Effects of exercise training on cardiac performance, exercise capacity and quality of life in patients with heart failure: a meta-analysis
van Tol B A, Huijsmans R J, Kroon D W, Schothorst M, Kwakkel G

CRD summary
The authors concluded that exercise training in stable patients with mild to moderate chronic heart failure results in improvements in exercise capacity and health-related quality of life, and small improvements in cardiac performance during exercise. However, the results may not be applicable to a general population. The review was generally well-conducted and points to the need for further research.

Authors' objectives
To evaluate the effect of exercise training compared with usual care in patients with chronic heart failure (CHF) on cardiac performance, exercise capacity and health-related quality of life (HRQL) measures.

Searching
MEDLINE, CINAHL, EMBASE, the Cochrane Controlled Trials Register, PEDro, SPORTDiscus, PiCarta and DocOnline were searched from January 1985 to October 2004; the search terms were reported. Only English, Dutch, German and French language studies were included. The reference lists of retrieved studies and guidelines of exercise therapy and management of CHF were also checked.

Study selection
Study designs of evaluations included in the review
Studies of randomised controlled trials (RCTs), including those of a crossover design, were eligible for inclusion.

Specific interventions included in the review
Studies that compared exercise training with standard medical treatment without additional exercise training were eligible for inclusion. Exercise training had to include at least one of the following: walking, cycling or resistive training of peripheral muscles. Studies in which only respiratory muscles or one isolated muscle group were trained were excluded. The interventions included were aerobic activities, sometimes combined with callisthenics or ball games, resistance training and interval training. The average training period duration was 13.0 (+/- 7.8) weeks, with a mean session duration of 50.0 (+/- 22.0) minutes and an average frequency of 3.7 (+/- 1.7) times per week.

Participants included in the review
Studies in patients with CHF, where diagnosis was based on clinical findings or a left ventricular ejection fraction (LVEF) of less than 40%, were eligible for inclusion. In the included studies the overall participant characteristics were: age 60.6 (+/- 7.5) years, height 1.72 (+/- 0.03) m, weight 79.6 (+/-6.3) kg, body mass index 26.9 (+/- 1.3), New York Health Association class 24 (+/- 0.2) and LVEF 27.7% (+/- 4.2). The primary aetiology was ischaemia in 55.2% (+/- 28.1) of the participants.

Outcomes assessed in the review
Studies that measured cardiac performance, exercise capacity and/or HRQL were eligible for inclusion. The included studies measured heart rate, systolic and diastolic blood-pressure (BP), LVEF, end-systolic and end-diastolic volume, cardiac output, cardiopulmonary exercise testing, peak oxygen consumption (VO2), anaerobic threshold and 6-minute walking distance (6-MWD). HRQL was measured using a range of scales including the Minnesota Living with Heart Failure Questionnaire.

How were decisions on the relevance of primary studies made?
Two reviewers applied the inclusion criteria independently. When data for the same patients were reported in more than 1 study, only the article that described the largest population was included.
Assessment of study quality
Methodological quality was assessed by applying the 'Delphi score' which includes concealment of randomisation procedure, blinding and intention-to-treat analysis. Two reviewers performed the quality assessment independently. Any disagreements were resolved between reviewers or referred to a third reviewer.

Data extraction
Two reviewers extracted the data independently. For crossover trials, only data at the baseline and results at the point of crossover after the first treatment phase were included in the quantitative analysis. One study had two exercise intervention programmes compared with a control, and this study was considered as 2 separate studies. Effect sizes (ES) for each included study were calculated using the pooled standard deviation of the baseline outcome measure in the treatment and control groups.

Methods of synthesis
How were the studies combined?
The trials were combined using a meta-analysis for each of the outcomes investigated. The calculated ES were weighted for sample size and summarised to obtain a weighted summary ES (SES) using a fixed-effect model. A random-effects model was applied when significant heterogeneity between individual ES was present. Publication bias was assessed by visual assessment of funnel plots and by using Egger's asymmetry test.

How were differences between studies investigated?
Heterogeneity was assessed using the I-squared method. A sensitivity analysis was undertaken to investigate the impact of methodological quality and type of intervention on the calculated pooled ES.

Results of the review
Thirty-five trials (n=1,486) were included: 31 parallel RCTs and 4 crossover trials.

The methodological quality score ranged from 3 to 7 out of 9 points. The main areas of methodological weakness were the lack of concealment of randomisation procedure and the absence of blinding procedures and intention-to-treat analysis.

Cardiac performance at rest.
The pooled ES for diastolic BP at rest showed a statistically significant improvement (7 trials, n=209; SES -0.33, 95% confidence interval, CI: -0.61, -0.05, p=0.021) as did end-diastolic volume (9 studies, n=527; SES -0.21, 95% CI: -0.39, -0.04, p=0.017). However, these effects in natural units were small. Heart rate (14 trials, n=528), systolic BP (11 trials, n=406), LVEF (14 trials, n=683), end-systolic volume (7 trials, n=485) and cardiac output at rest (4 trials, n=131) showed no statistical differences after a period of exercise.

Cardiac performance during maximum exercise.
There were statistically significant changes in favour of exercise training after a period of maximum exercise for heart rate (18 trials, n=683; SES 0.20, 95% CI: 0.05, 0.35, p=0.011), systolic BP (10 trials, n=382; SES 0.22, 95% CI: 0.02, 0.43, p=0.030) and cardiac output (3 trials, n=104; SES 0.58, 95% CI: 0.19, 0.97, p=0.004). However, there was no change in diastolic BP (4 trials, n=118) and the authors reported insufficient data to obtain the results of LVEF during exercise.

Exercise capacity.
There was significant improvement in the results for VO2 (31 trials, n=1,240; SES 0.60, 95% CI: 0.42, 0.79, p=0.000), maximal power output (19 trials, n=715; SES 0.57, 95% CI: 0.42, 0.73, p=0.000), ventilatory or lactic-derived anaerobic threshold (13 trials, n=511; SES 0.84, 95% CI: 0.48, 1.20, p=0.000) and 6-MWD (15 trials, n=599; SES 0.52, 95% CI: 0.36, 0.69, p=0.000). These measurements were all taken during the same cardiopulmonary exercise testing.
HRQL and symptoms.

The HRQL score assessed using the Minnesota Living with Heart Failure Questionnaire decreased significantly from baseline (9 trials, n=463; SES -0.41, 95% CI: -0.60, -0.22, p=0.000); this favoured training.

The authors reported that a sensitivity analysis showed no significant differences between studies with a high or low methodological rating. They reported no evidence of publication bias.

**Authors' conclusions**

Exercise training in stable patients with mild to moderate CHF resulted in statistically significant improvements in maximum heart rate, maximum cardiac output, VO2, anaerobic threshold, 6-MWD and HRQL. The authors also noted that a limitation of the study was that patients with CHF are often older than those included in the meta-analysis and may have additional co-morbidities which limit exercise; this may restrict the generalisability of the review results.

**CRD commentary**

The inclusion and exclusion criteria were clearly defined. Several relevant databases were searched and the authors attempted to locate published studies. Some language restrictions were applied and it is therefore possible that some relevant studies have not been included. The authors attempted to minimise bias and error in the review by carrying out the study selection, data extraction and quality assessment processes in duplicate. Validity was assessed using an aggregate quality score system.

Pooling appears to have been appropriate statistically; the contribution of the number of individual trials to the pooled results was clear. Some outcomes were based on a small number of studies and participants and may therefore be less reliable. Potential sources of heterogeneity and publication bias were explored. The results of any investigations into the effect of type, intensity and duration of exercise on the outcomes were not presented. The review appears to have been well-conducted, but the applicability of the results may be limited due to the fact that the general population outside the trial is potentially older and with a greater range of co-morbidities, which may limit exercise.

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

Practice: The authors did not state any implications for practice.

Research: The authors recommended that further studies be conducted, particularly in elderly patients and those with more severe CHF. They also made recommendations for adherence to methodological principles, in particular, for concealment of treatment allocation, blinding of outcome assessors, and adequate description and analysis of drop-outs. There is a need for general agreement on a core set of measurements to be used in CHF trials that investigate the effectiveness of exercise training, and greater understanding of the mechanisms responsible for improvements related to exercise training.

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