Effects of ischemic training on leg exercise endurance

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Abstract—This study tested whether ischemic exercise training (TrIS+EX) would increase endurance of ischemic (ExIS) and ramp exercise (ExRA) knee-extension tests more than exercise training (TrEX) alone. Ten healthy subjects performed pre- and posttraining tests with each leg. For ExRA, after subjects warmed up, a weight was added each minute until they were exhausted. ExIS was similar, but after warm-up, we inflated a thigh cuff to 150 mmHg instead of adding weights. One leg was chosen for TrIS+EX (cuff inflated to 150 mmHg during exercise) and the other for TrEX, both with a small weight on each leg, four to six times per daily session for 3 to 5 min each, 5 days per week for 6 weeks. ExIS duration increased 120% more ($p = 0.002$) in the TrIS+EX leg than in the contralateral TrEX leg, whereas ExRA duration increased only 16% (nonsignificant). TrIS+EX and TrEX significantly attenuated the ventilation increase (ergoreflex) during ExIS. The O₂ debt for ExIS was significantly lower and systolic blood pressure recovery was faster after TrIS+EX than after TrEX. Heart rate recovery after ExRA and ExIS was faster after TrIS+EX. Apparently, TrIS+EX with low-intensity resistance increases exercise endurance and attenuates the ergoreflex and therefore may be a useful tool to increase regional muscle endurance to improve systemic exercise capacity in patients.

Key words: congestive heart failure, ergoreflex, frequency spectrum, heart rate recovery, ischemia, ischemic training, oxygen debt, ramp exercise, surface-recorded electromyogram (sEMG), ventilation response.

INTRODUCTION

Exercise intolerance is one of the most prominent features of acute or chronic activity-disabling diseases, such as congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), and renal disease. Exercise curtailment results in impaired systemic exercise capacity required for ambulation and is associated with muscle

Abbreviations: CHF = congestive heart failure, COPD = chronic obstructive pulmonary disease, DVT = deep venous thrombosis, EMG = electromyogram, ExIS = ischemic endurance test, ExRA = ramp (progressive) exercise test, HR = heart rate, iEMG = integrated electromyogram, MVC = maximal voluntary contraction, NCV = nerve conduction velocity, O₂ = oxygen, SBP = systolic blood pressure, SEM = standard error of measurement, sEMG = surface electromyogram, TrEX = exercise training without ischemia, TrIS+EX = exercise training with ischemia, $V_{E}$ = pulmonary ventilation, $V_{O2}$ = oxygen uptake, $V_{O2p}$ = peak oxygen uptake, $V_{CO2}$ = carbon dioxide output.

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atrophy from inactivity. Many studies suggest that enhanced exercise capacity is associated with increased quality of life and longer survival [1]. However, these chronic diseases may restrict exercise intensity to less than what is required for an adequate training stimulus, and these patients often cannot perform sufficient activity to avoid progressive deconditioning.

Any peripheral exercise stimulus that prevents deconditioning or enhances training can be very beneficial for patients with a disabling disease. Training groups of skeletal muscles, e.g., leg muscles collectively required for large motor activities (e.g., walking, stair-climbing, cycling), without taxing the central circulation can improve whole body exercise capacity and metabolic performance of patients with CHF [2–4]—the ones most commonly studied. We have previously demonstrated that fairly high-intensity exercise training restricted to a small forearm muscle group can enhance performance without placing appreciable stress on the central circulation during training in patients [5]. However, intense regional training of larger muscle groups does place significant demand on the central circulation, so additional strategies to enhance aerobic capacity and endurance in these muscle groups important to daily life could offer additional help to the patients, especially those with CHF.

Research studies have shown that peak exercise performance is enhanced in healthy subjects by reducing blood flow to exercising muscles by 20 percent during training with lower-body positive pressure [6–7]. Other experiments have shown that vascular occlusion during high-intensity resistance exercise training of arm flexors can induce favorable biochemical changes in the muscle [8] and that similar training of knee extensors can benefit athletes [9]. These studies used high-intensity training in combination with reduced blood flow to enhance the training response. It is not known whether a reduction in blood flow during repeated exercise bouts with low-intensity workloads, appropriate for chronically ill patients, would also enhance muscle training, thereby reducing the intensity of exercise required to achieve endurance training.

Safety concerns of limb occlusion associated with exercise in nonathletes are an important issue. In a Medline search from 1966 to present, we found no reports of deep venous thrombosis (DVT) or other negative consequences associated with exercise and limb occlusion. Also, no reports were found of DVTs being triggered by the use of pneumatic cuffs, either at rest for hours during surgery, in studies of reactive hyperemia following exercise, or in studies of the "ergoreflex" (the systemic heart rate (HR) and ventilatory response to muscle ischemia).

The purpose of this study was to determine whether repetitive, low-intensity dynamic knee-extension exercise with marked reduction of blood flow (ischemic training) would increase work capacity of the knee extensors more than the same exercise without ischemia. If so, this type of training might be applied, in principle, to other limb movements and larger muscle groups to benefit patients with chronic diseases and limited exercise capacity. The specific hypothesis was that training knee extensors under ischemic conditions with low-intensity exercise would result in a greater increase in exercise endurance, compared with the training effect of the same exercise without ischemia in the contralateral knee extensors.

METHODS AND PROCEDURES

Subjects

Five men and five women volunteered as subjects. Informed, written consent was obtained from each, as approved by the Institutional Review Board of the University of New Mexico and the Albuquerque Department of Veterans Affairs Medical Center. Their mean age and body mass index (kilograms per meter squared) were 50 yr (range 35–68) and 23.5 kg/m² (range 21–27), respectively, ranging from being sedentary to running/jogging or cycling daily for 30 min. Exclusionary criteria included hypertension, any history of venous or arterial thrombosis, lower-limb arthritis, blood clotting abnormalities, and evidence of central or peripheral vascular disease. Prior to participation, subjects underwent a medical history and physical exam and ultrasound imaging of the leg veins to screen for DVTs.

Knee-Extension Exercise Tests

Maximal ramp and endurance knee-extension tests were performed on a Unex II exercise chair (model 2400, Sammons Preston; Bolingbrook, Illinois). Exercises were done to a metronome, whereby both knees alternately extended completely and relaxed through a 90° range so that each leg performed 20 knee extensions per minute [10]. For the ramp (progressive) exercise test (ExR), after resting measurements, the subject exercised for 2 min with no load added to the weight of the swing arms. At the midpoint of the leg range of motion, the weight of the chair arm
was 4.1 kg. This was approximately 12 percent (range 9%–14%) of a single maximal voluntary contraction (MVC) for these subjects. Each succeeding minute, a 2.3 kg weight was added to the swing arm on the side of the leg being tested. This was continued until the subject could no longer fully extend that knee or keep up with the metronome rhythm. The same exercise was performed for the ischemic endurance test (ExIS) as for the ExRA, but after 2 min of baseline exercise, a cuff (SC 10, Hokanson Co.; Bellevue, Washington), previously placed on the upper thigh, was inflated to 150 mmHg. This occlusion pressure was maintained until the exercise end point was reached, based on the same criteria as the ramp test. Whenever the systolic blood pressure (SBP) exceeded 150 mmHg during exercise, the leg cuff pressure was raised to 10 mmHg above the SBP.

Overall Protocol

Subjects were screened, enrolled in the study, and familiarized with the testing procedures. Pretraining testing consisted of ExRA performed on the left leg and then the right. Then ExIS testing was done on the left leg followed by the right with a 15 min rest between each test. A 6-week training period followed, with the same leg (randomly chosen for each subject) always made ischemic by an inflated cuff during the exercise training, repeating the same tests. Using a comparison of pre- and posttraining measurements of each leg’s exercise test duration and associated variables during ExRA and ExIS, we evaluated changes attributable to ischemia during training.

Training Protocol

During training, subjects performed the same exercise as for ExIS, with a 1.1 kg weight (approximately 3% of MVC, range 2%–4%) attached to each ankle, on a chair or bench in the laboratory or at home. Subjects performed knee-extension exercise with each leg four to six times per daily session for 3 to 5 min each, 5 days a week for 6 weeks. In these training exercises, the blood flow in the ischemically trained leg was reduced with a thigh cuff inflated to 150 mmHg (exercise training with ischemia [TrIS-EX]) and the other leg was exercised without the cuff (exercise training without ischemia [TrEx]). The four to six bouts of 3 to 5 min each were chosen as the exercise goal to achieve a total training time of 20 min, as recommended by the American College of Sports Medicine [11] for endurance training. Preliminary trials indicated that 3 to 5 min of ischemic exercise could be tolerated. As training progressed, if the subjects were able to increase bout duration, the number of bouts decreased to maintain the 20 min of exercise training each day.

Ancillary Measurements and Data Collection

Gas exchange was measured at the mouth before, during, and for 3 min after the exercise tests with a TrueMax 2400 breath-by-breath automated system (Parvomedics, Inc., Sandy, Utah) with incorporated software. These measurements included oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$) and pulmonary ventilation ($\dot{V}E$). The oxygen (O₂) debt was estimated from the duration during the 3 min recovery, minus preexercise resting $\dot{V}O_2$. Heart rate (HR) was obtained with a single-lead electrocardiogram. The same investigator measured the SBP with an arm sphygmomanometer at baseline rest and for each minute during and after exercise. Before and after the training period, we measured the thigh volume of each leg between the patella and 10 cm below the pubic symphysis by water displacement to estimate possible volume changes of the muscles involved in knee-extension training. The isometric strength of the quadriceps of each leg before and after training was measured with a tensiometer, as the peak knee-extension force exerted at an angle 45° from horizontal.

Electromyogram Recordings

Surface electromyogram (sEMG) recordings during ExRA and ExIS were used to estimate the differences in muscle fiber recruitment and fatigue during exercise. In addition to the inability to complete knee extensions, a shift to lower frequencies of motor-unit firing rates in the power spectrum of the quadriceps sEMG monitored the degree of muscle fatigue [12–13]. The sEMG analyses from a single-channel recording from the vastus lateralis were performed with a Noraxon 1200 system (Scottsdale, Arizona). Skin preparation for electrodes included shaving, sanding, and cleaning the skin with alcohol on the patella and on the vastus lateralis 2 and 4 cm proximal to the patella. The reference electrode was placed on the patella, and the two recording electrodes were placed on the vastus lateralis and remained there for the entire session of the ExRA and ExIS. Both raw and rectified sEMGs were collected for the last five bursts (contractions) of each minute of each exercise. By computer processing, these bursts were averaged and analyses were performed, including integrated electromyogram (iEMG) and spectral
analysis by fast Fourier transform. Total spectral power and mean and median frequencies were analyzed. The shift in frequency of the entire power spectrum with exercise duration was calculated from the area of the cumulative distribution function of the frequency spectra and expressed as percent change from baseline exercise.

**Data Analysis**

Each subject’s leg trained by TrEX (without ischemia) served as a control comparison for the leg trained by TrIS+EX. The differences between the pre- and posttraining changes in exercise duration in each leg were compared with paired t-test. Similarly, the differences in changes in electromyogram (EMG) parameters and gas exchange measurements between the pre- and posttraining tests were taken to represent the differences resulting from TrIS+EX. Differences in recovery values were tested by two-way (time and group) analysis of variance, with values at specific times compared with the use of Tukey’s post hoc test.

**RESULTS**

**Training Compliance**

Ultrasound imaging of deep and superficial upper-leg veins of these 10 subjects at rest, after exercise or cuff inflations, and before and after the study did not demonstrate any evidence of vascular clot formation. Training for one subject was stopped after 2 weeks at his request. Data from this subject were included. EMG recordings from two subjects were not analyzed because of inferior quality. Nine subjects trained for 30 out of 42 days (6 weeks), for a total of 20 min per day. Most were able to increase the exercise time per bout from 5 to 10 min, thus reducing the number of daily training bouts from four to two.

**Exercise Duration**

The average durations for the exercise tests before and after training are shown in Figure 1. The duration of ExIS increased 0.8 min (16%, nonsignificant) after TrEX and 5.5 min after TrIS+EX, a difference of 120 percent \((p = 0.002)\). For ExRA, the maximal workload is proportional to the test duration; the leg trained by TrEX had a small reduction in ExRA time from 6.1 to 5.7 min, and for the leg trained by TrIS+EX, the duration increased from 5.6 to 6.2 min. This 21 percent difference, corresponding to ischemic training, was positive in 7 of 10 subjects, but not statistically significant \((p = 0.17)\). The Cohen’s \(d\) and effect size values for the differences in exercise duration with training were, respectively, 1.39 and 0.63 for ExIS and 0.63 and 0.30 for ExRA.

To determine whether pretraining fitness level for this exercise influenced the results, we divided the 10 subjects into two groups of 5 each, based on a ranking of their average time on the pretests for both legs on the knee-extension ExIS and ExRA. The average time for the highest ranked group (“trained,” 6.3 min) was significantly \((p = 0.007)\) above that of the other (“untrained,” 4.1 min). Both groups increased their time on the ExRA by 0.9 min and the ExIS by 4.8 min. The percent increases were 13 percent for “trained” and 30 percent for “untrained” \((p = 0.55)\) on the ExRA and 108 percent for “trained” and 141 percent for

![Figure 1](image-url)

Changes in exercise duration in 10 subjects for (a) ischemic endurance and (b) ramp exercise tests pre- and posttraining. Average times indicated in Table of main text. Comparison of change in ischemic exercise duration after TrIS+EX with TrEX is significant \((p = 0.002)\), whereas the same comparison in ramp exercise duration is not \((p = 0.17)\). Cohen’s \(d\) values corresponding with \(p = 0.002\) for endurance exercise and \(p = 0.17\) for ramp exercise are 1.11 and 0.43, respectively. TrIS+EX = exercise training with ischemia; TrEX = exercise training without ischemia.
“untrained” \( (p = 0.65) \) on the \( \text{Ex}_{\text{IS}} \). Therefore, the pretraining exercise capacity did not have a significant influence on the improvement with training for this type of exercise.

### Oxygen Consumption

The peak oxygen uptake (\( \dot{V}O_2 \)) at maximal exercise ranged from 685 to 789 mL/min in the four \( \text{Ex}_{\text{IS}} \) (2.4–2.8 Met) (1 Met = resting \( \dot{V}O_2 \)) and from 949 to 1062 mL/min (3.4–3.8 Met) in the four \( \text{Ex}_{\text{RA}} \). The cumulative \( \dot{V}O_2 \) above resting levels after warm-up is shown in the Table. The \( O_2 \) used for the first 2 min of warm-up exercise averaged 479 mL for all eight tests. The \( O_2 \) cost during exercise after the warm-up corresponded with duration, as expected. After \( \text{Ex}_{\text{IS}} \), the recovery \( O_2 \) was significantly reduced after \( \text{Tr}_{\text{IS}+\text{EX}} \) compared with \( \text{Tr}_{\text{EX}} \). After training, the recovery \( O_2 \) decreased for both legs in \( \text{Ex}_{\text{RA}} \), but was only significant in the \( \text{Tr}_{\text{IS}+\text{EX}} \) group. The recovery \( O_2 \) as a percentage of the total \( O_2 \) cost was also reduced significantly more by \( \text{Tr}_{\text{IS}+\text{EX}} \) than \( \text{Tr}_{\text{EX}} \), and this difference was significant after both \( \text{Ex}_{\text{IS}} \) and \( \text{Ex}_{\text{RA}} \).

### Pulmonary Ventilation

The \( V_E \) changes for \( \text{Ex}_{\text{IS}} \) are shown in Figure 2. After ischemic training, the maximal \( V_E \) was significantly lower than the pretraining maximal value, even though the exercise duration was more than doubled (Figure 2(a)). The \( V_E \) attenuation was even greater comparing the pretraining \( V_E \) at maximal exercise with the posttraining \( V_E \) at the same exercise time. For the \( \text{Tr}_{\text{EX}} \) leg, \( V_E \) decreased significantly after training, even though this exercise duration was not significantly increased (Figure 2(b)). During \( \text{Ex}_{\text{RA}} \), the \( V_E \) increased similarly for all four tests from warm-up to \( \dot{V}O_2 \), by an average of 18 L/min (98%).

### Heart Rate and Systolic Blood Pressure Recovery After Exercise

After \( \text{Tr}_{\text{IS}+\text{EX}} \), recovery was faster for HR and SBP following \( \text{Ex}_{\text{IS}} \). After \( \text{Ex}_{\text{RA}} \), HR and SBP also both recovered faster after \( \text{Tr}_{\text{IS}+\text{EX}} \), but only the former was significant (Figure 3). The rate-pressure-product in the four \( \text{Ex}_{\text{IS}} \) at maximal exercise averaged 15,800 (standard error of measurement [SEM]: 990).

### Table.

Ischemic and ramp exercise duration and oxygen (\( O_2 \)) consumption of 10 subjects on two tests pre- and posttraining.

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Training</th>
<th>Test</th>
<th>Exercise Duration (min)</th>
<th>Cumulative ( O_2 ) Consumption</th>
<th>Recovery/Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Exercise (mL)</td>
<td>Recovery (mL)</td>
</tr>
<tr>
<td>( \text{Ex}_{\text{IS}} )</td>
<td>( \text{Tr}_{\text{IS}+\text{EX}} )</td>
<td>Pre</td>
<td>4.16</td>
<td>1,784</td>
<td>376</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post</td>
<td>9.72</td>
<td>3,375</td>
<td>308</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post – Pre</td>
<td>5.56*</td>
<td>1,591*</td>
<td>–68</td>
</tr>
<tr>
<td>( \text{Tr}_{\text{EX}} )</td>
<td></td>
<td>Pre</td>
<td>4.93</td>
<td>2,018</td>
<td>274</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post</td>
<td>5.68</td>
<td>1,909</td>
<td>328</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post – Pre</td>
<td>0.75</td>
<td>–109</td>
<td>54</td>
</tr>
<tr>
<td>( \text{Tr}<em>{\text{IS}+\text{EX}} – \text{Tr}</em>{\text{EX}} )</td>
<td>Post – Pre diff</td>
<td>4.81†</td>
<td>1,699†</td>
<td>–122†</td>
<td>–11.7†</td>
</tr>
<tr>
<td>( \text{Ex}_{\text{RA}} )</td>
<td>( \text{Tr}_{\text{IS}+\text{EX}} )</td>
<td>Pre</td>
<td>5.59</td>
<td>3,134</td>
<td>861</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post</td>
<td>6.18</td>
<td>3,456</td>
<td>662</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post – Pre</td>
<td>0.59</td>
<td>322</td>
<td>–199*</td>
</tr>
<tr>
<td>( \text{Tr}_{\text{EX}} )</td>
<td></td>
<td>Pre</td>
<td>6.06</td>
<td>3,388</td>
<td>649</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post</td>
<td>5.74</td>
<td>2,819</td>
<td>529</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post – Pre</td>
<td>–0.32</td>
<td>–569</td>
<td>–120</td>
</tr>
<tr>
<td>( \text{Tr}<em>{\text{IS}+\text{EX}} – \text{Tr}</em>{\text{EX}} )</td>
<td>Post – Pre diff</td>
<td>0.91</td>
<td>891</td>
<td>–79</td>
<td>–5.1†</td>
</tr>
</tbody>
</table>

*Value sign (difference \( p < 0.05 \) between pre- and posttraining)
†Difference (diff) value sign (difference between exercise + ischemia and exercise training)

\( \text{Ex}_{\text{IS}} \) = ischemic exercise test
\( \text{Ex}_{\text{RA}} \) = ramp exercise test
\( \text{Tr}_{\text{IS}+\text{EX}} \) = leg trained with exercise and ischemia
\( \text{Tr}_{\text{EX}} \) = leg trained with exercise only
Recovery = oxygen consumption above resting level during 3 min after exercise
Surface Electromyogram Recordings

Typical frequency power spectra are shown in Figure 4 for one subject. The frequency power spectra were always skewed to the right, with peak power (mean frequency) occurring at an average of 62.4 Hz (SEM: 1.0) during the baseline warm-up exercise before ischemia or workload increments were imposed. The shift to lower motor-unit firing frequencies during the exercises was taken as an estimate of motor-unit fatigue, and changes in the power (area under the curve) were considered proportional to recruitment of motor units. The average frequency shifts from baseline to peak exercise values were not significantly different between ExIS and ExRA or between recordings before and after training. During ExRA, the same reduction in frequency occurred, 14 percent from baseline to maximal workload for tests before and after TrEX. In the TrIS+EX leg, the shifts were –8 and –9 percent before and after training, respectively. For ExIS the frequency shift was –6 before TrEX and –11 percent after TrEX (p = 0.12), but –6 and –4 percent before and after training in the TrIS+EX leg (p = 0.27). These differences in frequency shifts were not statistically significant (p = 0.11). The total power during ExRA (Figure 4) increased from baseline to maximal exercise by an average of 720 percent, indicating increased recruitment, and by 40 percent for ExIS.
Figure 3.
Mean values for 10 subjects for (a) ischemic and (b) ramp exercises for heart rate (HR) and systolic blood pressure (SBP) during baseline and maximal (max) exercise and during 3 min of recovery (R), pre- and posttraining with exercise, and ischemia + exercise. All values shown as difference from max exercise value, with two pretraining tests averaged. Differences between pretraining recovery values and those following two types of training were evaluated by two-way analysis of variance, with overall $p$-values shown. *Values at 1 min significantly different ($p < 0.05$) with Tukey’s post hoc test.
with no significant changes or differences in changes related to training.

Ancillary Measurements

The isometric strength test showed no significant change in strength of either leg with training. No significant change was found in upper-leg volume after either training strategy ($p = 0.59$).

DISCUSSION

The results of this study demonstrate that training with a combination of ischemia and low-resistance exercise increased knee-extension exercise endurance under ischemic conditions. The effect of TrIS+EX on exercise with no ischemia could not be measured because the workload was too light for end points to be obtained. Earlier studies have noted significantly greater improvement in time-to-fatigue and one-legged VO$_2$P in ergometer exercise in legs trained for 45 min a day for 4 days a week for 4 weeks with a 20 percent blood flow reduction, as compared with control legs training without flow restriction [6–7]. Similar to our results, those improvements in the ischemically trained leg were greater when the test was performed with flow restriction than without flow restriction, demonstrating specificity in the training response. Other measurements during those studies, including muscle biopsies, determined

![Figure 4](image-url)

Typical recordings from one subject of frequency spectra as processed by fast Fourier transform, averaged from five contractions after ischemia + exercise training during last 15 s of baseline exercise and during last minute of (a) ischemic (ExIS) and (b) ramp exercise tests (ExRA). Power increased by factor of 6 during ramp exercise, indicating increased fiber recruitment with increasing load, but remained about the same for ExIS. Mean frequency shifted to lower value from start to end of exercise, indicating increasing fatigue, i.e., $100 \times (66 - 73)/73 = -10\%$ for ExIS, and $100 \times (59 - 68)/68 = -13\%$ for ExRA.
that ischemic training contributed to higher citrate synthase activity, lower lactate dehydrogenase isoenzymes, more type I and fewer type IIB fibers and more capillaries/fiber [14]. More recently, studies have also demonstrated that ischemically trained legs increased in the cross-sectional area, probably resulting from increases in contractile proteins, intracellular water, and mitochondrial volume [9,15]. Minimal hypertrophy has been noted after training at 50 percent of MVC, so we did not anticipate hypertrophy in either leg after endurance training, with or without ischemia, at these low levels of MVC (4 percent) and none was noted. However, increased capillarization and improved O₂ delivery would be expected. Studies in rats have shown that restricting blood flow during high-resistance training of an exercising limb enhanced exercise capacity corresponding to an increased arteriolar capillary density [16]. All these studies demonstrated that training using usual training intensities under ischemic conditions enhanced aerobic exercise capacity.

The main difference between those studies and the current one is that we used much lower-resistance exercise training, resulting in a doubling of exercise duration from controls. In this study, no significant training effect on exercise duration was demonstrated after training without ischemia, implying that this level of exercise intensity will not induce training by itself. And yet, using the same training intensity under ischemic conditions provoked a marked increase in exercise endurance, confirming the unique contribution of ischemia to exercise training. The starting fitness level to perform knee extensions did not significantly alter the improvement from the training.

One of the most important benefits of exercise training, particularly to heart failure patients, is the improvement in exercise dyspnea and HR response. The effect of training on these end points can be measured by the ergoreflex or muscle chemoreflex response to ischemia imposed during exercise. The usual physiological ergoreflex parameters measured include V̇E, SBP, and HR during and after ExIS.

The attenuation of V̇E during ExIS and after TrIS+EX and TrEX, shown in Figure 2, is striking and demonstrates a reduction of the exercise ventilatory stimulus after ischemic training. An equivalent reduction in V̇E was found during ExIS in response to ischemia in the leg not trained by ischemia (TrEX). This finding suggests that not only was the stimulus site in the exercising muscle affected by the training but also that the central site of the afferent limb of the ergoreflex was altered.

The main ventilatory stimulus from regional ischemia is thought to be the local concentration of H⁺ [17]. Eiken and Bjurstedt demonstrated that venous lactate concentration, V̇E, arterial blood pressure, HR, and V̇E/O₂̇ (ventilation equivalent for O₂, a measure of ventilatory drive) were significantly greater and VO₂p reduced by leg ischemia compared with no flow restriction [18]. In the present study, the reduced VO₂ in recovery from ExIS after TrIS+EX (Table) suggests that ischemic training lowered the O₂ debt, presumably by reducing accumulation of lactate and H⁺ during exercise, and therefore the release of these metabolites was diminished when exercise terminated and cuff pressure was released. This trend was less pronounced after ExRA, where the O₂ debts were larger and the decline in the percentage of the total cost was smaller, but still significant.

The recovery patterns of HR and SBP in Figure 3 indicate that TrIS+EX contributed to a faster recovery for both circulatory variables after ExIS, with some carryover benefit indicated for HR after ExRA (p = 0.008). More rapid recovery rates of SBP [19] and HR [20] following exercise, associated with vagal activation and sympathetic deactivation, are known to be directly related to exercise capacity and inversely related to mortality in patients with heart failure.

These findings suggest that blood flow restriction to the legs during exercise places additional metabolic stress on exercising muscles, enhancing the sympathetic response to exercise at a given workload compared with no ischemia. If metabolic stress to the muscles is the stimulus for a training response, then flow restriction should augment the leg training response. Ergoreflex responses are enhanced in patients with CHF, presumably because of peripheral muscle effects of the disease [21–22], and are reduced by nonischemic endurance training in these patients [23].

EMG recordings made during progressive exercise demonstrate a shift to lower EMG frequencies, presumably because of a larger contribution of slow-twitch muscle fibers (type I, having slower firing rates) as fast-twitch (type II) fibers fatigue [24–25]. This shift might also occur partly because of a decrease in average nerve conduction velocity (NCV) of motor units. Type II motor units operate with a faster NCV than do type I fibers, and as they fatigue first, the average NCV decreases as they are recruited less [26]. In the present study, the difference in frequency shift between control (TrEX) and TrIS+EX legs was not significantly different for either test exercise. This means that the rate of the shift with exercise time
was decreased during ExIS because duration was more than doubled. However, with the low exercise intensity (<4% MVC) used in the ischemic training, it is doubtful that type II fibers were significantly used or trained in these exercises [27], and the local ischemia probably affected them minimally. A previous study found that ischemia induced during an endurance exercise did not result in a frequency shift [25]. This suggests that the slower frequency shift with time of exercise after ischemic training may have resulted from an endurance training effect on type I fibers. These findings are in line with those of Esbjörnsson et al., who reported more aerobic or “endurance” type I and fewer type IIB fibers with ischemic training [14].

Other strategies to improve muscle O₂ delivery during training have been tested. Intermittent systemic hypoxic training has been used in healthy subjects to improve athletic performance [28] and to improve muscle energy supply during normoxic exercise [29]. For peripheral skeletal muscles, ischemic training may be more effective than hypoxic training because with ischemia the venous effluent blood has much higher partial pressure of carbon dioxide and H⁺ concentrations, reflecting changes in the perfused tissues [30–31], than with hypoxia causing the same reduction in O₂ delivery. In addition to providing a stronger training stimulus, regional ischemic training is safer to apply than systemic hypoxemia. For a given reduction in mixed venous O₂ level, the arterial oxygenation remains higher so that O₂ delivery to critical organs (e.g., brain, heart, and kidney) is not restricted and studies using complete occlusion of limbs during exercise in CHF patients have been conducted without any reported risk.

**CONCLUSIONS**

This study shows that endurance training can be achieved with dynamic, low-intensity resistance exercise with superimposed ischemia. Other studies have shown that ischemic training increases exercise tolerance in healthy individuals during high-resistance exercise [6,8–9] and general endurance training attenuates the ergoreflex and resulting dyspnea in patients with CHF [23,32]. Therefore, it seems probable that ischemic training would further reduce dyspnea and sympathetic responses and improve skeletal muscle metabolism and exercise capacity, especially in patients with CHF or other chronic diseases. Exercise training can improve exercise performance, quality of life, and endothelial function in nonexercising vascular beds in patients with CHF [33]. Ischemic training might also broaden the population of patients who could be trained, since regional ischemic training could be implemented in patients not typically able to comply with rehabilitation programs requiring more intense systemic training. Future studies will help define the role that ischemic training will have in enhancing the daily lives of patients with chronic disease characterized by inactivity.

**REFERENCES**


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