A plantar flexion device exercise programme for patients with peripheral arterial disease: a randomised prospective feasibility study.

Plantar flexion device exercise in peripheral arterial disease

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Abstract

Objectives: To determine if the use of a plantar flexion device (Step It pedal) in a newly developed exercise programme is of benefit to patients with peripheral arterial disease.

Design: Prospective feasibility trial with patients randomised to either standard care or the Step It exercise programme plus standard care.

Setting: Physiotherapy Department at Cumberland Infirmary, Carlisle, UK.

Participants: Patients were identified from the vascular team's referral list. In total, 42 patients agreed to take part; 18 in the control group and 24 in the intervention group.

Interventions: Eligible participants were randomised and received either standard care or took part in a plantar flexion resistance exercise programme, involving the Step It pedal, for a period of 12 weeks.

Main outcome measures: Maximum walking distance, claudication distance and ankle brachial pressure index.

Results: Eighty-three percent of patients completed the study. Improvements in median distance to claudication symptoms and maximum walking distance were observed in the intervention group but not in the control group. Nine out of 15 (60%) participants in the control group and 14 out of 20 (70%) participants in the intervention group improved their walking distance. Ankle brachial pressure index remained virtually unchanged in both

groups.

Conclusions: Due to the variability of patients' fitness in the sample, it cannot be concluded whether use of the Step It pedal has additional benefits to patients over standard care. However, the study completion rate implies that patients with peripheral arterial disease are receptive to undertaking exercise programmes.

Introduction

Peripheral artery disease is a common progressive disorder of the vasculature. The underlying aetiology of peripheral artery disease is atherosclerosis and therefore patients are at high risk of associated cardiovascular diseases such as myocardial infarction and stroke.[1,2] Narrowing of the arteries leads to reduced oxygen supply, thereby resulting in symptoms of intermittent claudication, limited capacity to exercise and an increased risk of tissue loss.[3] Peripheral arterial disease can be divided into Fontaine classification according absence or presence of intermittent claudication symptoms. In the United States alone approximately 6% of the population are affected by this disease.[4] A UK study involving 55 to 74-year olds found that 4.5% experienced intermittent claudication symptoms, which is exercise-induced pain experienced in the calves, thighs or buttocks.[5]

Patients who receive support, training and education with regards to exercise on average improve their walking distance by 150%.[6,7] Most previous research studies applied programs involving weight-bearing or aerobic exercise, e.g. walking, rowing and cycling to try and improve the maximum walking distance that patients can reach. Due to the increased risk of cardiovascular accidents in peripheral artery disease patients and, due to the underlying atherosclerosis, and the aversion to strenuous exercise by most patients, an alternative

exercise program that does not involve high impact aerobic exercise regimes may be more appropriate than the aforementioned cycling and rowing programs.

Supervised exercise programs have been shown to benefit patients.[8,9] One recent study by McDermott and colleagues has shown that supervised lower extremity resistance training has significant benefits over a normal management involving education and advice on diet and exercise.[10] A six-month program results in improved maximum treadmill walking time, although 6-minute walking distance does not improve over the control group. The type of lower extremity exercise involved repetitions of knee extensions, leg press and leg curls.

In this pilot clinical research study, for the first time, the 'Step It™' rocker pedal has been applied in peripheral arterial disease patients (Step It System AB, Saltsjöbaden, Sweden). It is a small device, very similar to the pedal used to operate a bass drum on a drum kit, which is easy to use from a seated position and was first devised to help alleviate the risk of economy syndrome for travellers on long haul flights. Patients may be receptive to this form of exercise in addition to walking, especially if they are elderly, frail, feel in fear of falling or have an aversion to the idea of 'exercise'. The aim of this initial randomized, controlled, prospective feasibility study was to determine the efficacy of the Step It pedal by measuring patients' maximum walking distance as well as ankle brachial pressure index. Both the control arm and the intervention arm received advice on diet and exercise and were monitored for physical parameters.

Methods

Study design and subjects

This concerned a pilot of a prospective, single-centre, controlled, randomized research study with 1:1 allocation to control or intervention arm. Patients were identified from referrals to vascular clinic at Cumberland Infirmary, Carlisle. Symptomatic peripheral arterial disease,

Fontaine IIa or higher, was diagnosed in patients by consultant vascular surgeons when first consulted on symptoms alone: exertional calf pain upon walking and an ankle brachial pressure index of < 0.90. [3,11] Adult patients with symptomatic intermittent claudication due to peripheral artery disease who were capable of giving informed consent were invited to participate in the study; there were no age restrictions. Patients were excluded according to the following criteria: unstable cardio/respiratory condition, such as uncontrolled hypertension, cardiovascular accident or myocardial infarction within last two months, surgery within six weeks of enrolling, a major amputation of one or more lower limbs, blood glucose level above 13 mmol/l (ie uncontrolled diabetes).[10,12] Following consent, the patient was allocated randomly to either the control or Step It plantar flexion intervention group. The study was performed unblinded and a non-restricted randomised sequence was obtained - and visible to researchers beforehand - for the whole sample using a freeware randomization programme (www.randomizer.org). The corresponding author, LJ, generated the randomisation sequence, and LR and JT enrolled patients and NT measured the study outcomes.

Interventions

Participants were randomized to either the control arm (standard care) or the intervention arm (standard care plus use of Step It pedal) for a period of 12 weeks. Neither participants nor researchers were blinded regarding the allocated intervention. All participants initially attended one exercise class in the hospital for baseline measurements, continuing their exercises, ie plantar flexion using Step It pedal, and care program unsupervised at home thereafter. Patients in all groups were advised to walk daily to their maximum walking distance and to attempt to increase distance as able. The second study appointment in the hospital took place at 12 weeks after patient enrolment. In addition to the standard care the control group receives, the intervention group was also asked to do exercises at home using

the Step It rocking pedal. This consists of lower limb exercise training (resisted plantar flexion) whilst seated. The resistance of the pedal is equivalent to approximately 6 kg. The exercise sessions were performed three times a week for 12 weeks, with the following pattern: 2 minutes exercise / 2 minutes rest for ten times, to equal 20 minutes exercise in total. The patients were shown how to use the Step It pedal at the baseline appointment, were asked to try it out to demonstrate they could use the instrument, and throughout the study program the participants were asked to record an exercise diary.

Primary and secondary outcomes

Outcome measures were recorded at baseline and at 12 weeks, with distance walked as the primary outcome measure. The data for the claudication distance, the distance at which there is onset of claudication pain, and maximum walking distance were obtained using a treadmill set at 3.2 km/hr (as reported by Hiatt and colleagues[13]) and a 10º gradient. If no claudication pain developed then the maximum walking distance was recorded as the claudication distance. The secondary outcome measurement was the ankle brachial pressure index, which was measured with a handheld Doppler machine. This tool is commonly used for diagnosis and monitoring of peripheral artery disease.[14] In healthy persons, the ankle brachial pressure index is at least one with the systolic blood pressure equal in all limbs or higher in the ankle.[3] The highest measure of the dorsalis pedis and posterior tibial pressure was divided by the brachial pressure in the right arm of the patient. Since the recruited participants had claudication symptoms in either the right leg, left leg or both legs, the ankle brachial pressure index score for either the affected leg (unilateral disease) or the average of the ankle brachial pressure index scores for both legs (bilateral disease) is presented to account for this.

Data analysis and sample size

In order to determine the required sample size, the assumption was made that distribution of data would be normal and it was estimated – based on previous studies - that the mean baseline maximum walking distance for all participants would be 300 meters with a standard deviation of 100 meters.[9,10] It was estimated, for the purpose of an a priori sample size calculation, that the intervention group would improve after 12 weeks by 20% with the control group remaining static. Applying a two-tailed unpaired t-test to compare means of control and intervention groups, and taking into account 80% power, 5% significance plus a 10% participant dropout rate, the required total number of participants required was 90 (45 in each treatment arm). The change in claudication pain distance, maximum walking distance and ankle brachial pressure index between baseline and 12-weeks within the control and intervention arm was determined. Statistical analyses were performed using SPSS version 17 (SPSS Inc., Chicago, USA).

Results

In total, 42 patients were recruited into the study; 18 in the control group and 24 in the intervention group. The CONSORT guidelines require a statement on the number of patients assessed for eligibility.[15] In this study it was not recorded, therefore no data is available on the number of patients who did not meet the inclusion criteria or declined to participate. Of these, 3 patients in the control group and 4 patients in the intervention group respectively discontinued during the 12 week study program. The reasons were surgical intervention (two cases, one in control group and one in intervention group – both had angioplasty) or no reason given (two in control group and 3 in intervention group). The control group and intervention group did not differ significantly in the demographic and clinical make-up of the participants (see Table 1). More diabetic patients were allocated to the intervention arm but this difference was not statistically significant.

The claudication distance and maximum walking distance was measured for all 35 participants who completed the study (15 control and 20 intervention), however, the ankle brachial pressure index was not available for one control participant at baseline and was therefore excluded from this outcome measurement. The trial was discontinued when an interim analysis was performed of the data. The primary reason was the variance observed in the values of the primary outcome measures, claudication distance and maximum walking distance (see results below). No unintended effects were observed in any of the participants. What follows is the data for the 42 participants enrolled, rather than the 90 participants originally planned.

[Table 1 to be inserted here]

Claudication distance and maximum walking distance

Both the claudication distance and the maximum walking distance measured in all patients showed a wide range – see Figure 1 and Figure 2 respectively. The claudication distance achieved by patients varied considerably; for example, from as short as 10 meters to as far as 520 meters long in the control group at baseline. In terms of median distance walked before claudication symptoms developed, for the control group this was 100 meters (inter-quartile range [IQR] 97 meters) at baseline and stayed exactly level (100 meters, IQR 120), and for the intervention group it changed from 65 meters (IQR 60 meters) to 85 meters (IQR 85 meters) over the 12-week period. It should be noted that participants did not always stop walking due to claudication pain. One control participant and three intervention participants did not experience any claudication pain before finishing their walking test; shortness of breath and tiredness were the reasons on these occasions. Where no claudication pain was experienced, the claudication distance was considered equal to the maximum walking distance. The maximum distance walked by participants ranged from 40 meters for one

patient to 770 meters for another patient. Over the 12-week trial program, on average the maximum distance walked by participants in the control group worsened; the median distance changed from 260 meters (IQR 225 meters) to 210 meters (IGR 290 meters). For participants in the intervention group, however, the median improved from a baseline 160 meters (IQR 171 meters) to 200 meters (IQR 198 meters) at the 12-week endpoint.

[Figure 1 and 2 to be inserted here]

The outcome measures maximum walking distance and claudication distance were further analysed to determine how many participants actually showed an improvement in distance walked for these two parameters. Table 2 shows that more participants who used the Step It pedal improved their claudication distance compared to those in the control arm. The number of participants who improved on their maximum walking distance was similar in both study arms, although more participants in the intervention arm improved their claudication distance.

[Table 2 to be inserted here]

Ankle Brachial Pressure Index

A secondary objective of this study was to conduct ankle brachial pressure index measurements to determine whether the plantar flexion exercise pedal could possibly have a positive effect. As shown in Figure 3, over the 12 week study period the median ankle brachial pressure index remained virtually unchanged. A marginal improvement was seen in the control group (at baseline: 0.73, IQR 0.44; at 12-weeks: 0.74, IQR 0.36) and in the intervention group the median ankle brachial pressure index decreased by a fraction (baseline: 0.64, IQR 0.36; 12-weeks: 0.63, IQR 0.19). Four control participants and three intervention participants had an ankle brachial pressure index of more than 0.9 at baseline,

despite patients being originally diagnosed with peripheral arterial disease by the vascular team using ankle brachial pressure measurements as a diagnostic tool.

[Figure 3 to be inserted here]

Discussion

Recently the first clinical study involving the Step It, conducted on healthy volunteers, was published.[16] The hypothesis that increased calf muscle exercise may alleviate the claudication symptoms experienced in peripheral arterial disease and thereby reduce the pain experienced in the lower extremities was therefore followed up using the Step It pedal in this pilot study. Out primary objective in this study was to determine whether an unsupervised exercise programme involving a plantar flexion pedal that stimulates calf muscle exercise can potentially reduce claudication symptoms in peripheral arterial disease patients. There was not much difference in the percentage of patients in the control group and intervention group who improved their walking distance the 12-week program as measured by claudication distance and maximum walking distance, and the effect size seen in either group would not likely to be clinically relevant. The average percentage improvement in median maximum walking distance for the Step It group was 25%, whereas an improvement of 30% is considered clinically significant.[17,18] As mentioned in the results section, the considerable variance in distance walked by patients led to the discontinuation of the study. In most cases the inter-quartile range was near identical to the median. Bearing in mind that peripheral arterial disease is a progressive disorder that worsens over time, a positive note is that neither the control nor the intervention group deteriorated a lot over the measured three month period in terms of measurement outcomes (see Figure 2 and Figure 3). Other studies have shown increases in peripheral artery disease patients' fitness with exercise programs, ranging from

50% to 200%.[5,9] The completed diaries provided by the participants did not indicate a high degree of non-compliance to the Step It exercise programme.

In order to gain an understanding of why the patients in this study did not improve dramatically, the baseline performance of participants in other studies was assessed. In studies by McDermott and Zwierska, the study the participants could walk a mean maximum of approximately 300 meters (SD of approximately 90 meters).[8,10] A Cochrane report also reported a baseline maximum distance walked by patients of 300 meters.[9] In the trial performed here the median maximum walking distance at baseline ranged from 160 meters for the intervention group to 260 meters for those participating in the control group. This implies that a proportion of the patients in our sample were less fit than in the two abovementioned studies in which a positive effect of an exercise program was demonstrated. In the study by Zwierska and colleagues the mean ankle brachial pressure index at baseline was 0.65 (improving to 0.68 after 24 –week exercise program), which is similar to the median 0.64 for intervention participants in the study presented here.[8] In their study the index changed to 0.68 after a 24-week exercise program, whereas in this study the median ankle brachial pressure index figure for the intervention group went down to 0.63. These results are in line with other evidence where it was shown that the ankle brachial pressure index does not change significantly with exercise in peripheral artery disease patients.[6] Our data is also concordant with one other study that evaluated a year-long exercise program in peripheral artery disease patients.[17] Crowther and colleagues' study had a similar drawback to ours in terms of sample size (total n =21), raising the possibility that a false-negative result is obtained. Another complication of using the ankle brachial pressure index as an outcome measure is that the measurements may differ depending on the experience of the person performing the measurements and the method applied.[19,20]

In another pilot study, involving a total 25 patients with peripheral arterial disease, Wang and colleagues randomized particpants to either a control group or plantar flexion exercise group and showed a 20% increase in time to exhaustion for the plantar flexion group.[21] The plantar flexion device used on that occasion was an ergometer (a pedal attached to a exercise bike) and the supervised training involved 4x 4 minute exercise intervals three times per week. Together with the data obtained in this study here, it may be that localized exercise of only the calf muscles is possibly not sufficient to resolve claudication symptoms due to the limited resistance of the pedal itself, limited exercise time, or lack of whole body aerobic exercise. It may, however, be of use to prepare patients before they embark on a more strenuous aerobic exercise program although more research on a larger scale is needed.[21]

Our exercise device of choice, the Step It pedal, was partly chosen because of the notion that even very unfit people can use it. Originally the Step It was designed for use in airplanes for long haul flights, so that the lower leg could be exercised with the aim of reducing economy syndrome, i.e. deep vein thrombosis during air travel. The data obtained with our sample size shows a considerable degree of variance and therefore it was not possible to determine if there is a significant benefit to the use of the Step It pedal. However, this could potentially be achieved with a larger sample size provided the study is perhaps better controlled in terms of the Fontaine classification that patients fall into and the maximum and minimum distance that people are able to walk at baseline.

This study has a number of limitations; our sample size is small. Because this concerns a single centre study, only patients from a certain area were recruited and together with the limited sample size the results may not be representative of a wider population. Cumbria is a county in the UK with a high prevalence of cardiovascular disease in its population. The two

study groups were, however, well balanced in terms of demographics and co-morbidities and this study does add to the recent literature about the application of specific lower limb exercise programs in patients with peripheral artery disease.[7,8,10,14,21] One other drawback may be that the exercise programme may not have intensive enough to cause any improvement in fitness levels. Nevertheless, a 20 minute exercise was likely to mean an increase compared the patients' usual level and frequency of doing exercise and is in alignment with other plantar flexion exercise programs used.[21] With unsupervised exercise there is always a risk that participants do not comply with the program. It has been shown that those in supervised exercise programs fair better than patients who are asked to exercise unsupervised. [9]

In conclusion, although exercise has been shown to be beneficial in general in peripheral arterial disease patients, further larger scale research is needed to determine whether intermittent claudication symptoms can be solved by applying exercise programmes that concentrate on the calf muscles. The pilot data obtained here could inform researchers when devising a research protocol and determining the required sample size.

Ethical approval: Ethics approval was obtained from the NHS National Research Ethics Service, West Midlands Committee (ref 09/H1014/38).

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Conflicts of interest: None.

References

1. Weitz JI, Byrne J, Clagett GP, et al. Diagnosis and treatment of chronic arterial insufficiency of the lower extremities: a critical review. Circulation 1996;94:3026-49.

2. Milani RV, Lavie, CJ: The role of exercise training in peripheral artery disease. Vasc Med 2007;12: 351-8.

3. Dieter RS, Chu WW, Pacanowski JP, McBride PE, Tanke TE. The significance of lower extremity peripheral arterial disease. Clin. Cardiol. 2002;25:3-10

4. Creasy TS, Fletcher EWL, Collin J. Peripheral vascular disease. BMJ 1989;299:1166.

5. Fowkes FGR, Housley E, Cawood EHH, MacIntyre CCA, Ruckley CV, Prescott RJ. Int J Epidemiology. 1991;20:384-92

6. Watson L, Ellis B, Leng GC. Exercise for intermittent claudication. Cochrane Database Syst Rev. 2008; 4: CD000990.

7. McGregor GS, Whyte G, Buckley JP, Houghton. The effect of weight-bearing and non-weight-bearing exercise on patients with intermittent claudication. J. of Sports Sci. 2000;19:59-60.

8. Zwierska I, Walker RD, Choksy SA, et al: Upper- vs lower-limb aerobic exercise rehabilitation in patients with symptomatic peripheral arterial disease: a randomized controlled trial. J of Vasc Surg 2005;42:1122-30.

9. Bendermacher BLW , Willigendael EM , Teijink JAW, Prins MH. Supervised exercise therapy versus non-supervised exercise therapy for intermittent claudication. The Cochrane Database of Systematic Reviews 2006.

10. McDermott MM, Ades P, Guralnik JM, et al. Treadmill exercise and resistance training in patients with peripheral arterial disease with and without intermittent claudication. JAMA 2009;301:165-74.

11. Scottish Intercollegiate Guidelines Network. Diagnosis and management of peripheral arterial disease, guideline nr 86, 2006.

12. Chipkin SR, Klugh SA, Chasan-Taber L. Exercise and diabetes. *Cardiol Clin* 2001 19:489–505.

13. Carter SA: Indirect systolic pressures and pulse waves in arterial occlusive diseases of the lower extremities. Circulation 1968; 37:624-37.

14. Hiatt WR, Regensteiner JG, Hargarten ME, Wlfel EE, Brass EP. Benefit of exercise conditioning for patients with peripheral arterial disease. Circulation 1990;81:602-9.

15. Schulz KF, Altman DG, Moher D, for the CONSORT group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c332.

16. Bergqvist D, Landin G, FLynner K, Heide B, Kusoffsky A. Anti-swelling effect of Step It – an active foot pump system. JAPMA. 2009;99:20-2

17. Crowther, R.G. et al. (2009) The influence of a long term exercise program on lower limb movement variability and walking performance in patients with peripheral arterial disease. Hum Mov Sci. 2009;28: 494-50.

18. Hiatt WR, Regensteiner JG, Hargarten ME, Wlfel EE. Benefit of exercise conditioning for patients with peripheral arterial disease. Circulation 1990;81:602-9.

19. Kaiser V, Kester ADM, Stoffers H, Kitslaar P, Knottnerus JA. The influence of experience on the reproducibility of the ankle-brachial systolic pressure ratio in peripheral arterial occlusive disease. Eur J Vasc Endovasc Surg. 1999;18:25-9.

20. Jeelani NU, Braithwaite BD, Tomlin C, MacSweeney ST. Variation of method for measurement of brachial artery pressure significantly affects ankle-brachial pressure index values. Eur J Vasc Endovasc Surg. 2000;20:25-8.

21. Wang E, Hoff J, Loe H, Kaehler N, Helgerud J. Plantar flexion: an effective training for peripheral arterial disease. Eur J Appl Physiol. 2008;104:749-56.

22. Helgerud J, Wang E, Mosti MP, Wiggen ON, Hoff J. Plantar flexion training primes peripheral arterial disease patients for improvements in cardiac function. Eur J Physiol. 2009;106:207-15.

Figure 1. Distance to claudication pain for control and intervention group.

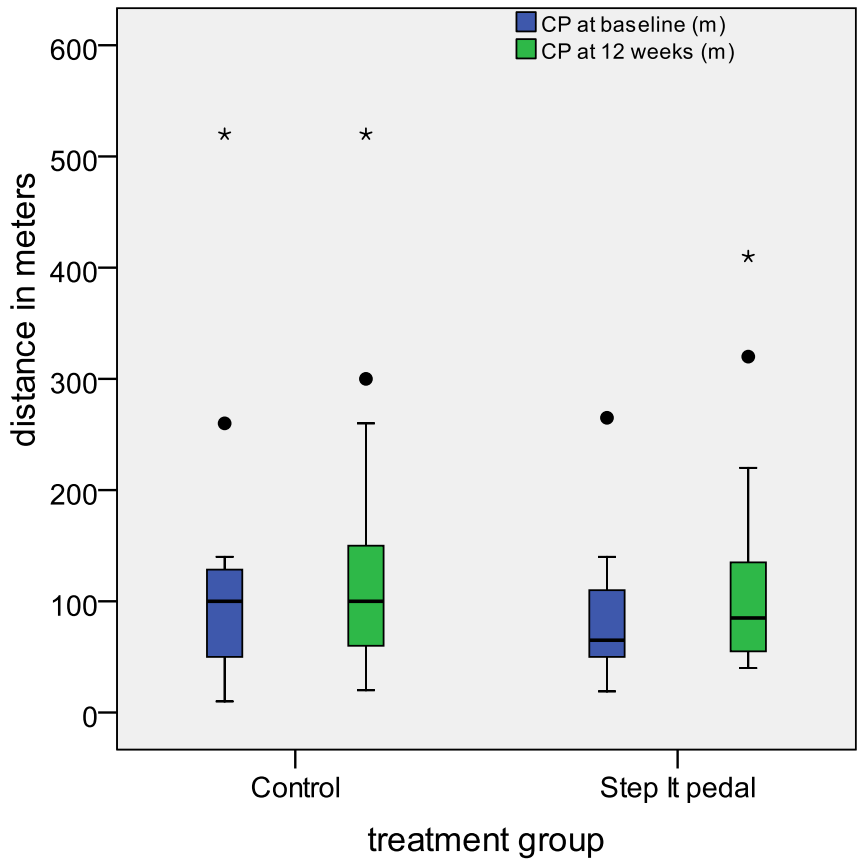

Figure 2. Maximum walking distance in control and intervention group.

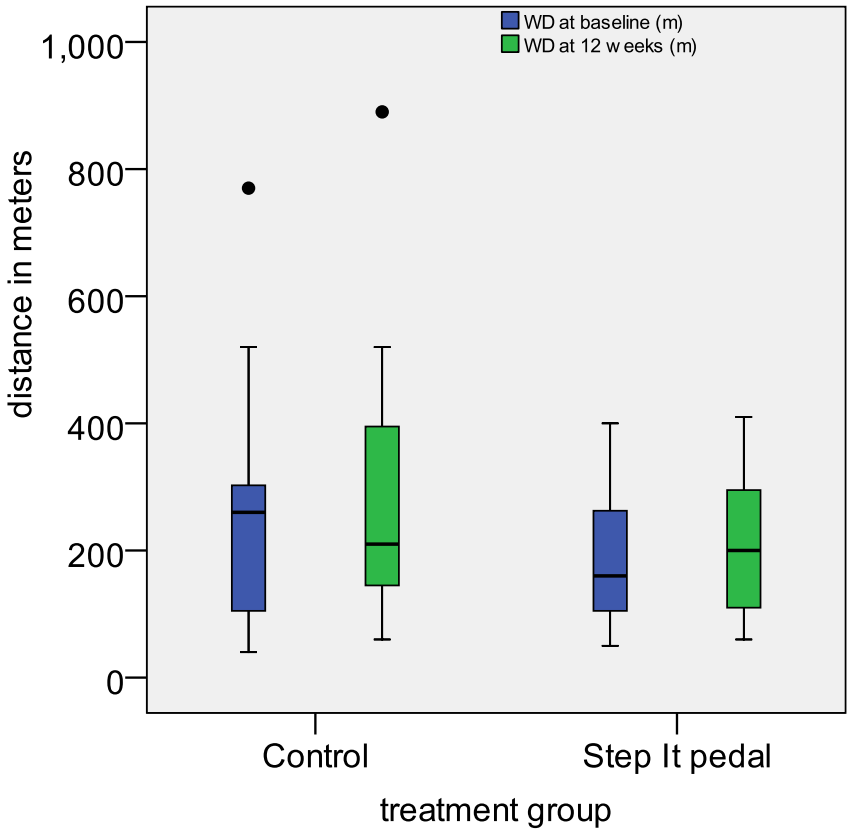

Figure 3. Ankle brachial pressure index score in control and intervention group.

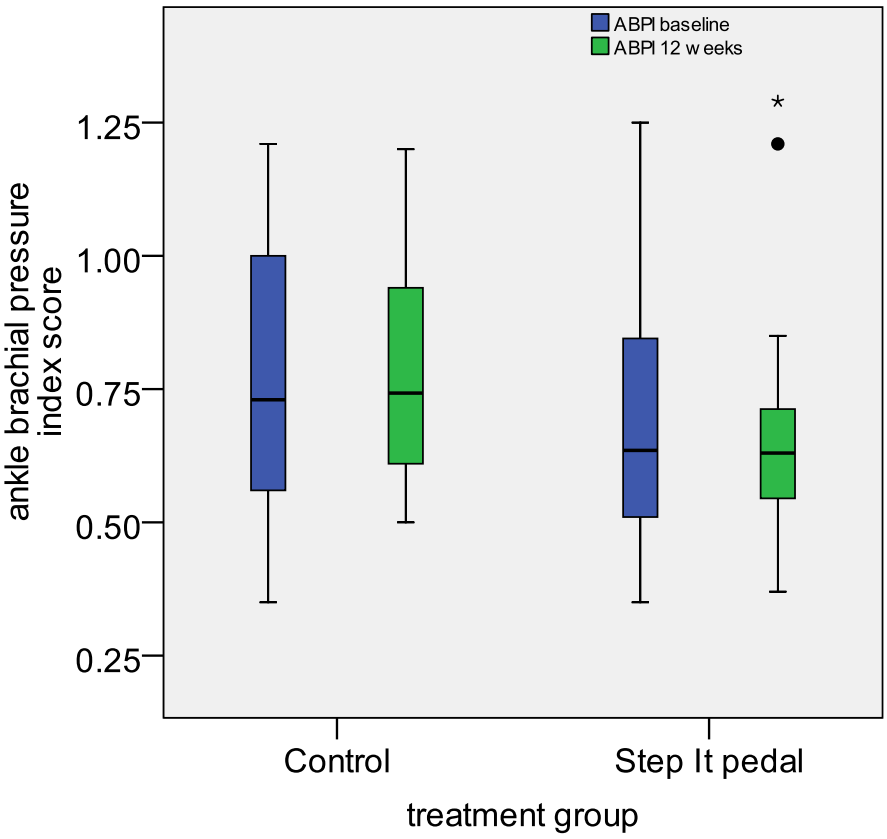

Table 1. Demographic overview of and completion rate in the two study groups

	Control group (n = 18)	*Plantar flexion group (n = 24)*	*P-value*
Mean age (range)	71 (47 – 86)	66 (45 – 77)	ns
Gender (M/F)	13/5	15/9	ns
Smoker	5 (28%)	7 (29%)	ns
Bilateral/Unilateral PAD	5 (28%) / 13 (72%)	7 (29%) / 17 (71%)	ns
Diabetes	0 (0%)	2 (8%)	ns
Betablocker	1 (6%)	2 (8%)	ns
Statin	17 (94%)	19 (79%)	ns
Completion rate	15/18 (83%)	20/24 (83%)	ns

ns: no significant difference between the two study groups when compared by one-way analysis for variance.

Table 2. Change in mean for claudication distance in control and intervention group.

	n	*Baseline in meters (SD)*	*12 weeks in meters (SD)*	*Change in mean (95% CI)*
Control group	15	122 (126)	139 (131)	16.9 (-16.4 to 50.1)
Intervention group	20	80.0 (56.7)	118 (97.3)	37.6 (-13.6 to 88.7)

CI, confidence interval; SD, standard deviation

Table 3. Maximum walking distance in control and intervention group.

	n	*Baseline in meters (SD)*	*12 weeks in meters (SD)*	*Change in mean (95% CI)*
Control group	15	258 (197)	287 (223)	29.7(-34.5 to 94.8)
Intervention group	20	183 (103)	205 (110)	22.7(-18.2 to 63.5)

CI, confidence interval; SD, standard deviation

Table 4. ABPI-score in control and intervention group.

	n	*Baseline score (SD)*	*12 weeks score (SD)*	*Change in mean (95% CI)*
Control group	14	0.74 (0.24)	0.85 (0.23)	0.11 (-0.01 to 0.23)
Intervention group	20	0.69 (0.24)	0.71 (0.25)	0.02 (-0.08 to 0.12)

CI, confidence interval; SD, standard deviation