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Effectiveness of conservative interventions including exercise, manual therapy and medical management in adults with shoulder impingement: a systematic review and meta-analysis of RCTs

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ABSTRACT

Objective To investigate the effectiveness of conservative interventions for pain, function and range of motion in adults with shoulder impingement.

Design Systematic review and meta-analysis of randomised trials.

Data sources Medline, CENTRAL, CINAHL, Embase and PEDro were searched from inception to January 2017.

Study selection criteria Randomised controlled trials including participants with shoulder impingement and evaluating at least one conservative intervention against sham or other treatments.

Results For pain, exercise was superior to non-exercise control interventions (standardised mean difference (SMD) −0.94, 95% CI −1.69 to −0.19). Specific exercises were superior to generic exercises (SMD −0.65, 95% CI −0.99 to −0.32). Corticosteroid injections were superior to no treatment (SMD −0.65, 95% CI −1.04 to −0.26), and ultrasound guided injections were superior to non-guided injections (SMD −0.51, 95% CI −0.89 to −0.13). Nonsteroidal anti-inflammatory drugs (NSAIDS) had a small to moderate SMD of −0.29 (95% CI −0.53 to −0.05) compared with placebo. Manual therapy was superior to placebo (SMD −0.35, 95% CI −0.69 to −0.01). When combined with exercise, manual therapy was superior to exercise alone, but only at the shortest follow-up (SMD −0.32, 95% CI −0.62 to −0.01). Laser was superior to sham laser (SMD −0.88, 95% CI −1.48 to −0.27). Extracorporeal shockwave therapy (ECSWT) was superior to sham (−0.39, 95% CI −0.78 to −0.01) and tape was superior to sham (−0.64, 95% CI −1.16 to −0.12), with small to moderate SMDs.

Conclusion Although there was only very low quality evidence, exercise should be considered for patients with shoulder impingement symptoms and tape, ECSWT, laser or manual therapy might be added. NSAIDS and corticosteroids are superior to placebo, but it is unclear how these treatments compare to exercise.

INTRODUCTION

Shoulder complaints are the third common musculoskeletal presentation after back and neck disorders in primary care, and shoulder disorders account for 10% of referrals to physiotherapy in the Netherlands.[1] The incidence of shoulder complaints is 29.3 per 1000 person-years[2] and the 1-year prevalence, 21%;[3] with the highest incidence and prevalence in women and persons aged 45–64 years. Among people with shoulder pain, shoulder impingement syndrome (SIS) has the highest prevalence and accounts for 36% of shoulder disorders.[4]

SIS is a generic term for injury of structures in the subacromial space, such as rotator cuff tendinosis, partial thickness tears of the rotator cuff and bursitis.[5] The aetiology of rotator cuff injury and its relationship to subacromial impingement, the encroachment of the involved structures, are still a matter of debate.[6]

The common consequences of SIS are pain and disability, loss of quality of life and sleep disturbances.[7] An ongoing impingement process with serious rotator cuff damage can lead to complete joint destruction and end in a replacement of the glenohumeral joint.[8] Tears in the rotator cuff tendons are common in symptomatic shoulders, whereas up to 16.9% of asymptomatic shoulders also demonstrate tears in the rotator cuff.[9] The prevalence increases with age.[10]

The main treatment goals for patients with SIS are to reduce the common impairments related to pain, and to improve upper extremity function.

Systematic reviews and meta-analysis[5 11–39] have investigated treatment effects in patients with shoulder impingement. However, missing are (1) a comprehensive overview of all relevant interventions, (2) outcomes from all levels of disability, that is, impairments and activity limitations or participation restrictions[40] and (3) an outcome selection based on an a priori stated hierarchy.

The aim of this systematic review and meta-analysis of randomised trials was to provide a comprehensive overview of the effectiveness of all relevant non-surgical interventions for adults with shoulder impingements and outcomes on impairment (pain and active range of motion (AROM)), activity limitation or participation restriction (shoulder function questionnaires) based on an a priori stated hierarchy.

METHODS

We followed the recommendations of the PRISMA statement for the conduct and reporting of this review.[41]

Information sources and search strategy

To answer the question about the relative effects of conservative interventions for shoulder impingement, the Cochrane Database of Systematic Reviews, Cochrane Controlled Clinical

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Table 1 Inclusion criteria

Selected studies	Inclusion criteria
Study population	► 18 years and older
Complaints of shoulder pain (Based on Michener *et al*)[5]	► Painful arc between 40° to 120° in abduction, flexion ► Pain with active arm elevation ► Test by Neer, Hawkins-Kennedy, Speed or Jobe ► Empty can test ► Resisted painful or weak shoulder abduction ► Resisted or weak shoulder external rotation ► Diagnosis based on criteria according to Cyriax (ie, painful arc, or painful resisted abduction test) ► Impingement test with lidocaine ► Tenderness to palpation of rotator cuff tendons
Intervention/comparator	► At least one conservative intervention was compared with any kind of interventions (including surgery)
Reported outcomes	► Pain, function, active range of motion
Study design	► Randomised controlled trials
Controlled follow-up period	► Based on predefined criteria
Excluded studies	► Case reports, treatments after surgery, did not meet our specified outcome parameters, traumatic incidents, written in Chinese and Farsi language

Trials Register (CENTRAL), Embase, Medline, CINAHL, and PEDro were searched (search strategy in online supplementary appendix 1) for randomised controlled trials, published as full text in peer-reviewed journals from inception to January 2017. Only Chinese and Farsi language articles were excluded. Relevant reviews and selected articles were also screened for potentially relevant studies (see flow chart in online supplementary appendix 1). Trials that enrolled patients with shoulder impingement diagnosed with a minimal set of diagnostic criteria (one criteria fulfilled of the box 'Complaints of shoulder pain' in table 1, or diagnosed by MRI or ultrasound) and any kind of conservative interventions were eligible for inclusions.

Trials were included if surgery was compared with conservative interventions but not if only different types of surgery or postoperative interventions were compared. Trials that included patients with calcifying tendinitis, frozen shoulders, treatments after surgery and secondary impingement were excluded.

The protocol of this review was presented to an expert committee but not published or registered. Some amendments were made to the protocol after inclusion of the studies but prior to data analysis. This refers, for example, to the amendment of the hierarchy of outcome measures, (ie, which outcome measure should be selected if several measures were used for one outcome) or the refraining from performing a network meta-analysis because of clinical heterogeneity.

Table 2 Hierarchies of outcome measures

	Hierarchy of outcome measures

Pain	► Pain with activity
	► Pain at night
	► Global pain
	► Pain at rest
	► Pain subscales of composite scales
	  ► Pain subscale of SPADI
	  ► Other
	► Pain unspecified

Overall function (activity limitations or participation restrictions)	► Mean of several function scores, if mean and SD calculated in study ► Disability subscale of SPADI (if available; else total score) ► Constant-Murley Total Score ► Disabilities of the arm, shoulder and hand (DASH) ► Oxford Shoulder Scale ► University of California Los Angeles Shoulder Rating Scale (UCLA) ► Shoulder Disability Questionnaire (SDQ) ► American Shoulder and Elbow Surgeons standardised shoulder assessment form (ASES) ► Shoulder Function Assessment (SFA) ► Short Form Functioning and other Algofunctional Scale ► Patients global assessments ► Physicians global assessments
Active range of motion (AROM)	► Active abduction ► Active flexion ► Active external rotation

SPADI, Shoulder Pain and Disability Index.

Study selection criteria and selection process

Each title and abstract was independently screened by pairs of researchers (RS, CK, SE, RH), based on established criteria. Full texts were independently screened by two authors (RS, RH). Disagreement was resolved by consensus, and a third author (MS) was consulted if consensus could not be reached.

Data extraction process

The lead author extracted data of the characteristics of the individual trials and all outcomes for all time points into spreadsheets. A second author (RH) checked the data for accuracy. The primary outcomes considered in this systematic review were pain and shoulder function. The secondary outcome was range of motion. Outcomes were extracted from the longest available follow-up (for main analysis) and the first time point available after the end of the intervention period (for sensitivity analysis). For all outcomes, we defined, a priori, a hierarchy of outcome measures based on the literature and theoretical considerations, and extracted data accordingly (table 2). When a study reported multiple scales for a given outcome, the highest on the hierarchy of pain and shoulder function related scale was chosen (table 2). If reported, change score from baseline to the follow-up were extracted, or else postintervention scores were used.[42]

Risk of bias

The Cochrane Collaboration's tool was used to assess the risk of bias in each included article.[43] Each article was graded (unclear, low or high risk of bias) based on sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, other possible bias, intention-to-treat analysis, selective reporting and baseline characteristics. The risk of bias assessment was completed by one author (RS) and checked by a second author (MS). Disagreements were resolved by discussion, and a third author (RH) was consulted if consensus could not be reached.

Quality of evidence

The Grades of Recommendation Assessment, Development, and Evaluation[44] tool was used to assess the overall quality of evidence. For every comparison, evidence started out to be strong. We decreased the level of evidence by 1 for each of the following factors: risk of bias, inconsistency of results, indirectness, imprecision and other biases, such as reporting bias.

This process of analysis was completed by using a combination of GRADE systematic and traffic alert action, that is, how

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confident we are that it is effective or useless for each intervention and for all outcomes (table 3; adapted from reference 45).[45]

Data management and synthesis

Individual study effect sizes were expressed as standardised mean differences (SMDs), calculated as the difference in means between the two groups, divided by the pooled SD of the measurement. For pain and shoulder function, the sign of the extracted scores was changed according to the idea that higher scores meant worse outcome. Hence, a negative effect size indicated a beneficial effect for the experimental group. AROM scores were intuitively handled differently with higher scores indicating a better outcome. A positive effect size indicated a beneficial effect for the experimental group. If data were missing, we tried to contact the corresponding author. If mean or SDs were not reported, we used different methods to estimate those values (eg, extracting these data from figures, using median and IQR, p values or CIs).[43]

Each intervention was compared against different control groups such as other treatments, usual care or sham treatments. In this review, we used the term active intervention or active control for all treatments that were not placebo, sham or 'doing nothing'. The term passive control was used for all sham or placebo interventions.[43]

Meta-analysis

We decided to use a random effects model a priori. Weighting factors were calculated using the DerSimonean and Laird method.[46] Presence of heterogeneity was tested using a χ^2 test (Q value) and its corresponding degrees of freedom and p value. The extent of heterogeneity was analysed using Higgins' I^2 value (expressed as %). We used a funnel plot to assess publication bias in those comparisons with at least 10 trials.[47]

To test the robustness of the overall weighted effect sizes, a sensitivity analysis was conducted by extracting results for the first time point available after the end of the intervention period. For example, if a study reported results at several follow-up time points (eg, immediately after the intervention period and at 3 months and 6 months), the 6-month data were used for the primary analysis (called longest follow-up) and the data from immediately after the intervention period were used for the sensitivity analysis (called shortest follow-up). Meta-analyses were performed in RevMan V.5.3.[48] In addition, for each risk of bias item, we calculated the differences in the effect sizes between studies with low risk of bias in this item and the studies with unclear or high risk of bias in this item. To test the influence of each risk of bias item on the effect size, we calculated the differences, and corresponding 95% CIs, between low risk and high risk of bias effect sizes. This was repeated for all risk of bias items.

RESULTS

Study selection and characteristics

The electronic database search yielded 9351 studies, from which we screened 324 articles in full text screening (figure 1). Ultimately, we included 200 articles for analysis—177 in the quantitative synthesis (meta-analysis) and 23 in the qualitative synthesis (appendix 2). Ten trials had small samples sizes (n<20),[49–54] whereas most of the studies had sample sizes ranging from 20 to 232 participants. Most studies included participants who were between 18 years and 65 years of age, while the duration of symptoms varied widely across the trials. Injection tests were used in 22 trials, 26 trials used unilateral shoulder problem as inclusion criteria. Two trials included only women or only men.[55 56] In 50 trials there was a greater proportion of female participants than male participants. Insufficient data were reported in 23 studies; we were able to obtain two additional data files.

Risk of bias and quality of evidence

In 90% (n=159) of trials the random sequence generation was adequate. Adequate allocation concealment was observed as low risk of bias in 30% (n=54), unclear in 61% (n=108) and high risk of bias in 9% (n=15) of the included trials. Outcome assessors were blinded in 64% (n=114), while incomplete outcome data in 54% (n=96), and intention-to-treat analysis

Table 3 Relationship between GRADE and traffic alert action

Effect		Grade		Traffic alert action
Favourable	Green	Strong and moderate quality evidence	Strong quality: We are very confident that the true effect lies close to that of the estimate of the effect. Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.	Do it—it is likely to be effective.
Favourable	Orange	Low and very low quality evidence	Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.	Uncertain, measure to determine if progress is made.
Unfavourable	Orange	Low and very low quality evidence		
Unfavourable	Red	Strong and moderate quality evidence	Strong quality: We are very confident that the true effect lies close to that of the estimate of the effect. Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.	Don't do it

were reported in 50% (n=89) of trials (see online supplementary appendix 5).

For all comparisons and outcomes, the quality of evidence was graded as very low.

It was appropriate to assess a funnel plot in one comparison (corticosteroids vs active controls) with 20 trials. The funnel plot had slight asymmetry, indicating a possible risk of publication bias. All other comparisons had less than 10 trials, so funnel plots were not examined.

Across all comparisons, trials with an unclear or high risk of bias on allocation concealment had a significantly greater effect than trials with correct allocation concealment for pain, indicating a small bias (SMD of 0.28 (95% CI 0.05 to 0.51)). For function, AROM, and other risk of bias items in our sensitivity analyses, such as blinded outcome assessor for observer-based outcomes and intention-to-treat, there was no significant difference between trials with high risk and low risk of bias.

Meta-analysis: outcome pain

Hundred and one comparisons from 184 trials with 10 529 patients were included in this meta-analysis. Table 4 summarises the significant results from comparisons including at least 100 patients. Online supplementary appendix 3a shows all summary effect sizes, the Higgins' I^2 measure of heterogeneity (in %) and the level of evidence from the GRADE rating approach. Online supplementary appendix 4a shows all forest plots for the 101 comparisons. The strongest, but still very low quality, evidence for the reduction in pain was found for the following treatments:

Corticosteroids

- Corticosteroids were superior to control (6 studies, n=372, SMD −0.65, 95% CI −1.04 to −0.26)
- Corticosteroids were superior to active controls (physical therapy modalities), but only at the shortest follow-up (20 studies, n=1394, SMD −0.25, 95% CI −0.46 to −0.05)
- Ultrasound guided corticosteroid injections were superior to blind injections (5 studies, n=298, SMD −0.51, 95% CI −0.89 to −0.13).

NSAIDS

- Nonsteroidal anti-inflammatory drugs (NSAIDs) had a small advantage over placebo (1 study; n=306, SMD −0.29, 95% CI −0.53 to −0.05)
- Local anaesthetics were inferior to corticosteroids, but only at the shortest follow-up (4 studies, n=207, SMD 0.45, 95% 0.17 to 0.73).

Exercise

- Exercise was superior to doing nothing (5 studies, n=189, SMD −0.94, 95% CI −1.69 to −0.19)
- Specific exercise was superior to non-specific exercise (2 studies, n=145, SMD −0.65, 95% CI −0.99 to −0.32)

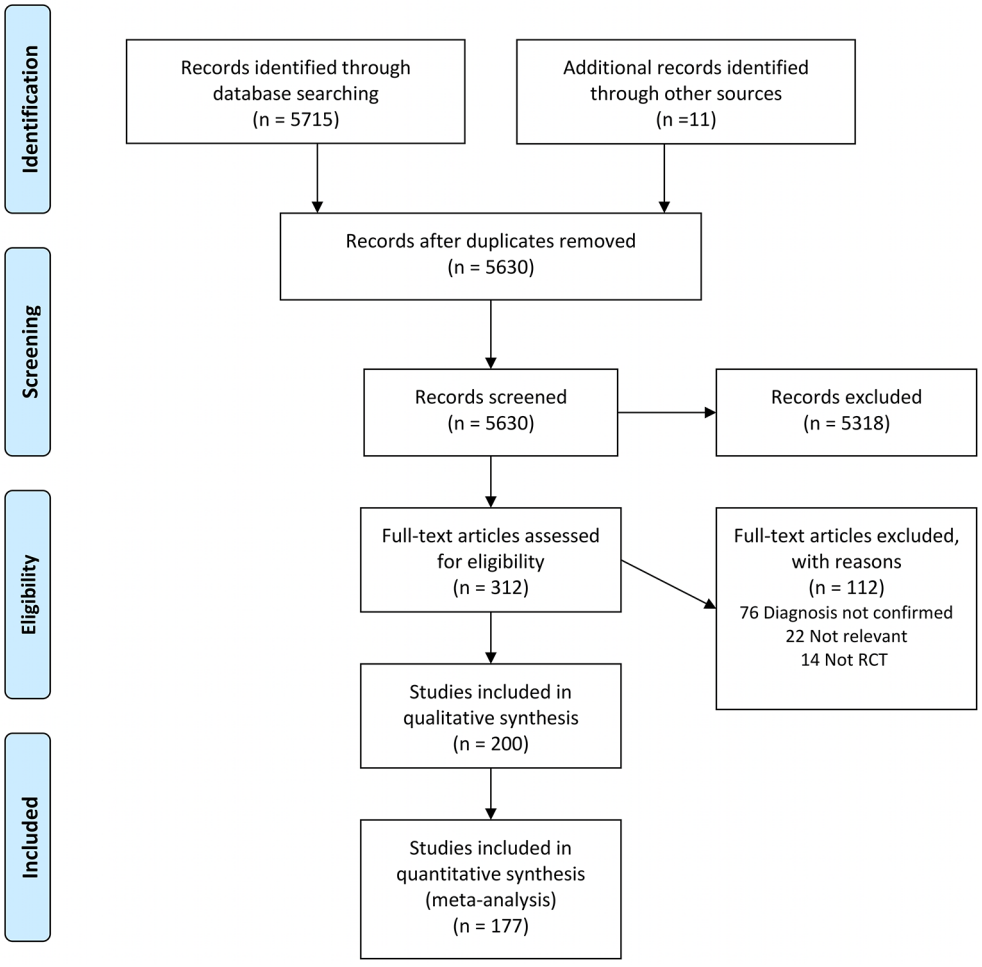

Figure 1 PRISMA flow diagram of the study selection process. RCT, randomised controlled trial.

Table 4 Conservative interventions, quality of evidence and recommendation

Conservative Interventions		« Traffic Light » statements and comments of the authors. Note: *the quality of the evidence is very low and we have but very little confidence in the effect size estimate: The true effect size is likely to be substantially different from the estimated effect size. This does not mean that our results and conclusions are meaningless. Future research might change the conclusions and therefore, practitioners need to reconsider our conclusions if new research becomes available. For all interventions, the readers should bear in mind that due to the insufficient reporting of unexpected adverse effects, no advice can be given with regard to potential harms.*
	Green	Do it—this intervention is effective.
	Orange	Uncertain effect—the effect of this intervention must be monitored, and alternative interventions need to be considered if the effect is not satisfactory.
	Red	Don't do it—this intervention is ineffective.
Corticosteroid injections	Orange	Corticosteroids were superior to doing nothing (pain −0.65, 95% CI −1.04 to −0.26; function −0.56, 95% CI −1.06 to −0.05). Compared with active control (physical therapy modalities), corticosteroids were superior only at the shortest follow-up (pain −0.25, 95% CI −0.46 to −0.05). Corticosteroids may be an alternative treatment if a patient disagrees on the use of other effective treatment options with less side effects, such as exercise. Ultrasound guided corticosteroid injections were superior to blind injections for pain (−0.51, 95% CI-0.89 to −0.13) and for function (−0.43, 95% CI −0.71 to −0.15). For active range of motion (AROM), local steroids were superior to systemic steroids (AROM 0.72, 95% CI 0.32 to 1.11). There was no conclusive evidence for the comparison between corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs).
Medicaments, other than corticosteroid injections	Orange	NSAIDs were superior to placebo (pain −0.29, 95% CI −0.53 to −0.05; AROM 2.62, 95% CI 2.25 to 3.00) but there is no evidence about how they compare to other treatments such as exercise. Local anaesthetics were inferior to corticosteroids at the shortest follow-up (pain 0.45, 95% CI 0.17 to 0.73).
Exercise	Orange	Exercise was superior to doing nothing (pain −0.94. 95% CI −1.69 to −0.19; function −0.57, 95% CI −0.85 to −0.29). Specific exercise was superior to non-specific exercise (pain −0.65, 95% CI −0.99 to −0.32; function −0.68, 95% CI −1.26 to −0.10; AROM 0.59, 95% CI 0.08 to 1.10). Exercise was less effective than surgery for pain but not for function (pain 31% risk difference, 95% CI 13% to 49%), supporting surgery if indication for surgery is given (ie, tears). Exercise was superior to non-exercise physical therapy (AROM 1.00, 95% CI 0.25 to 1.76).
Manual Therapy	Orange	Manual therapy was superior to doing nothing for pain (−0.35, 95% CI −0.69 to −0.01). Manual therapy plus exercise was superior to sham ultrasound and placebo gel for function (−0.42, 95% CI −0.78 to −0.06). Manual therapy combined with exercise was superior to exercise alone only for shortest follow-up (pain −0.32, 95% CI −0.62 to −0.01; function −0.41, 95% CI −0.71 to −0.11). There were immediate effects (after one session) for manual therapy versus placebo for pain (−0.62, 95% CI −0.97 to −0.28).
Laser	Orange	Laser plus exercise was superior to exercise plus sham laser for pain (−0.65, 95% CI −0.99 to −0.31). Laser was superior to sham laser for pain (−0.88, 95% CI −1.48 to −0.27).
Ultrasound	Orange	There was very low statistical precision for the effect estimates of ultrasound; the only significant effect was for long duration ultrasound (8 min) versus short duration (4 min) (pain −1.32, 95% CI −1.76 to −0.89; function −0.42, 95% CI −0.82 to −0.02).
Extracorporeal shockwave therapy (ECSWT)	Orange	ECSWT was superior to sham ECSWT for pain (−0.39, 95% CI −0.78 to −0.01) but there was not enough evidence for or against the use in combination with exercise. Because exercise showed the best effects, the use of ECSWT as stand-alone therapy may be questionable.
Tape	Orange	Tape was superior to sham tape for pain (−0.64, 95% CI −1.16 to −0.12).
Hyaluronate	Orange	Insufficient evidence for or against the use of hyaluronate.
Pulsed electromagnetic field	Orange	Insufficient evidence for or against the use of pulsed electromagnetic field.
Transcutaneous electrical nerve stimulation	Orange	Insufficient evidence for or against the use of transcutaneous electrical nerve stimulation.
Surgery (vs conservative treatment)	Orange	Very low evidence that surgery was superior to exercise or physiotherapy for pain (−0.66, 95% CI −1.06 to −0.26). We cannot exclude that a subset of patients will have a large benefit from surgery.
Acupuncture	Orange	Insufficient evidence for or against the use of acupuncture.
Diacutaneous fibrolysis	Orange	Insufficient evidence for or against the use of diacutaneous fibrolysis.
Nerve block	Orange	Nerve block was superior to control for pain and function (pain −0.91, 95% CI −1.27 to −0.54; function −0.55, 95% CI −1.01 to −0.08).
Myofascial trigger point	Orange	Insufficient evidence for or against the use of myofascial trigger point therapy.
Microwave	Orange	Insufficient evidence for or against the use of microwave.
Comprehensive physiotherapy	Orange	Insufficient evidence for or against the use of comprehensive physiotherapy.
Platelet rich plasma	Orange	Insufficient evidence for or against the use of platelet rich plasma therapy.
Interferential light therapy	Orange	Insufficient evidence for or against the use of interferential light therapy.
Massage	Orange	Insufficient evidence for or against the use of massage.
Microcurrent electrical stimulation	Orange	Insufficient evidence for or against the use of microcurrent electrical stimulation.
US guided percutaneous electrolysis	Orange	Not enough evidence for or against the use of US guided percutaneous electrolysis and eccentric exercises.

- Exercise was less effective than surgery if analysed with a dichotomised outcome (2 studies, n=105, risk difference 31%, 95% CI 13% to 49%).

Manual therapy

- Manual therapy was superior to placebo (4 studies, n=137, SMD −0.35, 95% CI −0.69 to −0.01)
- Manual therapy plus exercise was superior to exercise alone, but only at the shortest follow-up (9 studies, n=363, SMD −0.32, 95% CI −0.62 to −0.01)
- There were immediate effects after one session of manual therapy compared with sham (3 studies, n=134, SMD −0.62, 95% CI −0.97 to −0.28).

Ultrasound, laser, extracorporeal shockwave therapy (ECSWT), tape or nerve block

- Long duration ultrasound was superior to short duration ultrasound (1 study, n=100, SMD −1.32, 95% CI −1.76 to −0.89)
- Laser was superior to sham laser (3 studies, n=128, SMD −0.88, 95% CI −1.48 to −0.27)
- Laser plus exercise was superior to sham laser plus exercise (6 studies, n=313, SMD −0.65, 95% CI −0.99 to −0.31)
- ECSWT was superior to sham-ECSWT (3 studies, n=117, SMD of −0.39, 95% CI −0.78 to −0.01)
- Tape superior to sham tape (5 studies, n=272, SMD −0.64, 95% CI −1.16 to −0.12)
- Nerve block was superior to control (3 studies, n=129, SMD −0.91, 95% CI −1.27 to −0.54).

Miscellaneous

All other conservative interventions (hyaluronate, ultrasound, pulsed electromagnetic field, transcutaneous electrical nerve stimulation (TENS), myofascial trigger point therapy, acupuncture, diacutaneous fibrolysis, microwave and interferential light therapy) showed either non-significant results or significant results but with a very low number of patients (n<100).

Meta-analysis: outcome function

Ninenty-seven comparisons from 173 trials with 10 621 patients were included in this meta-analysis. Table 4 summarises the significant results from comparisons including at least 100 patients. Online supplementary appendix 3b shows all summary effect sizes, the Higgins' I^2 measure of heterogeneity (in %) and the level of evidence from the GRADE rating tool. Online supplementary appendix 4b shows all forest plots for all 97 comparisons.

The strongest, but still very low quality, evidence for the improvement in shoulder function was found for the following treatments:

Corticosteroids

- Corticosteroids were superior to control (5 studies, n=362, SMD −0.56, 95% CI −1.06 to −0.05)
- Ultrasound guided corticosteroid injections were superior to blind injections, but only for the shortest follow-up (4 studies, n=298, SMD −0.43, 95% CI −0.71 to −0.15).

Exercise

- Exercise was superior to doing nothing (4 studies, n=202, SMD −0.57, 95% CI −0.85 to −0.29)
- Specific exercise was superior to non-specific exercise (2 studies, n=145, SMD −0.68, 95% CI −1.26 to −0.10).

Manual therapy

- Manual therapy plus exercise was superior to sham ultrasound and placebo gel (1 study, n=120, SMD −0.42, 95% CI −0.78 to –0.06)
- Manual therapy plus exercise was superior to exercise alone, but only in the shortest follow-up (7 studies, n=301, SMD −0.41, 95% CI −0.71 to −0.11).

Ultrasound

- Long duration ultrasound was superior to short duration ultrasound (one study, n=100, SMD −0.42, 95% CI −0.82 to −0.02).

Tape

- Tape was superior to sham tape, but only in the shortest follow-up (3 studies, n=161, SMD −0.52, 95% CI −1.00 to −0.04).

Miscellaneous

All other conservative interventions (hyaluronate, laser, ECSWT, ultrasound, pulsed electromagnetic field, TENS, myofascial trigger point therapy, acupuncture, diacutaneous fibrolysis, microwave, interferential light therapy and nerve block) showed either non-significant results or significant results but with a very low number of patients (n<100).

Meta-analysis: outcome AROM

Sixty-nine comparisons from 113 trials with 6093 patients were included in this meta-analysis. Table 4 summarises the significant results from comparisons including at least 100 patients. Online supplementary appendix 3a shows all summary effect sizes, the Higgins' I^2 measure of heterogeneity (in %) and the level of evidence from the GRADE rating tool. Online supplementary appendix 4c shows all forest plots for all 69 comparisons.

The strongest, but still very low quality, evidence for the improvement in active shoulder range of motion was found for the following treatments:

NSAIDS

- NSAIDS were superior to control (one study, n=306, SMD 2.62, 95% CI 2.25 to 3.00 for celecoxib and SMD 3.10, 95% CI 2.69 to 3.50 for naproxen).

Exercise

- Exercise vs physical therapy modalities such as ultrasound, TENS, electrotherapy (four studies, n=152, SMD 1.00, 95% CI 0.25 to 1.76).

Miscellaneous

All other conservative interventions (manual therapy, hyaluronate, laser, ECSWT, ultrasound, pulsed electromagnetic field, TENS, myofascial trigger point therapy, acupuncture, diacutaneous fibrolysis, microwave, interferential light therapy and nerve block) showed either non-significant results or significant results but with a very low number of patients (n<100).

Numbers are effect sizes presented as SMDs with corresponding 95% CIs. Here, we only report effect sizes if they were statistically significant and if at least 100 patients were in the comparison. If both longest and shortest follow-up were statistically significant, we only present the longest follow-up. All summary effect sizes are reported in online supplementary appendix 4a (pain and function) and online supplementary

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appendix 3b (AROM). All complete forest plots are reported in online supplementary appendices 4a, 4b and 4c.

DISCUSSION

This systematic review and meta-analysis includes 200 trials comparing strategies to treat shoulder impingement. There was very low quality evidence that for pain and function (1) corticosteroid injections were superior to doing nothing, and ultrasound guided corticosteroid injection was superior to blind injection; (2) exercise was superior to doing nothing, and specific exercise was superior to non-specific exercise. For pain, (3) manual therapy was superior to doing nothing or sham, manual therapy plus exercise was superior to exercise alone (but only at the shorter follow-ups) and manual therapy had immediate effects; and (4) laser was superior to sham. Finally, (5) for AROM exercise was superior to non-exercise physical therapy modalities. The quality of evidence was very low for all comparisons because of high risk of bias, lack of precision, lack of consistency and clinical heterogeneity.

Strength and limitations of this review

There have been previously published reviews on SIS,[12 13 16 18 57] but only one review[57] included all conservative interventions for SIS, and reported the outcomes pain, shoulder function and AROM. Therefore, our meta-analysis provides a comprehensive overview. Another strength of this study is its systematic approach. We followed a stringent protocol and rigorously controlled every step of the process by two or more researchers. We are confident to have included most of the trials reporting on SIS. We used current recommendation to judge the risk of bias of the studies and we used the GRADE approach for the rating of the quality of evidence.[58] It could have been expected that the large number of studies and participants would allow to provide strong evidence for or against the different interventions. However, the methodological quality, the large clinical and statistical heterogeneity, and the low number of participants for most of the comparisons reduced the level of evidence to very low quality evidence. We have only low confidence in the overall effect size of our different meta-analyses. The underlying true population effect sizes might be substantially different from our estimated effect sizes. Nevertheless, some of the observed effects are large and therefore, despite the very low quality of evidence, we are confident that there is still a likely beneficial effect of the interventions.

The included trials had some specific limitations: There was a broad clinical diversity (such as duration of symptoms, diagnostic criteria used, sex ratio), and varying length of follow-up periods. Most of the included trials had a high risk of bias. It is suggested to either restrict the meta-analysis to studies with low risk of bias or to present the results of low risk of bias studies separately from those with high risk of bias. Because only few studies could be classified as low risk of bias, such an approach might have introduced selection bias in our systematic review.[59] Therefore, we decided to include all studies and to perform a sensitivity analysis to evaluate the influence of the high risk of bias studies.

There is a lack of uniformity in the concept of SIS. Braman *et al*[60] argued to abandon the diagnosis impingement syndrome and to investigate more homogenous groups of patients. Two reviews on diagnostic tests proposed to use a battery of tests to confirm SIS.[21 61] For example, to confirm SIS, three out of five tests need to be positive and SIS can be ruled out if less than three out of five tests are positive.[62] Furthermore, the use of multiple tests could help to build a more homogenous group. The use of modern diagnostic technics, so far not routinely used in randomised trials, will enhance the inclusion process and support homogenous grouping.[60] In our review only 61 trials out of 200 confirmed the diagnosis of shoulder impingement and related stage I–III with ultrasound or MRI. Because of insufficient reporting of patients' characteristics regarding classification of impingement (ie, stage I–III) we were not able to perform separate analysis for the different stages. This would be an important analysis, as each stage needs different intervention targets. The interventions might have varying effects in the different stages.

Including trials with varying length of follow-up periods resulted in additional heterogeneity. Follow-up periods in future trials need to be longer to learn more about the course of SIS.[63] In our meta-analysis 137 studies assessed patients within 2 weeks after end of treatment, 54 studies at 6 weeks, 52 studies at the end of 3 months, 24 studies up to 6 months, whereas only 21 studies had a follow-up longer than 6 months, and in 3 studies the length of follow-up was unclear.[51 64 65]

Not all interventions were compared against validated sham interventions or placebo. Non-valid sham interventions might disclose blinding of the participants and hence lead to a falsely increased (biassed) effect size in some of the comparisons against sham interventions. For example, there exist validated sham procedures for manual therapy.[66]

We found a higher proportion of women in the included trials, which is in line with survey data on 2144 Japanese patients having SIS, of whom 60% were women and 40% were men.[67] Hence, with regard to gender mix, our results are generalisable.

Unfortunately, we had to exclude several trials (n=23) for the quantitative analysis because of missing data. However, it is unlikely that those missing results would have changed our reported evidence on effect.

Comparisons with other studies

There exist several other reviews, although previous reviews have focused on fewer interventions.[14–16 19 28 57] The most important difference between our systematic review, and previously published reviews is that we have a more stringent assessment of the risk of bias and quality of included trials. This is important because the strength of recommendations (eg, in future guidelines) will be based on the quality of the evidence. Furthermore, we performed a meta-analysis and decided to evaluate heterogeneity with I^2 statistics, although we refrained from doing a network meta-analysis because of the high clinical heterogeneity.

For exercise, our results are in line with the other reviews, with the exception that we concluded that there is only very low quality evidence where other studies reported moderate[14] or even high or strong evidence.[15 38] Two reviews evaluated scapula-focused treatments, reporting moderate evidence,[36] and significant but clinically not relevant effects;[68] whereas we did not separately analyse the scapula-focused treatments.

Two previous reviews[18 57] concluded that exercise (stretching and strengthening of the rotator cuff and scapular muscles) was as effective as surgery. This contrasts with our interpretation that there is insufficient evidence to state whether exercise is as good as surgery. We classified studies comparing exercise to surgery as being at very high risk of bias. Therefore, our differing interpretation may be first due to our more severe rating of the risk of bias (eg, we classified Haahr *et al*[69 70] and Ketola *et al*[71 72] as high risk of bias studies, whereas Saltychev[18] classified them as low risk of bias. One argument for a high risk of bias rating was

the fact that in the study by Haahr *et al*[69 70] 6 out of 43 patients in the exercise group were operated, 5 of them because of unsatisfactory improvements with exercise, and in the study by Ketola *et al*[71 72] 14 patients from 70 allocated to the exercise group underwent surgery). Second, we also analysed a dichotomised pain outcome, which showed very low quality evidence for an advantage of surgery. However, we cannot exclude that a subset of patients may benefit from surgery.

Acupuncture has been recommended as a first choice to be added to exercises for the treatment of early stage shoulder impingement,[13] whereas we did not find enough evidence to make a statement in favour or against acupuncture. Our results for corticosteroid injections were in line with other reviews,[22 24] although we classified the evidence as a lower level of evidence (very low quality compared with moderate to strong in).[15] Our review supports previous findings[14] regarding low quality evidence for manual therapy. We found positive results for laser, although previous reviews are conflicting about whether laser is[16] or is not[13 57] effective. This might be because previous reviews have included fewer studies,[13] and have not performed a meta-analysis and probably based their statements of evidence on non-significance of the individual trials.[57] Our results for ultrasound therapy, hyaluronate, tape, pulsed electromagnetic field therapy, ECSWT, microwave and platelet-rich plasma support previous reviews.[11 13]

Implication for research

Larger trials that employ rigorous methodology to reduce the risk of bias studies and follow patients for longer than 6 months should be performed. Future trials must include homogenous populations, regarding clinical presentation, diagnostic criteria and duration of symptoms.[60] Also, health economic evaluations alongside such trials are needed to assess the cost-effectiveness and cost utility of different interventions. In studies comparing surgery with conservative interventions a clinical decision rule should be evaluated,[73] to distinguish patients who will only benefit from surgery from those who will recover with conservative treatments. Further research is also needed to evaluate exercise modalities and strategies to increase exercise adherence.

Implication for practice

Although our review only provides very low quality evidence, we suggest that exercise may be considered as the core conservative treatment for shoulder impingement. Furthermore, manual therapy, laser and tape might provide additional benefit. Surgery may be a valid alternative after unsuccessful conservative treatments, and for patients with clearly distinguished clinical signs. Most shoulder surgeons in the UK use a minimum period of 12 weeks of conservative treatments and at least two subacromial steroid injections.[74]

CONCLUSION

Exercise, especially shoulder-specific exercises, should be prescribed for all patients with shoulder impingement. The addition of manual therapy, tape, ECSWT and laser might add a small benefit. For other non-exercise physical therapy modalities, we cannot provide enough evidence for or against, therefore they should only be used in addition with exercise. Corticosteroid injections seems to be a valid alternative only when exercise or other modalities are not possible while NSAIDS can be helpful, if necessary, in addition to exercise. Future research should evaluate treatments applied to patients with a more clearly defined diagnosis.

What is already known?

- There exist several systematic reviews and meta-analyses on the treatment of shoulder impingement.
- A comprehensive review including all conservative treatments is missing.

What are the new findings?

- Exercise therapy was effective in improving pain, function and active range of motion.
- Specific exercises were more effective than general shoulder exercises.
- NSAIDS, corticosteroid injections (with an advantage for ultrasound guided injections), manual therapy, tape in combination with exercise, extracorporeal shockwave therapy and laser were also effective.
- The quality of evidence was very low, therefore clinicians should apply this evidence cautiously when making clinical decisions.

Correction notice This paper has been amended since it was published Online First. Owing to a scripting error, some of the publisher names in the references were replaced with 'BMJ Publishing Group'. This only affected the full text version, not the PDF. We have since corrected these errors and the correct publishers have been inserted into the references.

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