Effect of outpatient exercise training programmes in patients with chronic heart failure: a systematic review

Suzan van der Meer, Marlies Zwerink, Marco van Brussel, Paul van der Valk, Elly Wajon and Job van der Palen

European Journal of Cardiovascular Prevention & Rehabilitation published online 18 May 2011
DOI: 10.1177/1741826711410516

The online version of this article can be found at:
http://cpr.sagepub.com/content/early/2011/05/13/1741826711410516
Effect of outpatient exercise training programmes in patients with chronic heart failure: a systematic review

Suzan van der Meer1,2, Marlies Zwerink1, Marco van Brussel3, Paul van der Valk1, Elly Wajon4 and Job van der Palen1,5

Abstract

Background: Advantages of outpatient exercise training are reduced waiting lists, better compliance, reduced time investment by the patient with reduced travel expenses, and less dependence on other people to participate. Therefore, this systematic review studies the effects of outpatient exercise training programmes compared with usual care on exercise capacity, exercise performance, quality of life, and safety in patients with chronic heart failure.

Design: Systematic review with meta-analysis.

Methods: Randomized controlled trials concerning patients with chronic heart failure, with a left ventricular ejection fraction \( \leq 40\% \), were included. A meta-analysis was performed.

Results: Twenty-two studies were included. VO2max, 6-min walking test, and quality of life showed significant differences in favour of the intervention group of 1.85 ml/kg/min, 47.9 m, and 6.9 points, respectively. In none of the studies, a significant relationship was found between exercise training and adverse events.

Conclusion: This meta-analysis illustrates the efficacy and safety of outpatient training programmes for patients with chronic heart failure.

Keywords

Exercise, heart failure, meta-analysis, outpatient, quality of life, training

Received 23 August 2010; accepted 25 April 2011

Introduction

In Europe, there are at least 15 million patients with chronic heart failure (CHF), and the prevalence is rising due to ageing of the population and improved treatment options.1 Non-pharmacological management of CHF consists of weight monitoring, dietary rules, increasing daily activity, and exercise training. Systematic reviews and meta-analyses have shown that exercise training can reduce mortality and improve exercise capacity and quality of life.2–5 Therefore, nowadays the European Society of Cardiology advocates exercise training to all stable patients with CHF.1

Advantages of near-home exercise training for outpatients are reduced waiting lists, better compliance, reduced time investment by the patient with reduced travel expenses, and less dependence on other people to participate. Also, patients meet fellow patients living in the same neighbourhood which leads to more social contacts, and possibly diminishes social isolation.

It is important to know whether exercise training is effective and safe for outpatients, before making recommendations for this population. Therefore, this systematic review studied the effects of outpatient exercise training programmes compared with usual care on...
exercise capacity, exercise performance, quality of life, and safety in patients with CHF.

Methods

Information sources and search strategy

Studies on the efficacy of exercise training in patients with CHF published between January 1998 and March 2010 were independently identified by two researchers (SvdM and MZ) using PubMed, Cochrane Central Register of Controlled Trials, EMBASE, and PEDro. The PubMed search strategy contained the MESH terms heart failure, rehabilitation, exercise, exercise therapy, physical therapy, training, outpatient, community based, home based, randomized controlled trial, and clinical controlled trial, and was adapted for other databases. Additionally, the ISRCTN register, ClinicalTrials.gov, and the Dutch Trial Register were searched.

Eligibility criteria

Studies were included when the following criteria were met: (1) randomized controlled trials or controlled clinical trials; (2) patients with CHF New York Heart Association (NYHA) class II, III, or IV; (3) left ventricular ejection fraction (LVEF) ≤40%; (4) supervised outpatient training programmes at home, at a hospital, rehabilitation centre, or physiotherapy practice; (5) outcome measures were exercise performance, exercise capacity, and/or quality of life. Studies were excluded when not written in English, German, or Dutch, patients were <18 or >75 years of age, training period was <8 weeks, or when the controls also participated in an exercise programme.

Study selection

Two reviewers (SvdM, MZ) each independently screened the search results. When titles and abstracts suggested a potentially eligible study, the full-text paper was obtained. Disagreements between the authors regarding a study’s eligibility were resolved by discussion. When necessary, a third person (JvdP) acted as adjudicator. Additional reference tracking of eligible studies was performed.

Data collection process

Two reviewers (SvdM, MZ) independently extracted data at baseline and at the end of the intervention period, using the Renal Group Data Extraction Form. If data were missing, attempts were made to contact the study authors.

Risk of bias

The methodological quality of the studies was assessed by the reviewers (SvdM, MZ) using the Physiotherapy Evidence Database (PEDro) list (scores 0–10). Disagreement between the reviewers was assessed using Cohen’s Kappa. Publication bias was evaluated with the inverted funnel plot technique.

Methods of analysis

Outcomes included exercise capacity, exercise performance, quality of life, and number of adverse events. Exercise capacity was defined as the maximum amount of physical exertion that a patient can sustain. Exercise performance was defined as the patient’s ability to perform exercise on a submaximal level. Effect sizes were calculated with Review Manager 5. When necessary, standard deviations were calculated from the 95% confidence interval or standard error of the mean. For continuous outcomes a weighted mean difference between treatment and control group was calculated.

Heterogeneity was tested with I². In the situation of no heterogeneity a fixed effects model was used. When substantial heterogeneity (I² > 50%) was detected, the reviewers searched for explanations (e.g. participant selection, type of intervention), and a random effects model was used.

Results

Study selection

The search strategy identified 200 eligible studies. After screening titles and abstracts, 26 potentially relevant studies were included. Thirteen studies were excluded after reading the full text (Figure 1). Reference tracking provided nine additional studies, so 22 studies were included (Figure 1). No additional studies were found in the trial registers.

Study characteristics

The 22 studies included 3826 participants (mean age 60.1 range 52–71 years); of which 1942 received exercise training. Four exercise training programmes consisted merely of cycling, and one included only walking as type of exercise training. The exercise training programmes in the other 17 studies contained different types of aerobic training of which nine studies also included strength exercises. In 13 studies the intensity...
of aerobic training was based on heart rate,13,15–26 in five studies on VO2max (50–80%),11,12,14,27,28 in three studies on wattage of the speed ramp test29 or BORG scale,30,31 and one did not mention intensity.32 The training frequency ranged from 2–7 times per week, and the duration of a session from 10–60 min. All training programmes were supervised by a physical therapist, a physician, or a nurse.

Three studies were home based,15,20,31 one was community based,16 five were in a hospital or clinic,11,14,25,29,31 ten in a (rehabilitation) centre,12,17,18,21–23,26,27,30,32,33 and in three studies the location was not clearly stated.13,24,28 Table 1 provides additional information concerning patient characteristics, interventions, and settings.

Risk of bias

The PEDro scores varied from 4 to 8 points (Table 2). The main shortcomings were lack of concealment of the randomization procedure, absence of blinding procedures, and lack of intention-to-treat analysis. Agreement between the researchers regarding the methodological quality was 85%. No signs of publication bias were observed.

Synthesis of results

Eighteen studies measured exercise capacity with VO2max (Figure 2). Two of these studies21,53 were excluded due to insufficient data, and two19,30 because a treadmill test was used instead of cycle ergometry, which was used in all other studies.

A statistically significant difference of 1.85 ml/kg/min (95% CI 0.75–2.94) in favour of the experimental group was found, albeit with a heterogeneity of 89%. The maximal workload ($W_{\text{max}}$) achieved during the maximal exercise test was assessed in seven studies (Figure 3). It showed a statistically significant improvement of 14.0 Watt (95% CI 9.0–19.0) in favour of the intervention group, without heterogeneity.

The duration of the maximal exercise test was analysed in 11 studies (Figure 4). Data of three of these studies were excluded, two23,30 due to insufficient data, and one19 because a treadmill was used. The analysis showed a mean significant improvement of 2.1 min (95% CI 1.1–3.1) in favour of the intervention group, however with large heterogeneity.

In ten studies, the 6-min walking test (6MWT) was used to measure exercise performance (Figure 5).
### Table 1. Characteristics of the included studies

<table>
<thead>
<tr>
<th>Publication</th>
<th>Subjects exercise training (n)</th>
<th>Subjects control (n)</th>
<th>LVEF (mean %)</th>
<th>NYHA (I–IV)</th>
<th>Training time/frequency</th>
<th>Duration (months)</th>
<th>Training modality</th>
<th>Setting</th>
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<tr>
<td>Austin et al. (2005)</td>
<td>100</td>
<td>100</td>
<td>&lt;40</td>
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<td>2</td>
<td>A+S</td>
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<td>Hospital</td>
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<td>42</td>
<td>37</td>
<td>27</td>
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<td>10–60 min 5 times/week</td>
<td>3</td>
<td>A</td>
<td>Home</td>
</tr>
<tr>
<td>de Mello Franco et al. (2006)</td>
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<td>12</td>
<td>28</td>
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<td>1 h 3 times/week</td>
<td>4</td>
<td>A+S</td>
<td>Centre and home</td>
</tr>
<tr>
<td>Dracup et al. (2007)</td>
<td>86</td>
<td>87</td>
<td>27</td>
<td>II–III</td>
<td>10–45 min 4 times/week</td>
<td>6</td>
<td>A+S</td>
<td>Home</td>
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<td>45</td>
<td>25</td>
<td>II–III</td>
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<td>6</td>
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<td>Centre and home</td>
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<td>11</td>
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<td>II–III</td>
<td>30–60 min 5–7 times/week</td>
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<td>33</td>
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<td>1 h 4 times/week</td>
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<td>25</td>
<td>II–III</td>
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<td>3</td>
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<td>II–III</td>
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<td>23</td>
<td>27</td>
<td>36</td>
<td>I–III</td>
<td>15–45 min 2–3 times/week</td>
<td>4</td>
<td>A</td>
<td>Hospital</td>
</tr>
</tbody>
</table>

A, aerobic; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association Class; S, strength.
One study was excluded because of insufficient data. The 6MWT showed a significant difference of 47.9 m (95% CI 20.2–74.9) in favour of the intervention group. Heterogeneity was 82%.

In 11 studies quality of life was measured using the Minnesota Living with Heart Failure Questionnaire (MLHFQ), in which a lower score (scale 0–105) represents a better quality of life (Figure 6). Two studies

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### Table 2. PEDro scores of the included studies

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<th>Publication</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>Total score</th>
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<td>+</td>
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were excluded due to insufficient data. Meta-analysis showed a statistically significant difference of $-6.9$ points (95% CI $-10.9$ to $-2.9$) in favour of the intervention group. Heterogeneity was 57%.

In none of the studies, a significant relationship was found between exercise training and adverse events.

**Discussion**

This review shows that outpatient exercise training programmes can significantly improve exercise capacity, exercise performance, and quality of life in patients with CHF. The improvements are also clinically

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**Figure 3.** Maximal workload (W) achieved during the maximal cycle ergometer test.

**Figure 4.** Duration (min) of the maximal cycle ergometer test.

**Figure 5.** Distance walked (m) during the six-minute walking test.
relevant, and these programmes seem to be safe for clinically stable patients.

The meta-analysis shows an improvement in VO\textsubscript{2max} of 1.85 ml/kg/min, which is in line with Rees et al.\textsuperscript{5} and van Tol et al.\textsuperscript{4} To increase VO\textsubscript{2max}, either the cardiac output or the arterial–venous oxygen difference must rise.\textsuperscript{34} Patients with heart failure are not able to change their cardiac output to a large extent by physical training. Therefore, physical training of the peripheral muscles to improve the arterial–venous oxygen difference, and hence the VO\textsubscript{2max}, should be included in physical training programmes.

VO\textsubscript{2max} is a strong predictor of survival in patients with CHF. Mancini et al.\textsuperscript{35} showed that patients with a VO\textsubscript{2max} < 10 ml/kg/min had significantly reduced survival rates compared to patients with a VO\textsubscript{2max} > 14 ml/kg/min. So, although the relative improvement of 2 ml/kg/min found in this review might seem small, it could be considered clinical relevant, particularly in patients with a low VO\textsubscript{2max}. The mean differences in maximal workload of 14.0 Watt, and duration of 2.1 min are also considered to be clinically relevant, and in line with the results from earlier reviews.\textsuperscript{4,5}

To date, there has been little investigation on the minimal clinical important difference on 6MWT in patients with CHF. However, Spertus et al.\textsuperscript{36} found that a mean change in walking distance of 15.9–55.2 m was associated with a mild to moderate improvement in heart failure status. Considering this, the improvement of 47.9 m found in the current review can be classified as clinically relevant. These results are in line with the review articles by Rees et al.\textsuperscript{5} and van Tol et al.\textsuperscript{4} which show clinically and statistically significant differences of 41 and 46 m, respectively in patients with CHF.

The difference in health-related quality of life is 8.1 points in favour of the intervention group. This is largely in line with the findings of van Tol et al.\textsuperscript{4} and Garin et al.,\textsuperscript{37} where differences of 10.0 and 9.6 points were found, respectively. An improvement of 5 points in MLHFQ is the minimal clinically important change.\textsuperscript{38} We did not include the HF-ACTION trial in our meta-analysis for quality of life, since it was the only study that used the Kansas City Cardiomyopathy Questionnaire (KCCQ). In this study, a modest improvement of quality of life was found, but this was not considered to be clinically relevant.\textsuperscript{33}

The current review also showed that outpatient training programmes for patients with CHF are safe in the short term. This is in line with the review of Piepoli et al.\textsuperscript{3} in which the authors state that none of the adverse events were related to the exercise interventions. Moreover, they even reported an overall reduction in mortality due to the intervention.

Although all outcomes show an improvement in favour of the experimental group, it should also be noted that heterogeneity is large (57–83%). This can be explained by diversity in training interventions and patient selection.

The results of the current review are very similar to results found in earlier reviews investigating the effects of exercise programmes in patients with CHF. An explanation for the observed similarities may be that studies that have been published between 2005 and 2010,\textsuperscript{20,22,24–26,29,31–33} and that are included in this review exclusively, do not show stronger effects than the studies that were included in earlier reviews.

The results of this meta-analysis underline that patients with CHF, with an LVEF ≤ 40% and younger than 75 years can benefit from outpatient exercise training programmes. Although exercise training seems safe for these patients, it is important to keep in mind the contraindications for exercise training and testing since these were used as exclusion criteria in the majority of the included studies.\textsuperscript{39,40} The contents of the training interventions in the included studies were diverse. Therefore clear recommendations regarding the most

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**Figure 6.** Quality of life (points) by Minnesota Living with Heart Failure Questionnaire.
effective training type, intensity, duration, or setting cannot be made yet. This is also stated in the review of Carvalho and Mezzani. Furthermore, the studies in this review had a maximum follow-up of only 12 months and thus long-term efficacy is not ascertained. Future research on these topics can help to further sustain the evidence for exercise training in patients with CHF.

Another point of attention for future studies is the methodological quality. Twelve of the 22 studies scored < 6 points on the PEDro scale. The main shortcomings were lack of concealment of the randomization procedure, absence of a blinding procedure, and lack of intention-to-treat analysis in favour of per-protocol analysis. Although concealment and blinding are difficult to achieve in studies of rehabilitation, an intention-to-treat analysis is warranted, because a per-protocol analysis will lead to an overestimation of the effects of exercise training programmes.

In conclusion, this meta-analysis shows that outpatient exercise training programmes can lead to significant and clinically relevant improvements in exercise performance, exercise capacity, and quality of life in patients with chronic heart failure. Also, participation in exercise programmes seems to be safe for these patients. More research is needed concerning individual optimal training programmes and long-term effects of training.

Funding
This work was supported by the Netherlands Asthma Foundation [grant number AF07.038].

Conflict of interest
None.

References


