Single Limb Exercise Induces Femoral Artery Remodeling and Improves Blood Flow in the Hemiparetic Leg Poststroke

Sandra A. Billinger, PhD; Byron J. Gajewski, PhD; Lisa X. Guo, BA; Patricia M. Kluding, PhD

Background and Purpose—After stroke, individuals have decreased mobility of the hemiparetic leg, which demands less muscle oxygen consumption; thus, blood flow decreases. The purpose of this study was to determine the effect of single limb exercise (SLE) on femoral artery blood flow, diameter, and peak flow velocity in the hemiparetic leg after stroke.

Methods—Twelve individuals (60.6 ± 14.5 years of age; 5 male) with chronic stroke (69.1 ± 82.2 months; 5 with right-sided hemiparesis) participated in the study. The intervention consisted of a SLE knee extension/flexion protocol 3 times per week for 4 weeks. Using Doppler ultrasound, bilateral femoral artery blood flow, diameter, and peak flow velocity were assessed at baseline, after 2 weeks, and after 4 weeks of SLE.

Results—Using repeated-measures analysis of variance, femoral artery blood flow, arterial diameter, and blood flow velocity in the hemiparetic limb were significantly improved (P < 0.0001) after the SLE. No significant changes occurred in the nontrained limb for any outcome measures.

Conclusions—These data suggest that a 4-week SLE training program that increases muscular activity in the hemiparetic limb improves femoral artery blood flow, diameter, and peak velocity. SLE may be an important training strategy in stroke rehabilitation to minimize the vascular changes that occur poststroke due to decreased activity of the hemiparetic limb. (Stroke. 2009;40:3086-3090.)

Key Words: blood flow ■ stroke ■ vascular function

P hysiological functional changes such as vascular resistance and arterial remodeling may be associated with aging and disease-induced changes, including stroke. Specifically, people after stroke often present with decreased cardiorespiratory fitness and peripheral vascular adaptations (ie, reduced blood flow, decreased arterial diameter and endothelial dysfunction) in the hemiparetic leg. However, participation in regular physical activity such as aerobic exercise has altered these pathological vascular changes in people with obesity, Type 2 diabetes, spinal cord injury, and coronary artery disease.

Most exercise interventions for people poststroke focus on bilateral activity such as treadmill walking or cycling. However, during bilateral exercise, evidence has suggested a reduced work effort by the hemiparetic limb when compared with the other limb. This indicates a need to identify an exercise training strategy that would primarily focus on the hemiparetic limb to maximize work effort.

Participants in this study used single limb exercise (SLE) as an aerobic training intervention. The purpose of the present study was to characterize the effects of a 4-week SLE training intervention on cardiovascular function in the hemiparetic limb in people poststroke. It was hypothesized that after the SLE training intervention, significant improvements in femoral artery: (1) blood flow; (2) diameter; (3) peak blood flow velocity; and (4) conductance would be observed after the training period when compared with baseline measures. Lastly, to determine if systemic vascular function would improve after SLE, we hypothesized that the ankle–brachial index (ABI) would improve to the normal ranges (0.90 to 1.40).

Materials and Methods

Twelve participants with chronic stroke completed this within-subject design study. Inclusion criteria were: (1) a diagnosis of hemiparesis from a stroke at least 6 months ago confirmed by clinical assessment; (2) the ability to transfer from a sitting to standing position with minimal assist; (3) walking 10 m independently with or without an orthotic or assistive device; (4) mild to moderate stroke deficits defined by a lower extremity Fugl-Meyer score from 20 to 33/34; (5) 35° of active knee extension/flexion with movement against gravity; and (6) medical clearance from their primary care physician for exercise testing and prescription. Exclusion criteria consisted of the following: (1) Type 1 or 2 diabetes; (2) current participation in SLE or physical therapy; (3) peripheral vascular disease (ABI < 0.40) or known stenosis of the lower extremity vessels; (4) taking α-agonists to improve peripheral vasodilation; (5) a difference ≤ 2% between the hemiparetic and less affected limbs for arterial diameter and blood flow velocity; and (6) any medical condition that would preclude participation in exercise testing and prescription. Institutionally approved informed consent was obtained in writing before enrollment in the research study.
Table 1. Participant Demographics

<table>
<thead>
<tr>
<th>Characteristics (n=12)</th>
<th>Mean±SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: male</td>
<td>5</td>
</tr>
<tr>
<td>Age, years</td>
<td>60.6±1.7</td>
</tr>
<tr>
<td>Race/ethnicity</td>
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</tr>
<tr>
<td>Black</td>
<td>2</td>
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<tr>
<td>White</td>
<td>8</td>
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<tr>
<td>Hispanic</td>
<td>1</td>
</tr>
<tr>
<td>Native American</td>
<td>1</td>
</tr>
<tr>
<td>Body mass index (dual emission x-ray absorptiometry scan)</td>
<td>29.7±1.5</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
</tr>
<tr>
<td>β-blockers</td>
<td>4</td>
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<tr>
<td>Stroke characteristics</td>
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<tr>
<td>Time poststroke, months</td>
<td>69.1±28.8</td>
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<tr>
<td>Right-sided weakness</td>
<td>5</td>
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<tr>
<td>Type of stroke</td>
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<td>Ischemic</td>
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<tr>
<td>Hemorrhage</td>
<td>3</td>
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<tr>
<td>Stroke severity</td>
<td></td>
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<tr>
<td>Lower extremity Fugl-Meyer score</td>
<td>26.7±1.0</td>
</tr>
</tbody>
</table>

Dual Emission X-ray Absorptiometry

Lean tissue and fat mass for bilateral lower extremities was assessed at baseline and postintervention using dual emission x-ray absorptiometry scans (GE Lunar, Madison, Wisc). This allowed for within- and between-limb lean tissue comparison at the respective time points. The rationale for observing lean tissue changes was to ensure that improved blood flow was not the result of increased lean tissue.

Measures of Cardiovascular Function

At baseline, 2 weeks, and 4 weeks, Doppler ultrasound (MicroMaxx Doppler ultrasound; Sonosite, Inc, Bothell, Wash) measurements were performed on bilateral femoral arteries for diameter and peak blood flow velocity. With the image frozen on the screen, femoral artery diameter was obtained at peak systole using the R-wave from an electrocardiogram. Peak blood flow velocity was recorded as the highest speed at which blood flowed through the vessel. All arterial measures for both limbs were taken in duplicate and values averaged for data analysis. The individual performing the second measurement was blinded to limb at the time of assessment. Blood flow was calculated using baseline values. After the intervention, corrections were also performed to assess the relationship between percent change scores for blood flow and lean tissue.

Because the hemiparetic side was an area of interest, ABI was calculated for the affected side (ABIhemi). To perform the ABI test, the participant rested for 10 minutes in a supine position. Using a portable 5-MHz LifeDop hand-held Doppler probe (SummitDoppler, Golden Colo) to obtain systolic blood pressure, values were recorded and ABI was calculated.

Because the hemiparetic side was an area of interest, ABI was calculated for the affected side (ABIhemi).

Training Intervention

The SLE training intervention involved isokinetic (Biodex Medical Systems, Inc, Shirley, NY) extension/flexion using only the hemiparetic limb. Because no data were available in the literature to suggest a SLE protocol as an intervention in individuals poststroke, we developed this training regimen based on pilot data. Therefore, we had the participants exercise at 150°/sec with 40 repetitions per set. They were instructed to self-progress their exercise training with the goal of completing a total of 40 sets at the end of the intervention. A 30-second rest break in between each set allowed monitoring of heart rate and perceived exertion. Participants exercised 3 times per week for 4 weeks at an intensity of 60% to 70% of maximal heart rate. In an effort to limit compensatory movements to assist the hemiparetic leg, the participant was secured in place using straps for trunk, hip, and leg stabilization.

Statistical Analysis

The arithmetic mean and SE were used for descriptive statistics. At baseline, paired t tests were used to determine significant differences in vascular function between the hemiparetic and less affected limbs. To elucidate the relationship between the blood flow and lean muscle tissue in the hemiparetic limb, Pearson product moment correlations were calculated using baseline values. After the intervention, correlations were also performed to assess the relationship between percent change scores for blood flow and lean tissue.

Three different 2 side (hemiparetic; less affected)×3 time (baseline, T1, post) within-subject, repeated-measures analyses of variance with time as the repeating factor investigated the effects of SLE on the dependent measures: (1) blood flow; (2) arterial diameter; and (3) peak blood flow velocity. A significant side×time interaction suggested a statistically significant SLE effect and warranted further post hoc analysis. For post hoc analysis, the percent change was calculated from baseline to post for arterial diameter and BF velocity. Testing each side, a second set of repeated-measures analyses of variance determined if the percent change was significantly different from zero. Furthermore, vascular conductance was assessed using paired t tests to determine significant differences between baseline and postintervention values.

Because the pattern of variability of ABI and ABIhemi across time, which traditional repeated-measures analysis of variance does not account for, a linear mixed model was used to test statistical significance across time. All statistical analyses were conducted with a significance level of α=0.05.

Results

Baseline Measures

Baseline values between the hemiparetic and less affected limb were significantly different for resting femoral artery BF, diameter, and peak BF velocity (P<0.0001). Furthermore, femoral artery BF to the hemiparetic limb was 29.57% less compared with the other side. Baseline descriptive data are reported in Table 2.

At baseline, dual emission x-ray absorptiometry scans were performed to assess lean tissue composition. Lean tissue between the hemiparetic and less affected limb was significantly different at baseline (P=0.05). A weak, nonsignificant relationship between lean lower extremity tissue and femoral artery BF (r=0.14, P=0.665) was found.

Femoral Artery Adaptation to SLE

Femoral artery hemodynamics improved in the hemiparetic limb after the 4-week SLE training period, whereas nonsignificant changes were found in the control limb. Furthermore, no unanticipated or adverse events were reported as a result of the training intervention. Femoral artery BF significantly improved after SLE as indicated by an interaction of side (hemiparetic, less affected) and time (F[2,22]=12.12; P<0.0001; Figure 1). After the training period, a 41.84% increase in BF
was observed. This resulted in a 4.37% deficit for leg BF in the hemiparetic leg when compared with the other side. Furthermore, the significance between the 2 limbs disappeared after the training period (Table 2). Two-way repeated-measures analysis of variance with an effect of side*time indicated that both femoral artery diameter ($F_{2,22} = 24.76, P < 0.0001$; Figure 2) and peak BF velocity ($F_{2,22} = 27.97, P < 0.0001$) in the hemiparetic limb significantly improved after SLE. No significant differences were detected in the nontrained limb for femoral artery BF ($F_{2,22} = 0.905, P = 0.08$), diameter ($F_{2,22} = 0.651, P = 0.53$), and peak BF velocity ($F_{2,22} = 1.28, P = 0.30$). Post hoc analysis suggested a significant improvement in percent change scores for femoral artery diameter ($P < 0.001$) and peak BF velocity ($P < 0.001$) in the hemiparetic limb. The less affected limb did not demonstrate significant percent change scores for arterial diameter ($P = 0.78$) or BF velocity ($P = 0.15$). Vascular conductance significantly improved ($P < 0.0013$) in the trained limb but not the untrained side ($P = 0.38$).

### Lean Tissue Composition and the Relationship to BF

Baseline values for lean tissue mass in the hemiparetic and less affected limb were significantly different ($P = 0.05$). After the SLE intervention, lean tissue in the hemiparetic leg was not significantly different from baseline ($P = 0.56$). However, between-limb differences postintervention approached significance ($P = 0.06$).

The relationship between the BF and lean tissue was also explored after the training intervention. The percent change in BF from baseline to postintervention was not related to lean muscle tissue as evidenced by a weak correlation ($r = -0.07; P = 0.83$).

### Ankle–Brachial Index

ABI values were not significantly different after the training intervention ($F_{2,22} = 0.211, P = 0.81$). Further analysis of ABI$_{hemi}$ also identified nonsignificant changes ($F_{2,22} = 0.556, P = 0.58$).

### Discussion

This study examined the effect of a 4-week SLE training protocol on cardiovascular function and femoral artery BF in the femoral arteries in people poststroke. The primary findings were that a SLE training intervention that focused on the hemiparetic leg resulted in structural vascular adaptations with improved arterial diameter and BF to the trained limb.

### Femoral Artery Characteristics and BF Before SLE

After stroke, vascular remodeling may occur if the hemiparetic leg has a reduced metabolic demand due to the lack of physical activity or exercise$^{5,6,10}$ As demonstrated in our previous work$^{17}$ and by others,$^{5,6}$ resting femoral artery BF, diameter, and peak BF velocity in the hemiparetic limb is significantly lower than the less affected side. This study supports previous work that lean muscle tissue is significantly lower in the hemiparetic limb when compared with the less affected side.$^{24}$ Similar to the work by Ivey and colleagues,$^{5}$
a weak, nonsignificant relationship was found between resting BF and lean muscle tissue. Therefore, the difference in BF may, in fact, be due to lower oxygen demand in the hemiparetic limb.10

Effect of SLE Training
Results from this study suggest that after 4-weeks of SLE, vascular adaptations in the hemiparetic limb can be improved to reflect values of the control limb. After the exercise period, a 4.37% deficit, which was nonsignificant, remained between the 2 limbs for femoral artery BF. This is not surprising because exercise is a potent stimulus for inducing vascular changes. Miyachi and colleagues25 reported that healthy adults participating in a 6-week SLE training protocol induced femoral artery remodeling that resulted in a significant increase in the cross-sectional area of the artery. No significant changes were found in the nontrained limb. They concluded that exercise-induced BF changes during SLE facilitated arterial diameter expansion and may be the mechanistic factor driving vascular adaptations.

In the present study, we report similar vascular adaptations after the SLE training intervention. Femoral artery BF and diameter in the hemiparetic limb significantly improved after SLE, whereas the untrained limb demonstrated nonsignificant changes. The percent change in BF from baseline to postintervention was not related to increased lean muscle tissue. Therefore, vascular remodeling may be related more to metabolic activity25 rather than tissue composition.5,20 A peripheral “feedback mechanism”26 known as the flow-diameter relationship27 may also provide information regarding the vascular adaptations. With increased BF, greater shear stress is placed on the arterial wall. The endothelial cells detect changes in wall tension and undergo structural modification to increase vessel diameter.10,28

The intrinsic nature of the flow-diameter relationship would support the findings that vascular conductance improved after SLE. Vascular conductance is the product of mean arterial pressure and BF. The individuals in this study did not demonstrate a significant improvement in mean arterial pressure from baseline to posttraining, but BF significantly increased. Therefore, the improvement in vascular conductance likely resulted from peripheral rather than central adaptations.25 Using the less affected limb as the control limb, we were able to compare peripheral vascular changes that occurred over time in the hemiparetic limb as a result of the training intervention. Although a control group consisting of bilateral exercise would strengthen the study design, this work was an initial step to identify whether vascular changes could occur in the hemiparetic limb after an intense training period. Individuals engaging in stroke rehabilitation may benefit from encouraged use such as SLE to minimize peripheral vascular alterations that appear to be observed in people poststroke.

Despite the vascular adaptations that occurred for femoral artery BF and conductance, ABI values posttraining did not support improved endothelial function as suggested by Andreozzi and colleagues.29 In the present study, ABI values <0.90 were reported for only 4 individuals. Because 67% of the individuals were already considered in the normal range for ABI,14,22 a ceiling effect is likely.

Summary
The findings from this study support the hypotheses that a 4-week SLE training program that encourages use of the hemiparetic limb improves femoral artery BF, diameter, peak velocity, and vascular conductance. These peripheral vascular changes result from an exercise-induced stimulus that directly affects the flow-diameter relationship. Simply, if the arterial wall is chronically exposed to increased BF (ie, exercise), then the diameter expands to accommodate a larger volume of flow. However, systemic vascular function using ABI did not significantly improve after the intervention. Future research is needed to examine the role of exercise in the peripheral mechanisms (ie, nitric oxide-dependent vasodilation) behind vascular remodeling in the hemiparetic limb after stroke.

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Disclosures
None.

References


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