Discrepancy Between Cardiac and Physical Functional Reserves in Stroke

Djordje G. Jakovljevic, PhD*; Sarah A. Moore, BSc*; Lip-Bun Tan, FRSP, DPhil; Lynn Rochester, PhD; Gary A. Ford, FRCP; Michael I. Trenell, PhD

Background and Purpose—Understanding the physiological limitations to exercise after stroke will assist the development of targeted therapies to improve everyday function. This study defines (1) whether exercise capacity is limited by the cardiovascular system (oxygen supply) or skeletal muscles (oxygen utilization); and (2) cardiac function and pumping capability in people with stroke.

Methods—Twenty-eight male participants with mild ischemic stroke (70±6 years of age, 18±20 months poststroke) and 25 male, age-matched healthy control subjects performed a graded cardiopulmonary exercise test with gas exchange and noninvasive hemodynamic measurements. Maximal oxygen extraction was calculated as the ratio between peak oxygen consumption and peak cardiac output. Cardiac function and pumping capability were assessed by peak exercise cardiac power output (expressed in watts) and cardiac output.

Results—Peak oxygen consumption (18.4±4.6 versus 26.8±5.5 mL/kg/min, P<0.01) and arterial–venous O₂ difference (9.3±2.5 versus 12.6±1.9 mL O₂/100 mL of blood, P<0.01) were both reduced in stroke participants compared with healthy control subjects. In contrast, peak exercise cardiac power output (4.79±0.79 versus 4.51±0.96 W, P=0.49), cardiac output (16.4±3.1 versus 17.1±2.5 L/min, P=0.41), and the pressure-generating capacity of the heart (127±11 versus 125±14 mm Hg, P=0.97) were similar between stroke participants and healthy control subjects.

Conclusions—The ability of skeletal muscles to extract oxygen is diminished after stroke. However, cardiac function and pumping capability are maintained. Appropriate therapies targeting muscle oxygen uptake such as exercise rehabilitation may improve exercise capacity after stroke. (Stroke. 2012;43:1422-1425.)

Key Words: cardiac function ■ cardiac power ■ exercise performance ■ oxygen consumption
Table. Participant Characteristics and Medication Use

<table>
<thead>
<tr>
<th>Variable</th>
<th>Stroke (N=28)</th>
<th>Control (N=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>70±6</td>
<td>67±5</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>82±11</td>
<td>81±13</td>
</tr>
<tr>
<td>Height, cm</td>
<td>176±6</td>
<td>175±8</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27±4</td>
<td>26±4</td>
</tr>
<tr>
<td>Time from stroke to study entry, mo</td>
<td>19±21</td>
<td>NA</td>
</tr>
</tbody>
</table>

Stroke characteristics

<table>
<thead>
<tr>
<th>Stroke type,* no. (%)</th>
<th>TACI 4 (13%)</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PACI 13 (41%)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>LACI 11 (34%)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>POCI 1 (3%)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>ICH 3 (9%)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Side of stroke

| Right                  | 17 (53)      | NA |
| Left                   | 15 (47)      | NA |
| NIHSS score            | 2.4±2.4      | NA |

Mobility status

| 6-min walk distance, m  | 401±148      | NA |
| Walking speed, m/s      | 1.4±0.6      | NA |

Walking aid

| None                   | 25 (78%)     | NA |
| Stick                  | 7 (22%)      | NA |

Medication, no. (%)

| ACE inhibitors          | 16 (50%)     | NA |
| Diuretics               | 7 (22%)      | NA |
| Antarrhythmics          | 7 (22%)      | NA |
| Calcium channel blockers| 3 (9%)       | NA |

Smoking status

| Current smoker          | 5 (16%)      | 0  |
| Nonsmoker              | 27 (84%)     | 25 |

TACI indicates total anterior circulation infarct; PACI, partial anterior circulation infarct; LACI, lacunar infarct; POCI, posterior circulation infarct; ICH, intracerebral hemorrhage; NIHSS, National Institutes of Health Stroke Scale; ACE, angiotensin-converting enzyme; NA, not applicable.

*Oxford Community Stroke Project classification.

followed by 10-W increments every minute until volitional exhaustion. The standard 12-lead electrocardiogram was continuously monitored and blood pressure recorded. Peak exercise was defined as the absence of a rise in oxygen consumption with further increase in exercise intensity, respiratory exchange ratio >1.05, or inability of the patient to continue. Additionally, QT (assessed by CO2 rebreathing) and VO2 data at peak treadmill exercise were obtained from 25 male, age- and body weight-matched healthy participants who took part in a previous study.6

Cardiac power output, expressed in Watts, was calculated6:

\[
\text{cardiac power output} = (\text{QT} \times \text{MAP}) \times K
\]

where MAP is mean arterial pressure in mm Hg and K is the conversion factor (2.22×10⁻³). Peak arterial–venous oxygen difference, expressed in mL O₂/100 mL of blood, was calculated as the ratio between VO₂ and QT.

Independent-sample t tests were used for between-group comparison. The Pearson coefficient of correlation demonstrated relationships between variables. Statistical significance was indicated if P<0.05. All data are presented as means±SD unless otherwise indicated. Post hoc power analysis for the sample size of 28 demonstrated high power of the study (β=0.95).

Results

Stroke participants completed the maximal exercise testing with no adverse events and they achieved 87% of their age-predicted maximal heart rate. The mean peak exercise respiratory exchange ratio and the Borg scale scores were 1.10±0.10 (range, 1.02–1.18) and 19.5±1.2, suggesting that the patients demonstrated a high level of exertion.

Peak VO₂ was 31% lower in stroke participants (18.4±4.6 versus 26.8±5.5 mL/kg/min, P<0.01; Figure 1A) and was accompanied by a reduction in peak exercise arterial–venous oxygen difference of 26% (9.3±2.5 versus 12.6±1.9 mL O₂/100 mL of blood, P<0.01; Figure 1B). Peak cardiac power output was not significantly different (P=0.49) between control and stroke participants (Figure 1D) as were not QT (16.4±3.1 versus 17.1±2.5 L/min, P=0.41; Figure 1C) and mean arterial pressure (127±11 versus 125±14 mm Hg; P=0.97).

Peak VO₂ highly correlated with QT in healthy subjects (r=0.84, P<0.01) and only moderately in stroke participants (r=0.42, P<0.05; Figure 2).

Discussion

The 2 major findings of the present study suggest that in stroke participants (1) the ability of skeletal muscles to extract oxygen is diminished; and (2) cardiac pumping capability is maintained.

Our finding that peak exercise VO₂ is severely compromised in stroke survivors is in line with previous reports.5,8 The underlying physiological limitations of this finding have not been well defined, restricting the ability to target therapies. Some explanations include bedrest-induced deconditioning, concomitant left ventricular dysfunction, the associated severity of neurological involvement, and the increased aerobic requirements of walking.4 Cardiac function, measured at rest, has been found to be impaired after stroke9 and cardiac dysfunction appears to be associated with severity of stroke.3 Resting central hemodynamics, however, do not reflect peak VO₂ and pumping capability of the heart because they do not account for the reserve of cardiac function.10 Only 1 previous study has assessed QT during exercise in people with stroke.4 The authors argued that reduced peak VO₂ is secondary to a decline in peak and reserve QT,4 which was assessed in only 4 patients and therefore needs to be considered with caution. The present study, however, suggests that peak cardiac function is not diminished, whereas maximal arterial–venous oxygen difference is reduced by 26% in stroke participants. This suggests that maximal aerobic capacity in people with stroke is likely due to reduced ability of the working muscles to extract oxygen. Only a moderate relationship
between VO$_2$ and QT suggests that factors other than cardiac (ie, muscle) play an important role in the determination of maximal VO$_2$ in patients with stroke.

This study has several limitations. Patients with mild stroke were recruited and it remains to be elucidated whether cardiac pumping capability is preserved in those with severe residual disability. In contrast to our stroke participants, healthy control subjects performed a treadmill exercise test with CO$_2$ rebreathing cardiac output measurement. This may limit findings of the present study bearing in mind that the treadmill may elicit a 10% to 15% higher physiological response than cycling. However, this does not compromise our findings because peak VO$_2$ was reduced in patients with stroke by 31%.

In conclusion, the ability of skeletal muscles to extract oxygen is diminished after stroke but cardiac function and pumping capability are maintained. Appropriate therapies targeting muscle oxygen uptake such as exercise rehabilitation may improve exercise capacity after stroke.

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**Disclosures**
None.

**References**
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