recovered").¹⁷

Secondary Outcomes

We measured the maximum voluntary isometric contraction of elbow flexors and extensors (ICCs for elbow isometric tests ranging from 0.83 to 0.94),22 and the ECET thickness. A pilot within-day, intrarater reliability analysis was conducted with 30 minutes between test and retest (before and after the subjective examination), in the first 8 recruited patients (mean age \pm SD: 45 ± 5.03) for the isometric elbow muscle strength and for the tendon thickness measurements, and the results showed excellent reliability indices for flexors (ICC = 0.97, minimally detectable change (MDC) = 1.44 kg), extensors (ICC = 0.99, MDC = 1.16 kg), capitellar (ICC = 0.95, MDC = 0.6 mm), and radiocapitellar measurements (ICC = 0.97, MDC = 0.55 mm).

Elbow flexors and extensors strength was measured with a digital handheld dynamometer (BioFET MusTec). Participants were positioned in supine position with the elbow flexed in 90° and the wrist in supination.^{2,39,63} After a warm-up of 2-3 submaximal contractions, patients were instructed to perform 3 bilateral maximum voluntary isometric contractions of elbow flexion and extension (make-test over 5 seconds).2 The mean value (kilograms) of 3 efforts, separated by 30-second rest intervals, was calculated.2,39 Isometric elbow flexion and extension strength were calculated, analyzed, and presented as a ratio between the affected and the unaffected side.

Elbow common extensor tendon thickness was assessed using a portable ultrasound device (Alpinion minisono, 3-12 Hz) with patients seated, elbows flexed to 90°, the wrist pronated, and the arm resting on a table.60 The sonographer was a physiotherapist with 15 years of experience and blinded to patients' group allocation. Longitudinal scans were performed with the transducer on the lateral epicondyle with the linear array parallel to the tendon fibers.²¹ Tendon thickness was measured offline using ImageJ software at 2 locations: from the deepest point of the capitellum and the mid-point of the radiocapitellar joint (MCID>10%). 21,23,60

Sample Size

Based on previous studies that used exercise interventions in patients with LET, a sample size calculation (power 0.80, 2-sided significance level 0.05) was conducted by using PRTEE, PFGS, and pain reduction (GPower 3.1). A sample size of 17 in each group was estimated to be sufficient to detect an effect size of 1.0 on the PRTEE, ^{19,65} a sample size of 21 per group to detect an effect size of 17 per group to detect an effect size of 1.0 on pain reduction. ^{42,53} To allow for a 10% loss to follow-up, the sample size was increased to 23 per group.

Statistical Analysis

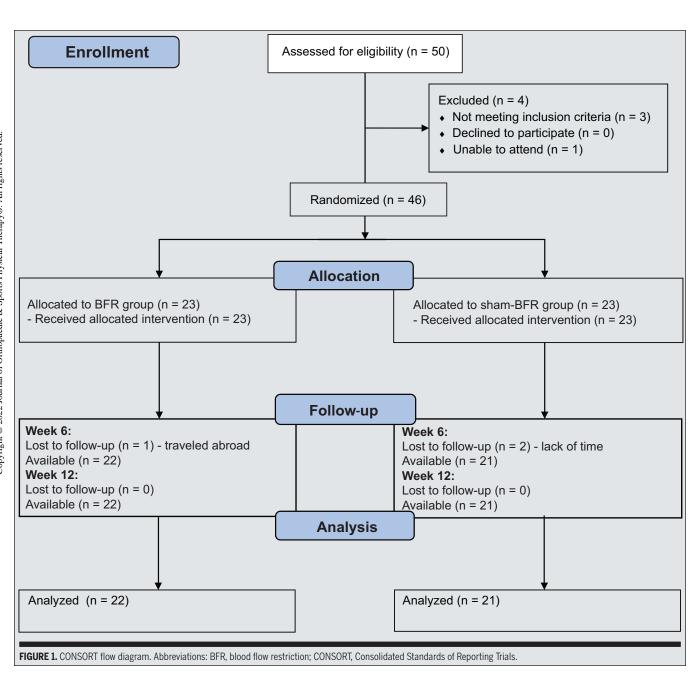
Normality of the data was checked visually with quantile-quantile (Q-Q) plots and tested statistically using the Shapiro-Wilk test. Descriptive statistics were used to summarize the baseline characteristics of the participants and the measurements. For the computation of success rates, participants' general improvement was dichotomized into successes ("complete recovered" or "much improved") and no successes for the rest of the responses in the GROC. 53,62

Data were analyzed for between-group differences using mixed-effects models with participant-specific random effects over the 3 measurements of time points (baseline, 6-, and 12-week follow-up).

Fixed effects included group, time, and group × time interactions. The parameter estimates were adjusted for covariates such as sex, chronicity, age, BMI, previous episodes, and dominant affected side. The choice of the best model for each variable was made on the basis of the Akaike information criterion. Models' comparison was conducted using the maximum likelihood method for estimating the parameters,

whereas the restricted maximum likelihood method was used for the rest of the estimation procedure by adding both intercept and slope as random.⁶¹

When there was a significant main effect or interaction, we performed post hoc testing with Bonferroni adjustments. There were no participants crossing over between groups. Mixed-models analysis of datasets was conducted and presented without imputation as there were only 1 and 2 participants lost to follow-up in the LLRT-BFR group and the LLRT-with-sham-BFR group, respectively. However, we performed a sensitivity analysis for the missing outcome data using last value carried forward. Cohen's d effect sizes were calculated using the pooled SD of baseline scores, and values of 0.2, 0.5, and 0.80 were considered the thresholds of a



small, moderate, and large effects, respectively. He Binary and categorical variables were analyzed using logistic regression. All data were analyzed with IBM SPSS (Version 25), and the level of significance was set at 0.05.

RESULTS

ROM JANUARY 2020 TO DECEMBER 2021, 50 patients with LET were assessed for eligibility, of which 4 patients were excluded, leaving 46 eligible participants remaining for randomization (FIGURE 1). Three participants were lost to follow-up: 1 from the LLRT-BFR group and 2 from the LLRT-with-sham-BFR group. None of the dropouts was related to side effects of the training. All remaining participants completed the 12 sessions (twice a week). The mean (±SD) age of the participants was 45.2 (±8.4) years with a median (interquartile range) duration of symptoms of 6 (4-26) weeks (TABLE 1).

Summary statistics of baseline-adjusted outcome measures by treatment group are presented in TABLE 2, whereas the main and interaction effects as well as the effects of covariates are presented in APPENDIX TABLE 1.

Between-Group Differences

A significant pain reduction with a moderate effect size (d = 0.68) in favor of the LLRT-BFR was observed at the 12week follow-up (-1.54, 95% CI: -2.89 to -0.18) (TABLE 2). A statistically significant between-group difference in favor of the LLRT-BFR group was found in the PRTEE score at the 6- and 12-week follow-up (-11.92, 95% CI: -20.26 to -3.59, and -15.23, 95% CI: -23.57 to -6.9, respectively) with a large effect size (d =0.88 and d = 1.13, respectively) (**TABLE 2**). A between-group statistically significant difference (0.20, 95% CI: 0.06 to 0.34) with a large effect size (0.83) was found in PFGS ratio only at the 6-week follow-up (TABLE 2). A significant difference in the odds of reporting a successful outcome using GROC was found between patients allocated to the LLRT-BFR group

TABLE 1

Participants' Baseline Characteristics in the LLRT-BFR and the LLRT-With-Sham-BFR Group^a

	LLRT-BFR Group	LLRT-With-Sham-BFR Group (N = 23)	
Characteristics	(N = 23)		
Women	9 (39%)	13 (56%)	
Age, mean (SD), years	43.3 (8.7)	47.08 (8.1)	
BMI, mean (SD)	24.8 (4.1)	26.8 (3.6)	
Symptom duration, median (IQR), weeks	6 (4-26)	6 (4-26)	
Dominant elbow affected	10 (43%)	10 (43%)	
Nonsmokers	22 (95%)	18 (78%)	
Previous episodes of LET	17 (74%)	19 (82%)	
Manual workers	5 (22%)	4 (17%)	
Alleged cause:			
- Sports or work related	10 (43%)	11 (48%)	
- Insidious onset	7 (30%)	9 (39%)	
- Other	6 (17%)	3 (13%)	

Abbreviations: LET, lateral elbow tendinopathy; LLRT-BFR; low-load resistance training with blood flow restriction; SD, standard deviation; IQR, interquartile range.

compared to patients allocated to the LLRT-with-sham-BFR group at 6-week (OR = 6.0, 95% CI: 1.5 to 23.9) and 12-week (OR = 4.09, 95% CI: 1.03 to 16.28) follow-up (TABLE 2).

Significant between-group differences were found at the elbow flexors strength ratio at both follow-up time points (0.2, 95% CI: 0.08 to 0.31, and 0.15, 95% CI: 0.04 to 0.27, respectively) with large effect sizes (d=1.2 and d=0.9, respectively) in favor of the LLRT-BFR group (APPENDIX TABLE 2 and FIGURE 2). There were no significant between-group differences for elbow extensors strength ratio and ECET thickness (FIGURE 2).

Compliance, Cointerventions, and Adverse Events

The implementation of home-based exercise was similar between the LLRT-BFR group and the LLRT-with-sham-BFR group (86% [19/22] and 85% [18/21], respectively). One patient from the LLRT-BFR group and one from LLRT-with-sham-BFR group reported using nonsteroidal anti-inflammatory drugs for 5 and 3 days, respectively. None of the

patients reported an adverse event due to BFR or exercise training.

Sensitivity Analysis

There was no difference in main or interactions effects compared to the primary analysis when imputing missing data (APPENDIX TABLE 3).

DISCUSSION

BFR Training Improves Disability and Promotes Functional Recovery in LET

The combination of LLRT-BFR with patient education, home exercise program, and massage significantly improved pain intensity, PRTEE score, and PFGS ratio as compared to the same intervention with sham-BFR application in patients with LET. A clinically significant between-group difference (>11 points in PRTEE score) in favor of the LLRT-BFR group was found in disability at the very-short (6 weeks) and the short-term (12 weeks) follow-up, and in PFGS ratio (>18%) at the 6-week follow-up.

Low-load resistance training with blood flow restriction led to significantly better

^aValues are presented as number (percentage), unless otherwise indicated. No significant differences were found between the groups at baseline (all P>.05).

TABLE 2

BETWEEN- AND WITHIN-GROUP DIFFERENCES OF BASELINE-ADJUSTED PRIMARY OUTCOME MEASURES IN PER-PROTOCOL ANALYSIS

	LLRT-BFR Group ^a	LLRT-With-Sham-BFR Group ^a	Between-Group Differences ^c	Odds Ratio ^c	P Value
Pain intensity (0-10)					0.014 ^d
Baseline	$7.47 \pm 2.2 \ (6.5 \text{ to } 8.4)$	6.64 ± 2.1 (5.71 to 7.5)		-	-
6th week	3.47 ± 2.1 (2.52 to 4.42)	4.62 ± 2.1 (3.65 to 5.59)	-1.14 ± 0.66 (-2.5 to 0.20), $d = 0.52$	-	0.09e
12th week	1.73 ± 2.1 (0.78 to 2.68)	3.27 ± 2.1 (2.3 to 4.24)	-1.54 ± 0.67 (-2.89 to -0.18), $d = 0.68$	-	0.026e
Change from baseline to 6 weeks	3.99 ± 0.7 (2.56 to 5.42), $d = 1.71$	2.01 ± 0.7 (0.57 to 3.46), d = 0.92	-	-	-
Change from 6 to 12 weeks	1.73 ± 0.7 (0.29 to 3.18), $d = 0.74$	1.34 ± 0.7 (-0.12 to 2.82), $d = 0.61$	-	-	-
Change from baseline to 12 weeks	5.73 ± 0.7 (4.3 to 7.16), d = 2.46	3.36 ± 0.7 (1.91 to 4.81), $d = 1.54$	-	-	-
PRTEE score					<0.001 ^d
Baseline	38.74 ± 13.2 (33.13 to 44.55)	36.99 ± 12.25 (31.29 to 41.87)	-	-	-
6th week	$12.75 \pm 13 \ (6.95 \ \text{to} \ 18.5)$	24.68 ± 13 (18.74 to 30.61)	-11.92 ± 4.1 (-20.26 to -3.59), $d = 0.88$	-	0.006e
12th week	$5.01 \pm 13.2 \ (0.79 \text{ to } 10.81)$	$20.24 \pm 13 \ (14.31 \ \text{to} \ 26.18)$	-15.23 ± 4.1 (-23.57 to -6.9), $d = 1.13$	-	<0.001e
Change from baseline to 6 weeks	26.08 ± 3.7 (18.64 to 33.53), $d = 1.86$	12.31 ± 3.7 (4.74 to 19.89), $d = 0.95$	-	-	-
Change from 6 to 12 weeks	7.74 \pm 3.7 (0.25 to 15.23), P = .04, d = 0.55	4.43 ± 3.8 (-3.24 to 12.11), $d = 0.34$	-	-	-
Change from baseline to 12 weeks	33.83 ± 3.7 (26.38 to 41.27), $d = 2.43$	16.75 ± 3.7 (9.17 to 24.32), $d = 1.29$	-	-	-
PFGS ^b					<0.001 ^d
Baseline	$0.71 \pm 0.2 (0.61 \text{to} 0.81)$	$0.75 \pm 0.2 (0.65 to 0.85)$	-	-	-
6th week	$0.93 \pm 0.2 \ (0.83 \ \text{to} \ 1.03)$	$0.73 \pm 0.2 (0.63 \text{to} 0.83)$	0.20 ± 0.06 (0.06 to 0.34), d = 0.83	-	0.005 ^e
12th week	$0.94 \pm 0.2 \ (0.84 \ to \ 1.04)$	0.80 ± 0.2 (0.70 to 0.91)	0.13 ± 0.06 (-0.009 to 0.27) $d = 0.54$	-	0.066e
Change from baseline to 6 weeks	-0.22 ± 0.05 (-0.32 to -0.12), d = 1.1	0.01 ± 0.04 (-0.08 to 0.11), $d = 0.04$	-	-	-
Change from 6 to 12 weeks	0.00 ± 0.04 (-0.09 to 0.09), $d = 0$	-0.05 ± 0.04 (-0.15 to 0.04), d = 0.2	-	-	-
Change from baseline to 12 weeks	0.22 ± 0.05 (-0.32 to -0.12), $d = 1.1$	-0.07 ± 0.04 (-0.17 to 0.02), d = 0.28	-	-	-
GROC n (% success rate) ^g					
At 6 weeks	18 (82%)	9 (43%)	-	6 (1.5 to 23.9)	0.011 ^f
At 12 weeks	18 (82%)	11 (52%)	-	4.09 (1.03 to 16.28)	0.018 ^f

Abbreviations: BFR, blood flow restriction; GROC, global rating of change; LLRT-BFR; low-load resistance training with blood flow restriction; PRTEE, patient-rated tennis elbow evaluation; PFGS, pain-free grip strength.

perceived GROC and success rates than the LLRT-with-sham-BFR group. Considering the lack of adverse events and the favorable outcomes, we suggest that LLRT-BFR

has potential as an add-on intervention to exercise loading and patient education to improve recovery in patients with LET, at least at the short-term.

Exercise interventions are superior for improving function than wait-andsee and corticosteroid injections at the short- and mid-term follow-up. However,

 $^{^{\}mathrm{a}}Values~are~means\pm SD~and~95\%~confidence~intervals.$

^bValue expressed as a ratio of the affected to the unaffected side.

 $^{^{}c}Values\ in\ parenthesis\ are\ 95\%\ confidence\ intervals.$

 $^{^{\}mathrm{d}}Intervention \times time.$

 $^{^{\}circ}\!Adjust ments\ were\ performed\ for\ post\ hoc\ multiple\ comparisons\ (Bonferroni).$

^fBetween-group comparison (chi-square test).

^{*}Successes at each time point were calculated from the responses of "much improved" and "complete recovery" in each group.

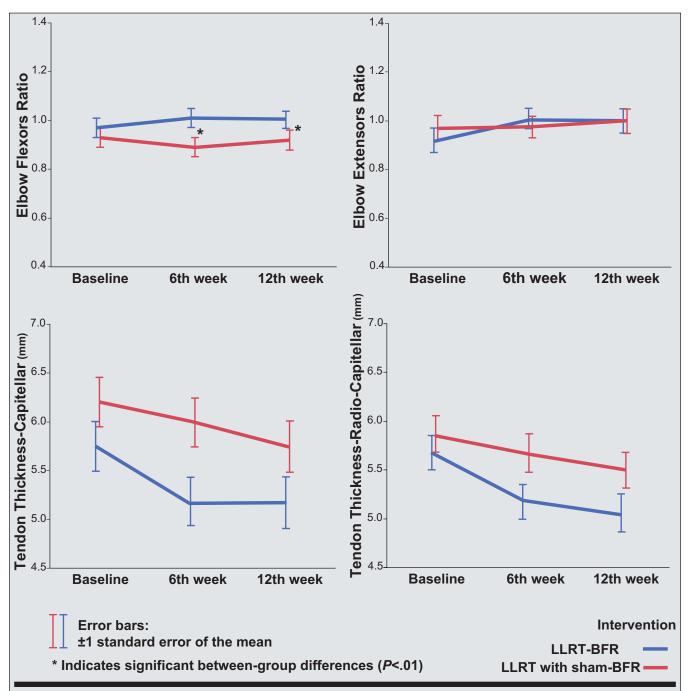


FIGURE 2. Mean scores for the secondary outcomes in LLRT-BFR and LLRT with sham-BFR at 6- and 12-week follow-up. Notes: Data are adjusted means from the linear mixed-effects analysis. Isometric elbow flexion and extension strength were calculated, analyzed, and presented as a ratio between the affected and the unaffected side. Error bars show standard errors. A detailed description of the between-group differences and the within-group changes of secondary outcomes is reported in Appendix B. Abbreviations: BFR, blood flow restriction; LLRT, low-load resistance training; PRTEE, patient-rated tennis elbow evaluation score.

the differences are small and not clinically significant.³⁵ In our study, the LLRT-BFR group had statistically and clinically significant improvement (>11 points) in PRTEE score at both follow-up time points, indicating that the BFR component might have played a key role in improving treatment outcomes. Our reports

mirror previous results of physiotherapy interventions with an exercise component in patients with LET at 6- and 12-week follow-up (47%-65% and 55%-76%,

respectively).5,53 Nevertheless, the proportion of patients in the LLRT-BFR group reported "complete recovery" or "much improved" was substantially higher (82%) at both time points.

A Pain-Monitoring BFR Approach **Was Effective for Improving Function** but Not for Reducing Pain

Several mechanisms may explain acute or long-term effects of LLRT-BFR in reducing pain, including (1) activating the endogenous opioid system via beta-endorphin,31 (2) recruiting high threshold motor units (similar to high-load resistance training),33 (3) a baroreceptor pathway due to increases in blood pressure,³⁰ and (4) a conditioned pain modulation phenomenon due to discomfort caused from the exercise loading.30 In our study, the intensity and volume of the wrist extensors loading (minimum free weight with pain<2/10, 3 sets of 10 reps) differed to BFR best practice guidelines (30% of 1 RM, 4 sets of 30-15-15-15 reps) to avoid symptom flare-up due to the increased volume of loading. A relative underloading of the wrist extensors might explain why the changes we observed in pain did not reach the clinical significance threshold.

Applying LLRT with BFR in the upper limb resulted in significant improvements in PFGS ratio. The between-group differences were statistically and clinically significant in favor of the LLRT-BFR group only at the 6-week follow-up and plateaued up to the 12-week follow-up. The LLRT-BFR displayed a significant mean PFGS ratio increase over the first 6 weeks exceeding 20%, whereas the LLRT-with-sham-BFR group remained relatively stable with a mean PFGS ratio increase that reached 5% at the 12-week follow-up. On one hand, the lack of clinically significant between-group differences could be attributed to the observed mean PFGS ratio in the LLRT-BFR group that reached a high limb symmetry (93% and 94% at 6- and 12-week follow-up, respectively). On the other hand, a longer application of BFR training during a progressive exercise loading program (ie, 8 to 12 weeks),^{27,28,32} similarly to studies in lower limb musculoskeletal conditions, could have facilitated the continuation of PFGS improvement over a longer period.

No Between-Group Differences in Tendon Thickness

Tendon thickness changes following BFR loading are inconsistent.^{7,9,10,47} Studies that have investigated healthy tendon thickness changes (rotator cuff,7 patellar,9 and Achilles tendon¹⁰) after LLRT-BFR have consistently shown within-group increases in thickness, which were at least comparable to high-load training without BFR. Our results supported a report in Achilles tendinopathy suggesting reduced tendon thickness following BFR training.47 Despite that an increased ECET thickness has been documented as part of the tendinopathic changes observed in LET,40 this ultrasonographic finding is weakly correlated with clinical outcomes such as pain and disability.^{13,45} In addition, the use of the method as a diagnostic or stand-alone assessment tool has several limitations, including the increased variability in asymptomatic tendon thickness, substantial heterogeneity in equipment and operators, and the small detectable changes found in patients with LET.34,40

Limitations and Future Studies

We acknowledge the noninclusion of GROC as a primary outcome measure in the sample size calculation. In addition, our results cannot be generalized to patients receiving cointerventions for LET (injections, brace, etc) or with risk factors for adverse events from the use of BFR. We also did not strictly controlled for the total volume of exercise.

Future research should consider time under tension along with total load as independent factors that may influence any pain or function effect independent of BFR. We suggest that an important area of future research is determining the mechanisms of action of BFR application in subgroups of patients with LET as indicated by relative risk factors and PRTEE scores.

CONCLUSIONS

HEN DELIVERED AS PART OF A 6-week progressive exercise therapy program, LLRT-BFR can improve function, reduce pain, and improve self-perceived recovery compared to LLRT with sham-BFR in patients with LET. •

KEY POINTS

FINDINGS: A 6-week low-load resistance training program with blood flow restriction (BFR) was more effective in improving function and self-perceived recovery than a similar program with sham-BFR in patients with lateral elbow tendinopathy (tennis elbow) at the short term (12 weeks).

IMPLICATIONS: Considering the statistically (and clinically for function) significant changes in favor of lowload resistance training with BFR, the method can be suggested as a valuable additive intervention to improve recovery in patients with lateral elbow tendinopathy.

CAUTION: Pain reduction was greater in the BFR training group compared to sham intervention at the 12-week follow-up. However, the between-group differences did not reach the clinical significance threshold. Clinicians should consider that the low-load resistance training protocol implemented in this study for the wrist extensors deviated from BFR best practice guidelines in terms of load volume.

STUDY DETAILS

AUTHORS CONTRIBUTIONS: S.K. as a PhD student contributed in the planning, conduct, data collection, analysis, synthesis, and reporting of this study. M.M. contributed in data collection. V.K. contributed in reporting and revising this study. S.X., E.T., and G.G. contributed in planning and revising the work. DATA SHARING: Data are available on

request.

PATIENT AND PUBLIC INVOLVEMENT: There was no patient or public involvement in this study.

REFERENCES

- Aben A, De Wilde L, Hollevoet N, et al. Tennis elbow: associated psychological factors. J Shoulder Elbow Surg. 2018;27:387-392. https://doi.org/10.1016/j.jse.2017.11.033
- 2. Andrews AW, Thomas MW, Bohannon RW. Normative values for isometric muscle force measurements obtained with hand-held dynamometers. *Phys Ther*. 1996;76:248-259. https://doi.org/10.1093/ptj/76.3.248
- Association WM. World medical association declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310:2191-2194. https://doi.org/10.1001/jama.2013.281053
- 4. Bhabra G, Wang A, Ebert JR, Edwards P, Zheng M, Zheng MH. Lateral elbow tendinopathy: development of a pathophysiology-based treatment algorithm. Orthop J Sports Med. 2016;4:2325967116670635. https://doi.org/10.1177/2325967116670635
- 5. Bisset LM, Beller E, Jull G, Brooks P, Darnell R, Vicenzino B. Mobilisation with movement and exercise, corticosteroid injection, or wait and see for tennis elbow: randomised trial. BMJ. 2006;333:939. https://doi.org/10.1136/ bmj.38961.584653.AE
- Bisset LM, Vicenzino B. Physiotherapy management of lateral epicondylalgia. J Physiother. 2015;61:174-181. https://doi.org/10.1016/j. jphys.2015.07.015
- Brumitt J, Hutchison MK, Kang D, et al. Blood flow restriction training for the rotator cuff: a randomized controlled trial. *Int J Sports Physiol. Perform*. 2020;1-6. https://doi.org/10.1123/ ijspp.2019-0815
- 8. Cancio JM, Sgromolo NM, Rhee PC. Blood flow restriction therapy after closed treatment of distal radius fractures. J Wrist Surg. 2019;08:288-294. https://doi. org/10.1055/s-0039-1685455
- 9. Centner C, Jerger S, Lauber B, et al. Low-load blood flow restriction and high-load resistance training induce comparable changes in patellar tendon properties. *Med Sci Sports Exerc*. 2021. https://doi.org/10.1249/MSS.000000000000002824
- Centner C, Lauber B, Seynnes OR, et al. Low-load blood flow restriction training induces similar morphological and mechanical Achilles tendon adaptations compared with high-load resistance training. *J Appl Physiol*. 2019;127:1660-1667. https://doi.org/10.1152/japplphysiol.00602.2019
- 11. Charles D, White R, Reyes C, Palmer D. A systematic review of the effects of blood flow restriction training on quadriceps muscle atrophy and circumference post ACL reconstruction. *Int J Sports Phys Ther*. 2020;15:882-891. https://doi.org/10.26603/ijspt20200882
- 12. Chen Z, Baker NA. Effectiveness of eccentric strengthening in the treatment of lateral elbow tendinopathy: A systematic review with

- meta-analysis. *J Hand Ther*. 2021;34:18-28. https://doi.org/10.1016/j.jht.2020.02.002
- Clarke AW, Ahmad M, Curtis M, Connell DA. Lateral elbow tendinopathy: correlation of ultrasound findings with pain and functional disability. Am J Sports Med. 2010;38:1209-1214. https:// doi.org/10.1177/0363546509359066
- Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd ed. Lawrence Erlbaum Associates: New York, NY; 1988.
- Cook CJ, Kilduff LP, Beaven CM. Improving strength and power in trained athletes with 3 weeks of occlusion training. Int J Sports Physiol Perform. 2014;9:166-172. https://doi.org/10.1123/ ijspp.2013-0018
- Cook SB, Clark BC, Ploutz-Snyder LL. Effects of exercise load and blood-flow restriction on skeletal muscle function. Med Sci Sports Exerc. 2007;39:1708-1713. https://doi.org/10.1249/ mss.0b013e31812383d6
- 17. Coombes BK, Bisset L, Brooks P, Khan A, Vicenzino B. Effect of corticosteroid injection, physiotherapy, or both on clinical outcomes in patients with unilateral lateral epicondylalgia: A randomized controlled trial. *JAMA*. 2013;309:461-469. https://doi.org/10.1001/ jama.2013.129
- 18. Coombes BK, Connelly L, Bisset L, Vicenzino B. Economic evaluation favours physiotherapy but not corticosteroid injection as a first-line intervention for chronic lateral epicondylalgia: evidence from a randomised clinical trial. Br J Sports Med. 2016;50:1400. https://doi.org/10.1136/bjsports-2015-094729
- Croisier J-L, Foidart-Dessalle M, Tinant F, Crielaard J-M, Forthomme B. An isokinetic eccentric programme for the management of chronic lateral epicondylar tendinopathy. Br J Sports Med. 2007;41:269-275. https://doi. org/10.1136/bjsm.2006.033324
- 20. Cuyul-Vásquez I, Leiva-Sepúlveda A, Catalán-Medalla O, Araya-Quintanilla F, Gutiérrez-Espinoza H. The addition of blood flow restriction to resistance exercise in individuals with knee pain: a systematic review and meta-analysis. Braz J Phys Ther. 2020;24:465-478. https://doi.org/10.1016/j.bjpt.2020.03.001
- 21. Del Baño-Aledo ME, Martínez-Payá JJ, Ríos-Díaz J, Mejías-Suárez S, Serrano-Carmona S, de Groot-Ferrando A. Ultrasound measures of tendon thickness: intra-rater, inter-rater and inter-machine reliability. Muscles Ligaments Tendons J. 2017;7:192-199. https://doi. org/10.11138/mltj/2017.71.192
- 22. Douma RK, Soer R, Krijnen WP, Reneman M, van der Schans CP. Reference values for isometric muscle force among workers for the Netherlands: a comparison of reference values. BMC Sports Sci Med Rehabil. 2014;6:10. https://doi.org/10.1186/2052-1847-6-10
- du Toit C, Stieler M, Saunders R, Bisset L, Vicenzino B. Diagnostic accuracy of power Doppler ultrasound in patients with chronic tennis elbow. Br J Sports Med.

- 2008;42:872-876. https://doi.org/10.1136/bjsm.2007.043901
- 24. Early KS, Rockhill M, Bryan A, Tyo B, Buuck D, McGinty J. Effect of blood flow restriction training on muscular performance, pain and vascular function. *Int J Sports Phys Ther*. 2020;15:892-900. https://doi.org/10.26603/ ijspt20200892
- 25. Farup J, de Paoli F, Bjerg K, Riis S, Ringgard S, Vissing K. Blood flow restricted and traditional resistance training performed to fatigue produce equal muscle hypertrophy. Scand J Med Sci Sports. 2015;25:754-763. https://doi.org/10.1111/sms.12396
- 26. 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. *Clinical Rehabilitation*. 2020;34:1378-1390. https://doi.org/10.1177/0269215520943650
- 27. Ferraz RB, Gualano B, Rodrigues R, et al. Benefits of resistance training with blood flow restriction in knee osteoarthritis. *Med Sci Sports Exerc*. 2018;50. https://doi.org/10.1249/ MSS.00000000000001530
- 28. Giles L, Webster KE, McClelland J, Cook JL. Quadriceps strengthening with and without blood flow restriction in the treatment of patellofemoral pain: a double-blind randomised trial. *Br J Sports Med.* 2017;51:1688-1694. https://doi.org/10.1136/bjsports-2016-096329
- 29. Heales L, Hill C, Kean C, Stanton R. Within- and between-session test-retest reliability of pain-free grip strength in individuals with lateral elbow tendinopathy. *J Sci Med Sport*. 2021;24:S79. https://doi.org/10.1016/j.jsams.2021.09.196
- Hughes L, Patterson SD. Low intensity blood flow restriction exercise: rationale for a hypoalgesia effect. Med Hypotheses. 2019;132:109370. https://doi.org/10.1016/j.mehy.2019.109370
- 31. Hughes L, Patterson SD. The effect of blood flow restriction exercise on exercise-induced hypoalgesia and endogenous opioid and endocannabinoid mechanisms of pain modulation. J Appl Physiol. 2020;128:914-924. https://doi. org/10.1152/japplphysiol.00768.2019
- 32. Hughes L, Patterson SD, Haddad F, et al. Examination of the comfort and pain experienced with blood flow restriction training during post-surgery rehabilitation of anterior cruciate ligament reconstruction patients: a UK National Health Service trial. *Phys Ther Sport*. 2019;39:90-98. https://doi.org/10.1016/j.ptsp.2019.06.014
- Jessee MB, Mattocks KT, Buckner SL, et al. Mechanisms of blood flow restriction: the new testament. *Tech Orthop*. 2018;33. https://doi. org/10.1097/BTO.00000000000000252
- 34. Karanasios S, Korakakis V, Moutzouri M, et al. Diagnostic accuracy of examination tests for lateral elbow tendinopathy (LET) – a systematic review. J Hand Ther. 2021. https://doi. org/10.1016/j.jht.2021.02.002
- **35.** Karanasios S, Korakakis V, Whiteley R, Vasilogeorgis I, Woodbridge S, Gioftsos G.

- Exercise interventions in lateral elbow tendinopathy have better outcomes than passive interventions, but the effects are small: a systematic review and meta-analysis of 2123 subjects in 30 trials. *Br J Sports Med*. 2021;55:477-485. https://doi.org/10.1136/bjsports-2020-102525
- **36.** Karanasios S, Koutri C, Moutzouri M, Xergia SA, Sakellari V, Gioftsos G. The effect of body position and the reliability of upper limb arterial occlusion pressure using a handheld Doppler ultrasound for blood flow restriction training. *Sports Health*. 2021;19417381211043877. https://doi.org/10.1177/19417381211043877
- 37. Korakakis V, Whiteley R, Epameinontidis K. Blood flow restriction induces hypoalgesia in recreationally active adult male anterior knee pain patients allowing therapeutic exercise loading. *Phys Ther Sport*. 2018;32:235-243. https://doi. org/10.1016/j.ptsp.2018.05.021
- 38. Korakakis V, Whiteley R, Giakas G. Low load resistance training with blood flow restriction decreases anterior knee pain more than resistance training alone. A pilot randomised controlled trial. Phys Ther Sport. 2018;34:121-128. https:// doi.org/10.1016/j.ptsp.2018.09.007
- Kotte SHP, Viveen J, Koenraadt KLM, The B, Eygendaal D. Normative values of isometric elbow strength in healthy adults: a systematic review. Shoulder Elb. 2018;10:207-215. https:// doi.org/10.1177/1758573217748643
- Krogh TP, Fredberg U, Ammitzbøll C, Ellingsen T. Clinical value of ultrasonographic assessment in lateral epicondylitis versus asymptomatic healthy controls. Am J Sports Med. 2020;48:1873-1883. https://doi.org/10.1177/0363546520921949
- **41.** Loenneke JP, Abe T, Wilson JM, Ugrinowitsch C, Bemben MG. Blood flow restriction: how does it work? *Front Physiol* . 2012;3:392-392. https://doi.org/10.3389/fphys.2012.00392
- 42. Martinez-Silvestrini JA, Newcomer KL, Gay RE, Schaefer MP, Kortebein P, Arendt KW. Scientific/clinical article: chronic lateral epicondylitis: comparative effectiveness of a home exercise program including stretching alone versus stretching supplemented with eccentric or concentric strengthening. J Hand Ther. 2005;18:411-420. https://doi.org/10.1197/j.jht.2005.07.007
- **43.** Minniti MC, Statkevich AP, Kelly RL, et al. The safety of blood flow restriction training as a therapeutic intervention for patients with musculoskeletal disorders: a systematic review. *Am J Sports Med*. 2020;48:1773-1785. https://doi.org/10.1177/0363546519882652
- 44. Ortega-Castillo M, Medina-Porqueres I. Effectiveness of the eccentric exercise therapy in physically active adults with symptomatic shoulder impingement or lateral epicondylar tendinopathy: a systematic review. J Sci Med Sport. 2016;19:438-453. https://doi.org/10.1016/j. jsams.2015.06.007
- **45.** Palaniswamy V, Ng S-K, Manickaraj N, et al. Relationship between ultrasound detected

- tendon abnormalities, and sensory and clinical characteristics in people with chronic lateral epicondylalgia. *PIOS One*. 2018;13:e0205171. https://doi.org/10.1371/journal.pone.0205171
- 46. Patterson SD, Hughes L, Warmington S, et al. Blood flow restriction exercise: considerations of methodology, application, and safety. Front Physiol. 2019;10:533. https://doi.org/10.3389/ fphys.2019.00533
- 47. Picón-Martínez M, Chulvi-Medrano I, Cortell-Tormo JM, Alonso-Aubin DA, Alakhdar Y, Laurentino G. Acute effects of resistance training with blood flow restriction on Achilles tendon thickness. J Hum Kinet. 2021;78:101-109. https:// doi.org/10.2478/hukin-2021-0032
- Poltawski L, Watson T. Measuring clinically important change with the patient-rated tennis elbow evaluation. Hand Therapy. 2011;16:52-57. https://doi.org/10.1258/ht.2011.011013
- Rompe JD, Overend TJ, MacDermid JC. Validation of the patient-rated tennis elbow evaluation questionnaire. *J Hand Ther*. 2007;20:3-10. https://doi. org/10.1197/j.jht.2006.10.003
- 50. Sanders TL Jr, Maradit Kremers H, Bryan AJ, Ransom JE, Smith J, Morrey BF. The epidemiology and health care burden of tennis elbow: a population-based study. Am J Sports Med. 2015;43:1066-1071. https://doi.org/10.1177/0363546514568087
- Shiri R, Viikari-Juntura E. Lateral and medial epicondylitis: role of occupational factors. Best Pract Res Clin Rheumatol. 2011;25:43-57. https:// doi.org/10.1016/j.berh.2011.01.013
- 52. Shiri R, Viikari-Juntura E, Varonen H, Heliövaara M. Prevalence and determinants of lateral and medial epicondylitis: a population study. Am J Epidemiol. 2006;164:1065-1074. https://doi.org/10.1093/aje/kwj325
- 53. Smidt N, van der Windt DAWM, Assendelft WJJ, Devillé WLJM, Korthals-de Bos IBC, Bouter LM. Corticosteroid injections, physiotherapy, or a wait-and-see policy for lateral epicondylitis: a randomised controlled trial. *Lancet*. 2002;359:657-662. https://doi.org/10.1016/S0140-6736(02)07811-X
- 54. Song JS, Spitz RW, Yamada Y, et al. Exercise-induced hypoalgesia and pain reduction following blood flow restriction: a brief review. *Phys Ther Sport*. 2021;50:89-96. https://doi.org/10.1016/j.ptsp.2021.04.005
- Stasinopoulos D, Papadopoulos C, Antoniadou M, Nardi L. Greek adaptation and validation of the Patient-Rated Tennis Elbow Evaluation (PRTEE). J Hand Ther. 2015;28:286-290. https:// doi.org/10.1016/j.jht.2014.12.005
- 56. Stasinopoulos D, Stasinopoulos I. Scientific/ clinical article: comparison of effects of eccentric training, eccentric-concentric training, and eccentric-concentric training combined with isometric contraction in the treatment of lateral elbow tendinopathy. J Hand Ther. 2017;30:13-19. https://doi.org/10.1016/j.jht.2016.09.001

- 57. Stratford P, Gill C, Westaway M, Binkley J. Assessing disability and change on individual patients: a report of a patient specific measure. *Physiotherapy Canada*. 1995;47:258-263. https://doi.org/10.3138/ptc.47.4.258
- Stratford P, Levy K, Miseferi D, Levy, DR, Gauldie S. Extensor carpi radialis tendonitis: a validation of selected outcome meaures. *Physiotherapy Canada*. 1987;39:250-2255.
- 59. Takarada Y, Takazawa H, Sato Y, Takebayashi S, Tanaka Y, Ishii N. Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. *J Appl Physiol*. 2000;88:2097-2106. https://doi.org/10.1152/ jappl.2000.88.6.2097
- **60.** Toprak U, Ustüner E, Uyanık S, et al. Comparison of ultrasonographic patellar tendon evaluation methods in elite junior female volleyball players: thickness versus cross-sectional area. *Diagn Interv Radiol*. 2012;18:200-207. https://doi.org/10.4261/1305-3825.DIR.4339-11.2
- Twisk JW. Applied Multilevel Analysis: A Practical Guide for Medical Researchers. Cambridge, UK: Cambridge University Press; 2006. https://doi. org/10.1017/CB09780511610806
- 62. van der Windt DA, Koes BW, Devillé W, Boeke AJ, de Jong BA, Bouter LM. Effectiveness of corticosteroid injections versus physiotherapy for treatment of painful stiff shoulder in primary care: randomised trial. BMJ. 1998;317:1292-1296. https://doi.org/10.1136/bmj.317.7168.1292
- **63.** Vermeulen HM, de Bock GH, van Houwelingen HC, et al. A comparison of two portable dynamometers in the assessment of shoulder and elbow strength. 2005;91:101-112. https://doi.org/10.1016/j.physio.2004.08.005
- **64.** Vicenzino B. Masterclass: Lateral epicondylalgia: a musculoskeletal physiotherapy perspective. *Manual Therapy*. 2003;8:66-79. https://doi. org/10.1016/S1356-689X(02)00157-1
- 65. Vuvan V, Vicenzino B, Mellor R, Heales LJ, Coombes BK. Unsupervised isometric exercise versus wait-and-see for lateral elbow tendinopathy. *Med Sci Sports Exerc*. 2020;52:287-295. https://doi.org/10.1249/ MSS.00000000000002128
- 66. Yasuda T, Fukumura K, lida H, Nakajima T. Effects of detraining after blood flow-restricted low-load elastic band training on muscle size and arterial stiffness in older women. SpringerPlus. 2015;4:348. https://doi.org/10.1186/s40064-015-1132-2
- 67. Yasuda T, Ogasawara R, Sakamaki M, Ozaki H, Sato Y, Abe T. Combined effects of low-intensity blood flow restriction training and high-intensity resistance training on muscle strength and size. Eur J Appl Physiol. 2011;111:2525-2533. https:// doi.org/10.1007/s00421-011-1873-8



APPENDIX

DESCRIPTION OF THE INTERVENTIONS PROVIDED IN PATIENTS WITH LATERAL ELBOW TENDINOPATHY

The management of all patients with lateral elbow tendinopathy (LET) included the following:

- (a) massage,
- (b) advice and education,
- (c) supervised exercises, and
- (d) a home exercise program by providing an exercise instruction booklet.

A. Massage

A course of massage was applied on the soft tissues of the elbow around the lateral epicondyle and the wrist extensors for 7-8 minutes. Deep pressure and mobilization techniques of the soft tissue were provided with a pain monitoring approach (acceptable pain <2 out of 10).

B. Advice and education

Education:

- Pain and disability are not related to changes in the tendons (imaging), which means that improvement will be seen regardless of whether the tendon structure changes or not in imaging.
- The main goal of the therapeutic program is to increase the endurance of the muscles around the elbow and wrist and, subsequently, to improve their ability to do repetitive tasks without pain and to sustain higher load.
- In order to achieve this goal, they should follow the exercises provided, which contain stretching and strengthening of the muscles attached to the tendon and other muscles as well as tendons of the upper limb, which will help and promote the healing process.
- The main aim of the process is to improve function and return to daily activities, sports, and other recreational activities.
- The therapeutic approach should last at least 6-12 weeks, while it might be necessary to continue the exercises for a longer time after the completion of the treatment plan to maintain health of their elbow.

Advice:

- Pain should be avoided during activities, positions, or exercises.
- It would be better to carry objects with the palm up and close to the body (elbow flexed).
- Decrease manual work/activities/sports during the therapeutic program.
- Do not fully unload the tendon.

APPENDIX (CONTINUED)

C. Supervised exercises Determining 1 repetition maximum (RM) for elbow flexors and extensors





After warming up, the load was set at 80% of the predicted 1 RM. Following each successful repetition, the load was increased from 0.5-1 kg until the patients failed to execute the exercise through the entire range of motion, used improper form to complete the repetition, needed assistance, and reported pain. We have allowed 2-3 minutes of rest between each attempt to ensure recovery.1

BFR application



Each session started with determining arterial occlusion pressure in the standard anatomical position.² Participants rested in the standing position for 3-5 minutes before measurement to ensure restoration of blood flow circulation, and a cuff was placed in the most proximal part of their painful upper-limb. BFR application was conducted by using an automatic personalized tourniquet system (Mad-Up Pro, France).

APPENDIX (CONTINUED)

Supervised low-load resistance training (LLRT) with blood flow restriction (BFR) program (biweekly for 6 weeks)

1st Stage

For LLRT-BFR, 40%-50% of arterial occlusion pressure with intermittent application was used.

For sham LLRT-BFR, a <20% of arterial occlusion pressure with the cuff minimally inflated to the point that were comfortably positioned on the proximal site of the limb (with enough room for 2 fingers between the cuff and the skin).³



Elbow Flexion (concentric-eccentric), 30% of 1 RM using dumbbells, 4 sets (30-15-15-15 repetitions).



Elbow Extension (concentric-eccentric), 30% of $1\,\mathrm{RM}$ using dumbbells, $4\,\mathrm{sets}$ (30-15-15-15 repetitions).

APPENDIX (CONTINUED)



Wrist flexion (concentric-eccentric), 3 sets of 10 repetitions, minimum free weight using a pain-monitoring approach (acceptable pain during the exercise: <2 out of 10).



Wrist supination-pronation (concentric-eccentric), 3 sets of 10 repetitions, minimum free weight using a pain-monitoring approach (acceptable pain during the exercise: <2 out of 10).



Wrist extension (concentric-eccentric), 3 sets of 10 repetitions, minimum free weight using a pain-monitoring approach (acceptable pain during the exercise: <2 out of 10).

APPENDIX (CONTINUED)



Static stretching exercises of wrist extensors (3 times × 30 seconds).

Pace: 2-second concentric and 2-second eccentric phases using a metronome.

Break between sets: 30 seconds.

Break between exercises: 1-minute (the cuff was deflated).

Progression: Load was increased weekly from 0.5-1 kg using a pain-monitoring approach (acceptable pain during the exercise: <2 out of 10)



Static stretching exercises of wrist flexors (3 times × 30 seconds).

APPENDIX (CONTINUED)

2nd Stage

(After at least 2 weeks of training and if patients did not report pain with 1st stage exercises)

All 1st-stage exercises with wrist flexion, extension, and supination exercises performed with a fully straightened elbow and the arm lifted so that it is no longer supported. Additional exercises:



Wall push-ups, 3 sets of 10 repetitions, (concentric-eccentric), using a pain-monitoring approach (acceptable pain during the exercise: <2 out of 10).

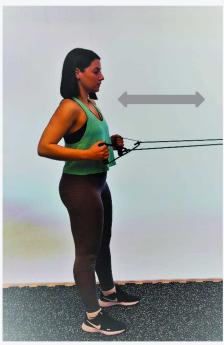


Wrist extension-flexion using a rubber bar, 3 sets of 10 repetitions, using a pain-monitoring approach (acceptable pain during the exercise: <2 out of 10).

APPENDIX (CONTINUED)



Hand grip using a soft ball, 3 sets of 10 repetitions using a pain-monitoring approach (acceptable pain during the exercise: <2 out of 10).



Standing row with a TheraBand, 3 sets of 10 repetitions using a pain-monitoring approach (acceptable pain during the exercise: <2 out of 10).

APPENDIX (CONTINUED)

D. Home exercise program

Guidelines:

- > Keep 30-second breaks between sets.
- > Keep a 1-minute break between different exercises.
- > Perform your exercises every second day.
- > Hold up and down for 2 counts during each repetition.
- Use minimum free weight with acceptable pain during the exercise less than 2 out of 10.
- > If pain is more than 2 out of 10 during an exercise, then use less load or no load.
- > If pain persists after exercise, communicate with your physiotherapist.

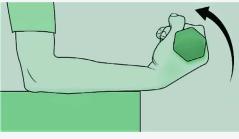


Elbow Flexion

Stand up straight. Hold a hand weight next to your body with your elbow in contact with your ribs. Bend your elbow and lift the weight up to your shoulder.

4 sets (30-15-15-15 repetitions).

Load:....kg



Wrist flexion

Support your forearm on a table with the flexed elbow in 90°. Your palm should face up. Bend your wrist up as far as you can reach.

3 sets × 10 repetitions.

Load:....kg

Progression: straighten your elbow and lift your arm so that it is no longer supported.

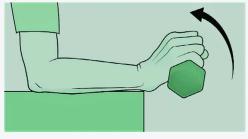


Elbow Extension

Stand up straight. Hold a hand weight over your head. Straighten your elbow and lift the weight up until the elbow is fully extended. Do not move your shoulder during elbow extension.

4 sets (30-15-15-15 repetitions).

Load:....kg



Wrist extension

Support your forearm on a table with the flexed elbow in 90°. Your palm should face down.

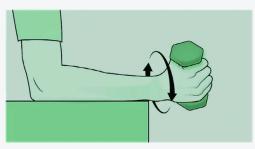
Bend your wrist up as far as you can reach.

3 sets × 10 repetitions.

Load:....kg

Progression: straighten your elbow and lift your arm so that it is no longer supported.

APPENDIX (CONTINUED)

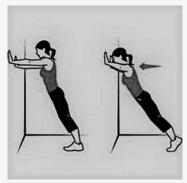


Wrist supination-pronation

Support your forearm on a table with the flexed elbow in 90° . Your palm should face down. Slowly turn the palm facing up and then return back to the starting position. 3 sets \times 10 repetitions

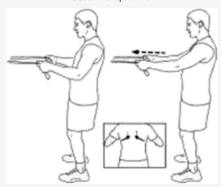
Load:....kg

Progression: straighten your elbow and lift your arm so that it is no longer supported.



Wall push-ups

Position your arms on a wall. Bend your elbows so you can nearly touch your nose to the wall, and then straighten your elbows. $3 \text{ sets} \times 10 \text{ repetitions}.$



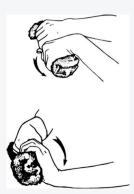
Rowing exercise with TheraBand

Stand holding the band with your elbows bent parallel to your body. Pull your elbows back and return to the starting position. $3 \text{ sets} \times 10 \text{ repetitions}.$



Hand grip with a soft ball

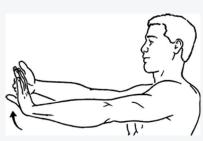
 $3\ sets\times 10\ repetitions.$ Start with elbow flexed and progress by straightening your elbow.



Wrist flexion-extension with a towel

 $\label{eq:wing} Wring a towel and twist downward-upward. \\ 3 sets \times 10 \ repetitions.$ Start with elbows flexed and progress by straightening your elbows.

APPENDIX (CONTINUED)

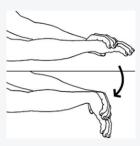


Wrist flexors stretching

Straighten your affected elbow with your palm facing up. Using the unaffected arm, bend backward your wrist gently.

3 repetitions × 30 seconds.

This should be performed at the end of the exercise program.



Wrist extensors stretching

Straighten your affected elbow with your palm facing down. Using the unaffected arm bend forward your wrist gently.

3 repetitions × 30 seconds.

This should be performed at the end of the exercise program

- 1 Abe T, Kearns CF, Sato Y. Muscle size and strength are increased following walk training with restricted venous blood flow from the leg muscle, Kaatsu-walk training. *J Appl Physiol.* 2006;100:1460-1466. https://doi.org/10.1152/japplphysiol.01267.2005
- 2 Karanasios S, Koutri C, Moutzouri M, Xergia SA, Sakellari V, Gioftsos G. The effect of body position and the reliability of upper limb arterial occlusion pressure using a handheld Doppler ultrasound for blood flow restriction training. Sports Health. 2021;14(5). https://doi.org/10.1177/19417381211043877
- 3 Giles L, Webster KE, McClelland J, Cook JL. Quadriceps strengthening with and without blood flow restriction in the treatment of patellofemoral pain: a double-blind randomised trial. Br J Sports Med. 2017;51:1688-1694. https://doi.org/10.1136/bjsports-2016-096329

APPENDIX TABLE 1

MAIN EFFECTS AND INTERACTION, AND COVARIATE SIGNIFICANT EFFECTS (P VALUES)^a

Outcome	Intervention	Time	Intervention × Time	Covariates ^b
Pain intensity (0-10)	0.183	<0.001	0.014	0.045 (symptoms duration)
PRTEE score	0.014	<0.001	<0.001	0.007 (symptoms duration)
PFGS ratio	0.11	<0.001	<0.001	0.003 (symptoms duration)
Elbow flexors ratio	0.03	0.9	0.073	0.025 (symptoms duration)
(affected/unaffected side)				
Elbow extensors ratio	0.7	0.65	0.13	>0.05 (all)
(affected/unaffected side)				
Tendon thickness capitellar (mm)	0.105	<0.001	0.522	>0.05 (all)
Tendon thickness	0.108	<0.001	0.212	>0.05 (all)
radio-capitellar (mm)				

Abbreviations: PRTEE, patient-rated tennis elbow evaluation; PFGS, pain-free grip strength.

 $^{{}^{\}mathtt{a}} Bold\ indicates\ statistical\ significance;\ results\ were\ analyzed\ using\ an\ intention\mbox{-}to\mbox{-}treat\ analysis.}$

 $^{{}^{\}mathrm{b}}Significant\ covariate\ effects.$

APPENDIX TABLE 2

SECONDARY OUTCOMES AT EACH DATA COLLECTION TIME POINT

	LLRT-BFR Group ^a	LLRT-With-Sham-BFR Group ^a	Between-Group Differences ^b	P Value
Elbow flexors ratio (Affected/ unaffected side)				0.073°
Baseline	$0.97 \pm 0.17 (0.90 \text{to} 1.05)$	0.93 ± 0.23 (0.85 to 1.05)	-	-
6th week	$1.09 \pm 0.17 (1.02 \text{to} 1.17)$	$0.89 \pm 0.17 (0.81 \text{to} 0.97)$	0.2 ± 0.05 (0.08 to 0.31) $d = 1.2$	0.001^{d}
12th week	1.07 ± 0.11 (1.05 to 1.15)	$0.92 \pm 0.17 (0.84 to 1.0)$	0.15 ± 0.05 (0.04 to 0.27) $d = 0.9$	0.009^{d}
Change from baseline to 6 weeks	-0.11 ± 0.05 (-0.23 to -0.006), $d = 0.55$	0.03 ± 0.05 (-0.07 to 0.15), $d = 0.23$	-	-
Change from 6 to 12 weeks	-0.01 (-0.09 to 0.13), $d = 0.05$	-0.02 ± 0.05 (-0.14 to 0.8), $d = 0.08$	-	-
Change from baseline to 12 weeks	-0.09 (-0.21 to 0.01), $d = 0.45$	0.1 ± 0.05 (-0.1 to 0.12), $d = 0.76$	-	-
Elbow extensors ratio (Affected/ unaffected side)				0.137°
Baseline	$0.92 \pm 0.24 (0.82 \text{to} 1.03)$	$0.97 \pm 0.25 (0.86 \text{to} 1.08)$	-	-
6th week	1.08 ± 0.23 (0.98 to 1.19)	0.98 ± 0.24 (0.87 to 1.09)	0.1 ± 0.07 (-0.05 to 0.26), $d = 0.43$	0.205^{d}
12th week	1.02 ± 0.23 (0.91 to 1.12)	$1.01 \pm 0.24 (0.89 \text{to} 1.11)$	0.02 ± 0.08 (-0.14 to 0.18), $d = 0.08$	0.797 ^d
Change from baseline to 6 weeks	-0.16 ± 0.06 (-0.28 to -0.04), $d = 0.84$	-0.01 ± 0.06 (-0.13 to 0.11), $d = 0.03$	-	-
Change from 6 to 12 weeks	0.06 ± 0.05 (-0.05 to 0.18), $d = 0.31$	0.01 ± 0.06 (-0.14 to 0.1), $d = 0.01$	-	-
Change from baseline to 12 weeks	0.09 ± 0.05 (-0.21 to 0.02), $d = 0.47$	-0.02 ± 0.06 (-0.15 to 0.09), $d = 0.07$	-	-
Tendon thickness capitellar (mm)				0.522°
Baseline	5.75 ± 1.23 (5.22 to 6.28)	6.2 ± 1.22 (5.67 to 6.73)	-	-
6th week	$5.28 \pm 1.2 \ (4.74 \ to \ 5.81)$	6.0 ± 1.17 (5.46 to 6.53)	-0.72 ± 0.37 (-1.47 to 0.03), $d = 0.69$	0.06^{d}
12th week	$5.18 \pm 1.2 (4.64 \text{to} 5.71)$	5.82 ± 1.18 (5.21 to 6.28)	-0.56 ± 0.37 (-1.32 to 0.18), $d = 0.54$	0.138^{d}
Change from baseline to 6 weeks	0.47 ± 0.2 (0.05 to 0.88), $d = 0.36$	0.2 ± 0.2 (-0.21 to 0.61), $d = 0.16$	-	-
Change from 6 to 12 weeks	0.1 ± 0.2 (-0.3 to 0.5), $d = 0.09$	0.25 ± 0.2 (-0.16 to 0.67), $d = 0.2$	-	-
Change from baseline to 12 weeks	0.57 ± 0.2 (0.16 to 0.98), $d = 0.44$	0.45 ± 0.2 (0.04 to 0.87), $d = 0.37$	-	-
Tendon thickness radio-capitellar (mm)				0.212°
Baseline	5.68 ± 0.83 (5.32 to 6.04)	$5.86 \pm 0.8 (5.5 \text{to} 6.2)$	-	-
6th week	5.12 ± 0.82 (4.82 to 5.55)	$5.68 \pm 0.75 $ (5.31 to 6)	-0.49 ± 0.26 (-1.01 to 0.02), $d = 0.57$	0.06^{d}
12th week	$5.04 \pm 0.82 \ (4.67 \ to \ 5.4)$	5.49 ± 0.81 (5.13 to 5.87)	-0.46 ± 0.25 (-0.98 to 0.05), $d = 0.53$	0.079^{d}
Change from baseline to 6 weeks	0.49 ± 0.16 (0.15 to 0.83), $d = 0.55$	0.17 ± 0.16 (-0.16 to 0.52), $d = 0.2$	-	-
Change from 6 to 12 weeks	0.14 ± 0.16 (-0.19 to 0.48), $d = 0.15$	0.18 ± 0.16 (-0.16 to 0.52), $d = 0.21$	-	-
Change from baseline to 12 weeks	0.64 ± 0.16 (0.30 to 0.98), $d = 0.72$	0.36 ± 0.17 (0.01 to 0.70), $d = 0.42$	-	-

 $Abbreviations: BFR, blood flow\ restriction; LLRT-BFR, low-load\ resistance\ training\ with\ blood\ flow\ restriction.$

 $^{^{\}mathrm{a}}Values$ are means and 95% confidence intervals.

 $^{{}^{\}mathrm{b}}Values\ in\ parenthesis\ are\ 95\%\ confidence\ intervals.$

Intervention imes time

 $^{^{\}mathrm{d}}\!Adjustments$ were performed for post hoc multiple comparisons (Bonferroni).

APPENDIX TABLE 3

PRIMARY OUTCOMES AT EACH DATA COLLECTION TIME POINT IN AN INTENTION-TO-TREAT SENSITIVITY ANALYSIS

	LLRT-BFR Group ^a	LLRT-With-Sham-BFR Group ^a	Between-Group Differences ^c	Odds Ratio ^c	P Value
Pain intensity (0-10)					0.047 ^d
Baseline	7.22 (6.18 to 8.26)	6.77 (5.74 to 7.8)	-	-	-
6th week	3.52 (2.53 to 4.61)	4.77 (3.73 to 5.81)	-1.2 (-2.7 to 0.30), $d = 0.54$	-	0.124e
12th week	1.94 (0.9 to 2.98)	3.68 (2.6 to 4.72)	-1.74 (-3.27 to -0.2), $d = 0.79$	-	0.026
Baseline-6 weeks	3.64 (2.15 to 5.14), <i>d</i> = 1.56	2.0 (0.51 to 3.49), d = 0.91	-	-	-
6-12 weeks	1.62 (0.13 to 3.11), d = 0.69	1.09 (2.4 to -0.4), $d = 0.0.5$	-	-	-
Baseline-12 weeks	5.27 (3.78 to 6.78), d = 2.26	3.36 (1.91 to 4.81), d = 1.61	-	-	-
PRTEE score					<0.001d
Baseline	39.08 (32.9 to 45.2)	37.05 (30.89 to 43.22)	-	-	-
5th week	13.25 (7.08 to 19.41)	26.22 (20.06 to 32.29)	-12.97 (-22.11 to -2.84), $d = 0.95$	-	0.006
12th week	6.27 (0.1 to 12.43)	21.74 (15.58 to 27.91)	-15.47 (-24.61 to -6.33), $d = 1.14$	-	<0.001e
Baseline-6 weeks	25.83 (17.9 to 33.76), d = 1.84	10.83 (2.9 to 18.76), d = 0.83	-	-	-
5-12 weeks	6.97 (-0.95 to 14.9), d = 0.49	4.48 (-3.454 to 12.4) d = 0.34	-	-	-
Baseline-12 weeks	32.8 (24.8 to 40.73), d = 2.33	15.31 (7.38 to 23.24), d = 1.17	-	-	-
PFGS ^b					<0.001 ^d
Baseline	0.70 (0.60 to 0.80)	0.76 (0.66 to 0.86)	-	-	-
5th week	0.93 (0.83 to 1.03)	0.73 (0.63 to 0.83)	0.20 (0.05 to 0.34), d = 0.83	-	0.01e
12th week	0.91 (0.81 to 1.01)	0.82 (0.72 to 0.92)	0.09 (-0.05 to 0.24) d = 0.37	-	0.21e
Baseline-6 weeks	-0.22 (-0.32 to -0.12), $d = 0.91$	0.02 (-0.07 to 0.12), $d = 0.08$	-	-	-
6-12 weeks	0.02 (-0.08 to 0.11), $d = 0.08$	-0.08 (-0.18 to 0.01) $d = 0.3$	-	-	-
Baseline-12 weeks	0.2 (-0.3 to -0.1), d = 0.83	-0.05 (-0.15 to 0.04), $d = 0.2$	-	-	-

 $Abbreviations: BFR, blood\ flow\ restriction; LLRT-BFR; low-load\ resistance\ training\ with\ blood\ flow\ restriction; PRTEE,\ patient-rated\ tennis\ elbow\ evaluation; PFGS,\ pain\ free\ grip\ strength.$

 $^{^{\}mathrm{a}}Values~are~means~and~95\%~confidence~intervals.$

^bValue expressed as a ratio to the unaffected side.

 $^{^{\}circ}Values~in~parenthesis~are~95\%~confidence~intervals.$

 $^{^{\}mathrm{d}}Intervention \times time.$

 $^{{}^{\}rm e}\!Adjust ments\ were\ performed\ for\ post\ hoc\ multiple\ comparisons\ (Bonferroni).$