Efficacy of resistance exercises in rheumatoid arthritis: meta-analysis of randomized controlled trials

CRD summary
This review concluded that resistance exercises for rheumatoid arthritis were safe and significantly improved muscle strength, disability, and functional capacity. The review process was generally good, but limitations to the trial quality and size suggest that the authors’ conclusions should be considered to be tentative.

Authors’ objectives
To evaluate the efficacy and safety of resistance exercises for rheumatoid arthritis.

Searching
PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov, were searched to 18 November 2009 for articles published in English or French; search terms were reported. References from relevant articles and reviews were handsearched, as were abstracts, published over the previous five years, of meetings of the American College of Rheumatology (ACR), European League Against Rheumatism (EULAR), and the French Society of Rheumatology (SFR).

Study selection
Randomised controlled trials (RCTs) of resistance exercise in adults diagnosed with rheumatoid arthritis, as defined by the American Rheumatism Association (ARA) or ACR criteria, were eligible for inclusion. Trials of rehabilitation after surgery were excluded. Resistance exercises were defined as repetitive exercises, specifically designed to increase muscle strength through increased or adjusted resistance. The control group had to received non-aerobic rehabilitation, defined as static, range of motion, isometric, seated immersion, relaxation, stretching, no attention, or usual care; trials with aerobic exercise controls were excluded. Relevant outcomes were tender joint counts, pain and disability. The safety of the interventions was assessed by withdrawals and adverse events. Trials were excluded if they did not report extractable data.

Exercises were supervised in half the studies. Exercise programmes were targeted at different parts of the body. Where reported, sessions lasted from 15 to 60 minutes, ranging from daily to three times per week, for three to 104 weeks. The control groups received usual care, motion exercises, or non-aerobic exercise. The outcomes included: muscle strength; disability level, assessed by the Health Assessment Questionnaire (HAQ); functional capacity; disease activity level; swollen and tender joint count; pain on a visual analogue scale (VAS); the erythrocyte sedimentation rate, measured at one hour; exercise tolerance; and radiological damage. Mean age ranged from 41.4 to 62 years. Only 20% of trials specifically included early rheumatoid arthritis patients; in the other trials, disease had been diagnosed from 0.8 to 16.3 years in intervention groups and from 0.7 to 12.3 years in control groups.

Two independent reviewers selected studies, with disagreements resolved by discussion and with a third reviewer if necessary.

Assessment of study quality
Two independent reviewers assessed quality, using the Jadad scale, to give a score out of five for randomisation, blinding and withdrawals. Disagreements were resolved by discussion and with the help of a third reviewer if needed.

Data extraction
Two independent reviewers extracted the data, with disagreements resolved by discussion, including a third reviewer if necessary. Mean differences with 95% confidence intervals were calculated, for each group.

For most outcomes, the mean scores after the intervention were compared between groups. For the HAQ and muscle strength, the changes from baseline values were also compared. Where median values were reported, the median was used as the mean. Standard deviations were estimated conservatively if not reported. Inter-reviewer reliability was
moderate for data extraction and Jadad scoring (κ=0.60, 95% CI 0.47 to 0.73).

Methods of synthesis
Mean differences were pooled to give weighted mean differences with 95% confidence intervals. For tolerance, the results were pooled to give the relative risk of withdrawal or an adverse event, with 95% confidence interval. A random-effects model was used. Inter-study heterogeneity was assessed using an extension of the Cochran Q-test and using $I^2$, which was considered significant when it was over 50%. Statistically significant results were compared with published values to identify minimum clinically important differences.

Sensitivity analyses were conducted to find the effect of removing individual trials from the meta-analysis. For HAQ changes, sensitivity analyses were conducted to find the effect of publication date, trial quality, disease duration, and intervention parameters. Heterogeneity between subgroups was assessed using $X^2$. Publication bias was assessed using the Begg and the Egger tests, and by viewing funnel plots.

Results of the review
Ten RCTs were included, with 547 patients (range 24 to 100). The mean Jadad score was 2.3 (SD 0.6); five trials scored two, one scored one, and four scored three. Only three of these four trials had an intention-to-treat analysis. Completers ranged from 70.2% to 100% for the intervention group and 66.7% to 100% for the control group, where reported.

Efficacy: Resistance exercises significantly increased muscle strength versus controls for isokinetic strength (WMD 23.7%, 95% CI 11.0 to 36.4; $I^2=0$; three trials), isometric strength (WMD 35.8%, 95% CI 24.4 to 47.1; $I^2=68$%; five trials), and grip strength (WMD 26.4%, 95% CI 12.3 to 40.5; $I^2=0$; four trials). Resistance exercises significantly improved disability (HAQ change; WMD -0.22, 95% CI -0.35 to -0.10; $I^2=36$%; nine trials); functional capacity (50 foot walking test; WMD -1.90 seconds, 95% CI -2.95 to -0.85; $I^2=35$%; five trials); joint count (WMD -5.36, 95% CI -9.00 to -1.72; $I^2=73$%; six trials); and erythrocyte sedimentation rate (WMD -5.17mm, 95% CI -8.77 to -1.58; $I^2=0$; three trials). Resistance exercises had no significant effect on pain using VAS ($I^2=57$%; five trials).

Safety: There were no significant differences between resistance exercise and control groups in withdrawals and in total adverse events ($I^2=0$; seven trials, for both).

The sensitivity analyses for HAQ change found that publication date, disease duration, exercise duration, supervision and frequency had a negligible impact, but exercise intensity and trial quality had a slight but not significant impact on the results, with a trend towards higher efficacy in lower quality trials and with higher exercise intensity. There was no evidence of publication bias.

Authors' conclusions
Resistance exercise for rheumatoid arthritis was safe. The improvement in most outcomes, including muscle strength, disability and walking performance, was statistically significant and could be clinically relevant.

CRD commentary
The review addressed a well-defined question for study design, participants, interventions, and outcomes. Relevant databases were searched and unpublished trials were sought, but only those published in English and French were included; some relevant trials might have been missed. Publication bias was assessed and there was no evidence of it, but only 10 trials were analysed. Trial quality was assessed using suitable criteria and was found to be moderate to low. Efforts were made to reduce error and bias throughout the review process. Relevant trial details were reported.

The synthesis seems to have been appropriate, but the values for changes from baseline were not available for many outcomes, which considerably reduces the quality of the evidence. Some of the analyses had high statistical heterogeneity. The authors stated that most of the trials were of middle-aged patients so the results might not apply to older patients. The overall number of participants was low.

The review process was generally good, but the limitations in trial quality and size, suggest that the authors' conclusions should be considered to be tentative.

Implications of the review for practice and research
Practice: The authors did not specifically report any implications for practice, but they implied that physicians should
recommend resistance exercises to rheumatoid arthritis patients.

**Research:** The authors suggested that further RCTs should assess: the medical cost impact of resistance exercises; falls and fractures; quality of life; structural damage; the long-term maintenance and molecular mechanisms of the benefits; and both aerobic and resistance exercise. Trials should compare the effectiveness of supervised and home-based exercise and define relevant adverse events in advance.

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