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ABSTRACT

PURPOSE: This study aimed to investigate the effect of unsupervised isometric exercise compared to a wait-and-see approach on pain, disability, global improvement and pain-free grip strength in individuals with lateral elbow tendinopathy (LET). **METHODS:** Forty participants with unilateral LET of at least 6 weeks' duration were randomised to either wait-and-see (N=19) or a single supervised instruction session by a physiotherapist, followed by an 8-week unsupervised daily program of progressive isometric exercise (N=21). Primary outcomes were Patient-Rated Tennis Elbow Evaluation (PRTEE), global rating of change on a 6-point scale (GROC, dichotomised to success and no success) and pain-free grip strength at 8 weeks. Secondary outcomes were resting and worst pain on an 11-point numerical rating scale (NRS), and thermal and pressure pain thresholds as a measure of pain sensitivity. **RESULTS:** Thirty-nine (98%) participants completed 8-week measurements. The exercise group had lower PRTEE scores compared to wait-and-see at 8 weeks (standardised mean difference (SMD) -0.92, 95% CI -1.58 to -0.26). No group differences were found for success on GROC (29% exercise vs 26% wait-and-see (risk difference 2.3%, 95% CI -24.5 to 29.1)), or pain-free grip strength (SMD -0.33, 95% CI -0.97 to 0.30). No differences were observed for all secondary outcomes except for worst pain, which was moderately lower in the exercise group (SMD -0.80, 95% CI -1.45 to -0.14). **CONCLUSION:** Unsupervised isometric exercise was effective in improving pain and disability, but not perceived rating of change and pain-free grip strength when compared to wait-and-see at 8 weeks. With only one out of the three primary outcomes being significantly different following isometric exercises, it is doubtful if this form of exercise is efficacious as a sole treatment.

Keywords: Lateral epicondylalgia, tennis elbow, exercise, isometric, pain

INTRODUCTION

Lateral elbow tendinopathy (LET) is characterised by lateral elbow pain with manual tasks involving gripping. It is a common persistent pain condition of the upper limb (1) affecting 1-3% of the general population (2, 3), with tennis players (4) and workers involved in highly repetitive hand tasks (5, 6) at higher risk. Research indicates resistance exercise improves pain and function in LET, with most studies to date investigating the effects of isotonic (concentric and/or eccentric) exercises (7, 8).

Isometric exercise has recently been advocated as a means of pain relief in tendinopathy (9). Early promising results in this regard were reports of immediate pain relief in patellar tendinopathy with isometric exercise (10, 11). The only study of the immediate effects of isometric exercise in LET reported an increase in pain, not a decrease in pain immediately after exercise (12). This contrasts with findings from two studies in LET reporting beneficial effects of isometric exercise combined with eccentric-concentric exercise compared to exercise without isometric mode (4 and 8 weeks) (13), and isometric exercise compared to nonsteroidal medication (4 weeks) (14). There are two issues that arise with this body of work. First, the description of the exercise dose was incomplete in these studies, leaving question regarding the role of isometric exercise in LET (8). Second, Stasinopoulos and Stasinopoulos (13) did not study isometrics as a mono-therapy and Park et al. (14) compared isometrics to medication. This leaves unanswered what is the absolute effect of a program of isometrics (when compared to no treatment).

The primary aim of this study was to investigate the effect of an 8-week unsupervised program of isometric exercise compared to a wait-and-see approach on pain, disability, global improvement and pain-free grip strength in participants with unilateral LET. The secondary aim was to investigate its effect on pain sensitivity as a means of exploring possible mechanisms of any effect of isometric exercise. It was hypothesised that the unsupervised program of isometric exercise would be superior to a wait-and-see approach after 8 weeks.

METHODS

We performed a superiority randomised clinical trial to compare the effects of an 8-week unsupervised program of isometric exercise and a wait-and-see approach for participants with chronic unilateral LET. The trial was registered in the Australian New Zealand Clinical Trial Registry (ACTRN12615001136594). The trial had ethical approval by The University of Queensland Medical Research Ethics Committee (2015001134) and all participants provided written informed consent. Reporting of this trial follows CONSORT guidelines for reporting of randomized clinical trials (15) and the Consensus on Exercise Reporting Template (CERT) (16).

Participants

Participants were recruited from the greater Brisbane region of Australia between September 2015 and July 2017 through print and online advertisements. Participants underwent online and phone screening, with potentially eligible participants invited to The University of Queensland, Brisbane, Australia for a clinical examination. The assessor responsible for confirming inclusion and data collection was a registered physiotherapist with a Masters in Musculoskeletal Physiotherapy qualification and 9 years of clinical experience. Inclusion criteria were: age 18-70

years; unilateral lateral elbow pain ≥ 6 weeks duration; average pain severity during the past week ≥ 2 on a 11-point numerical rating scale (NRS, 0 = no pain, 10 = worst pain imaginable); provoked by at least 2 of: gripping, palpation of the lateral epicondyle, stretching of forearm extensor muscles, or resisted wrist, second or third finger extension; and reduced pain-free grip strength. Exclusion criteria were other primary sources of elbow pain (e.g. exacerbation of elbow pain with neck movements or manual palpation, pain localised over the radiohumeral joint, abnormal findings on neural examination); concomitant musculoskeletal pain conditions reported by participants to be their predominant complaint; major neurological, inflammatory or systemic conditions; treatment by a healthcare practitioner within the preceding 3 months; injections within the preceding 6 months; or major trauma, fracture or surgery in the last year.

Interventions

All participants received a 20-minute individualised session with the trial physiotherapist who had a postgraduate Master's degree-level qualification. Participants were provided written and verbal general advice regarding self-management and ergonomics. Participants assigned to the exercise group received additional information and advice to complete an unsupervised program of isometric exercise in a home setting for 8 weeks. The program consisted of daily isometric wrist extension exercise, performed using a container of water with a handle as resistance (see Figure, Supplemental Digital Content 1, which illustrates the water container used, <http://links.lww.com/MSS/B725>), and progressed weekly by adding water to the container or increasing the duration of exercise, according to standardised criteria. Table 1 details the exercise parameters as per Toigo and Boutellier (17). Participants were instructed to hold the water-filled container in the affected arm, with the forearm resting on the edge of a table (upper body in

sound postural alignment, elbow approximately 90° flexion, forearm pronated, wrist 30° extension). The other hand was used to lower the water container to the floor between sets. To determine the starting load, the maximal voluntary contraction (MVC) of the wrist extensors on the unaffected arm was measured using a digital force gauge (Chatillon DFX II, Ametek, USA). The force gauge was fitted with an identical handle to that of the water bottle and the upper limb position was similar to the exercise position. The unaffected arm was selected to determine a more accurate maximum load without provoking pain in the affected elbow. The starting load was equivalent to 20% MVC of the unaffected side and increased to 35% by week 7. Participants were instructed to add the equivalent of 5% MVC more water to the container each fortnight (week 3, 5, 7). To keep track of load progressions the water bottle was marked with a waterproof marker. On alternate weeks, to accommodate for increases in intensity (load), the time under tension (TUT) was alternated between 4 x 30 s isometric holds (TUT 120s) and 3 x 45 s isometric holds (TUT 135s). In order to reduce the risk of adverse events in an unsupervised exercise program, we adopted a standardised protocol that enabled a gradual, progressive increase in total exercise dose (Time x Intensity) each week (see Figure, Supplemental Digital Content 2, which illustrates weekly progression of total exercise dose, <http://links.lww.com/MSS/B726>). The exercise dose was based on pilot testing of 6 participants prior to the commencement of this study. In that pilot trial, we evaluated pain perception during a sustained isometric exercise task at 20% MVC and found an average pain rating of 34/100 at 30 seconds and four of the participants had reached 60/100 by 2 minutes.

Participants in the exercise group were asked to complete a paper-based daily exercise diary to record adherence to the prescribed load, duration and sets achieved, and to record symptoms

during and following exercise. For each exercise session, participants rated their perceived exertion on a category-ratio scale (RPE-CR10, 0 = nothing at all, 10 = extremely strong), and their pain intensity on a 11-point NRS. Participants also rated how long it took for their pain to settle after completion of each exercise session using a 5-point category scale (0 = 0-60s, 1 = 1-4.9min, 2 = 5-9.9min, 3 = 10-19min, 4 = 20-59min, 5 = $\geq$ 1hr). Participants were asked to send the exercise diaries to the trial physiotherapist at the end of each week to help monitor and improve adherence. Adherence to the exercise program was determined as the percentage of exercise sessions completed according to the exercise dose prescribed out of a possible 56 sessions.

Outcome measures

Outcome measures were collected at baseline and at the 8-week follow-up time point by an assessor blinded to treatment allocation. Primary outcome measures were the Patient-Rated Tennis Elbow Evaluation, which is a condition-specific, valid and reliable questionnaire of pain and disability that is sensitive to change (PRTEE, 0 = no pain or disability, 100 = worst pain or disability) (18, 19); global rating of change (from baseline) on a 6-point Likert scale (GROC, 6 = completely recovered, 5 = much improved, 4 = improved, 3 = same, 2 = worse, 1 = much worse); and pain-free grip strength (N) of the affected arm. Pain-free grip strength of the affected arm was measured using a digital grip dynamometer (MIE, Medical Research, UK). Participants were positioned in supine, with the arm in full elbow extension and forearm pronated and resting on the bed. Participants were instructed to grip the dynamometer at a consistent rate and to stop at the first onset of pain. Triplicate measures were collected with 30 second rest intervals and mean values used for analysis.

Secondary outcome measures were recorded in order to provide data and information that might direct further evaluation of potential underlying mechanism(s). These were related to pain severity and sensitivity (pressure and thermal pain thresholds), which have been shown to be features of LET (20, 21). Resting and worst pain in the past week was measured using an 11-point NRS. Pain thresholds were measured over the affected lateral epicondyle with the participant positioned in supine, with the elbow in flexion and hand resting on the abdomen. Pressure pain threshold (kPa) was measured using a hand-held digital algometer (probe size of 1cm²) (Somedic AB, Farsta, Sweden) with pressure applied at a rate of 40kPa/s (21). Cold and heat pain thresholds were measured initially using the Modular Sensory Analyzer (MSA) Thermotest (probe size of 12.5cm²) (Somedic AB, Farsta, Sweden). The PATHWAY applicant tracking system (ATS) (probe size of 9cm²) (MEDOC, Israel) was later used due to malfunction of the MSA Thermotest during the study. The baseline temperature was 32°C with temperature increase or decrease occurring at 1°C/s and cut-out temperatures of 5°C and 50°C (21). For all pain threshold tests the participants were instructed to press a button at the first onset of pain. Triplicate measures with 30 second rest intervals were collected for pain thresholds and mean values used for analyses.

Information on not per protocol treatments were collected during follow-up for both groups.

Randomisation

A computer-generated randomisation sequence was performed by a researcher not involved in data collection. Randomisation was stratified based on baseline worst pain ratings of 5 or less

(low pain) or 6 or more (high pain) on an 11-point NRS. Following baseline measurements, participants were randomly allocated using concealed opaque envelopes to either the exercise or wait-and-see group.

Sample size

Based on the assumption of a similar response of isometric exercise to that of a previous study of eccentric exercise (22), a sample size of 17 in each group was estimated to be sufficient to detect an effect size of 1 on the PRTEE, with 80% power ($\alpha = 0.05$). To allow for a 15% loss to follow-up, the sample size was increased to 20 per group.

Statistical analysis

Statistical analyses were performed on an intention-to-treat basis with Stata version 14 software (StataCorp, College Station, TX, USA). Testing was 2-sided with an alpha level set at $P < 0.05$. Continuous outcome measures were analysed using linear regression, with group allocation as the fixed factor, and baseline value of the outcome and stratifying variable of baseline pain as covariates. Standardised mean differences (SMD) were calculated using RevMan statistical software version 5.3 (Nordic Cochrane Centre, The Cochrane Collaboration) to illustrate the size of the treatment effect. A SMD between 0.2 and 0.6 was defined as a small effect, a SMD between 0.6 to 1.2 as a moderate effect, and a SMD of greater than 1.2 as a large effect (23). Responses on the GROC scale were dichotomised to success (much improved, completely recovered) or no success (much worse, worse, same, improved), consistent with other studies of LET (24, 25). The dichotomous measure of success was compared between groups using binary logistic regression adjusting for the stratifying variable of baseline pain. Risk difference (RD)

was used as the point estimate of the treatment effect and was modelled with logistic regression as the difference between the mean predicted probabilities. Sensitivity analyses of the GROC dichotomisation were performed to assess between-group differences when dichotomised to improved (improved, much improved, completely recovered) or not improved (much worse, worse, same), and on a per-protocol basis (e.g. by excluding participants that had other treatments).

RESULTS

533 volunteers responded to a public call for participants between September 2015 and July 2017 and were screened using an online survey and over the phone. Potential participants were then invited to the laboratory for a clinical examination. See figure 1 for participant flow and reasons for exclusions. In total, 40 participants met the eligibility criteria and agreed to participate, thus were randomised to the exercise group ($n = 21$) or wait-and-see group ($n = 19$). Follow-up at 8 weeks was completed by 39 (98%) of 40 participants. One participant in the exercise group was not available to attend the 8-week follow-up session. For this participant, the primary outcomes PRTEE and pain-free grip strength could not be collected, however a GROC score was obtained via telephone. Baseline characteristics were similar in the 2 groups (Table 2).

Primary outcomes

The exercise group had better PRTEE scores at 8 weeks compared to the wait-and-see group (SMD -0.92, 95% CI -1.58 to -0.26, $P = 0.006$) (Table 3). No difference was found between the exercise and wait-and-see group for rate of success on the GROC (29% (6/21) vs 26% (5/19), respectively; RD 2.3, 95% CI -24.5 to 29.1, $P = 0.866$) (Table 3, Figure 2). A sensitivity analysis

of the GROC dichotomised to improved or not improved showed an 86% (18/21) rate of improvement with isometric exercise compared to 63% (12/19) in the wait-and-see group, with the difference not being statistically significant (RD 22.6, 95% CI -1.3 to 46.6, $P = 0.086$). Interestingly, 3 participants reported worse on the GROC scale at 8 weeks in the exercise group compared to none in the wait-and-see group. No difference was observed between groups for pain-free grip strength of the affected arm (SMD -0.33, 95% CI -0.97 to 0.30, $P = 0.297$) (Table 3). Baseline pain levels as a stratifying variable did not influence these findings.

Secondary outcomes

At 8 weeks, worst pain was lower in the exercise group compared to the wait-and-see group (SMD -0.80, 95% CI -1.45 to -0.14, $P = 0.017$), whereas no difference was observed between groups for pain at rest (SMD -0.20, 95% CI -0.83 to 0.42, $P = 0.516$) (Table 3). No differences were observed between groups for pressure pain threshold (SMD -0.34, 95% CI -0.97 to 0.29, $P = 0.289$), cold pain threshold (SMD -0.06, 95% CI -0.69 to 0.57, $P = 0.849$) or heat pain threshold (SMD -0.24, 95% CI -0.87 to 0.38, $P = 0.454$) at the elbow (Table 3).

Exercise diaries were obtained from 20 (95%) of the 21 participants in the exercise group. Mean (SD) adherence to the exercise program was 87 (16) %, based on reported total number of sessions completed out of a possible 56 sessions. 18 of the 20 participants (90%) completed greater than 71% of prescribed sessions which is equivalent to 5 out of 7 sessions per week on average. Average pain experienced during exercise sessions, as well as time for pain to settle are summarised in Figure 3. The 3 participants in the exercise group who reported being worse at 8 weeks had an average pain score of 5, 4 and 4 out of 10 during exercise sessions. Of these

participants, 2 reported their pain settled on average 10-19 minutes and 1 reported on average 20-59 minutes after exercise. The remainder of participants in the exercise group reported a mean (SD) pain score of 1.9 (1.4) out of 10 during exercise sessions, and a median (IQR) time of 0-60 seconds (0-5 minutes) for their pain to settle on completion of exercise sessions.

No participants reported a serious adverse event. Use of co-interventions was similar between groups. An elbow brace was used by 6 participants in the exercise group and 5 participants in the wait-and-see group. Pain-relieving medication was used occasionally by 3 participants in each group. Other treatments were sought by 1 participant in the exercise group (massage) and 2 participants in the wait-and-see group (GP visit, physiotherapy). Results for per-protocol analyses (exclusion of the 3 participants who had other treatments) were consistent with those of the intention-to-treat analyses (Table 3).

DISCUSSION

This randomised controlled trial with assessor blinded outcomes demonstrated that isometric exercise on the whole is not better than wait-and-see when applied as a mono-therapy in persons with LET. Only one of the primary outcomes registered a significant difference. Isometric exercise resulted in less pain and disability (as measured by PRTEE), but there were no differences on GROC and pain-free grip strength. Interestingly, while there was a significant difference in pain intensity at 8 weeks, there was no difference in mechanical or thermal hyperalgesia.

The inconsistency in treatment effects across outcome measures may reflect the multidimensional domains of health. An accepted model of health, the International Classification of Functioning, Disability and Health (ICF) (26), indicates health and function can be influenced by 3 key domains: body structure and function, limitation in activity, and restriction in participation. Pain-free grip strength, mechanical and thermal hyperalgesia, which quantify the amount of gripping force, pressure, heat or cold before the onset of pain, represent one aspect of the body structure and function domain within the ICF i.e. sensitivity to noxious stimuli. In contrast, the PRTEE captures several aspects across the 3 key health domains with items on pain, limitation in specific activities and difficulty performing personal, work and recreational sporting activities (27, 28). Exercise showed moderate-sized effects on all PRTEE subscales (pain: SMD -0.75, 95% CI -1.40 to -0.10, $P = 0.024$; specific activities: SMD -0.86, 95% CI -1.52 to -0.20, $P = 0.010$; usual activities: SMD -1.05, 95% CI -1.72 to -0.37, $P = 0.002$). The secondary outcome of pain severity, which could also be categorized in the ICF body structure and function domain, was significantly different following isometric exercise. These findings suggest that isometric exercise may have an effect on a broad spectrum of pain and functional limitations that may not be linked to pain sensitivity.

There are several possible explanations for the lack of between-group differences observed on GROG. First, unlike the other outcome measures that are directed towards measuring change in a specific or limited domain of the patient's health status, the GROG allows patients themselves to decide on what factors they consider as representing overall improvement (29). The health aspects patients took into account when rating their improvement may have varied which may have influenced GROG outcomes. Second, the GROG (measured using a 6-point scale and

dichotomised to success and non-success) may have not been sufficiently sensitive to change. A sensitivity analysis showed a meaningful difference of 23% between groups when the GROC was dichotomised to improved and not improved, though not statistically significant (rate of improvement: 86% (18/21) with isometric exercise vs 63% (12/19) in the wait-and-see group). Third, it is highly plausible that an unsupervised program of isometric exercise may be insufficient for improving a person's overall perception of tendon-related health. This is supported by similar success rates for participants in the current trial (29% and 26% for exercise and wait-and-see groups, respectively) to those of the wait-and-see group in two larger clinical trials, measured at similar time points (i.e. 6-8 weeks) (27% in Bisset et al. (24) and 34% in Smidt et al. (30)). In a previous randomised clinical trial by Bisset et al. (24) the success rate (using GROC) at 6 weeks for a physiotherapy intervention, combining 8 thirty minute sessions of elbow manipulation and isotonic exercise was 65%. Other factors may explain the lack of benefit in the current study, including fewer clinician sessions (i.e. 1 compared to 8 sessions in the previous study), different exercise modes (i.e. isometric versus isotonic), and a mono versus multi-modal therapy (i.e. inclusion of manual therapy techniques) (24).

A comparison of the effects of isometric exercise on pain severity in the other two studies of isometric exercise can potentially provide some direction to its application in clinic (13, 14). Pain severity was significantly lower following exercise in all three studies. In the two studies that only included isometric exercise compared to effectively a control condition (wait-and-see, nonsteroidal medication) the differences were approximately the same and clinically meaningful at 2.1 points (11-point NRS) in the current study and 20 mm (100 mm VAS) in the study of Park et al. (14). Different exercise time under tension (TUT) and resistance were used in these studies.

The TUT for the current study was only 2 hours in total over 8 weeks compared to 11 and 16 hours over 4 weeks for the studies of Stasinopoulos and Stasinopoulos (13) and Park et al (14). Stasinopoulos and Stasinopoulos (13) had a total effective exercise TUT of 19 hours, which comprised of eccentric, concentric and isometric exercise. The TUT for isometric exercise was additional to the eccentric and concentric components. Another major difference was that the current study used an average resistance of 27.5% MVC, compared to hand limb segment lifts without any added resistance (i.e., gravity only) in the study of Park et al. (14), whilst the resistance was unspecified in the study of Stasinopoulos and Stasinopoulos (13). It would seem that isometric exercise done on average at 27.5% MVC for approximately 5 minutes of TUT per day is similar to 33 minutes per day against gravity in the study of Park et al. (14). Future research might evaluate further efficiencies in isometric exercise on pain severity (e.g., can load be increased at a greater rate and with less TUT). Nevertheless, our current protocol was not superior to wait-and-see on a range of measures (GROC, pain-free grip strength) and as such is likely not a first line mono-therapy.

A strength of our study is that it provides detailed description of the exercise intervention according to the Toigo and Boutellier mechanobiological exercise descriptors (17) and internationally endorsed Consensus on Exercise Reporting Template (CERT) (16). A progressive load was applied, commencing at 20% of MVC and increasing to 35% by week 6. This load was different to the average loads of our previous trial (38% and 55% MVC) in which we observed an acute increase in pain after exercise, not a decrease (12). We used different exercise doses because in the previous trial 10 sets of 10 second holds into pain (20% higher than pain threshold) resulted in 30 minutes of post exercise pain. We deemed this to be a barrier to

participants completing the 8 weeks of daily exercise in this study and thus devised a program that started at a lower level of resistance that with progressions would approximate the prior trial's loads. This current study showed that the loads we selected for this uni-modal exercise program were largely ineffectual in changing pain-free grip strength, GROC and pain sensitivity (hyperalgesia).

Although excellent adherence to the program and no serious adverse events were reported, 3 out of 21 participants in the exercise group reported feeling worse on the GROC compared to none in the wait-and-see group. Although speculative, we propose that symptom behaviour during and immediately following exercise may provide an early indicator of participants at risk of poor response. For example, pain intensity during exercise was higher for these 3 individuals and took longer for pain to settle after exercise. Although further research is needed to confirm these thresholds, a simple rule of thumb may be to adjust (lower) the dose of isometric exercise if the participant reports pain intensity during exercise of 3 or more (on a 11-point NRS) or if their pain lasts beyond 10 minutes after ceasing the exercise. More importantly, it is essential that participants who are prescribed an unsupervised exercise program be warned about possible aggravation of symptoms and to seek advice from their clinician should symptoms not improve over a 6 to 8-week period.

Our study has several limitations that should be taken into consideration. First, our study was powered to detect group differences on the PRTEE, and may have been underpowered to detect an effect of isometric exercise on GROC and pain-free grip strength. Notwithstanding this, it is unlikely that even with a larger sample size isometric exercises would effect change on these

outcomes because the point estimates of effect for success on GROC and pain-free grip strength were small. Second, given improvements in pain and disability but not overall rating of change and pain-free grip strength, isometric exercise may have had an effect on other factors not measured in this study, for example, pain self-efficacy. Third, many of the baseline measures indicate that our sample was reasonably non-severe LET. For example, mean PRTEE scores (mean (SD) 35.4 (13.0)) and cold pain threshold scores at baseline (mean (SD) 12.3 (8.6)) were low for the entire group, with 17 out of the 40 participants having cold pain thresholds below the cut-off temperature of 5°C, compared to the severe subgroup of LET in the study by Coombes et al. (21). Hence, our results may not be generalised to patients with severe LET. Fourth, 2 different probe sizes were used to measure thermal pain thresholds due to equipment malfunction which may have impacted the accuracy of study findings. This small difference in thermode size would at most lead to a 0.5°C difference in threshold (31, 32) and considering the small and imprecise differences we observed, it is unlikely to have impacted on our overall findings.

The isometric exercise program used in this study demonstrated some benefit on pain and disability for patients with LET, and was time-efficient and also of low cost (i.e. taking a total of <10 minutes per day and with the cost of a water flask approximately \$10). Research to directly compare a low-cost unsupervised exercise program with more intensive physiotherapy programs might lead to more broadly implementable treatment for LET. This should include studies that evaluate different sub-populations of LET for which isometric exercise is an optimal intervention, in line with a stratified approach to low back pain for which economic evaluations have shown cost-effectiveness (33, 34).

CONCLUSION

Unsupervised isometric exercise was effective in improving pain and disability, but not perceived rating of change and pain-free grip strength when compared to wait-and-see at 8 weeks. With only one out of the three primary outcomes being significantly different following isometric exercises, it is doubtful if this form of exercise is efficacious as a sole treatment.

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REFERENCES

1. Roquelaure Y, Ha C, Leclerc A, et al. Epidemiologic surveillance of upper-extremity musculoskeletal disorders in the working population. *Arthritis Rheum.* 2006;55(5):765-78.
2. Allander E. Prevalence, incidence, and remission rates of some common rheumatic diseases or syndromes. *Scand J Rheumatol.* 1974;3(3):145-53.
3. Shiri R, Viikari-Juntura E, Varonen H, Heliovaara M. Prevalence and determinants of lateral and medial epicondylitis: a population study. *Am J Epidemiol.* 2006;164(11):1065-74.
4. Gruchow HW, Pelletier D. An epidemiologic study of tennis elbow. Incidence, recurrence, and effectiveness of prevention strategies. *Am J Sports Med.* 1979;7(4):234-8.
5. Chiang HC, Ko YC, Chen SS, Yu HS, Wu TN, Chang PY. Prevalence of shoulder and upper-limb disorders among workers in the fish-processing industry. *Scand J Work Environ Health.* 1993;19(2):126-31.
6. Kurppa K, Viikari-Juntura E, Kuosma E, Huuskonen M, Kivi P. Incidence of tenosynovitis or peritendinitis and epicondylitis in a meat-processing factory. *Scand J Work Environ Health.* 1991;17(1):32-7.
7. Bisset LM, Vicenzino B. Physiotherapy management of lateral epicondylalgia. *J Physiother.* 2015;61(4):174-81.
8. Raman J, MacDermid JC, Grewal R. Effectiveness of different methods of resistance exercises in lateral epicondylitis--a systematic review. *J Hand Ther.* 2012;25(1):5-25.

9. Cook J, Purdam C. Tendon overuse injury (tendinopathy). In Brukner P, Khan KM, editors. *Brukner & Khan's clinical sports medicine. Volume 1: injuries*. 5th ed. New South Wales: McGraw-Hill Education Australia; 2017. p. 46-51.
10. Rio E, Kidgell D, Purdam C, et al. Isometric exercise induces analgesia and reduces inhibition in patellar tendinopathy. *Br J Sports Med*. 2015;49(19):1277-83.
11. Rio E, van Ark M, Docking S, et al. Isometric Contractions Are More Analgesic Than Isotonic Contractions for Patellar Tendon Pain: An In-Season Randomized Clinical Trial. *Clin J Sport Med*. 2017;27(3):253-9.
12. Coombes BK, Wiebusch M, Heales L, Stephenson A, Vicenzino B. Isometric Exercise Above but not Below an Individual's Pain Threshold Influences Pain Perception in People With Lateral Epicondylalgia. *Clin J Pain*. 2016;32(12):1069-75.
13. Stasinopoulos D, Stasinopoulos I. 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(1):13-9.
14. Park JY, Park HK, Choi JH, et al. Prospective evaluation of the effectiveness of a home-based program of isometric strengthening exercises: 12-month follow-up. *Clin Orthop Surg*. 2010;2(3):173-8.
15. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. *J Pharmacol Pharmacother*. 2010;1(2):100-7.
16. Slade SC, Dionne CE, Underwood M, Buchbinder R. Consensus on Exercise Reporting Template (CERT): Explanation and Elaboration Statement. *Br J Sports Med*. 2016;50(23):1428-37.

17. Toigo M, Boutellier U. New fundamental resistance exercise determinants of molecular and cellular muscle adaptations. *Eur J Appl Physiol.* 2006;97(6):643-63.
18. Newcomer KL, Martinez-Silvestrini JA, Schaefer MP, Gay RE, Arendt KW. Sensitivity of the Patient-rated Forearm Evaluation Questionnaire in lateral epicondylitis. *J Hand Ther.* 2005;18(4):400-6.
19. Rompe JD, Overend TJ, MacDermid JC. Validation of the Patient-rated Tennis Elbow Evaluation Questionnaire. *J Hand Ther.* 2007;20(1):3-10; quiz 1.
20. Fernández-Carnero J, Fernández-de-las-Peñas C, de la Llave-Rincón AI, Ge H-Y, Arendt-Nielsen L. Widespread mechanical pain hypersensitivity as sign of central sensitization in unilateral epicondylalgia: a blinded, controlled study. *Clin J Pain.* 2009;25(7):555-61.
21. Coombes BK, Bisset L, Vicenzino B. Thermal hyperalgesia distinguishes those with severe pain and disability in unilateral lateral epicondylalgia. *Clin J Pain.* 2012;28(7):595-601.
22. Croisier JL, Foidart-Dessalle M, Tinant F, Crielaard JM, Forthomme B. An isokinetic eccentric programme for the management of chronic lateral epicondylar tendinopathy. *Br J Sports Med.* 2007;41(4):269-75.
23. Hopkins WG. A new view of statistics [Internet]. Internal Society for Sport Science; 2000 [cited 2019 Feb 02]. Available from: <http://www.sportsci.org/resource/stats/>.
24. Bisset L, 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(7575):939.

25. 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(5):461-9.
26. World Health Organization. International classification of functioning, disability and health: ICF [Internet]. Geneva: World Health Organization; 2001 [cited 2019 Mar 16]. Available from: <http://www.who.int/iris/handle/10665/42407>.
27. MacDermid JC, Silbernagel KG. Outcome Evaluation in Tendinopathy: Foundations of Assessment and a Summary of Selected Measures. *J Orthop Sports Phys Ther*. 2015:1-34.
28. Vincent JJ, MacDermid JC, King GJ, Grewal R. Linking of the Patient Rated Elbow Evaluation (PREE) and the American Shoulder and Elbow Surgeons - Elbow questionnaire (pASES-e) to the International Classification of Functioning Disability and Health (ICF) and Hand Core Sets. *J Hand Ther*. 2015;28(1):61-7; quiz 8.
29. Kamper SJ, Maher CG, Mackay G. Global rating of change scales: a review of strengths and weaknesses and considerations for design. *J Man Manip Ther*. 2009;17(3):163-70.
30. Smidt N, van der Windt DA, Assendelft WJ, Deville WL, Korthals-de Bos IB, Bouter LM. Corticosteroid injections, physiotherapy, or a wait-and-see policy for lateral epicondylitis: a randomised controlled trial. *Lancet*. 2002;359(9307):657-62.
31. Rolke R, Baron R, Maier C, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): standardized protocol and reference values. *Pain*. 2006;123(3):231-43.
32. Defrin R, Urca G. Spatial summation of heat pain: a reassessment. *Pain*. 1996;66(1):23-9.

33. Whitehurst DG, Bryan S, Lewis M, Hill J, Hay EM. Exploring the cost-utility of stratified primary care management for low back pain compared with current best practice within risk-defined subgroups. *Ann Rheum Dis*. 2012;71(11):1796-802.
34. Hill JC, Whitehurst DG, Lewis M, et al. Comparison of stratified primary care management for low back pain with current best practice (STarT Back): a randomised controlled trial. *Lancet*. 2011;378(9802):1560-71.

FIGURE CAPTIONS

Figure 1. Participant flow diagram.

Figure 2. Percentage of participants reporting perceived improvements across categories from ‘completely recovered’ to ‘much worse’.

Figure 3. Exercise diary characteristics. (A) Mean (SD) pain experienced during exercise sessions, and (B) Percentage of participants reporting time for pain to settle following exercise sessions across categories from ‘0-1min’ to ‘20-59min’.

Missing diary entries: one in weeks 4 and 5, three in weeks 6 and 7, five in week 8.

NRS, numerical rating scale.

Supplemental Digital Content 1. Figure that illustrates the water container used. tif

Supplemental Digital Content 2. Figure that illustrates weekly progression of total exercise dose. Tif

Figure 1

Figure 2

Figure 3

Table 1. Description of the isometric exercise protocol

Exercise descriptors	Isometric exercise program
1. Load	Week 1-2: 20% MVC Week 3-4: 25% MVC Week 5-6: 30% MVC Week 7-8: 35% MVC
2. Repetitions	Week 1, 3, 5, 7: 4 repetitions Week 2, 4, 6, 8: 3 repetitions
3. Sets per session	1 set
4. Rest between sets	NA
5. Sessions per week	7 per week
6. Duration of exercise program	8 weeks
7. Contraction mode and duration per repetition	Week 1, 3, 5, 7: 30s isometric hold Week 2, 4, 6, 8: 45s isometric hold
8. Rest between repetitions	30s
9. Time under tension	Week 1, 3, 5, 7: 120s total /session Week 2, 4, 6, 8: 135s total /session
10. Contraction failure in each set	No
11. Range of motion	Static (isometric)
12. Rest between exercise sessions	~24 h
13. Anatomical definition of the exercise	Affected arm was positioned with forearm resting on the edge of table, upper body in sound postural alignment, elbow ~90° flexed, forearm pronated, wrist ~30° extended, neutral radial/ulnar deviation. Participant was instructed to hold a water-filled container whilst maintaining this position.

MVC, maximal voluntary contraction of wrist extensors on the unaffected arm.

Table 2. Baseline demographic and clinical characteristics.

Characteristic	Total n = 40	Exercise n = 21	Wait-and-see n = 19
Age, y	48.5 (9.0)	48.0 (7.9)	49.0 (10.2)
Female, no. (%)	11 (28)	7 (33)	4 (22)
Height, cm	173.9 (10.2)	174.1 (10.7)	173.6 (9.9)
Mass, kg	79.5 (15.5)	79.6 (19.9)	79.3 (9.0)
BMI, kg/m ²	26.2 (4.0)	26.0 (5.0)	26.4 (2.7)
Smoker, no. (%)	2 (5)	1 (4.7)	1 (5.3)
Repetitive/manual tasks at work, no. (%)	33 (82.5)	17 (81.0)	16 (84.2)
Gripping sport, no. (%)	30 (75)	15 (71.4)	15 (79.0)
Dominant side affected, no. (%)	24 (60)	14 (67)	10 (53)
Pain duration, median (IQR), months	4 (2-8)	6 (2-8)	3 (2-6)
EQ-5D /1	0.77 (0.10)	0.78 (0.06)	0.77 (0.13)
Sleep disturbed by pain, no. (%)	30 (75)	14 (66.7)	16 (84.2)
PRTEE total /100	35.4 (13.0)	33.4 (12.1)	37.6 (13.9)
- PRTEE pain /50	19.6 (6.2)	18.5 (5.0)	20.8 (7.4)
- PRTEE specific activities /60	18.0 (10.8)	16.9 (11.8)	19.3 (9.8)
- PRTEE usual activities /40	13.5 (7.5)	12.8 (11.8)	14.3 (7.6)
Resting pain NRS /10	1.7 (1.5)	1.6 (1.1)	2.0 (1.9)
Worst pain NRS /10	7.3 (1.7)	6.8 (1.8)	7.8 (1.4)
PFG affected N	104.9 (64.2)	98.7 (56.7)	111.8 (72.6)
PFG unaffected N	375.5 (127.2)	369.6 (116.8)	382.1 (140.7)
CPT elbow °C	12.3 (8.6)	12.9 (9.3)	11.7 (7.9)
HPT elbow °C	43.6 (4.6)	43.4 (5.1)	43.8 (4.1)
PPT elbow kPa	333.6 (93.1)	332.0 (98.4)	335.2 (89.6)

Values are expressed as mean (SD) unless stated otherwise. BMI, body mass index; IQR, interquartile range; EQ-5D, EuroQol (Health-related quality of life, 1 = perfect health); PRTEE, Patient-Rated Tennis Elbow Evaluation (100 = worst pain and disability); NRS, numerical rating scale (10 = worst imaginable pain); PFG affected, pain-free grip strength for affected side; PFG unaffected, pain-free grip strength for unaffected side; CPT, cold pain threshold; HPT, heat pain threshold; PPT, pressure pain threshold.

Table 3. Primary and secondary outcome measures at 8 weeks (continuous outcomes adjusted for baseline scores and stratification variable) and study group comparisons.

	Exercise	Wait-and-see	Mean difference (95% CI) between groups
Primary outcomes			
PRTEE total /100	17.1 (11.2)	27.6 (11.2)	-10.5 (-17.8 to -3.2)*
- PRTEE pain /50	10.8 (6.4)	15.7 (6.5)	-4.9 (-89.2 to -0.7)*
- PRTEE specific activities /60	7.0 (6.8)	12.9 (6.8)	-5.9 (-10.3 to -1.5)*
- PRTEE usual activities /40	5.9 (4.7)	10.9 (4.7)	-5.1 (-8.1 to -2.0)*
GROC			
- No. (%) of participants reporting success ^a †	6/21 (28.6%)	5/19 (26.3%)	2.3 (-24.5 to 29.1)
- No. (%) of participants reporting improved ^b †	18/21 (85.7%)	12/19 (63.1%)	22.6 (-1.3 to 46.6)
PFG affected N	156.0 (101.9)	190.7 (102.0)	-34.7 (-101.3 to 31.8)
Secondary outcomes			
Resting pain NRS /10	0.8 (0.9)	0.9 (0.9)	-0.2 (-0.7 to 0.4)
Worst pain NRS /10	4.2 (2.6)	6.3 (2.6)	-2.1 (-3.8 to -0.4)*
CPT elbow °C	12.6 (6.2)	13.0 (6.1)	-0.4 (-4.4 to 3.6)
HPT elbow °C	43.4 (2.7)	44.0 (2.7)	-0.7 (-2.4 to 1.1)
PPT elbow kPa	378.1 (118.5)	419.0 (118.5)	-40.9 (-118.0 to 36.21)

Values expressed as mean (SD) unless stated otherwise.

* Statistically significant difference ($P < 0.05$)

^a Success = Participants reported “much improved” or “recovered” on the GROC scale

^b Improved = Participants reported “improved”, “much improved” or “recovered” on the GROC scale

[†] Risk difference between groups (95% CI)

PRTEE, Patient-Rated Tennis Elbow Evaluation (100 = worst pain and disability); GROC, Global rating of change; PFG affected, pain-free grip strength for affected side; NRS, numerical rating scale (10 = worst imaginable pain); CPT, cold pain threshold; HPT, heat pain threshold; PPT, pressure pain threshold.

SDC 1. Water container used.

Week	1	2	3	4	5	6	7	8
% MVC	20	20	25	25	30	30	35	35
TUT sec	120	135	120	135	120	135	120	135

SDC 2. Weekly progression of total exercise dose.

MVC, maximal voluntary contraction of wrist extensors on the unaffected arm; TUT, time under tension.