Plantar flexion training primes peripheral arterial disease patients for improvements in cardiac function

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Abstract This study investigated if initial calf muscle training immediately followed by whole body training improved aerobic power and cardiovascular function in peripheral arterial disease (PAD) patients. The training group \((n = 10)\) pursued 8 weeks of high aerobic intensity plantar flexion interval training continued by 8 weeks of high aerobic intensity treadmill training. The control group \((n = 11)\) received advice according to exercise guidelines. Treadmill \(\text{VO}_2\text{peak}\) and time to exhaustion increased significantly with 16.8 and 23.4\% during the plantar flexion training period while no changes occurred in heart stroke volume (SV). Following treadmill training, SV increased with 25.1\% while treadmill \(\text{VO}_2\text{peak}\) and time to exhaustion increased 9.9 and 16.1\%. Plantar flexion training was effective for increasing treadmill \(\text{VO}_2\text{peak}\) and time to exhaustion in PAD patients and amplified the effects of the additional treadmill training, as SV increased and treadmill \(\text{VO}_2\text{peak}\) and time to exhaustion improved further. This study suggests that calf muscle training prime PAD patients for cardiovascular adaptations when applying whole body exercise.

Keywords Intermittent claudication · Exercise · Stroke volume · Oxygen consumption · Cardiovascular health

Introduction

Peripheral arterial disease

Peripheral arterial disease (PAD) is caused by arterial narrowing in the lower extremities because of atherosclerosis and leads to thickening of the arterial wall. This inhibits blood flow to the legs, causing lactic acid formation and impaired walking ability (Weitz et al. 1996). Symptoms of PAD may vary from intermittent claudication to pain at rest. Intermittent claudication is caused by critical leg ischemia and is the most severe symptom of PAD (Hiatt 2001). Claudication is defined as pain induced by walking which is only relieved by rest. The pain appears in one or both legs during activity and mainly affects the calves (Stewart et al. 2002), but might also be present in the buttocks and thighs (Weitz et al. 1996).

Physical capacity, measured as maximal oxygen consumption (\(\text{VO}_2\text{max}\)), is a more powerful predictor of mortality amongst males than other established risk factors for cardiovascular disease (Myers et al. 2002). Exercise training is known to improve physical capacity, reduce symptoms and slow the progression of PAD (Gardner et al. 2005; Stewart et al. 2002). Further, it is shown that the intensity of the training cannot be compensated for by longer duration and that training with high aerobic intensity...
is shown to be superior to training of low aerobic intensity (Slordahl et al. 2005). Although PAD is localized in the lower extremities it is a manifestation of systemic cardiovascular disease (Weitz et al. 1996) and it is critical to not only provoke training adaptations in peripheral muscle metabolism, but also the overall cardiovascular system. The importance of cardiovascular improvements also becomes evident by the elevated risk of cardiovascular events these patients suffer (Weitz et al. 1996). Presently, exercise training studies with PAD patients which show improvements in lower limb blood flow, measured in the femoral and/or popliteal arteries, and in central blood flow, measured as cardiac output (Q) and stroke volume (SV), are limited (Slordahl et al. 2005; Tan et al. 2000).

It has been demonstrated that maximal work performed by an isolated small skeletal muscle is not sufficient to tax the supply components of aerobic endurance (Shephard et al. 1988). Thus, it seems likely that the calf pain which PAD patients experience restricts them from overloading the cardiovascular system when pursuing exercise training. In practical terms claudication pain in the calf may be seen as the main factor limiting physical capacity in PAD patients. Most studies on PAD patients have used exercise training interventions of large muscle groups (e.g., treadmill walking). However, it has been shown that reducing the muscle mass involved in exercise induces higher rates of muscle blood flow and metabolic extraction (Klausen et al. 1982; Richardson et al. 1999; Saltin 1985). Further, it has been documented that the main factor limiting small muscle work is the steady power output that can be developed by the active muscle fibers, rather than oxygen delivery (Shephard et al. 1988). Small muscle work may be seen as arm plus shoulder ergometry in the Shephard et al. (1988) study or as calf muscle work in the present study. A study confirmed the assumptions of calf muscle limitations and possible benefits of small muscle training in PAD patients by applying a training intervention using only the individual leg. The study showed effective adaptations in whole body physical capacity and walking distance (Wang et al. 2008).

Training the isolated calf muscle alone is not sufficient to tax the cardiovascular system (Shephard et al. 1988). Improvements in the cardiovascular system should therefore include training with large muscle groups. The calf muscle as the limiting factor for exercise performance in PAD patients must be overcome and training suitable for causing adaptations in the cardiac function applied. Identifying cardiovascular adaptations to exercise training in PAD patients would suggest a change in limitations to VO₂max in PAD patients, as they would go from being more limited from peripheral factors to being more limited by central factors. In the present study it was hypothesized that initial plantar flexion interval training using high aerobic intensity would improve treadmill peak oxygen consumption (VO₂peak) and time to exhaustion, but without any observed changes in cardiac function. Further, it was hypothesized that additional high aerobic intensity interval training on a treadmill (continued immediately after the plantar flexion training period) would improve cardiac function, as well as treadmill VO₂peak and time to exhaustion.

Methods

Subjects

In all 21 subjects (17 males and 4 females), all diagnosed with mild to moderate-severe claudication, classified as Fontaine stage II PAD (Hirsch et al. 2006), participated in this study. Inclusion criteria were functional limitations from intermittent claudication defined as difficulties with performing social, recreational or vocational activities; a history of intermittent claudication together with resting unilateral or bilateral ankle-brachial index of systolic blood pressure (ABI) ≤0.9. Subjects were excluded from the study if they were more than 75 years of age, had asymptomatic PAD classified as Fontaine stage I PAD, ischemic rest pain classified as Fontaine stage III PAD, undergone a revascularization operation the last 6 months, if they could not perform the plantar flexion or treadmill exercise (e.g., different movement restrictions), and if their physical capacity was limited by other factors than intermittent claudication, the exercise pain was not of vascular origin, and/ or they were unable to perform plantar flexion/treadmill test procedures. One subject reported mild symptoms of angina, but that exercise tolerance was not limited by this, but the symptoms of claudication. Also, subjects in the training group were excluded if not pursuing at least 85% of the planned training bouts. The subjects were told not to change medications or other possible treatments throughout the length of this study.

From another study which investigated the effect of plantar flexion exercise alone (Wang et al. 2008), subjects had already been randomly assigned to a training intervention group (TG) and a control group (CG). The TG in the present study was based on volunteers from the earlier TG who had already been performing plantar flexion exercise for 8 weeks and now immediately continued additional 8 weeks of treadmill exercise. Ten of the 14 PAD patients in the previous study (Wang et al. 2008) volunteered to participate in the present study. Of the four patients that did not want to continue, two gave the reason that they were travelling abroad, and that this prevented them from participating, one said no because of personal reasons, and one gave lack of motivation as the reason for not participating.
From the original TG (N = 10) in the present study one subject withdrew from the TG due to personal reasons and two subjects were excluded from the TG due to not pursuing the required amount of training. The CG (n = 11) received exercise guidelines in accordance to the recommendations for PAD patients from the American Heart Association (Hirsch et al. 2006). The CG was post-tested after the first 8 weeks of participation. As no changes were observed in the control group during this period, the chances of changes within the same timeframe the next 8 weeks was considered small. The patients in the control group received advice of training with a higher intensity, which is documented to be more effective for PAD patients and other patient groups (Rognmo et al. 2004; Slordahl et al. 2005; Wisloff et al. 2007; Tjonna et al. 2008). All participants reviewed and signed an informed consent form, in accordance with the Declaration of Helsinki. The study was approved by the regional medical ethics committee. The patients’ physical characteristics are presented in Table 1.

Treadmill testing

After a 10-min warm-up period, $\text{VO}_{2\text{peak}}$ was measured (Metamax II, Cortex, Leipzig, Germany) using a graded treadmill protocol (Hiatt et al. 1990). The treadmill velocity was held constant at 3.2 km h\(^{-1}\), and inclination starting at 0% and increased by 3.5% steps every 3 min until patients were stopped by claudication pain. $\text{VO}_{2\text{peak}}$ was measured as the mean of the highest 30-s interval as was expiratory exchange ratio and ventilation. Peak heart rate (HR\(_{\text{peak}}\)) was measured using a heart rate monitor (Polar Electro, Kempele, Finland). Blood samples were drawn from fingertip for measurement of lactate in blood ([Lac]\(_b\)) using a YSI 1500 Sport Lactate Analyzer (Yellow Springs Instrument Co, Yellow Springs, Ohio, USA) within 1 min after the test.

Work economy was determined using oxygen uptake at a standard sub-maximal workload of 0% inclination at 3.2 km h\(^{-1}\).

Stroke volume

$Q$ and $SV$ were measured using a Sensorsmedics Vmax Spectra 229 (Sensorsmedics, Pennsylvania, USA). The test was performed at the workload representing the subjects $\text{VO}_{2\text{peak}}$. The workload corresponding to maximal aerobic velocity was known from the treadmill test. Thus, the highest intensities and total exhaustion could be avoided. $\text{VO}_{2\text{peak}}$ was reached about 10 heart beats below the maximal intensities. The single breath acetylene uptake (SB) procedure started with complete expiration followed by complete inspiration of a gas mixture containing 0.3% carbon monoxide (CO), 0.3% methane (CH\(_3\)), 0.3% acetylene (C\(_2\)H\(_2\)), 21% oxygen (O\(_2\)), balanced with nitrogen (N\(_2\)). The inspiration was followed by a continuous complete expiration. Before the test started, multiple training bouts were carried out to familiarize subjects to the technique. The SB technique has been validated with the indirect Fick CO\(_2\) rebreathing method and compared with open circuit acetylene uptake (Dibski et al. 2005). Both techniques were valid and reliable for measures of $Q$ and $SV$. CoV was 7.6% at an intensity of 200 W. The test procedure was however concluded to be more difficult to perform at the highest exercise intensities. However, the patients in the present study were walking on the treadmill which made it easier to do the proper procedure, compared to athletes doing much more vigorous work. Their respiratory frequency was also lower compared to the athletes. Although not directly measured, maximal arteriovenous oxygen differences [C(a – v)\(_2\)] were calculated from the equation $\text{VO}_{2\text{peak}} = \text{CO} \times [\text{C(a} – \text{v})\text{O}_2]$.

### Table 1 Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Control group ((n = 11))</th>
<th>Training group ((n = 10))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>8/3</td>
<td>9/1</td>
</tr>
<tr>
<td>Age (years)</td>
<td>67.1 ± 7</td>
<td>68.2 ± 7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>92.5 ± 15.8</td>
<td>87.5 ± 17.1</td>
</tr>
<tr>
<td>Body mass index ((\text{kg/m}^2))</td>
<td>31.8 ± 5.8</td>
<td>30.0 ± 4.9</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Current smoker</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Previous congestive heart failure</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Previous cerebrovascular events</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Data for age, weight and body mass are mean ± SD

### Plantar flexion test

Patients performed an exercise test using a plantar flexion ergometer (Wang et al. 2008). Frequency was held constant at 1 Hz, displayed by a monitor. Resistance started at 0 W and was increased by steps of 1 W every minute until exhaustion, while subjects performed plantar flexion training working against the footplate. The bicycle flywheel provided constant resistance and returned the pedal to the proper position between plantar flexion pushes. Range of motion was 10 cm with the starting position perpendicular to horizontal (Haseler et al. 2007; Wang et al. 2008). Patients were given one training session to familiarize with the ergometer before the test. In addition to power output, time to exhaustion and pulmonary oxygen consumption were measured continuously during the test protocol. Oxygen consumption was measured as the mean of the highest...
Due to Q–Q plots examining the line of best fit (investigating the data distribution) and the low number of subjects \((n = 7, n = 11)\) non-parametric statistics were used. Wilcoxon signed rank tests were used to detect differences within groups, and Mann–Whitney \(U\) tests were used to detect differences between groups. In order to compare the results with other studies, data are presented as arithmetic mean and standard deviation (SD). In figures data are presented as arithmetic mean and standard error (SE). Level of significance was set at \(P < 0.05\).

**Results**

No differences were apparent between the TG and CG at pre-training tests. Absolute changes in \(V\text{O}_{2\text{peak}}\) and time to exhaustion should be reported here, both for plantar flexion and treadmill training.

**Plantar flexion interval training (8 weeks)**

After performing 8 weeks of plantar flexion interval training, the TG improved plantar flexion \(V\text{O}_{2\text{peak}}\) from 0.77 ± 0.15 to 0.89 ± 0.19 L min\(^{-1}\) (14.8%) \((P = 0.008)\), plantar flexion time to exhaustion from 443 ± 117 to 664 ± 132 s. (58.5%) \((P = 0.010)\) and peak power output by 7.1 ± 1.7 to 10.8 ± 1.9 W (61.4%) \((P = 0.010)\). Furthermore, treadmill \(V\text{O}_{2\text{peak}}\) increased from 2.13 ± 0.60 to 2.39 ± 0.41 L min\(^{-1}\) (16.8%) \((P = 0.001)\). These improvements were apparent both within and between groups. The TG also showed a within-group increase in treadmill time to exhaustion from 1,130 ± 277 to 1,326 ± 201 s. (23.4%) \((P = 0.041)\). The results are presented in Table 2 and Fig. 1.

**Treadmill interval training (8 weeks)**

After performing 8 weeks of treadmill interval training, the TG improved treadmill \(V\text{O}_{2\text{peak}}\) from 2.39 ± 0.41 to 2.62 ± 0.36 L min\(^{-1}\) (9.9%) \((P < 0.001)\) while treadmill time to exhaustion increased from 1,326 ± 201 to 1,526 ± 144 s. (16.1%) \((P < 0.001)\). \(Q\) and SV improved by 33.4% \((P < 0.001)\) 25.1% \((P = 0.027)\), respectively. These improvements were apparent both within and between groups. Results are presented in Tables 2 and 3; Fig. 2.

**Discussion**

The main findings in this study were that plantar flexion interval training was effective in increasing treadmill \(V\text{O}_{2\text{peak}}\) and time to exhaustion in PAD patients. Additional
Changes in physiological parameters from the treadmill and plantar flexion tests

<table>
<thead>
<tr>
<th></th>
<th>TG-PF (n = 7)</th>
<th>TG-TM (n = 7)</th>
<th>CG (n = 11)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Pre-training</td>
<td>Mid-training</td>
<td>Post-training</td>
</tr>
<tr>
<td><strong>Peak treadmill test</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO(_{2\text{peak}}) (L min(^{-1}))</td>
<td>2.13 ± 0.60</td>
<td>2.39 ± 0.41(^{§})</td>
<td>2.62 ± 0.36(^{§})</td>
</tr>
<tr>
<td>(mL min(^{-1}) kg(^{-1}))</td>
<td>23.7 ± 3.4</td>
<td>27.0 ± 3.6(^{§})</td>
<td>29.8 ± 2.5(^{§})</td>
</tr>
<tr>
<td>(mL min(^{-1}) kg(^{-0.75}))</td>
<td>72.7 ± 12.0</td>
<td>82.4 ± 8.4(^{§})</td>
<td>91.0 ± 3.5(^{§})</td>
</tr>
<tr>
<td>HR(_{\text{peak}}) (beats min(^{-1}))</td>
<td>142 ± 13</td>
<td>149 ± 11(^{§})</td>
<td>158 ± 10(^{§})</td>
</tr>
<tr>
<td>[La(^{-})](<em>{b}) at VO(</em>{2\text{peak}}) (mmol L(^{-1}))</td>
<td>3.97 ± 2.12</td>
<td>4.76 ± 1.63(^{§})</td>
<td>6.73 ± 1.54(^{§})</td>
</tr>
<tr>
<td>TE (seconds)</td>
<td>1,130 ± 277</td>
<td>1,326 ± 20(^{†})</td>
<td>1,526 ± 144(^{§})</td>
</tr>
<tr>
<td>Respiratory exchange ratio (R)</td>
<td>1.02 ± 0.05</td>
<td>1.04 ± 0.05</td>
<td>1.10 ± 0.06(^{§})</td>
</tr>
<tr>
<td>VE (L min(^{-1}))</td>
<td>71.7 ± 22.5</td>
<td>78.5 ± 15.9(^{§})</td>
<td>93.8 ± 12.0(^{§})</td>
</tr>
<tr>
<td>VE/V(_{O_2})</td>
<td>33.4 ± 3.8</td>
<td>32.8 ± 3.1</td>
<td>36.0 ± 3.6(^{§})</td>
</tr>
<tr>
<td>VE/V(_{CO_2})</td>
<td>32.5 ± 2.6</td>
<td>31.4 ± 2.1</td>
<td>32.9 ± 2.9</td>
</tr>
<tr>
<td><strong>Treadmill work economy</strong></td>
<td></td>
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<tr>
<td>VO(_{2}) (mL min(^{-1}) kg(^{-0.75}))</td>
<td>35.8 ± 5.4</td>
<td>37.2 ± 6.0</td>
<td>35.0 ± 4.4</td>
</tr>
<tr>
<td><strong>Plantar flexion test</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO(_{2\text{peak}}) (L min(^{-1}))</td>
<td>0.77 ± 0.15</td>
<td>0.89 ± 0.19(^{§})</td>
<td>1.02 ± 0.26</td>
</tr>
<tr>
<td>TE (s)</td>
<td>443 ± 117</td>
<td>664 ± 132(^{§})</td>
<td>862 ± 185</td>
</tr>
<tr>
<td>Watt(_{\text{peak}})</td>
<td>7.1 ± 1.7</td>
<td>10.8 ± 1.9(^{§})</td>
<td>14.0 ± 3.1</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>89.1 ± 19.0</td>
<td>90.1 ± 18.8</td>
<td>88.9 ± 18.4(^{§})</td>
</tr>
</tbody>
</table>

Data are mean ± SD. The mid-test was used as post-test for the plantar flexion training period (TG-PF) and pre-test for the treadmill training period (TG-TM).

TG-PF, plantar flexion training period; TG-TM, treadmill training period; CG control group, lasted 8 weeks and ran in parallel with the plantar flexion training period; VO\(_{2}\), oxygen consumption; VCO\(_{2}\), carbon dioxide production; HR\(_{\text{peak}}\), peak heart rate; [La\(^{-}\)]\(_{b}\), blood lactate; Watt\(_{\text{peak}}\), peak power output; TE time to exhaustion; VE, ventilation

\(^{§}\) Different from pre-training within group, \(P < 0.05\); \(^{†}\) difference between groups from pre-training to post-training, \(P < 0.05\); \(^{§}\) difference between groups from pre-training to post-training, \(P < 0.01\)

Plantar flexion training intervention

Plantar flexion training increased plantar flexion VO\(_{2\text{peak}}\) and time to exhaustion, and this led to an improved treadmill VO\(_{2\text{peak}}\) and time to exhaustion in a ramp protocol. The ~17% improvement in treadmill VO\(_{2\text{peak}}\) after the first 8 weeks in the present study (~27% after 16 weeks) is comparable to the largest improvements seen in previous studies, especially if the duration of the training intervention is taken into consideration. Gardner et al. (2001, 2005) showed a ~7 and ~11% VO\(_{2\text{peak}}\) improvement after 6 months of supervised treadmill exercise (3 days a week), whereas other studies have shown increases of ~4% after 6 (3 days a week) weeks (Hiatt et al. 1990), ~13% (Hiatt et al. 1994) to ~30% (Hiatt et al. 1990) after 12 (3 days a week) weeks. A potential problem with reporting changes in VO\(_{2\text{peak}}\) is that they do not take possible changes in body weight with training into consideration. A decrease in bodyweight will overestimate the improvement in VO\(_{2\text{peak}}\) in relation to bodyweight (mL min\(^{-1}\) kg\(^{-1}\)). Changes in bodyweight from 24 weeks of exercise training could have occurred and changes in VO\(_{2\text{peak}}\) could be due to an average decrease in bodyweight. The increases in treadmill time to
Table 3  Changes in maximal cardiac output and stroke volume during treadmill testing

<table>
<thead>
<tr>
<th></th>
<th>TG-PF (n = 7)</th>
<th>TG-TM (n = 7)</th>
<th>CG (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stroke volume</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV (mL beat⁻¹)</td>
<td>78.9 ± 21.0</td>
<td>83.4 ± 19.8</td>
<td>102.9 ± 24.4*</td>
</tr>
<tr>
<td>(mL beat⁻¹ kg⁻¹)</td>
<td>0.89 ± 0.25</td>
<td>0.95 ± 0.24</td>
<td>1.19 ± 0.31*</td>
</tr>
<tr>
<td><strong>Cardiac output</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q (L min⁻¹)</td>
<td>10.40 ± 3.16</td>
<td>11.37 ± 2.03</td>
<td>14.93 ± 2.49*</td>
</tr>
</tbody>
</table>

Data are mean ± SD. The mid-test was used as post-test for the plantar flexion training period (TG-PF) and pre-test for the treadmill training period (TG-TM)

TG-PF, plantar flexion training period; TG-TM, treadmill training period; CG control group, lasted 8 weeks and ran in parallel with the plantar flexion training period; SV stroke volume of the heart; Q, cardiac output

* Different from pre-training within group, P < 0.05, P < 0.01, § difference between groups from pre-training to post-training, P < 0.05, † difference between groups from pre-training to post-training, P < 0.01

As no significant changes in Q occurred during the initial 8 weeks of plantar flexion training, the VO₂peak improvement must be due to an increased a – v O₂ difference. In the present study, calf muscle metabolism, measured as plantar flexion VO₂peak, increased with 0.12 ± 0.10 L min⁻¹. Also peak power output during plantar flexion increased by 3.7 ± 2.1 W. The improved muscle metabolism together with the absence of blood flow adaptations is in line with most previous findings from exercise training studies with PAD patients (Slordahl et al. 2005; Tan et al. 2000). From studies investigating the mechanisms behind “local” muscle training response, an improved demand function, measured as oxidative enzyme activities, has been well documented (Hiatt et al. 1996; Lundgren et al. 1989). This supports the assumption of the present study that improved 

exhaustion found in many studies (Gardner et al. 2001; Gardner and Poehlman 1995; Hiatt et al. 1994) have most often been measured at additional sub-maximal continuous testing protocols, making their results difficult to compare with the present study. It should also be noted that the pre-test VO₂peak values was higher for the participants in the present study (23.7 ± 3.4 mL min⁻¹ kg⁻¹) than for other studies (Gardner et al. 2001; Hiatt et al. 1994). One might speculate that the high VO₂peak values in this study indicate a better trained selection of patients than regularly shown. However, all patients showed an ABI <0.9. Furthermore, low [La]b concentrations and low respiratory exchange ratios before training, together with a large improvement in HRpeak with training, indicated that the patients did not reach their true VO₂max, and thus were limited by peripheral factors and intermittent claudication pain.
muscle VO$_{2\text{peak}}$ is due to “peripheral” adaptations in the calf muscles.

PAD patients are by definition limited by claudication pain when pursuing exercise, thus probably not reaching their true potential for maximal effort. Increased metabolic capacity in muscles is the best documented factor contributing to reduced symptoms of claudication pain (Stewart et al. 2002). HR$_{\text{peak}}$, [La$^-\text{peak}$], and ventilation increased after the plantar flexion training period, indicating that these patients are working harder during whole body exercise at post-test. This means that they are closer to fulfilling the criteria’s for maximal effort than before training (Bassett and Howley 2000), most likely due to improved metabolic capacity in the calf muscles. Thus, it appears that an emphasis on reducing the symptoms of calf pain by plantar flexion exercise is an effective treatment for increasing whole body VO$_{2\text{peak}}$ in PAD patients.

Treadmill training intervention

The heart SV increased by 25.1% following the treadmill interval training. PAD patients suffer from an elevated risk of cardiovascular events (Weitz et al. 1996), and this adaptation should be of importance. The finding suggests that there has been a change in limitations to VO$_{2\text{peak}}$ in the PAD patients participating in this study displaying a larger importance of supply factors. However, it is important to consider supply and demand oxygen transport adaptations as series of linked factors that all may contribute with different order of magnitude to VO$_{2\text{peak}}$ limitation. As argued by Wagner (Wagner 2000), SV improvements demonstrate an improved blood flow in response to training. Earlier studies which have identified blood flow improvements following exercise training have used “local” calf blood flow measurements (Gardner et al. 2001; Hiatt et al. 1990). There seems to be some agreement between the present study and previous studies (Gardner et al. 2001) with regard to percentage change in blood flow, despite the diversity of measuring cardiovascular adaptations “centrally” versus “peripherally”. Furthermore, the changes in SV from the present study were similar to what is seen in healthy, young individuals (Helgerud et al. 2007).

In contrast, another study applying high aerobic intensity interval training (Slordahl et al. 2005) found no change in maximal calf blood flow after 8 weeks of high aerobic intensity interval treadmill training. This probably demonstrates how crucial the plantar flexion training period was in amplifying the effects of the treadmill training period in the present study. However, this could also indicate that 8 weeks of exercise was not enough to induce cardiovascular adaptations in this group of patients.

Treadmill VO$_{2\text{peak}}$ increased by an additional 9.9% during the treadmill training period. Also treadmill time to exhaustion increased by 16.1% during the 8-week period. The use of high aerobic intensity may be one explanation for the size of improvement. This is in line with previous findings (Slordahl et al. 2005) documenting large increases following high aerobic intensity training. It seems to be a consistent finding that intensity of training cannot be compensated for by longer duration when emphasizing on improving VO$_{2\text{peak}}$, and that high aerobic intensity training is superior to training of low/moderate intensity, both in healthy and different groups of patients (Helgerud et al. 2007; Rognum et al. 2004; Slordahl et al. 2005; Tjonna et al. 2008; Wisloff et al. 2007).

Work economy did not change throughout the treadmill training period. This is in contrast to other findings from training studies with PAD patients (Hiatt et al. 1990; Stewart et al. 2002; Womack et al. 1997). The most likely explanation for the findings in the present study is that the subjects pursued their treadmill training at inclinations from 14% and steeper, while the work economy walking test was performed at 0% inclination. When accounting for the specificity of aerobic exercise and oxygen consumption (Åstrand et al. 2003) it seems like the inclined treadmill interval training had little or no transfer to the horizontal walking test. The result might have been different if a steeper inclination had been used during the work economy test.

Comparison of the two training interventions

When evaluating the training intervention as a whole (8 weeks of plantar flexion training +8 weeks of treadmill training) an interesting finding is that the two different training periods induced divergent training adaptations which seem to contribute to improved treadmill VO$_{2\text{peak}}$ and time to exhaustion. The plantar flexion training intervention improved parameters measured “locally” at the calf, such as muscle VO$_{2\text{peak}}$ and peak power output during the maximal plantar flexion test. As supply factors remained unchanged, these improvements seem to be the major contributors in accounting for improved treadmill performance post-test. In contrast, during the treadmill training period no significant improvements occurred in any of the plantar flexion parameters. The treadmill training period improved supply factors which seem to be most the important contributors to improved VO$_{2\text{peak}}$ and time to exhaustion at post-test. However, it should be noted that there was a tendency of improvements in plantar flexion VO$_{2\text{peak}}$ at post-test ($P = 0.083$).

The diverse training response from the two different training interventions can be explained by the unequal dependence on peak power output and muscle VO$_{2\text{peak}}$, and on whether leg pain and muscle metabolism limits exercise performance and the level of trained state. The high aerobic intensity treadmill training apparently involves enough
muscle mass to challenge the supply properties of aerobic fitness, also in PAD patients when they become more fit, and less limited from leg pain.

Study limitations

More explicit measurements of calf muscle training adaptations such as calf muscle biopsies and direct measurements of $a - v O_2$ difference would have been preferable. This could reveal to what degree muscle metabolism accounts for increased $V_{O2peak}$ compared with Q adaptations during a treadmill training intervention. Further, the method for measuring stroke volume is difficult, and is dependent on the patient’s ability to perform the correct breathing procedure. However, if the ventilation frequency is low, and/or calf pain is limiting exercise performance, as in most PAD patients, this can be overcome by multiple training bouts. Pulmonary measuring of planter flexion $V_{O2peak}$ might increase the sensitivity for variations between tests, but the variation can be reduced by proper instructions given to the subjects before and during testing. Another weakness of the present study is that the control group lasted for only 8 weeks. Though chances of changes in the last 8-week period are considered small, it would have been preferable to have it running concurrently also during the last 8 weeks. However, it is an ethical topic if patients should continue to receive advices with small or no effect. Finally, a higher number of subjects included in the study would have been preferable and made the study less exposed to the risk of not being representative for the patient population.

Conclusions

These results demonstrate that the small muscle mass in the leg may limit whole body performance and that training of the small muscle mass on each individual leg is effective for improving whole body exercise performance in PAD patients. These data also suggest that improving calf muscle limitations in PAD patients enhances further cardiovascular improvements when applying whole body exercise.

Acknowledgments  The experiments in the present study comply with the current laws of the country in which they were performed.

Conflict of interest statement  The authors declare that no conflict of interest existed in the present study.

References


the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease); endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. Circulation 113:e463–e654. doi:10.1161/CIRCULATIONAHA.106.174526


