REVIEW

Editor's Choice — The Effect of Supervision on Walking Distance in Patients with Intermittent Claudication: A Meta-analysis CME

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> **WHAT THIS PAPER ADDS**
> This is the largest meta-analysis to date to evaluate the efficacy of exercise programmes in patients with intermittent claudication. A supervised exercise therapy regimen is superior to other conservative treatment modalities. A dose—response trend is found between the intensity of support and improvement in walking capacity in this patient population.

Background: A number of reviews have reported the influence of exercise therapy (ET) for the treatment of intermittent claudication (IC). However, a complete overview of different types of ET is lacking. The aim of this meta-analysis was to study the effect of supervision on walking capacity in patients with IC. It was hypothesized that there was a positive treatment effect in relation to the intensity of supervision and improvement in walking capacity (i.e., a "dose—response" hypothesis).

Methods: A systematic search in the Cochrane Central Register of Controlled Trials, MEDLINE, and EMBASE databases was performed. Only randomized controlled trials (RCTs) evaluating the efficacy of an ET in IC were included. Type of supervision, treadmill protocol, length of ET, total training volume, and change in walking distance were extracted. RCTs were categorised according to type of support: no exercise, walking advice, home-based exercise (HB-ET), and supervised exercise therapy (SET). A standardised mean difference between pre- and post-training maximal walking distance (MWD) and pain-free walking distance (PFWD) was calculated for all subgroups at 6 weeks, and 3 and 6 months of follow up.

Results: Thirty studies involving 1406 patients with IC were included. The overall quality was moderate-to-good, although number of included patients varied widely (20—304). The intensity of supervision was directly related to MWD and PFWD. SET was superior to other conservative treatment regimens with respect to improvement in walking distances at all follow-ups. However, the difference between HB-ET and SET at 6 months of follow up was not significant.

Conclusion: Supervised exercise therapy for intermittent claudication is superior to all other forms of exercise therapy. Intensity of supervision is related to improved walking distance.

INTRODUCTION

In 2010, 202 million people worldwide were coping with peripheral arterial occlusive disease (PAOD).[1] During the preceding decade, the number of affected individuals increased by 13.1% and 28.7% in high- and low—middle-income countries, respectively.[1] These huge numbers illustrate that PAOD has become a global health problem affecting vast numbers of individuals. Some 50—80% of patients with PAOD are symptomatic and suffer from intermittent claudication (IC), the mildest manifestation of in PAOD.[2]

To protect patients from cardiovascular events and related morbidity and mortality, international guidelines indicate that the treatment of IC should consist of cardiovascular risk management. Moreover, supervised exercise therapy (SET) is advised to reduce symptoms and restore physical function.[2,3] However, widespread implementation

of SET is restricted by the combination of an insufficient number of available facilities and issues of reimbursement, awareness, and motivation.[2,4–6] To overcome some of these problems in the Netherlands, a community-based network for SET was implemented.[5] Community-based SET solves the problem of transportation time and costs for individual patients, as well as the restricted capacity of hospital-based SET.[7,8] Others have suggested the initiation of exercise programmes in a home-based environment, thereby diminishing the amount of labour-intensive supervision.[9,10] A recent published trial revealed promising results regarding the effect of such an approach.[11]

Several reviews are currently available regarding the value of different conservative treatment options in IC.[12–16] However, no meta-analysis has yet compared SET with home-based exercise, non-supervised regimens, and a control group. A recently updated Cochrane review compared unsupervised exercise with supervised exercise with regard to improvement in walking.[16] A second review that was aimed at identifying components of SET contributing to maximal improvement of walking capacity only compared supervised exercise with no exercise at all.[13] Despite the use of strict inclusion criteria in both reviews, some overlap in included trials was inevitable. Moreover, the latter reported that intensity, duration, or programme content were not independently associated with improvement in maximal or pain-free walking distance, but the role of support was not addressed.

The present effort aimed to evaluate the effect of various grades of supervision on walking capacity by providing a meta-analysis of the existing literature concerning exercise programmes for IC. It was hypothesised that a dose—response relationship was present between supervision and improvement in walking capacity.

METHODS

Eligibility criteria

Only randomised controlled trials (RCTs) of patients with IC (Fontaine II/Rutherford 1—3) were eligible for inclusion in this meta-analysis. An RCT was included if each intervention group received at least one type of exercise, if the type of supervision was different between study groups, if supervision and duration of exercise therapy (ET) exceeded 6 consecutive weeks, and if > 50% of the exercise time included lower limb training. Outcomes had to be reported as maximal walking distance/time (MWD/T) or pain-free walking distance/time (PFWD/T), or both. Only English or Dutch studies were included. Trials with a control group undergoing invasive therapy or specific drug treatment were excluded.

Trial selection strategy

An electronic search was conducted in MEDLINE (for the period January 1966—March 2013), EMBASE (January 1974 to March 2013), and the Cochrane Central Register of Controlled Trials (CENTRAL) database (January 1966 to September 2012). The search strategy contained the following medical subject heading terms: "Arteriosclerosis", "Arterial Occlusive Diseases", "Intermittent Claudication", "Peripheral Vascular Diseases", "Exercise", "Exercise Therapy", "Physical Exertion", "Sports", "Exercise Movement Techniques", "Locomotion", "Leisure Activities", "Fitness Centers, Physical Exertion". In addition, reference lists of papers identified from these searches were hand-searched for additional trials. Three authors (LG, RS, and HF) independently selected trials on the basis of title and abstract. A definite selection was based on full-text evaluation of the report. Disagreement between the reviewers was discussed and resolved by consensus.

Risk of bias assessment

The included articles were assessed by two authors (LG and RS) using the Cochrane scale to determine methodological quality and to assess the risk of bias. Blinding of staff and patients during exercise programmes is not possible and was therefore not taken into account. Study quality was determined using a table of risk of bias on the basis of a checklist of design components, including random sequence generation, allocation concealment, incomplete outcome data, and selective reporting (Appendix 1). The adequacy of each category was assessed as "low", "unclear", or "high" risk, as suggested in the Cochrane Collaboration Handbook.[17]

Data collection and processing

Trial data were extracted by three authors (LG, HF, and RS) using a standardised data extraction form that was checked by a fourth author (SH). Study characteristics, year of publication, study location, and type of supervision were collected, as well as patient group characteristics, including mean age and sex, number of patients in each group, and walking distances (MWD and PFWD, pre- and post-training). The authors of individual articles were contacted for additional information when there was ambiguity or missing data.

Where MWD/PFWD were reported, conversion into distances (metres) was performed by multiplying the time spent on the treadmill by the given walking speed (m/s). If standard errors (SEs) were available (and the authors did not reply or declined the request to release unpublished data), we converted these values into standard deviations (SDs). In articles that reported nonparametric data, the SD was calculated by dividing the interquartile range by 1.35, as suggested by the Cochrane Handbook.[17]

Labelling of supervision

Two authors (RS and LG) independently categorised treatment arms per study by classifying the type of supervision given per arm, and the following groups were defined.

1. Control group (NO-ET): Participants were mainly advised to consolidate current levels of activities, while some additionally received best medical treatment.
   Supervised walking exercise or a walking advice was not provided during the treatment period.