



WHAT ARE THE EFFECTS OF DIFFERENT MODES OF EXERCISE TRAINING FOR INTERMITTENT CLAUDICATION? - A COCHRANE REVIEW SUMMARY WITH COMMENTARY

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The aim of this commentary is to discuss from a rehabilitation perspective the published Cochrane Review "Modes of exercise training for intermittent claudication"⁽¹⁾ by Jansen SCP et al¹, under the direct supervision of Cochrane Vascular. This Cochrane Corner is produced in agreement with the Journal of Rehabilitation Medicine by Cochrane Rehabilitation.

Key words: Cochrane Review Summary, exercise training, intermittent claudication, systematic review, walking

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BACKGROUND

Peripheral arterial disease (PAD) of lower limbs is an atherosclerotic cardiovascular disease in which the arteries carrying blood become narrowed and obstructed. It is a common problem and estimated to affect over 200 million people worldwide (2). Major risk factors include smoking, diabetes, and dyslipidemia. The most common symptom of PAD is intermittent claudication (2). It is defined as inadequate blood flow to the muscles of the lower limb causing cramping pain which appears during walking activity and is relieved with a short period of rest (3). Pain during activity can adversely affect quality of life and restricts activities of daily living (4). Exercise is recommended for intermittent claudication due to PAD in order to improve walking capacity, claudication symptoms and quality of life, and for secondary prevention of cardiovascular disease (5).

¹This summary is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2020, Issue 8, Art. No.: CD009638, DOI: 10.1002/14651858.CD009638.pub3 (see www.cochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review. The views expressed in the summary with commentary are those of the Cochrane Corner authors and do not represent the Cochrane Library or Wiley..

MODES OF EXERCISE TRAINING FOR INTERMITTENT CLAUDICATION

(Jansen SCP, Abaraogu UO, Lauret GJ, Fakhry F, Fokkenrood HJP, Tejjink JAW, 2020)

WHAT IS THE AIM OF THIS COCHRANE REVIEW?

The aim of this Cochrane Review was to evaluate the effects of alternative modes of supervised exercise therapy compared to traditional walking exercise in patients with intermittent claudication.

WHAT WAS STUDIED IN THE COCHRANE REVIEW?

This review is an update of the 2014 review published on the same topic (6). This review addressed adults over the age 18 years with clinically diagnosed intermittent claudication (of grade being Fontaine II or Rutherford 1 to 3) who were selected for conservative management. The interventions studied were alternative modes of exercise (arm ergometer, strength training, cycling, Nordic walking, etc.) or combination of these forms of exercise'. The intervention was compared to traditional walking exercise. To be included in the review the exercise program had to be supervised at least twice a week during six consecutive weeks of training. The primary outcome measure was maximal treadmill walking distance or time (MWD/T) and the secondary outcome measures included Pain-free treadmill walking distance or time (PFWD/T), Health-related quality of life scores (HR-QoL) and Self-reported functional impairment (Walking Impairment Questionnaire).

SEARCH METHODOLOGY AND UP-TO-DATENESS OF THE COCHRANE REVIEW?

The review authors searched for studies that had been published up to 4 March 2019 from Cochrane Vascular

Specialised Register, Cochrane Central Register of Controlled Trials, MEDLINE, Embase Ovid, CINAHL Ebsco and AMED Ovid. Two trial registries were also searched including World Health Organization International Clinical Trials Registry Platform and Clinicaltrials.gov. The reference lists of relevant studies identified by the above search strategies were further explored to identify other relevant studies.

WHAT ARE THE MAIN RESULTS OF THE COCHRANE REVIEW?

The review included 10 RCTs (including 2 quasi randomised trials) with 527 participants. The mean age of the participants ranged from 62 and 73.4 years. All studies included both male and female participants. The female participants ranged from 7% to 54%. Most studies were carried out in high income countries (Australia, Poland and the USA) with one study from Brazil.

Alternative modes of exercise training compared to traditional walking exercise after 12 weeks of training:

- Maximum walking distance (MWD) at 12 weeks of training was reported in six studies ($n=274$). MWD was reported in lower-extremity resistance training by three studies with (standardised mean difference (SMD) -0.02 , 95% confidence interval (CI) -0.59 to 0.55 ; $p=0.94$ ($n=94$); Nordic walking in two studies (SMD 0.31 , 95% CI -0.12 to 0.74 ; $p=0.15$, $n=88$); combined exercise modes in three studies (SMD -0.19 , 95% CI -0.66 to 0.29 ; $p=0.44$ ($n=74$) and arm ergometer in one study SMD -0.84 , 95% CI -1.87 to 0.19 ($n=18$). When compared to traditional walking there was no clear difference for any of the alternative mode of exercise after 12 weeks of training (SMD -0.01 , 95% CI -0.29 to 0.27 ; $p=0.95$) (low certainty evidence).
- Pain free walking distance (PFWD) at 12 weeks of training was reported in five studies ($n=249$). PFWD was reported in lower-extremity resistance training by two studies (SMD 0.11 , 95% CI -0.32 to 0.55 ; $p=0.61$ ($n=80$), Nordic walking by two studies (SMD 0.14 , 95% CI -0.28 to 0.57 ; $p=0.51$ ($n=88$), combined exercise modes by two studies ($n=63$) and arm ergometer by one study (SMD -0.22 , 95% CI -0.74 to 0.30 ; $p=0.40$ ($n=18$). There was no clear difference for PFWD between alternative mode of exercise compared to traditional walking after 12 weeks of training with (SMD -0.01 , 95% CI -0.26 to 0.25 ; $p=0.97$) (low certainty evidence).

Alternative modes of exercise training compared to traditional walking exercise at end of training:

- Maximum walking distance (MWD) at the end of training was reported by nine studies ($n=412$). The

duration of exercise programs varied from 6 to 24 weeks. MWD was reported in lower-extremity resistance training in 4 studies (SMD -0.06 , 95% CI -0.48 to 0.35 ; $p=0.77$ ($n=127$), Nordic walking in three studies (SMD 0.04 , 95% CI -0.47 to 0.54 ; $p=0.88$ ($n=165$), combined exercise modes in three studies ($n=74$), arm ergometer in one study ($n=18$) and cycling in one study (SMD -0.31 , 95% CI -1.06 to 0.43 ; $p=0.41$ ($n=28$). There was no clear difference for MWD in alternative modes of exercise training compared to traditional walking exercise at end of training (SMD -0.11 , 95% CI -0.33 to 0.11 ; $p=0.32$. (low certainty evidence).

- Pain free walking distance (PFWD) at end of training was reported by eight studies ($n=382$). PFWD was reported in lower-extremity resistance training by 3 studies (SMD 0.01 ; 95% CI -0.37 to 0.38 ; $p=0.98$ ($n=108$), Nordic walking in three studies had little to no difference between groups (SMD 0.21 ; 95% CI -0.10 to 0.52 ; $p=0.19$) ($n=165$), combined exercise modes in two studies ($n=63$), arm ergometer in one study ($n=18$) and cycling in one study (SMD -1.01 , 95% CI -1.81 to -0.22 ; $p=0.01$; ($n=28$). There was no clear difference for PFWD in alternative modes of exercise training compared to traditional walking exercise at end of training SMD of -0.06 (95% CI -0.30 to 0.17 ; $p=0.59$. (low certainty evidence).
- Health-related quality of life (HR-QoL) at the end of the training was reported in four studies. Due to the heterogeneity in outcome measure meta-analysis was not done.
 - Two studies reported the physical functioning score of the SF-36 and found improvement in both exercise groups.
 - One study used Medical Outcomes Study (MOS) SF-20 to assess HR-QoL. It consists of five domain scores: physical functioning score, social functioning score, role functioning score, overall health score, and well-being score. After 12 weeks of training, the physical functioning scores improved by 24% (95% CI 9 to 39) for the walking group, and the well-being scores increased by 9% (95% CI 2 to 16) for the lower-extremity resistance training group. No improvement in the other MOS domains was detected.
 - One study used the Australian Vascular Quality of Life Index and reported improvement both in treadmill walking group ($n=15$) and the combination exercise group ($n=12$) with mean decrease of 1.6 points (SD 2.4) and 3.3 points (SD 3.9), respectively ($p=0.18$).
- Self-reported functional impairment was reported in three studies using Walking Impairment Questionnaire. Meta-analysis was performed for two studies

only ($n=96$) and it showed little or no difference between alternative modes of exercise and walking exercise with a mean difference of -5.52 (95% CI -17.41 to 6.36 , $p=0.36$). (low certainty evidence).

HOW DID THE AUTHORS CONCLUDE?

The authors concluded that for patients with intermittent claudication due to PAD there was little to no difference between alternative exercise programs and supervised walking exercise when using maximum walking distance and pain free walking distance as outcomes measures. This was mainly because of risk of bias, small sample size and clinical inconsistency in the included studies. Authors also concluded that alternative exercise modes may be useful when supervised walking exercise is not an option. They recommended the need for better trials with a larger sample size and robust methodology to provide better evidence and a clear answer.

WHAT ARE THE IMPLICATIONS OF THE COCHRANE EVIDENCE FOR PRACTICE IN REHABILITATION?

Between 10%–35% of patients with PAD have classic intermittent claudication (7). It can adversely affect the mobility and quality of life of the person experiencing these symptoms. Supervised and home-based exercise plans are recommended as a first line of management. Walking is the modality of exercise with the strongest evidence and is recommended in several national and international guidelines (8). It is suggested that the structured walking programs improve pain-free walking distance better than pharmacologic therapy alone (9). In a large cohort of more than 54,000 Dutch patients, those who received supervised exercise training as a primary intervention had fewer lower limb revascularizations and demonstrated better survival than patients undergoing primary endovascular revascularisation or open surgery (10). Despite the evidence for supervised exercise, it remains an underutilized tool (11). Rehabilitation professionals are experts in the provision of exercise and need to understand the value of providing different forms of exercises in a tailored manner to the individual patients presenting with intermittent claudication. They should encourage and support the patients to adhere to a home-based exercise plan. In patients with PAD, active participation in a home-based exercise program was associated with a lower rate of death and better long-term clinical outcome (11). It is also important that the rehabilitation professionals identify and address the barriers towards exercise in patients with intermittent claudication. These may include exercise-induced pain and

depression (12). This approach is likely to improve the outcomes and reduce symptoms.

However, the current review suggests that the evidence for different forms of exercise in patients with intermittent claudication is low. Therefore, it is imperative that rehabilitation professionals conduct high quality rigorous trials to determine the true effectiveness of different forms of exercise for intermittent claudication.

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