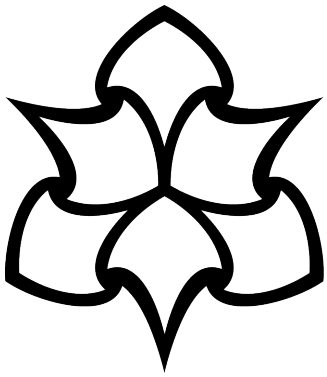

The efficacy of higher versus lower dose exercise in rotator cuff tendinopathy: A systematic review of randomised controlled trials

Running head: Exercise dose and rotator cuff tendinopathy

Abstract

Objective: to compare the effectiveness and harms of higher exercise dose, including higher exercise load and/or higher volume, with lower exercise dose (lower load and/or lower volume) in people with rotator cuff tendinopathy

Design: Systematic review (PROSPERO: CRD42017077478)

Data sources: CENTRAL, MEDLINE, EMBASE, CINAHL from inception to March 2019.

Study selection: Randomised controlled trials comparing higher versus lower dose exercise that investigated function and pain (overall, activity, night) and adverse event outcomes were independently determined by two reviewers.

Data extraction and risk of bias: Two authors independently extracted data and assessed risk of bias using the Cochrane tool. The primary endpoint was >six weeks to three months (other endpoints included up to six weeks & beyond three months) and GRADE was used to assess evidence certainty.

Data synthesis: Three trials (N=283), none at low risk of bias for all domains, were included. Low certainty evidence (1 trial, N=102) indicated improved function (20 points [95% CI 12 to 28 points] on 0-100 point scale) with higher load and volume exercise at three months, but little or no clinically important between-group difference in activity or night pain (overall pain not reported). Very low certainty evidence (1 trial, N=120) indicated higher load exercise conferred no function benefits over lower load exercise at six weeks. Very low certainty evidence (1 trial, N=61) indicated benefit of uncertain clinical importance in function with higher versus lower volume exercise at three months and clinically important benefit at >3 months (pain outcomes not reported). Risk of adverse events was uncertain.

Conclusions: There are few studies that investigate higher dose exercise for rotator cuff tendinopathy. There was low to very low certainty and conflicting evidence about the value of higher exercise dose in people with rotator cuff tendinopathy.

Key Words: Rotator cuff tendinopathy, dose-response, exercise

Introduction

Shoulder pain is estimated to have a prevalence between 15 to 30% in the general population, with prevalence increasing with age [1]. Rotator cuff tendinopathy is the most common cause, accounting for up to 80% of all cases of shoulder pain in primary care [2]. While often self-limiting, up to 50% of patients who present for care may continue to experience ongoing pain and disability beyond 12 months [2]. This results in significant morbidity and health resource utilisation given shoulder function is essential to personal hygiene, dressing and work [2].

Clinical guidelines recommend clinician-prescribed exercise for rotator cuff tendinopathy[3, 4]. However, there are conflicting data about its benefits [5-7]. An updated Cochrane review synthesised exercise and manual therapy evidence for rotator cuff tendinopathy from 60 trials (3,620 participants) up until 2015. The authors reported high quality evidence from a single trial (120 participants) [8] indicating that manual therapy and exercise provided no patient-reported benefits in pain and function outcomes over placebo at 22 weeks follow-up. However, the exercise component was not loaded progressively so could be defined as lower load [6]. This lack of benefit in pain and function outcomes was supported by very low quality evidence from two trials (89 participants) that compared manual therapy and exercise to no treatment although only one trial progressed exercise load in the active group [9, 10]. By contrast low quality evidence from one trial of exercise versus placebo (80 participants in these treatment groups) that did progress load in the exercise group reported pain and function outcome benefit favouring the exercise group for overall pain and function but not activity pain or night pain [11].

While the overall body of evidence indicates a lack of consensus regarding the benefit of exercise for rotator cuff tendinopathy, previous systematic reviews have not generally considered whether exercise dose parameters such as load progression and repetitions influence outcomes. Higher load may be more beneficial for neuromuscular adaptation and higher volume might develop greater muscular endurance [12, 13]. Greater neuromuscular adaptation and muscular endurance could improve function and improve shoulder symptoms [14]. In a systematic review of prescription parameters reported in randomised controlled trials (RCTs) of exercise interventions for rotator cuff tendinopathy, trials that progressively loaded exercise were more likely to report improvements in shoulder function compared with trials where exercise was not progressively loaded [15]. However, it is unclear if these improvements are clinically important or if these findings are robust in view of potential biases in the included studies. Further exploration of the relationship between exercise dose and outcomes in rotator cuff tendinopathy therefore appears warranted.

The aim of this systematic review was to compare the effectiveness and harms of higher exercise dose, including higher exercise load and/or higher volume, with lower exercise dose (lower load and/or lower volume) in people with rotator cuff tendinopathy.

Methods

Criteria for considering studies for this review

We adopted similar methods to the updated Cochrane review of manual therapy and exercise interventions for rotator cuff tendinopathy [6]. Our review was conducted in accordance with the PRISMA statement guidelines (Preferred Reporting Items for Systematic reviews and Meta-Analyses) [16] and was registered with the International Prospective Register of Systematic Reviews (PROSPERO; reference CRD42017077478).

Types of studies

We included RCTs of any design (e.g. parallel, factorial, cross-over) and controlled trials using a quasi-randomised method of allocation. There were no restrictions based on language.

Types of participants

We included trials that recruited participants aged 16 years and over with a primary complaint (any duration) of shoulder pain (with or without referral into the arm) labelled and/or diagnosed as rotator cuff tendinopathy by any means. Rotator cuff tendinopathy has many synonyms in the literature including rotator cuff disease, rotator cuff related pain, subacromial impingement syndrome, rotator cuff tendinitis, supraspinatus, infraspinatus or subscapularis tendonitis or tendinopathy, subacromial bursitis and rotator cuff tears. Trials using these synonyms were included as were trials where participants had unspecified shoulder pain provided that the inclusion/exclusion criteria were compatible with a diagnosis of rotator cuff disease (i.e. anterolateral shoulder pain that is made worse by active and resisted shoulder elevation and associated with preserved passive range of motion [4]). We included trials with participants with multiple shoulder disorders, if data were presented separately for our population of interest.

Trials were excluded if they included participants with a full thickness tear involving more than one rotator cuff tendon (based on presentation or imaging findings), gross shoulder instability, significant shoulder trauma, previous shoulder surgery, shoulder osteoarthritis, patients with hemiplegia affecting the shoulder, a complex myofascial neck/shoulder/arm

pain condition, suspected cervical spine referred pain, or a systemic inflammatory condition (e.g. rheumatoid arthritis).

Types of interventions

We included trials that utilised exercise designed to load the shoulder joint, this could include any active movement in any shoulder plane. Passive movements and pendular movements (also classified as passive [e.g. [17]]) were excluded. Trials were included if they compared higher versus lower dose exercise as defined in the trials. Higher dose could include heavier load (using external weight or resistance) or greater volume (repetitions x sets x frequency). The volume was defined as a total of all sessions they performed, including supervised and/or home-based exercise. There was no minimum dose (volume or load) because diverse exercise interventions can lead to neuromuscular adaptations [12, 13]. Trials needed to explicitly state the load or volume, or both, in each group so there was certainty that these dose parameters varied. The comparator group needed to be the same setting (e.g. home-based, supervised, or a combination) and type of exercise (e.g. isometric, isotonic, eccentric) so dose was the primary variable being investigated. Trials that also progressed other exercise parameters such as the range of motion or the type of exercise (static to dynamic) were included if these were identical in both treatment groups. Co-interventions, including mobilisation, manipulation and massage modalities, glucocorticoid injections and analgesia were allowed even if they were not applied equally to groups.

Types of outcome measures

For effectiveness we included patient-reported shoulder function, and the following pain outcomes (as per the Page et al review [6]): overall shoulder pain, activity and night pain in the shoulder. When data for more than one function scale was reported within a trial, we

extracted data from the function scale highest on the shoulder function scale hierarchy reported by Page et al [6]:

- Shoulder Pain and Disability Index (SPADI) [18]. Scored on a 0 to 100-point scale, where 0 best;
- Croft Shoulder Disability Questionnaire [19] Scored on a 0 to 22-point scale, where 0 is best;
- Constant-Murley Score [20] Scored on a 0 to 100-point scale, where 100 is best;
- any other shoulder-specific function scale.

Overall pain, pain with activity and night pain could be measured on a visual analogue scale (VAS), numerical or categorical rating scale. For harms we included the proportion of participants experiencing adverse events.

Outcome times were selected to identify short (up to 6 weeks), medium (>six and up to three months) and longer-term (>three months) effects of the exercise interventions. The longest timepoint was extracted where multiple timepoints were reported within a given range. We chose >six weeks and up to three months as the primary endpoint given this is enough time for exercise to lead to greater muscle volume and strength, and potentially, better function [12].

Data sources and search

Relevant trials published up to March 2015 were identified from the updated Cochrane review of manual therapy exercise interventions for rotator cuff tendinopathy [6]. Given we focused on exercise for rotator cuff tendinopathy, the search strategy from the Page et al. [6] was modified to exclude terms related to adhesive capsulitis as well as non-exercise

interventions. For more recent papers we repeated the search in the Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library March* 2019, Issue 3), Ovid MEDLINE (March 2015 to March 2019), Ovid EMBASE (March 2015 to March 2019), and CINAHL Plus (EBSCO, March 2015 to March 2019).

The updated search strategies for all databases are shown in Supplementary appendix 1. We also searched gray literature via OpenGray and ongoing trials via the National Institute of Health (clinicaltrials.gov) and the World Health Organisation (http://www.who.int/ictrp) International Clinical Trials Registries, using the terms 'rotator cuff disease' [condition] and 'exercise' [intervention] up to March 2019.

Selection of studies

Two authors (PM, GS) independently screened titles and abstracts for potentially eligible trials, based on a predetermined checklist of inclusion criteria. The full text of potentially eligible trials was retrieved and independently assessed by the same two authors to determine eligibility. Any discrepancies were resolved via discussion, or by consulting a third author where necessary (CL).

Data extraction

Two authors (PM, GS) independently extracted data onto a standard data extraction form. Discrepancies were resolved through discussion until consensus was reached, otherwise a third author (RB) was consulted to adjudicate.

The following data were extracted from each study:

- Trial characteristics (sample size, first author name, year of publication, type of trial [e.g. parallel, crossover], country, source of funding, trial registration status [registration number if reported]).
- Participant characteristics (inclusion and exclusion criteria, age, gender, duration of symptoms,).
- Intervention including exercise characteristics (exercises performed, sets, repetitions, frequency, duration, how exercise was loaded, how exercise was progressed and how often, adherence measures, advice about pain during exercise)
- Comparator intervention exercise characteristics
- Co-interventions in each group, if any
- Outcomes reported, including the measurement instrument used and timing of outcome assessment.

To minimise potential bias, we used the following a priori decision rules for selecting outcome data:

- Preference was given to data that were adjusted for baseline values (e.g. ANCOVA) if available and intention-to-treat.
- Where follow-up and change scores were reported for the same outcome, we planned to extract follow up scores.
- For cross-over RCTs, we planned to only extract data for the first period.

Risk of bias assessment

Risk of bias for each study was performed using the Cochrane Collaboration's tool for assessing risk of bias, described fully in the Cochrane Handbook for Systematic Reviews of Interventions *[21]*. Risk of bias was performed independently by two of three authors (PM,

GS or RJ) and discrepancies were resolved through discussion until consensus was reached, otherwise a third author (RB) was consulted to adjudicate.

The following domains were rated as high risk of bias if they were not performed adequately, unclear risk of bias if it was not clearly reported or low risk of bias if performed adequately: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, outcome reporting bias, and other sources of bias (i.e. baseline imbalance, unequal application of co-interventions across treatment groups). All domains had to achieve a low risk of bias rating for the study to be classified as being at low overall risk of bias.

Measures of treatment effect

Review Manager (RevMan) 5.3 was used to calculate measures of treatment effect. Adverse events were expressed as relative risk (RR) and 95% confidence intervals. Mean pain was expressed as mean difference (MD) and 95% confidence intervals on a 0 to 100-point VAS scale, with a higher score indicating more pain. Mean function was also expressed as MD and 95% confidence intervals with a lower score indicating less disability or better function. So that zero was best function in all scales, we reversed scores for scales such as the Constant-Murley score and Shoulder Rating Questionnaire (SRQ) where a higher score indicates less disability or better function. For the SRQ we also transformed scores from a scale of 17 to 90 to 0 to 100 scale [22]. We assumed a minimal clinically important difference of 10 on a 100-point scale for function and 15 points on a 100-point scale for pain [6]. A clinically important difference was defined as a confidence interval where even the lower band (closest to null) was greater than 10 (for function) or 15 points (for pain).

Study authors were contacted (twice over four weeks) via email in any instances of missing data. If the data were not retrieved from the study authors, we planned to calculate standard deviation (SD) from the standard errors (SE), 95% CIs or P values, or use median and the Inter-quartile range (IQR) to approximate the mean and SD (SD=width of IQR/35), respectively.

Data synthesis

Meta-analysis was planned to pool results of trials with similar characteristics (e.g. participants, interventions, outcomes), however there was insufficient data to undertake data pooling.

Summary of findings

We created summary of findings tables [23] for a priori comparisons that included outcomes at the primary endpoint of >six weeks to three months. We rated the overall grading of the certainty of the evidence based on the GRADE approach (Grades of Recommendation, Assessment, Development and Evaluation Working Group) [24]. From an initial starting point of high certainty evidence, the level of evidence was downgraded (to moderate, low or very low) for each of the following: risk of bias, inconsistency of results, indirectness, imprecision, and publication bias.

For dichotomous outcomes (e.g. adverse events), we planned to calculate absolute risk difference expressed as a percentage and relative percent change (the risk ratio – 1) expressed as a percentage. For continuous outcomes (e.g. function), we planned to calculate absolute change which is the difference in mean of higher and lower load groups at follow-up standardised to the original units and expressed as a percentage. The relative percent change

was also calculated as the mean difference between groups at follow-up divided by the mean of the lower load group at baseline, expressed as a percentage.

Results

Study selection

Two eligible trials were identified from the Page et al. [6] systematic review [14, 25]. An additional 915 records (730 unique studies) were identified from the updated search conducted from 2015 to 9 March 2019. Of these, we assessed 12 in full text and identified one additional trial for inclusion [26] (Figure 1). Two trials were registered in trial registries [14, 26], (Table 1) but none published their protocol.

We excluded eleven trials after full text assessment for the following reasons: four compared different types of exercise as opposed to dose [27-30], one compared home versus group supervised group exercise [31], one compared pendular exercise with and without load [32], one compared painful vs painfree exercise [33], one compared home versus individual supervised exercise [34], one used the uninvolved asymptomatic shoulder as a control [35], one study compared the effect of the sequence in which exercises were performed [36] and one study included high dose exercise in both treatment arms (higher load and lower volume exercise versus lower load and higher volume exercise) [37], meaning it could not contribute to an understanding of the role of high versus low dose of exercise.

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 flow diagram for literature search results.

Trial, participant and intervention characteristics

The three included trials were all parallel group RCTs and included 283 participants [14, 25, 26]. All trials had similar inclusion criteria (see Supplementary appendix 2). The trial, participant and intervention characteristics of the included trials are shown in table 1. Mean age varied between 46 and 55 years (slight male dominance) and symptom duration between three months and four years. Mean baseline function scores varied between 49 to 63 out of 100 (lower score indicates better function).

One trial compared 12 weeks of either higher load and higher volume exercise or lower load and lower volume exercise [14]; one trial compared higher versus lower load exercise over six weeks [26]; and one trial compared 12 weeks of either higher or lower volume exercise [25]. With regards to the comparators, two trials simply utilised active shoulder movements without additional load that can be considered subtherapeutic [14, 26]. In contrast, the comparator in Osteras et al [25] still contained progressive load exercise but of lower volume. No trials reported the actual load during exercise or exercise intensity. Exercise intensity (e.g. >70% 1 repetition maximum) was not reported in any trial [12]. Repetitions per week were higher in the 'higher volume' (2160 to 3150) compared with the 'lower volume' comparators (300 to 420) [14, 25].

One trial supervised all exercise sessions [25] while the other two trials included home exercise. Pain during exercise was permitted in all intervention and comparator groups, aside from the Holmgren et al. [14] trial where this detail was not described for the comparator group. All trials included active non-weightbearing exercises in anatomical planes (e.g. flexion, abduction, external rotation). All trial participants received a glucocorticoid injection at baseline in one trial [14]. This trial also provided manual therapy 'when necessary' to participants in only the higher load and volume exercise group.

All three trials assessed function with one trial measuring function using two instruments [14]. One trial used the SPADI [26], one used the Constant-Murley Score [14] and one used the SRQ [25]. Holmgren et al. [14] also used the Disability of the Arm and Shoulder Score (DASH) but we extracted data from the Constant-Murley Score. No trial reported overall pain, and Heron et al. [26] did not report pain at all. One trial reported activity pain [14] and one trial reported night pain [14]. Two trials also reported pain at rest (or inactivity) [14, 25] but as this was not a pre-specified outcome, we did not extract data for this outcome. Only two trials reported outcomes at our primary endpoint of >6 weeks to three months (both at three months) [14, 25]. Østeras et al. [25] also reported outcomes at nine and 15 months and data were extracted at 15 months for the >three months endpoint. Although Holmgren et al. [14] reported results at 12 months participants were offered surgery after the three-month assessment and data were reported sub-grouped by whether or not participants underwent surgery. Therefore the 12-month data were not extracted for this review. One trial only reported outcomes at 6 weeks [26].

Table 1: Study, participant and exercise characteristics

Risk of bias in included trials

The risk of bias for each of the included trials is summarised in Figure 2. One trial was rated at low risk of bias for all domains other than performance bias, which was rated as uncertain [14]. Of note, this trial was rated at low risk of bias for all domains in the Page et al. Cochrane review [6]. While participants and the outcome assessor were blinded, the trial did not report whether the exercise explanations and verbal interaction (of potential effect and mechanisms) were identical between groups. Two of the remaining trials were susceptible to

performance [25, 26] and one trial was at risk of detection biases [25] due to lack of blinding of either participants or investigators; one trial was also at risk of attrition bias due to differences in the proportion of drop outs between groups [26]; and two trials were at risk of selective reporting [25, 26] because they reported one self-reported outcome measure and there were no associated trial protocols so it is unclear whether all outcomes were reported.

Figure 2: Risk of bias summary: judgements about each risk of bias item for each included study.

Comparison 1: higher load and higher volume versus lower load and lower volume

There may be clinically important improvement in function with higher load and higher volume exercise at three months (Figures 3 & 4). Function was 47.5 points in the lower dose group and this improvement was 20 points better (95% CI 12 to 28) in the high dose group. There was little or no clinically important benefit of higher dose exercise for pain outcomes at > 6 weeks to three months. Activity pain was 41 points with low dose exercise and 16.0 (95% CI 5.4 to 26.6) points better with high dose. Similarly, night pain was 27 points with low dose exercise and 12.0 points better (95% CI 2.1 to 21.9) with high dose. Overall pain and adverse events were not reported. This evidence arose from a single trial (97 participants for all reported outcomes) [14] and was low certainty (downgraded for bias and imprecision).

Figure 3: Effects of higher load and higher volume versus lower load and lower volume exercise

Figure 4: Summary of findings for the comparison of higher load and higher volume versus lower load and lower volume

Comparison 2: higher load versus lower load

Given outcomes were not reported at the primary endpoint for this comparison no summary of findings table was produced. There was no benefit with higher compared with lower load exercise for function at six weeks (Figure 5). Function was 42 points in the lower load group and this improvement was 5 points better in the higher load group (95% CI 15.9 better to 5.9 worse). Overall, activity or night pain and adverse events outcomes were not reported. This evidence was from a single trial (61 participants for function outcome) and was low certainty (downgraded for risk of bias and imprecision due to the very short follow-up time). Note that only two ('open chain' and 'range of movement') of the three trial arms were eligible and included in this review.

Figure 5: Effects of higher vs lower load exercise

Comparison 3: higher volume versus lower volume

There was benefit of uncertain clinical importance with higher volume exercise in function at three months (Figures 6 & 7). Function was 45.4 points in the lower volume group and 12.9 points better (95% CI 7.6 to 18.1 points better) in the higher volume group. There was clinically important benefit at >three months; function was 43.1 points in the lower volume group and 17.8 points better in the higher volume group (95% CI 11.8 to 23.8 points better). Overall, activity or night pain were not reported. There was no reliable estimate of the adverse event rates. One participant in the higher volume group was reported to sustain a neck injury (no adverse events reported for the lower volume group). This evidence arose from one trial (56 participants for all reported outcomes) and was very low certainty (downgraded for risk of bias and imprecision).

Figure 6: Effects of higher vs lower volume exercise

Figure 7: Summary of findings for the comparison of higher volume versus lower volume

Discussion

We found low to very low certainty and somewhat conflicting evidence about the value of higher exercise dose in people with rotator cuff tendinopathy. There was low certainty evidence from a single trial suggesting that higher load and higher volume exercise may result in a clinically important benefit in function but not activity or night pain at >six weeks to three months. There was also very low certainty evidence from another small single trial indicating that higher volume exercise might provide benefit of uncertain clinical importance for function at >six weeks to three months compared with lower volume exercise, although no data for pain were collected. Very low certainty evidence from one trial indicated that higher load exercise does not provide clinically important benefit over lower load exercise with respect to function up to six weeks. We are uncertain if there is an increased risk of adverse events with higher dose exercise, given the incomplete reporting of events and the low event rates. The evidence was downgraded for a variety of reasons including risk of performance and detection bias, imprecision and indirectness due to short follow-up times.

The exercise programs examined in the three included trials generally reflected the interventions that are delivered in practice and in the rotator cuff tendinopathy literature [6]. Load was progressed when the exercise could be performed easily or with a defined pain response. None of the studies reported the specific intensity (e.g. repetition maximum) or absolute load. In contrast, trials that evaluated the effect of volume utilised fixed rather than progressive volumes and these were at least five times greater in the high volume (2160 to

406 3150 repetitions per week) versus the lower volume (300 to 420 repetitions per week) trial
407 arms. Importantly, comparisons were unloaded active movements in two studies [14, 26] but
408 still contained progressive load with lower volume [25] in one study. Given the poorly
409 reported and heterogeneous interventions we cannot make any specific comments about the
410 level of load (or intensity) and volume that may confer greater benefit. Final follow-up for
411 the trial included in the higher load versus lower load exercise comparison was between four
412 to six weeks which may not be enough time to demonstrate a beneficial effect of higher load
413 exercise if one is present. Littlewood et al. [15] reported that maintenance of an exercise
414 program for at least 12 weeks may be needed to demonstrate improvements in function.
415
416 Adequate description of comparative load and volumes were part of our inclusion criteria. It
417 was common across studies for other exercise parameters to be incompletely described,
418 including pain during loading, exercise adherence, rest between exercise sets and exercise
419 tempo (see Table 1). This limitation is important because clinicians are unable to implement
420 incompletely described exercise interventions. Further, given adherence was poorly
421 described, it is impossible to be certain of the dose in each comparator group, and therefore
422 whether exercise dose or other mechanisms influenced outcome. For example, giving a
423 patient permission to perform progressively loaded exercise, or do more exercise, may reduce
424 fear, increase general shoulder use, and thereby improve outcome. Future exercise trials
425 should consider reporting guidelines such as the Consensus on Exercise Reporting Template
426 (CERT) [38] to ensure findings are translatable to practice.
427
428 **Comparison to the literature**
429 Littlewood et al (2015) reported superior function outcomes with resisted and greater volume
430 (repetitions and sets) [15], but this was based on a narrative synthesis. Fourteen studies were

included in the Littlewood review, and only one of these studies specifically examined the effect of exercise dose and was also included in the current review [25]. Our systematic review investigated the effect of higher exercise dose (load and/or volume) on function and pain outcomes in rotator cuff tendinopathy. While our review suggested that higher load and higher volume exercise or higher volume exercise might confer superior functional outcomes compared to their lower dose comparisons, we did not find that higher load exercise was better than lower load exercise. However, if an exercise program needs to be maintained for at least 12 weeks before any benefit on function is evident as proposed by Littlewood et al. [15], this may explain the lack of observed benefit in the higher load versus lower load exercise comparison as exercise intervention and outcome reported extended only four to six weeks.

A randomized trial by Ingwersen et al. [37] compared higher load but lower volume with lower load but higher volume exercise for rotator cuff tendinopathy. This study was not eligible for the current review but is worthy of discussion. The authors in this study equalized the work (volume multiplied by intensity) undertaken in each group. This is a worthwhile approach because it is able to identify whether load or volume is beneficial when accounting for overall work. In contrast, in the current review we were interested in whether additional load (and work) or additional volume (and work) or a combination of both were beneficial. The Ingwersen et al. [37] trial reported meaningful benefit in pain and function in both groups at 12 weeks with no between groups differences for higher intensity or higher volume exercise when work is equalized. This suggests that greater work may explain the between groups differences observed in studies in this review with higher load and volume or higher volume interventions, but this requires investigation in future trials.

Strengths of the systematic review

Our methods were based on a prior Cochrane review of exercise interventions for rotator cuff tendinopathy and adhered to best practice guidelines as outlined by the Cochrane collaboration and PRISMA to minimise potential sources of bias. Inclusion and exclusion criteria were determined a priori and were clearly defined to minimise selection bias.

Limitations

The main limitation is that only three trials met our inclusion criteria. We performed a comprehensive search and did not find any ongoing trials in trial registries, so publication bias is not likely. A further substantial limitation is diversity between exercise interventions. Comparators in two of the three trials were unloaded and could be considered subtherapeutic [14, 26], while the third trial included substantial progressive load in the higher load arm [25]. This, coupled with the sparse literature, makes it impossible to provide guidance about specific levels of load (or intensity) or volume that may be beneficial for individuals. A potential limitation among the included trials that may influence interpretation is contamination (e.g. lower does groups receiving higher dose or vice versa) between exercise interventions.

Future research

Only three studies that meet our selection criteria were identified. High quality adequately powered randomised trials are needed to investigate the value of exercise for rotator cuff tendinopathy. Future research should seek to determine optimal dose parameters for improvement in pain and function outcomes among people with rotator cuff tendinopathy. Future trialists should consider using function as the primary outcome given that the higher dose interventions in this review seemed to confer less differential benefit between exercise

interventions. These trials should adequately describe exercise interventions according to published guidelines such as the CERT [38] Checklist [39]. Robust monitoring of exercise fidelity (e.g. appropriately implementing progressive load) and adherence is also required in order to draw valid conclusions about the effect of dose on outcomes.

Implications for practice

Despite conflicting data, clinical guidelines continue to recommend clinician-prescribed exercise for rotator cuff tendinopathy. Based upon the currently available low to very low certainty evidence, exercise that progressively increases load and utilises greater volume may confer superior function outcomes compared with lower dose exercise regimens, although the certainty of these findings need to be confirmed in high quality trials. Clinicians should explain to patients that it is unclear whether exercise improves pain, while exercise may need to be maintained for at least 12 weeks before benefits in function become evident.

Conclusions:

There are few studies that investigate higher dose exercise for rotator cuff tendinopathy. There was low to very low certainty and conflicting evidence about the value of higher exercise dose in people with rotator cuff tendinopathy.

503 List of Figures and Tables

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