STUDY PROTOCOL
AND
STATISTICAL ANALYSIS PLAN

Official Title:

Comparison of the Effectiveness of Blood Flow Restriction Exercise and Eccentric Exercise in Patients Diagnosed with Lateral Epicondylitis: A Randomized Controlled Trial

NCT Number: [To be assigned]

Document Date: May 2026

Protocol Version: 1.0 (October 2021)

Ethics Approval: 2021/28-31 (13 October 2021)

Study Status: Completed

Enrollment Period: November 2021 – October 2024

This document does not contain the names of research participants.

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1. STUDY SYNOPSIS

Study Title	Comparison of the Effectiveness of Blood Flow Restriction Exercise and Eccentric Exercise in Patients Diag
Study Design	Prospective, randomized controlled trial, three parallel groups
Study Site	Dokuz Eylul University, Department of Orthopedics and Traumatology, Izmir, Turkey
Study Population	Patients aged 18 years and older diagnosed with unilateral lateral epicondylitis
Sample Size	27 patients (9 per group)
Intervention Groups	Group 1: Blood flow restriction exercise (BFRE) + stretching + orthosis Group 2: Eccentric exercise + stretching + orthosis Group 3: Orthosis + stretching only
Treatment Duration	6 weeks
Primary Outcome	Pain intensity (Visual Analog Scale, 0-10 cm)
Secondary Outcomes	Hand grip strength (JAMAR dynamometer, kg) Pinch strength (Pinch meter, kg) Upper extremity function (DASH questionnaire, 0-100)
Assessment Time Points	Baseline and 6 weeks
Statistical Methods	Mixed model ANOVA, paired t-tests, one-way ANOVA
Ethics Approval	Dokuz Eylul University Non-Interventional Research Ethics Committee, No: 2021/28-31, Date: 13 October
Enrollment Period	November 2021 – October 2024
Study Completion	October 2024

2. BACKGROUND AND RATIONALE

Lateral epicondylitis (tennis elbow) is a musculoskeletal disorder characterized by pain and tenderness at the lateral epicondyle of the elbow, affecting approximately 1–3% of the general population. The condition results from degenerative changes in the extensor carpi radialis brevis (ECRB) tendon caused by repetitive microtrauma.

Eccentric exercise has been widely recommended as a first-line conservative treatment. However, eccentric protocols typically require loading at 70% or more of one-repetition maximum (1-RM), which may not be tolerated by patients experiencing significant pain.

Blood flow restriction exercise (BFRE) is a training method involving the application of external pressure to the proximal limb using pneumatic cuffs, partially restricting arterial flow and completely restricting venous return during low-load resistance exercise (20–40% of 1-RM). BFRE has demonstrated effectiveness in various musculoskeletal conditions but evidence for lateral epicondylitis remains limited.

This study was designed to compare the effectiveness of BFRE with eccentric exercise and standard orthosis treatment in lateral epicondylitis.

3. STUDY OBJECTIVES AND HYPOTHESES

Primary Objective: To compare the effectiveness of BFRE, eccentric exercise, and orthosis use on pain reduction in patients with lateral epicondylitis.

Secondary Objectives: To compare the effects of the three interventions on hand grip strength, pinch strength, and upper extremity functional disability.

Hypotheses:

H0: There is no difference between BFRE, eccentric exercise, and orthosis groups in terms of functional level, pain, and grip strength.

H1: BFRE has a significant effect on functional level, pain, gross and fine grip strength in patients with lateral epicondylitis.

H2: Eccentric exercise has a significant effect on functional level, pain, gross and fine grip strength compared with BFRE in patients with lateral epicondylitis.

4. STUDY DESIGN

This study was designed as a prospective, three-arm, parallel-group, randomized controlled trial. Patients were randomly allocated to one of three treatment groups using block randomization. Assessments were performed at baseline (pre-treatment) and at the end of the 6-week intervention period (post-treatment).

5. STUDY POPULATION

5.1 Inclusion Criteria

1. Clinical diagnosis of lateral epicondylitis confirmed by an orthopedic surgeon
2. Age 18 years or older
3. Unilateral lateral epicondylitis
4. Signed written informed consent form

5.2 Exclusion Criteria

1. Bilateral lateral epicondylitis
2. Cervical radiculopathy
3. History of elbow, forearm, or wrist pathology (previous surgery, tendon rupture, fracture, osteoporosis, neurological involvement, nerve paralysis)
4. Physiotherapy within the preceding 6 weeks
5. Malignancy
6. Cardiac arrhythmia, pacemaker use, coagulation disorders, anticoagulant therapy, or history of deep vein thrombosis
7. Systemic or neurological disease
8. Peripheral vascular disease or endothelial dysfunction
9. Conditions associated with endothelial dysfunction (uncontrolled hypertension, cardiovascular disease, systemic inflammation, obesity, diabetes, atherosclerosis)
10. Active infection

6. INTERVENTIONS

6.1 Group 1 — Blood Flow Restriction Exercise (BFRE)

Arterial occlusion pressure (AOP) was individually determined using a pneumatic cuff and pulse oximetry (Zeng et al., 2019). Cuff pressure was gradually increased until the pulse and SpO2 waveform disappeared on the pulse oximeter, which was recorded as AOP.

Exercise was performed at 30% of individually determined AOP. A sphygmomanometer cuff was applied to the proximal upper arm. Pressure was maintained throughout exercise sets and rest intervals. Exercise load was set at 30% of 1-RM.

Protocol: 3 sets x 15 repetitions, 1-minute rest between sets, twice weekly for 6 weeks.

Stretching: 3 repetitions x 30 seconds before and after each session (45-second rest between stretches).

Non-exercise days: Home stretching program 2 times/day, 3 repetitions x 30 seconds.

Orthosis: Wrist extension orthosis (15–20 degrees) worn throughout the study.

6.2 Group 2 — Eccentric Exercise

Slow eccentric wrist extensor exercises were performed with the elbow in full extension and forearm in pronation. From a wrist extension position, the weight was slowly lowered into flexion over approximately 30 seconds.

Protocol: 3 sets x 10 repetitions, 1-minute rest between sets, five times weekly for 6 weeks, at 70% of 1-RM.

Stretching and orthosis protocols were identical to Group 1.

Non-exercise days: Home stretching program 2 times/day, 3 repetitions x 30 seconds.

6.3 Group 3 — Orthosis (Reference Standard Conservative Treatment)

Participants wore a wrist extension orthosis maintaining 15–20 degrees of extension throughout the day, removing it only during sleep, bathing, and stretching exercises.

Stretching: Home stretching program 2 times/day, 3 repetitions x 30 seconds.

6.4 Exercise Progression

Exercise protocols were kept constant throughout the 6-week period without progression. This decision was based on: (1) the risk of exacerbating tendon symptoms with rapid progression; (2) ensuring standardized comparison across groups; (3) allowing sufficient time for tendon adaptation; and (4) improving patient compliance by reducing protocol complexity.

6.5 Stretching Protocol (All Groups)

Shoulder at 90 degrees flexion, elbow in full extension, forearm in pronation, wrist in flexion and ulnar deviation. The contralateral hand was used to apply a sustained stretch for 30 seconds, repeated 3 times with 45-second rest intervals.

7. OUTCOME MEASURES

7.1 Primary Outcome

Visual Analog Scale (VAS): A 10-cm horizontal line where 0 = no pain and 10 = worst imaginable pain. Patients marked their current pain level. Assessed at baseline and 6 weeks.

7.2 Secondary Outcomes

Hand Grip Strength: Measured using a JAMAR hydraulic hand dynamometer (kg). Standardized position: elbow at 90 degrees flexion, forearm in neutral. Mean of 3 consecutive trials recorded.

Pinch Strength: Measured using a pinch meter (kg). Three pinch types assessed: lateral, palmar, and tip-to-tip. Mean of 3 trials across all types recorded.

DASH Questionnaire: Disabilities of the Arm, Shoulder and Hand. 30-item self-report questionnaire scored 0 (no disability) to 100 (maximum disability). Turkish validated version used.

8. SAMPLE SIZE CALCULATION

Sample size was calculated using G*Power software (version 3.1.9.4, Faul et al., 2007).

Parameters: Effect size = 1.8 (based on previously reported pain reduction rates in lateral epicondylitis exercise studies); Type I error rate alpha = 0.05; Statistical power = 95% (1 - beta = 0.95).

Result: Minimum 9 participants per group, total N = 27.

9. RANDOMIZATION

Participants were allocated using block randomization with blocks of nine. Each block contained three assignments for each group (BFRE, Eccentric, Orthosis), ensuring equal distribution. Randomization was performed by a researcher not involved in patient assessment or treatment delivery.

10. DATA COLLECTION PROCEDURES

All outcome measures were assessed by the same examiner at two time points: baseline (before initiation of treatment) and at the end of the 6-week intervention period.

JAMAR dynamometer and pinch meter measurements were performed according to the American Society of Hand Therapists (ASHT) standardized protocols. Three consecutive measurements were recorded for each strength test, with 30-second rest intervals between trials.

Home exercise adherence was monitored using exercise diaries. Patients recorded the date, number of sets and repetitions, and pain level for each session. Diaries were reviewed during weekly clinical sessions.

For the BFRE group, SpO2 monitoring was performed throughout each session for safety.

11. STATISTICAL ANALYSIS PLAN

11.1 Software

All analyses were performed using IBM SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA).

11.2 Descriptive Statistics

Continuous variables: mean +/- standard deviation (SD). Categorical variables: frequency (n) and percentage (%).

11.3 Normality Testing

The Shapiro-Wilk test was used to assess normality of data distribution, as recommended for small sample sizes ($n < 50$). Visual assessment was also performed using histograms and Q-Q plots.

11.4 Baseline Comparisons

One-way ANOVA was used to compare baseline demographic and clinical characteristics across the three groups. This was performed to verify successful randomization and ensure no significant pre-existing differences.

11.5 Primary Analysis — Time x Group Interaction

Mixed model ANOVA (repeated measures ANOVA with between-subjects factor) was used as the primary analytical method. This approach simultaneously evaluates:

- Within-subjects effect (time: pre vs. post-treatment)
- Between-subjects effect (group: BFRE vs. Eccentric vs. Orthosis)
- Time x Group interaction (differential treatment effects)

The time x group interaction was the primary focus, testing whether one treatment method produced a statistically significantly different rate or magnitude of improvement compared to the others.

11.6 Within-Group Comparisons

Paired t-tests were used to compare pre- and post-treatment values within each group. This analysis assessed the statistical significance of change for each intervention separately.

11.7 Post-Hoc Analyses

When significant differences were detected by ANOVA, post-hoc pairwise comparisons were performed to identify the source of the difference.

11.8 Significance Level

The significance level was set at $p < 0.05$ for all analyses (two-tailed).

11.9 Effect Size and Percentage Change

Percentage change from baseline was calculated for each outcome measure within each group to provide clinically interpretable effect magnitudes: [(Post - Pre) / Pre] x 100.

11.10 Handling of Missing Data

All 27 enrolled patients completed the 6-week protocol. There were no dropouts or missing data. Therefore, no imputation methods were required.

11.11 Justification for Parametric Tests

Although several variables showed deviation from normality on the Shapiro-Wilk test, parametric tests (paired t-test, ANOVA) were used based on: (1) the robustness of these tests to moderate departures from normality; (2) most variables meeting normality criteria; and (3) the advantages of parametric methods for detecting treatment effects in small samples.

12. ETHICAL CONSIDERATIONS

This study was approved by the Dokuz Eylul University Non-Interventional Research Ethics Committee (approval number: 2021/28-31, date: 13 October 2021, File No: 6471-GOA).

The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment. Participants were informed about the study purpose, procedures, risks, and their right to withdraw at any time without consequences.

Personal data were kept confidential and used for research purposes only. No true control (untreated) group was included due to ethical considerations; the orthosis group received standard conservative treatment.

13. STUDY TIMELINE

Period	Activity
April 2021	Thesis proposal preparation and presentation
May – October 2021	Literature review and ethics committee application
October 2021	Ethics committee approval obtained
November 2021 – October 2024	Patient recruitment, assessments, and interventions
December 2024	Statistical analyses and results evaluation
January 2025 – January 2026	Thesis writing and defense preparation
January 20, 2026	Doctoral thesis defense

14. LIMITATIONS

1. Small sample size (n = 9 per group) limiting statistical power and generalizability.
2. Single-center study design limiting external validity.
3. Open-label design (no blinding of patients or therapist).
4. Short-term follow-up (6 weeks only, no long-term data).
5. No exercise progression applied during the 6-week protocol.
6. AOP determined by pulse oximetry rather than Doppler ultrasonography.
7. The trial was not prospectively registered in a clinical trial registry.

15. REFERENCES

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