Efficacy of cardiorespiratory aerobic exercise in rheumatoid arthritis: meta-analysis of randomized controlled trials


CRD summary
The authors concluded that aerobic exercise was safe and effective in patients with rheumatoid arthritis. Given some methodological limitations in the review process and reliance on a large number of studies of uncertain quality, the authors' conclusion and recommendation for practice appears overstated.

Authors' objectives
To evaluate the efficacy of aerobic exercise on quality of life, function, clinical and radiologic outcomes in patients with rheumatoid arthritis.

Searching
PubMed, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to July 2009 for articles in English, French or German. Search terms were reported. Reference lists, review articles and relevant conference abstracts were scanned. ClinicalTrials.gov was searched for unpublished studies.

Study selection
Randomised controlled trials (RCTs) that evaluated cardiorespiratory exercise (50% to 90% of maximal heart rate) compared to non-aerobic rehabilitation in adult patients with rheumatoid arthritis (American College of Rheumatology definition) were eligible for inclusion. Studies of post-surgery rehabilitation were excluded.

Where reported, 47% to 100% of included participants were women. Mean age ranged from 44 to 68 years. Disease duration ranged from one to 16 years. Comparator interventions included non-aerobic and range-of motion classes, and education; more than half of the studies used usual care. Outcomes of interest were tender joint count, swollen joint count, pain and disability. Specific outcome measures included several quality of life scales: health assessment questionnaire (HAQ), disease activity score in 28 joints (DAS28), Ritchie articular Index, visual analogue scale for pain and Larsen's method to evaluate radiologic outcomes. Withdrawals and adverse effects were presented to indicate intervention compliance and safety. Studies were conducted in North America and Europe; there were no UK studies.

One reviewer selected studies for inclusion in the review.

Assessment of study quality
Trial quality was assessed using the Jadad scale (scores ranged from zero to 5) and the Checklist to Evaluate a Report of a Non-Pharmacological Trial (CLEAR-NPT) (scores ranged from zero to 14). Highest scores indicated high quality.

One reviewer carried out the quality assessment.

Data extraction
Data were extracted to enable calculation of mean differences (MDs) and 95% confidence intervals (CI) for all outcomes except intervention safety, for which odds ratios (ORs) were calculated. Data were collected at baseline, one month ± two weeks, three months ± four weeks, six months ± two months, one year and two years or more.

One reviewer extracted data. This process was supervised every two months by two other reviewers.

Methods of synthesis
Standardised mean differences (SMDs) and 95% CIs were synthesised in a fixed-effect meta-analysis (no statistically significant heterogeneity) or a random-effects model (statistically significant heterogeneity). Statistical heterogeneity
was assessed using Cochran’s test and quantified using the $I^2$ statistic (>50% indicated significant heterogeneity).

Subgroup analysis was carried out according to publication date, Jadad score, disease characteristics (mean disease duration and functional status class I to II or including class III), intervention parameters (supervised or home based, individual session and overall intervention duration and frequency). Sensitivity analyses explored the impact of removing one study at a time. Publication bias was assessed using a funnel plot and Begg’s and Egger’s tests.

**Results of the review**

Fourteen RCTs (n=723) were included in the meta-analysis. Jadad scores ranged from 1 to 3 (mean 2.4). The proportion of completers was similar across the study groups.

Small statistically significant beneficial effects of aerobic exercise were found for quality of life (SMD 0.39, 95% CI 0.23 to 0.56, $I^2$=45%; five studies), health assessment questionnaire (SMD 0.24, 95% CI 0.10 to 0.38, $I^2$=29%; nine studies), visual analogue scale pain (SMD 0.31, 95% CI 0.06 to 0.55, $I^2$=30%; six studies) and radiologic outcome (joint preservation) (SMD 0.36, 95% CI 0.16 to 0.56, $I^2$=17%; three studies). No statistically significant differences were reported for joint count, disease activity score and adverse events.

Sensitivity analyses did not materially alter the main results. Subgroup analyses revealed that aerobic exercise was more likely to improve health assessment questionnaire results in patients with class I or II functional status, improve pain where patients with established rheumatoid arthritis were involved in short-term programmes and improve quality of life in patients with early rheumatoid arthritis. Supervised exercise and programmes that lasted at least 60 minutes carried out fewer than three times per week had a greater effect on quality of life than home-based interventions and those with shorter duration carried out more frequently.

There was some evidence of publication bias in the analysis of health assessment questionnaire.

**Authors’ conclusions**

Cardiorespiratory aerobic exercises improved some of the most important outcomes in patients with rheumatoid arthritis. These exercises are safe in those with a stable condition.

**CRD commentary**

The research question was clear. Reproducible inclusion criteria were presented for study design, intervention and participants. The search strategy attempted to locate published and unpublished studies from several relevant sources. Language restrictions meant that studies might have been missed. The authors acknowledged the potential limitations imposed by a single author carrying out data extraction and validity assessment. There was no indication that errors and bias were minimised in the study selection. A relevant quality assessment tool was used.

The results of the Jadad composite score indicated that included studies were of suboptimal quality. It was not possible to determine how the studies scored on individual quality items. Study characteristics were presented in sufficient detail. The authors appropriately advised caution in generalising the review findings beyond middle-aged adults. Statistical heterogeneity was assessed and explored. The chosen methods of synthesis seemed justified. Various difficulties were highlighted by the authors in relation to the study of exercise interventions.

Given the methodological limitations in the review process and reliance on a large number of studies of uncertain quality, the authors’ conclusion and recommendation for practice appears a little overstated.

**Implications of the review for practice and research**

**Practice:** The authors stated that the review supported the frequent recommendation of exercise to patients with rheumatoid arthritis.

**Research:** The authors stated that future trials should investigate clinical and economic impacts of aerobic exercise in the management of rheumatoid arthritis. In particular, aerobic exercise should be rigorously compared with conventional pharmacologic treatment.
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