



## Review

## Upper versus lower limb exercise training in patients with intermittent claudication: A systematic review



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## ABSTRACT

Lower extremity (LE) exercise training has been shown to contribute to improvements in Maximum Walking Distance (MWD), Claudication Distance (CD), peak oxygen uptake (VO<sub>2peak</sub>) and Quality of Life (QoL) in patients with intermittent claudication (IC). However, little is known regarding the efficacy of upper extremity (UE) exercise training in comparison to the widely used LE training. The objective of this systematic literature review is to identify and synthesize the available literature on the effects of UE versus LE exercises using the International Classification of Functioning (ICF) conceptual framework. A total of 6 randomized controlled trials comparing UE to LE exercises were included in this study. Two of the articles were considered to be of high quality using the PEDro grading list. Both UE and LE training groups demonstrated significant improvements in MWD, CD, VO<sub>2peak</sub> and QoL in comparison to the control group but LE was not better than UE training. This supports the use of UE training as an alternative to LE, which could provide symptomatic relief to patients with IC without the discomfort caused during the LE training.

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## 1. Introduction

Peripheral arterial disease (PAD) broadly encompasses the atherosclerotic occlusion of the arteries, excluding coronary and intracranial vessels [1]. Its incidence is growing, probably reflecting a general increase in the incidence of atherosclerotic diseases, currently affecting up to 20% of the population worldwide, and constituting a serious global problem [2]. Intermittent claudication (IC) is the cardinal symptom in the clinical presentation of PAD [3], affecting approximately a third of those with PAD [4]. It is consistently manifested as pain and/or cramping in the legs during ambulation that subsides with rest [3,5]. IC results from a failure of the arterial system to deliver an adequate flow of oxygenated blood

to peripheral tissues [6], causing ischemia and thus, pain. The localization of symptoms is typically distal to the arterial occlusion. Atherosclerosis most commonly affects the femoral and popliteal arteries, thus, IC is usually experienced in the calves [5,7]. IC can result in severe functional limitations [8,9] and diminished quality of life (QoL) [9–13]. First-line treatment of IC aims to improve the patient's quality of life (QoL) by relieving the symptoms as well as to manage the risk factors related to cardiovascular morbidity and mortality. The choice of intervention is made on a selective, patient-specific basis.

Exercise therapy is an inexpensive alternative to invasive treatments for symptomatic PAD [14,15]. In accordance with the exercise principle of specificity, most rehabilitation programs have involved the lower extremities (LE) and have included some form of walking exercise [15,16]. The TASC-II working group recommends walking to a moderate-high level of claudication pain as an initial treatment [17], but exercise therapy guidelines differ in the published literature [16,18]. Current recommendations include

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'walking to a moderate level of claudication pain, rest and repeat as often as possible' [17], or less specifically, 'simple walking regimens, dynamic and static leg exercise, individualized treadmill exercise' [18]. However, the frequency and severity of ischemic pain induced by walking could discourage many patients from participating in LE exercise rehabilitation. Moreover, the high rates of comorbidity pose particular challenges to the execution of LE exercises and deter some patients from engaging in those programs. These barriers could be overcome by alternative training strategies such as exercises of the upper extremity (UE) that could reduce or prevent the claudication pain during the training. Such exercise programs could potentially have additional effects, reinforced by contemporary understanding of peripheral endothelial function [19]. This underlines the importance of exploring and determining the role of various modes of exercises other than the conventional walking or LE training regimen. Therefore, the aim of this systematic literature review was to investigate the effects of UE exercise in comparison to LE exercise in patients with PAD who were experiencing IC.

The outcome measures considered within this review were evaluated by means of the International Classification of Functioning, Disability and Health (ICF) conceptual framework. This model facilitated the realization that considering 'Illness' alone only supplies a partial perspective of health status. This is an important factor especially when designing a treatment program. Endorsing a more holistic approach has proven successful in the overall rehabilitation of a patient [20].

## 2. Methods

### 2.1. Literature search

A literature search was carried out by two researchers independently (NT, CF) targeting randomized controlled trials (RCTs) until February, 2014 in 4 databases: PubMed, PEDro, ScienceDirect and Google Scholar. A preliminary search using Cochrane was conducted to ensure the absence of any prior reviews comparing UE and LE exercises in treatment of PAD patients. PubMed is the most widespread free scientific database for clinicians and researchers in the biomedical field [21], and therefore the main database used to carry out the search. The reference list of all relevant articles was manually screened for missing references.

The following key words and MESH terms were used: 'Peripheral Arterial Disease', 'Intermittent Claudication', 'Upper Limb Exercise', 'Lower Limb Exercise', 'Upper Limb Training', 'Lower Limb training', 'Arm' and 'Treadmill'. No dates of publication filters were applied.

### 2.2. Study selection

#### 2.2.1. Inclusion criteria

The RCTs comparing UL and LE aerobic forms of exercise interventions in PAD patients, older than 18 years of age and experiencing IC symptoms for at least 12 months were included in this review, in which PAD was diagnosed by a Doppler assessment of the ankle brachial pressure index (ABPI) with a score of <0.9. The outcome measures used in the RCTs must have included at least one of the following: maximum walking distance (MWD), pain-free walking distance (PFWD) or claudication distance (CD), aerobic capacity or peak ( $VO_{2peak}$ ) or maximum oxygen uptake ( $VO_{2max}$ ) and QoL.

#### 2.2.2. Exclusion criteria

Articles which were not RCTs and were not written in English were not included in this review. Moreover, they were excluded if they examined patients who experienced IC symptoms for less than

12 months, had undergone a revascularization within the last year before the recruitment and had a limited exercise capacity due to health problems other than IC, e.g., arthritis, impeding gangrene, shortness of breath, angina pectoris or recent myocardial infarction.

### 2.3. Quality assessment

The included RCTs were evaluated for methodological quality using the PEDro scale. The PEDro scale is a method commonly employed to conduct a sensitivity analysis or meta-regression and exclude low quality trials or weight them less heavily in a meta-analysis [22]. As the healthcare paradigm has shifted towards evidence-based practice, it has become highly important to ascertain the most efficient and effective approach to achieve the desired outcomes. Studies with better methodological quality provide greater evidence regarding which intervention might be the most advantageous to utilize in a clinical setting. Therefore, it should be noted that studies demonstrating the greatest improvement in  $VO_{2peak}$ , MWD, PFWD, CD or QoL do not necessarily provide the strongest evidence in support of a particular exercise intervention if they had a low score in the PEDro list. In this review, reporting the methodological quality is intended to provide clinicians with a valuable guide to distinguish trials that are more likely to be valid and contain appropriate statistical information to be interpretable from those that are not [23]. An RCT is considered to be of 'excellent' quality if it scored 9 or 10 on the PEDro scale. Scores ranging from 6 to 8 are indicative of 'good' quality, while 4–5 are of 'fair' quality. A score below 4 is considered to show 'poor' quality. The choice of these cut-off points was made arbitrarily in an effort to simplify the interpretation of each trial's quality level [24].

## 3. Results

The literature search identified 1051 potentially relevant articles, of which 798 articles were excluded because they were not RCTs or they were not written in English (Fig. 1). The titles and abstracts of the remaining 253 articles were analyzed, resulting in the exclusion of 244 articles. Full text analysis of the remaining 9 articles followed, which resulted in the exclusion of 3 articles due to mismatching of the outcomes used. Finally, 6 RCTs were included and evaluated for their methodological quality via the PEDro scale. The score of each study and its estimated level of quality are illustrated in Supplementary Table 1. The two studies by Saxton et al. [25,26] were considered of high quality and the remaining of fair quality.

### 3.1. Participants

A total sample of  $n = 503$  subjects was studied from the included RCTs ranging from Bronas et al. [27] ( $N = 28$ ) to Saxton et al. [25] and Zwierska et al. [28] ( $N = 104$ ). Males and females were not equally represented in the sample; males accounting for the 77% of included patients (387). Participants' age ranged from 50 to 85 years and the mean age ranged from 63 to 72 years. All subjects were confirmed as PAD patients by means of the Doppler assessment of the ABPI; the mean ABPI ranged from .64 to 0.71. Subjects were included in the studies when no other severe cardiovascular pathology was present and IC symptoms lasted >12 months (15–68 months). The demographic characteristics of all participants included in the 6 RCTs are presented in Table 1.

All the selected articles compared the effects of UL and LE on a variety of outcomes in patients with IC who shared similar baseline characteristics. In 5 out of 6 studies the participants were randomized to 3 groups: UE training, LE training and a control group that did not engage in any exercise program, yet they were

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