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

Running title: Exercise training and intermittent claudication

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Manuscript Type: Review

Word Count: 4230

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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_{2peak}) 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_{2peak} 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.

Keywords: peripheral arterial disease, maximum walking distance, claudication distance, functional capacity

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 '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 into 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 awere 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 to be successful in the overall rehabilitation of a patient.[20]

Methods

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.

Study selection

Inclusion criteria. ~~Randomized controlled trials (~~Those 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.

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.

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 a 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 6-8 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]

Results

The literature search identified 1,051 potentially relevant articles, of which 798 articles were excluded because they were not RCTs or they were not written in English (**Figure 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 ~~Table 1~~ **(Supplementary file 1)**. The two studies by Saxton et al[26,29] were considered of high quality and the rest of fair quality.

Comentario [NT1]: Does the reference order need to change as now Saxton appears first? Eso tú, Fab

Participants

A total sample of n=503 subjects was studied from the included RCTs ranging from Bronas et al.[25] (N=28) to Saxton et al.[26] and Zwierska et al.[27] (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 0.64-0.71. 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 12**.

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 instructed to keep an active lifestyle. Treat-Jacobson et al[28] created a 4th group in which both UE and LE exercises were performed.

Interventions

As displayed in **Table 32**, the types of intervention were arm cranking exercises as UE intervention in all included RCTs and leg cranking/cycling exercises as LE intervention with the exception of Bronas et al[25] and Treat-Jacobson et al[28], which used treadmill walking as a substitute. Arm and leg cranking exercises were set at an intensity of 85-90% of limb specific VO_{2peak} in the RCTs carried out by Saxton et al.[26,29,30] Zwierska et al[30] employed the Borg Rating of Perceived Exertion (RPE) as an additional intensity parameter, and the RPE score had to remain between 13-16 on the 6-20 version of the RPE scale. RPE was also used by Bronas et al[25] and Treat-Jacobson et al[28], in which the intensity values were progressively adjusted to maintain a score of 13-15. Walker et al.[31] assessed all subjects prior to training and adjusted the intensity to the achieved workload before failure. After 3 weeks of training, Treat-Jacobson et al[28] and Walker et al[31] increased intensity to the maximum workload achieved (leading to failure) during the baseline assessment. After this time period, Treat-Jacobson et al[28] continued increasing the training intensity every 2 to 3 weeks by extending the training and decreasing the resting interval. The same approach was followed by Bronas et al[25] while Saxton et al[26,29] and Zwierska et al[27] performed incremental tests to determine the maximum tolerance at 6, 8 and 12 weeks and adjusted the training intensity accordingly.

The majority of the included RCTs had a frequency of 2 supervised training sessions per week with duration of 40 minutes and intervals of 2 min exercise/2 min rest. The exceptions were the studies by Bronas et al[25] and by Treat-Jacobson et al[28], which included 3 sessions per week lasting 60-70 minutes. Recovery periods during the treadmill training varied and were determined by level of leg discomfort due to IC.

The controls did not participate in formal supervised exercise. However, they were encouraged to maintain an active lifestyle possibly including engagement in unsupervised training. The amount of unsupervised exercise was only monitored by Bronas et al[25] and Treat-Jacobson et al[28].

Outcome measures

The MWD and CD or PFWD were used as outcome measures in all RCTs. Baseline and final measurements also included an incremental shuttle walk test with a standard protocol,[26,29-31] or a symptom-limited graded cardiopulmonary treadmill exercise test (GXT).[25,28] To determine UL/LE maximum power[31] or VO_{2peak}[28,29] cycle ergometers for the UEupper and LElower extremity were employed and incremental arm cranking tests or leg cranking tests were performed. QoL and activity limitations were measured by a variety of questionnaires: 36-Item Short Form Health Survey (SF-36), European Quality of Life Visual Analogue Scale (EQ-VAS), Walking Impairment Questionnaire (WIQ), and PAD Physical Activity Recall (PAR). The times that the measurements were obtained varied amongst the included studies.[26,27] and Treat-Jacobson et al[28] tested the participants systematically during the training period to monitor and evaluate progression, whereas Bronas et al,[25] Saxton et al[29] and Walker et al[31] limited the assessment to a pre- and a post- training test. Saxton et al[26] were the only who implemented an additional follow-up assessment at 48 and 72 weeks.

The outcomes and the timing of when the assessments took place are shown in **Table 4 (Supplementary file 2)**.

Maximum Walking Distance. All 6 RCTs reported significant improvements in MWD in both exercising groups compared to baseline and to the control group. There was a tendency for a greater improvement in the LE training group ranging from 31% to 69%,[25,27] compared to the UE group where the improvement ranged from 29% to 53%.[27,28] However, the difference in magnitude of improvement between the exercising groups did not reach statistical significance (**Table 35**).

Claudication Distance. The CD increased significantly for the UE and the LE groups compared to baseline ranging from 56% to 123%[28,29] and from 54% to 93% (**Table 46**).[28,31] Both training groups improved significantly more than the control, with two exceptions. Treat-Jacobson et al[28] reported no statistically significant differences between the LE versus control and the UE versus control for both 12 and 24 weeks. Moreover, Saxton et al[26] found no significant differences for either of the training groups compared to controls at 6 weeks. The improvements observed in the UE and LE groups were comparable to each other in all RCTs despite a trend towards greater CD increase in the UE group.

Functional capacity. The peak oxygen consumption (VO_{2peak}) improved significantly in both exercising groups as documented in all studies, with two exceptions **[Table 7 ((Supplementary file) 3]**. Treat-Jacobson et al[28] detected no significant differences between the intervention groups and the controls. There were also no significant differences found by Zwierska et al[27] at 6 weeks. The differences between the UE and the LE groups were consistently non-significant (p>.05).

Quality of life. Three RCTs assessed the health-related QoL using a variety of outcome measures. Walker et al[31] reported significant improvements (p<.05) in the SF-36 domains of physical functioning and role limitation-physical only with exercise. Saxton et al[26] demonstrated that the magnitude of improvement for only UE group exceeded that of the controls in the domains of physical functioning, bodily pain and mental health at 24 weeks, whereas general health and vitality were significantly higher for both intervention groups when compared to the controls **[Table 8 (Supplementary file 4)*]**.

Saxton et al[26] additionally used the EQ-VAS and the WIQ. Higher EQ-VAS scores were revealed in both the UE and LE groups (mean difference, 7.85-8.46, p<.03) at 48 and 72 weeks. The perceived walking distance at weeks 24,48 and 72 as well as calf pain and stair climbing at 6 weeks as measured by the WIQ were found to be significantly improved (p<.05) only in the UE group when compared to the control **[Table 9 (Supplementary file 5)*]**.

Zwierska et al[27] assessed the QoL using the PAD-PAR questionnaire. Both exercising groups improved significantly compared to baseline in the domain of leisure activities **[Table 10 (Supplementary file 6)*]**. No differences observed in the domain of work activities and household work reached statistical significance.

** Only domains where at least one significant difference was observed are shown.*

Discussion

This review compared the effectiveness of UE versus LE training in patients with IC in the ICF domains of body functions (VO_{2peak}), activities (MWD, CD) and participation (QoL). Participants in a 6-24 weeks arm crank training program demonstrated substantial improvements in both MWD and CD to a similar extent as those participating in an equivalent LE training program. This is in line with existing evidence regarding the effectiveness of exercise in decreasing claudication symptoms.[16,32,33] Yet, the amount of training implemented within the included RCTs was less than what is recommended in the literature in order to have a clinically relevant effect, that is:t; a minimum of 3 sessions per week for 30-45 minutes and for a minimum duration of 12 weeks. This methodological drawback might have resulted in underrating the extentd of potential positive or negative effects of either form of exercise training in the considered outcomes. Future research should take into account

Comentario [NT2]: Reference 18

Hirsch, A. T., Haskal, Z. J., Hertzer, N. R., Bakal, C. W., Creager, M. A., Halperin, J. L., Hiratzka, L. F., Murphy, W. R., Olin, J. W., Puschett, J. B., Rosenfield, K. A., Sacks, D., Stanley, J. C., Taylor, L. M., Jr., White, C. J., White, J., White, R. A., Antman, E. M., Smith, S. C., Jr., Adams, C. D., Anderson, J. L., Faxon, D. P., Fuster, V., Gibbons, R. J., Hunt, S. A., Jacobs, A. K., Nishimura, R., Ornato, J. P., Page, R. L. and Riegel, B., ACC/AHA Guidelines for the Management of Patients with Peripheral Arterial Disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Associations for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (writing committee to develop guidelines for the management of patients with peripheral arterial disease)--summary of recommendations, J Vasc Interv Radiol, 2006, 17: 1383-1397; quiz 1398.

international guidelines and its experimental design regarding exercise prescription should reflect actual clinical practice.

The improvements in MWD for both intervention groups were not significantly different from each other in either of the included studies. This supports the notion that training improvements in the walking ability of PAD patients is not only due to the limb specific exercise-induced adaptations in the affected leg muscles but also due to general systemic changes that occur during traning.[19,25,34,35]

An increase in the CD occurred in both type of intervention groups, LE and UE. Despite a trend towards a greater improvement as a result of the UE training, most of the studies did not display significant differences when compared to LE. An exception was Treat-Jacobson et al,[28] which did not observe significant improvement of the LE group in relation to the control. This could be attributed to a high variability in the response of walking training on the CD, similar to what has been previously documented in the literature.[36,37] Since only two of the included studies compared UE training versus walking as a form of LE training,[25,28] this review cannot resolve uncertainties regarding the comparison of these two exercise regimes.

Although PAD guidelines suggest walking as an exercise form for patients with IC, preferably at a level in which a high degree of claudication symptoms -are achieved during training,[17,18] such a prescription may be behaviorally counterintuitive and lead to low adherence rates.[38] Conversely, UE training is not likely to be limited by the claudication symptoms and therefore, might offer a more preferable mode of exercise for those with IC. Furthermore, evidence has demonstrated an increase of inflammatory markers following a walking exercise program[39,40] which could cause further endothelial damage.[41] This highlights the need for further definitive and robust comparisons between walking and UE training in order to build evidence and optimize current exercise prescriptions and guidelines for PAD.

Both intervention groups evoked similar improvements in lower leg VO_{2peak} versus the control group. The differences between UE and LE did not reach statistical significance. This finding, together with the absence of evidence of superiority of either of the training modes in MWD and CD might be interpreted as evidence for training induced adaptations of both central origin and nature.[42] A potential mechanism including systemic changes has been consistently suggested by all included RCTs. Even though local muscle adaptations to exercise-induced ischemia could have accounted for the changes observed in the LE group, this is not likely to have occurred in the UE group. The observed improvements following UE training could be attributed to a general improvement in the oxygen delivery system[25,35,36] and to the so called ‘cross transfer effect’.[34,42-44] This implies that the UE training improves oxygen delivery not only in the muscles of the arms but also the legs. For that to be conceivable, several underlying mechanisms have been proposed including improvements in stroke volume,[31,35] endothelial function,[19,45,46] and blood rheological properties.[35,47] An enhancement of lower-limb endothelial vasodilator function as a response to UE training is also a prospect that merits consideration, as supported by data regarding the improvement~~efficacy~~ induced by~~of~~ aerobic exercise training in the endothelial function of ~~in~~the untrained limbs of~~in~~ IC patients~~ with intermittent claudication~~. In addition, UE exercise training results in a decrease in systemic inflammatory markers and, consequently, might have a positive impact on systemic endothelial function. On the contrary, improved endothelial function has been reported also in response to LE training – particularly cycling, yet the results have been attributed to a predominantly local effect rather than to a systemic effect. This

Comentario [NT3]: Reference 41

Andreozzi, G. M., Leone, A., Laudani, R., Deinite, G. and Martini, R. (2007) Acute impairment of the endothelial function by maximal treadmill exercise in patients with intermittent claudication, and its improvement after supervised physical training. Int. Angiol. 26, 12-17

Comentario [NT4]: Reference 29

Saxton, J. M., Zwierska, I., Hopkinson, K., Espigares, E., Choksy, S., Nawaz, S., Walker, R. and Pockley, A. G. (2008) Effect of upper- and lower-limb exercise training on circulating soluble adhesion molecules, hs-CRP and stress proteins in patients with intermittent claudication. Eur. J. Vasc. Endovasc. Surg. **35**, 607-613

Comentario [NT5]: Loffredo, L., Marcoccia, A., Pignatelli, P., Andreozzi, P., Borgia, M. C., Cangemi, R., Chiarotti, F. and Violi, F. (2007) Oxidative-stress-mediated arterial dysfunction in patients with peripheral arterial disease. Eur. Heart J. 28, 608-612

Adamopoulos, S., Parissis, J., Kroupis, C., Georgiadis, M., Karatzas, D., Karavolias, G., Koniavitou, K., Coats, A. J. and Kremastinos, D. T. (2001) Physical training reduces peripheral markers of inflammation in patients with chronic heart failure. Eur. Heart J. 22, 791-797

Comentario [NT6]: http://www.sciencedirect.com/science/article/pii/S0002914902024335 prospect has been confined by the possibility of endothelium damage in people engaging into LE activities.

This review revealed the absence of significant differences between the effects of UE and LE exercises in health related QoL. However, the improvement due to UE training displayed a positive trend in a wider range of QoL domains than the LE. This might be indicative of the suggested general systemic effects that can be triggered by UE rather than the local muscle adaptations as a response to LE training. The improvement in physical conditioning and functioning might be reflected in the patient's execution of activities of daily living as well as in QoL.

The population examined by the studies reviewed herein was comprised of participants who experienced IC but had no other comorbidities that impaired their ability to engage int~~o~~ a LE training program. Nonetheless, several ~~the presence of~~ comorbidities are usually prevalent in ~~is common among~~ this population, such as ~~with a high prevalence of~~ diabetes, arthritis, peripheral neuropathies or~~,~~ hypertension~~n etc~~. This should be taken into consideration when prescribing exercise training because different needs may account for different conditions and associated impairments. For instance, up to 30% of the diabetic population develops IC. Exercise has been proven an effective means for the control of the blood glucose levels amongst diabetes patients. However, most of the studies have examined the effect of LE or whole-body exercises as a form of training despite those being particularly susceptible to low training adherence rates as they are often infeasible to follow due to disease-associated impairments. Leelayuwat et al. demonstrated beneficial effects of UE~~arm~~ exercise on the glycemic control in patients with type 2 diabetes. Data from Jeng et al. also support the positive role of UE exercise for diabetics with the duration of the exercise being the key factor in determining the glucose response to UE training. Arm

Comentario [NT7]: Reference 41

Andreozzi, G. M., Leone, A., Laudani, R., Deinite, G. and Martini, R. (2007) Acute impairment of the endothelial function by maximal treadmill exercise in patients with intermittent claudication, and its improvement after supervised physical training. Int. Angiol. 26, 12-17

Comentario [NT8]: http://vmj.sagepub.com/content/6/3/157.full.pdf+html

http://bjgp.org/content/bjgp/54/500/196.full.pdf

http://www.ncbi.nlm.nih.gov/pubmed/20121883

Comentario [NT9]: http://europepmc.org/abstract/med/19543188

Comentario [NT10]: http://www.ncbi.nlm.nih.gov/pubmed/11559268

Comentario [NT11]: http://link.springer.com/article/10.1007%2Fs00125-007-0910-y

http://link.springer.com/article/10.1007/s40279-013-0128-8#page-1

http://bjgp.org/content/bjgp/54/500/196.full.pdf

Comentario [NT12]: **http://www.sciencedirect.com/science/article/pii/S0168822708003872**

Comentario [NT13]: http://www.ncbi.nlm.nih.gov/pubmed/12244521 exercises have also been suggested to be suitable for patients with other limiting pathologies such as osteoarthritis or peripheral neur~~t~~opathies. Nonetheless, the prospect of UE training in particular groups with conditions that impede LE training which might principally benefit from ~~it~~ has ~~not~~ received little~~a lot of~~ attention ~~in research~~ and evidence is lacking. The need ~~o~~for consensual research on this domain is, therefore, highlighted.

Another point that should raise attention is the generalizability of the results in both men and women. ~~It is evident that w~~Women are comparatively underrepresented in IC research and, thus, the applicability of the findings remains questionable. In a recent study, gender based distinctions to exercise response was revealed with women responding less than men. The data provided herein are insufficient to clarify whether responses to UE or LE are similar amongst the two sexes~~genders~~. Moreover, they are confounded by the small percentage of women included, i.e.,~~;~~ 23% of the sample. However, evidence suggests that women experience greater LE~~lower limp~~ limitations than men. This could provide support to the choice of UE over LE exercises as UE training would seem more feasible. Nonetheless this prospect remains to be scientifically addressed.

Limitations

The heterogeneity in the reporting methods of the included RCTs prevented the execution of a meta-analysis. Confidence intervals and effect sizes were not consistently calculated or reported, and consequently are not presented in this review. Instead, the p-values indicating significant differences between the compared groups are provided yet are not informative for the magnitude of the differences. With

Comentario [NT14]: http://www.ncbi.nlm.nih.gov/pubmed/12892243?dopt=Abstract

http://www.ncbi.nlm.nih.gov/pubmed/15180224?dopt=Abstract

http://www.rehab.research.va.gov/JOUR/06/43/4/pdf/maire.pdf

Comentario [NT15]: Vinik AI, Erbas T: Neuropathy. In Handbook of Exercise in Diabetes. 2nd ed. Ruderman N, Devlin JT, Schneider SH, Kriska A, Eds. Alexandria, VA, American Diabetes Association, 2002, p. 463–496

Levin ME: The diabetic foot. In Handbook of Exercise in Diabetes. 2nd ed. Ruderman N, Devlin JT, Schneider SH, Kriska A, Eds. Alexandria, VA, American Diabetes Association, 2002, p. 385–399

Comentario [NT16]: http://circ.ahajournals.org/content/125/11/1449.full

Comentario [NT17]: http://www.sciencedirect.com/science/article/pii/S0741521413019253

Comentario [NT18]: http://jama.jamanetwork.com/article.aspx?articleid=199161

http://www.jabfm.org/content/19/2/132.abstract?ijkey=a7fd92ba5beaeac58dca453cf59b84d38aa02c92&keytype2=tf_ipsecsha

http://www.ncbi.nlm.nih.gov/pubmed/12439070?dopt=Abstract

http://www.ncbi.nlm.nih.gov/pubmed/19223136?dopt=Abstract regards to the validity of the RCTs, the same groups of researchers were involved in the studies which might have led to publication bias.

Research Recommendations

Only two of the included articles compared UE to walking as a form of LE training. Given that walking is the most commonly prescribed exercise regimen for the management of IC, there is a compelling rationale for additional well-designed research on the comparison of walking versus UE training. Moreover, future research should direct its focus on subgroups of IC with comorbidities that restrict the participation into LE training programs and account for gender-dependent differences.

Conclusion

This review demonstrated the effectiveness of both UE and LE training in improving MWD, CD, VO_{2peak} but neither of these forms of exercise was found superior to the other. The physical discomfort experienced by the patients while performing LE exercise is the main reason why, even though widely used amongst therapists, this type of exercise is usually not favorably received by the patients. Alternative exercise regimens such as UE training might provide an attractive/complementary alternative therapy for symptomatic relief to patients with IC without the discomfort caused by the LE training. The absence of statistically significant results regarding the superiority of either of the exercise regimens does not necessarily downgrade the clinical importance of the findings of this review. Clinicians should design individualized exercise rehabilitation prescriptions taking into consideration the patients' needs, disease severity, exercise tolerance and preferences. UE training can be used as an alternative to LE training preventing the discomfort commonly experienced during the latter.

Conflicts of Interest and Source of Funding: The authors declare no conflict of interest and no source of funding. All authors have read and approved the manuscript.

Aknowledgements

The authors would like to Louisa Borlu, Denise McCathey, Sofia Quintana, Anastasia Pochard and Lynn Prea for their contribution to the study.

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Figure Legend

Figure 1. Literature search flow.

Table 2. Demographic characteristics. Abbreviations: ABPI; BMI, Body Mass Index; LE, lower extremities; NS, non-significant; RCT, randomized controlled trial; UE, upper extremities. Saxton et al (2008) & Zwierska et al (2005) reported median age (range), rest; mean age ±SD or (range). P-value refers to the differences among the groups.

Table 3. Intervention parameters. Abbreviations: LE, lower extremities; mph, miles per hour; rpm, repetitions per minute; UE, upper extremities; RCT, randomized controlled trial; VO_{2peak}, peak oxygen uptake.

Table 5. Maximum walking distance. Abbreviations: LE, lower extremities; MI, mean improvement; N/A, not applicable; NS, not significant; RCT, randomized controlled trial; UE, upper extremities. *Data present the p value the differences of each group compared to baseline. †Data present the p value of the differences between the groups. ‡Data present the p value between the 3 exercising groups; UE, LE and UE+LE.

Table 6. Claudication distance. Abbreviations: LE, lower extremities; MI, mean improvement; N/A, not applicable; NS, not significant; RCT, randomized controlled trial; UE, upper extremities. * Data present the p value the differences of each group compared to baseline. †Data present the p value of the differences between the groups. ‡Data present the p value between the 3 exercising groups; UE, LE and UE+LE.

Table 2.

RCT	Saxton et al (2011)					Saxton et al (2008)					
Group	Total	UE	LE	Control	P	Total	UE	LE	Control	P-value	
Age (years)	68 (50-85)	68 (54-84)	68 (50-85)	71 (56-85)	NS	69(50-85)	66 (54-82)	68 (50-85)	72 (56-84)	NS	
Participants (n)	104	34	37	33		92	30	32	30	NS	
Sex											
Male (n)	81	27	30	24	NS	70	23	25	22	NS	
Female (n)	23	7	7	9	NS	22	7	7	8	NS	
BMI (kg/m^2)	-	28.6 ± 0.7	26.6 ± 0.6	27.8 ± 1.0	NS	-	29.1 ± 0.7	26.4 ± 0.6	27.8 ± 1.0	NS	
Duration of claudication (months)	-	50 ± 8	59 ± 9	55 ± 7	NS	-	46 ± 7	58 ± 9	56 ± 7	NS	
Resting ABPI	-	0.65± 0.03	0.6 ± 0.03	0.69 ± 0.03	NS	-	0.65±0.03	0.64 ± 0.03	0.69 ± 0.03	NS	
RCT	Bronas et al (2011)					Zwierska et al (2005)					
Group	Total	UE	LE	Control	P	Total	UE	LE	Control	P-value	
Age (years)	65.6 ± 8.5	64 ± 8.6	63 ± 11.5	70 ± 7.8			66 (54-84)	69 (50-85)	72(56-84)	NS	
Participants (n)	28	10	10	8	NS	104	34	37	33	NS	
Sex											
Male (n)	21	8	6	7		81	27	30	24	NS	
Female (n)	7	2	4	1		23	7	7	9	NS	
BMI (kg/m^2)	28.5 ± 4.3	29.9 ± 8.8	26.4 ± 3.3	29.2 ± 5.4			28.6 ± 0.6	26.6 ± 0.6	27.8 ± 1.0	NS	
Duration of claudication (months)	-	-	-	-	-	-	50	59	55	NS	
Resting ABPI	0.68 ± 0.1	0.66± 0.15	0.68 ± 0.11	0.69 ± 0.15			0.65 ± 0.03	0.64 ± 0.03	0.69 ± 0.03	NS	
RCT	Walker et al (2000)					Treat-Jacobson et al[28]					
Group	Total	UE	LE	Control	P	Total	UE	LE	UE + LE	Control	P-value
Age (years)		68 (63-70)	70 (61-73)	71 (70-77)	NS		64 ± 8.6	64 ± 11.7	71.9 ± 11.3	70 ± 7.8	NS
Participants (n)	67	26	26	15		41	10	11	12	8	NS
Sex											
Male (n)	53	22	22	9	NS	29	8	7	7	7	NS
Female (n)	14	4	4	6	NS	12	2	4	5	1	NS
BMI (kg/m^2)	-	-	-	-	-	-	-	-	-	-	-
Duration of claudication (months)	24(15-31)	24 (18-33)	24 (15-31)	24 (24-36)	NS	-	-	-	-	-	-
Resting ABPI	0.67 (0.56-0.8)	0.67 (0.56-0.73)	0.64 (0.6-0.8)	0.71 (0.61-0.79)	NS	0.67 ± 0.1	0.66 ± 0.15	0.68 ± 0.11	0.65 ± 0.1	0.69 ± 0.15	NS

Table 3.

RCT	UE	LE	Mode	Duration (training period)	Frequency	Intensity	Session duration	Characteristics	Adjustment
Saxton et al(2011)	arm cranking	leg cranking	supervised	24 weeks	twice/week	85-90% of limb-specific VO2peak	40 minutes (20min exercise	2 min at 50rpm/ 2 min rest	Incremental tests for max tolerance at weeks 6, 8, 12
Saxton et al(2008)	arm cranking	leg cranking	supervised	24 weeks	twice/week	85-90% of limb-specific VO_{2peak}	40 minutes (20min exercise	2 min at 50rpm/ 2 min rest	Incremental tests for max tolerance at weeks 6, 8, 12
Bronas et al(2011)	arm cranking	treadmill	supervised	12 weeks	three times/week	Borg scale (13-15)	60 minutes (5min warm up & 5 min cool down)	UL--> 2min at 50rpm and 10W less than their maximum/2min rest, LL --> 2mph, 0% grade till severe claudication 3-4 (scale 0-5), rest seated, progressively increased by 0.5% grade up to 10% grade, increase by 0.1 to 0.2 mph	UL --> every 2,3 weeks ↑exercise period (up to 5min) ↓rest (up to 1 min)
Treat-Jacobson et al(2009)	arm cranking	treadmill	supervised	12 weeks	three times/week	Borg scale (13-15)	70 minutes (5min warm up & 5 min cool down)	UL -->2 min at 50 rpm and 10W below their maximum/2 min rest	UL --> 3 weeks ↑exercise load to maximum W, then every 2,3 weeks ↑exercise period by 1 min (up to 5min) ↓rest (up to 1 min)
Zwierska et al(2005)	arm cranking	leg cranking	supervised	24 weeks	twice/week	85-90% of limb-specific VO_{2peak}, Borg scale (13-16)	40 minutes (20min exercise)	2 min at 50rpm/ 2 min rest	Incremental tests for max tolerance at weeks 6, 8, 12
Walker et al(2000)	arm cranking	leg cranking	supervised	6 weeks	twice/week	Workload achieved during baseline assessment	40 minutes (20min exercise)	2 min at 50rpm/ 2 min rest	After 3 weeks workload was adjusted to maximum

Table 5.

RCT	Time of measurement	UE		UE vs. Control	LE		LE vs. Control	Control		UE vs. LE (vs.UE+LE)	UE+LE		UE+LE vs. Control
		MI	P^*	$P^\dagger$	MI	P^*	$P^\dagger$	MI	P^*	$P^\ddagger$	MI	P^*	$P^\dagger$
Saxton et al(2011)	6 weeks	-	-	<.001	-	-	<.001	-	-	NS	N/A	N/A	N/A
	24 weeks	-	-	<.001	-	-	<.001	-	-	NS	N/A	N/A	N/A
	48 weeks	-	-	<.001	-	-	<.001	-	-	NS	N/A	N/A	N/A
	72 weeks	-	-	<.001	-	-	<.001	-	-	NS	N/A	N/A	N/A
Saxton et al(2008)	24 weeks	30%	<.001	<.05	35%	<.001	<.05		NS	NS	N/A	N/A	N/A
Bronas et al(2011)	12 weeks	43%		.023	61%		.002	13%		NS	N/A	N/A	N/A
Treat-Jacobson et al(2009)	12 weeks	53%	-	.002	69%	-	<.001	11%	-	NS‡ (1.00)	68%	–	<.001
	24 weeks	-	-	.01	-	-	.02	-	-		-	-	NS (0.73)
Zwierska et al(2005)	6 weeks		<.01	<.05		<.01	<.05		NS		N/A	N/A	N/A
	12 weeks		<.01	<.05		<.01	<.01		NS		N/A	N/A	N/A
	18 weeks		<.01	<.05		<.01	<.01		NS		N/A	N/A	N/A
	24 weeks	29%	<.01	<.05	31%	<.01	<.001		NS		N/A	N/A	N/A
Walker et al(2000)	6 weeks	47%	.003	<.05	50%	<.001	<.05		NS	NS	N/A	N/A	N/A

Table 6.

RCT	Time of measurement	UE		UE vs. Control	LE		LE vs. Control	Control		UE vs. LE (vs. UE+LE‡)	UE+LE		UE+LE vs. Control
		MI	P^*	$P^{\ddagger}$	MI	P^*	$P^{\ddagger}$	MI	P^*	$P^{\ddagger}$	MI	P^*	$P^{\ddagger}$
Saxton et al(2011)	6 weeks	-	-	NS (.072)	-	-	NS (.753)	-	-	NS	N/A	N/A	N/A
	24 weeks	-	-	.035	-	-	.044	-	-		N/A	N/A	N/A
	48 weeks	-	-	.038	-	-	.049	-	-		N/A	N/A	N/A
	72 weeks	-	-	.041	-	-	.046	-	-	NS	N/A	N/A	N/A
Saxton et al(2008)	24 weeks	56%	<.001	-	65%	<.001	-	-	NS	NS	N/A	N/A	N/A
Bronas et al(2011)	12 weeks	82%	.004	.004	62%	.048	.028	2.8%	NS	NS	N/A	N/A	N/A
Treat-Jacobson et al(2009)	12 weeks	82%	-	.03	54.%	-	NS (.20)	1%	-	NS(1.00)-‡	60%	-	NS (.11)
	24 weeks	123%	-	.01	80%	-	NS (.11)	18%	-	NS‡	38%	-	NS (1.00)
Zwierska et al(2005)	6 weeks	-	<.05	-	-	<.05	-	-	NS	NS	N/A	N/A	N/A
	12 weeks	-	<.01	-	-	<.01	-	-	NS	NS	N/A	N/A	N/A
	18 weeks	-	<.01	-	-	<.01	-	-	NS	NS	N/A	N/A	N/A
	24 weeks	51%	<.01	<.001	57%	<.01	<.001	-	NS	NS	N/A	N/A	N/A
Walker et al(2000)	6 weeks	122%	<.001	<.05	93%	<.001	<.05		NS	NS	N/A	N/A	N/A