Cardiac Reserve and Pulmonary Gas Exchange Kinetics in Patients With Stroke

Corey R. Tomczak, MSc; Anwar Jelani, MD; Robert G. Haennel, PhD; Mark J. Haykowsky, PhD; Robert Welsh, MD; Patricia J. Manns, PhD

Background and Purpose—Cardiovascular and pulmonary factors contributing to impaired peak oxygen uptake ($\dot{V}O_2$) in patients with stroke (SP) are not well known. We assessed cardiovascular function, pulmonary gas exchange, and ventilation in SP and healthy age, gender, and activity-matched control subjects.

Methods—Ten hemiparetic SP and 10 control subjects were enrolled. Subjects completed cycle ergometry testing to assess peak and reserve $\dot{V}O_2$, carbon dioxide production, ventilation (tidal volume; breathing frequency; minute ventilation), and cardiac output. $\dot{V}O_2$, carbon dioxide production, and minute ventilation were measured throughout peak exercise recovery (off-kinetics) and at exercise onset (on-kinetics) along with heart rate during low-level exercise.

Results—Peak $\dot{V}O_2$ was 43% lower ($P<0.001$) in SP secondary to reduced peak and reserve cardiac output and minute ventilation. The impaired cardiac output reserve ($P<0.001$) was due to a 34% lower heart rate reserve ($P=0.001$). The impaired minute ventilation reserve ($P=0.013$) was due to a 41% lower tidal volume reserve ($P=0.009$). Stroke volume and breathing frequency reserve were preserved. $\dot{V}O_2$ off-kinetics were 29% slower in SP ($P<0.001$) and related to peak $\dot{V}O_2$ ($R=–0.72$, $P<0.001$) and peak cardiac output ($R=–0.75$, $P<0.001$) for the study group. Additionally, carbon dioxide production ($P=0.016$) and minute ventilation ($P=0.023$) off-kinetics were prolonged in SP. $\dot{V}O_2$ on-kinetics were 29% slower ($P=0.031$) during low-level exercise in SP.

Conclusions—The impaired peak $\dot{V}O_2$ in SP is secondary to a decline in peak and reserve cardiac output and ventilation. Prolonged $\dot{V}O_2$ kinetics in SP are associated in part with deconditioning and may be mediated by reduced $O_2$ availability and/or the rate of muscle $O_2$ use. (Stroke. 2008;39:3102-3106.)

Key Words: cardiac output ■ exercise ■ oxygen uptake kinetics ■ stroke

The cardiopulmonary factors that contribute to the abnormal oxygen uptake ($\dot{V}O_2$) in patients with stroke (SP) are not well known. Although left ventricular function may be compromised in acute SP, cardiac function during exercise has not been evaluated. Circulatory impairments adversely impact peak $\dot{V}O_2$ in addition to the recovery of $\dot{V}O_2$ after exercise, yet this relationship has not been established in SP. Additionally, it is not known whether impairments in the rate of $\dot{V}O_2$ readjustment are present during low-level exercise comparable to activities of daily living in SP.

We tested the hypotheses that (1) peak and reserve $\dot{V}O_2$ and cardiac output ($Q$) would be lower in SP; (2) pulmonary gas exchange and ventilation off-kinetics would be slower in SP; (3) slower $\dot{V}O_2$ off-kinetics would be associated with a lower peak $\dot{V}O_2$ and $Q$; and (4) $\dot{V}O_2$ on-kinetics would be prolonged during low-level exercise in SP compared with healthy control subjects.

Materials and Methods

Ten hemiparetic SP and 10 healthy control subjects were enrolled (Table 1). This investigation was approved by the research ethics board at the University of Alberta and participants provided written and informed consent.

Testing was completed on a custom-modified recumbent cycle ergometer to assess peak and reserve ($peak–rest$) $\dot{V}O_2$, carbon dioxide production ($\dot{V}CO_2$), ventilation (tidal volume, $V_T$; breathing frequency; minute ventilation, $VE$; Parvomedics, Salt Lake City, Utah), and $Q$ (Minnesota Impedance Cardiograph, model 304B; Surcom, Minneapolis, Minn). $\dot{V}O_2$, $\dot{V}CO_2$, and $VE$ off-kinetics were determined. On a separate day, subjects completed 3 square-wave exercise protocols separated by 25 minutes to assess $\dot{V}O_2$, $\dot{V}CO_2$, $VE$, and heart rate (HR) on-kinetics. A 5-minute resting baseline was followed by 5 minutes of cycling at a power output approximating 80% of the ventilatory threshold.

Breath-by-breath off-kinetics data were averaged into 10-s bins for curve fitting and on-kinetics data from the 3 repeats were interpolated to 1-s intervals, time-aligned, averaged to yield a single response, and averaged into 5-s bins. $\dot{V}O_2$, $\dot{V}CO_2$, and VE off-kinetics (Eq 1) and on-kinetics (Eq 2) were determined using the following equations:

1. \[ Y_{(peak)} = Y_{(peak)} - A \left[ 1 - e^{-(c-d-TD)/t} \right] \]
2. \[ Y_{(rest)} = Y_{(rest)} + A \left[ 1 - e^{-(c-d-TD)/t} \right] \]
where Y is the parameter at any time (t), peak is the greatest 30-s value of Y, and rest is the value of Y over 1 minute before exercise onset. A is the amplitude change in Y, τ is the time to reach a 63% change in Y, and TD is the time delay before the exponential change in Y.

Phase II VO₂, VCO₂, and VE on-kinetics were determined and HR on-kinetics were measured from exercise onset. The best curve fit was defined by minimization of the residual sum of squares (Origin 7.5; OriginLab Corp, Northampton, Mass).

Analysis of variance was used for between-group comparisons and correlation regression to determine variable relationships. Data are mean±SEM and P<0.05 was significant.

Results

Peak VO₂, VCO₂, VE, HR, stroke volume (SV), Q, systemic vascular resistance, and power output were lower in SP
The major new findings of this investigation are that (1) the power output was lower at the ventilatory threshold in SP (45±4 versus 96±5 W; P<0.001). 

V̇O₂, and VE off-kinetics were prolonged in SP (Figure A). V̇O₂ and VE off-kinetics were correlated (R=0.80, P<0.001) and V̇O₂ off-kinetics related to peak V̇O₂ (R=−0.72, P<0.001) and peak Q̇ (R=−0.75, P<0.001).

The power output was lower during low-level exercise (26±3 versus 59±5 W; P<0.001) and V̇O₂ on-kinetics slower in SP (Figure B). V̇O₂ (66±10 versus 62±6 s; P=0.800), VE (63±11 versus 66±6 s; P=0.764), and HR (45±9 versus 32±8 s; P=0.307) on-kinetics were not different between SP and healthy control subjects, respectively. There was no relation between time poststroke and V̇O₂ on-kinetics (R=−0.60, P=0.064).

### Discussion

The major new findings of this investigation are that (1) the reduction in peak and reserve V̇O₂ in SP is secondary to an impaired peak and reserve Q̇ and Q̇, but not SV reserve were lower in SP (Table 2). Power outputs were lower at the ventilatory threshold in SP (45±4 versus 96±5 W; P<0.001). 

V̇O₂, and VE off-kinetics were prolonged in SP (Figure A). V̇O₂ and VE off-kinetics were correlated (R=0.80, P<0.001) and V̇O₂ off-kinetics related to peak V̇O₂ (R=−0.72, P<0.001) and peak Q̇ (R=−0.75, P<0.001).

The power output was lower during low-level exercise (26±3 versus 59±5 W; P<0.001) and V̇O₂ on-kinetics slower in SP (Figure B). V̇O₂ (66±10 versus 62±6 s; P=0.800), VE (63±11 versus 66±6 s; P=0.764), and HR (45±9 versus 32±8 s; P=0.307) on-kinetics were not different between SP and healthy control subjects, respectively. There was no relation between time poststroke and V̇O₂ on-kinetics (R=−0.60, P=0.064).

V̇O₂ and VE off-kinetics were prolonged in SP (Figure A). Prolonged V̇O₂ kinetics are explained by a greater CO₂ tension in the skeletal muscle secondary to buffering of exercise-induced lactate. This is consistent with the ventilatory threshold occurring at a lower exercise intensity in SP, suggesting a more immediate reliance on anaerobic glycolysis. The lower Q̇ may also have exacerbated the delay in recovery V̇CO₂. Resulting CO₂ levels likely contributed to the

### Table 2. Pulmonary Gas Exchange, Ventilation, and Cardiovascular Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Rest Stroke</th>
<th>Control</th>
<th>P Value</th>
<th>Peak Exercise Stroke</th>
<th>Control</th>
<th>P Value</th>
<th>Reserve Stroke</th>
<th>Control</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Power output, W</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>85±10</td>
<td>173±11</td>
<td>&lt;0.001</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>V̇O₂, mL/kg/min</td>
<td>3.2±0.3</td>
<td>3.7±0.2</td>
<td>0.149</td>
<td>16.0±1.2</td>
<td>28.1±2.0</td>
<td>&lt;0.001</td>
<td>12.8±1.2</td>
<td>24.4±2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>V̇O₂, L/min</td>
<td>0.25±0.02</td>
<td>0.27±0.02</td>
<td>0.460</td>
<td>1.33±0.16</td>
<td>2.06±0.14</td>
<td>0.003</td>
<td>1.08±0.15</td>
<td>1.79±0.14</td>
<td>0.003</td>
</tr>
<tr>
<td>V̇CO₂, mL/kg/min</td>
<td>2.8±0.2</td>
<td>3.2±0.2</td>
<td>0.195</td>
<td>17.7±1.9</td>
<td>32.7±2.6</td>
<td>&lt;0.001</td>
<td>14.9±1.9</td>
<td>29.6±2.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VE, L/min</td>
<td>9.6±0.6</td>
<td>9.5±0.7</td>
<td>0.934</td>
<td>49.4±6.4</td>
<td>76.5±7.9</td>
<td>0.016</td>
<td>39.8±6.2</td>
<td>67.0±7.6</td>
<td>0.013</td>
</tr>
<tr>
<td>Breathing frequency (breaths/min)</td>
<td>18±2</td>
<td>15±2</td>
<td>0.208</td>
<td>36±3</td>
<td>35±3</td>
<td>0.897</td>
<td>17±2</td>
<td>20±3</td>
<td>0.498</td>
</tr>
<tr>
<td>V̇̇L (L)</td>
<td>0.55±0.05</td>
<td>0.66±0.05</td>
<td>0.147</td>
<td>1.43±0.21</td>
<td>2.16±0.15</td>
<td>0.012</td>
<td>0.88±0.17</td>
<td>1.50±0.12</td>
<td>0.009</td>
</tr>
<tr>
<td>V̇CO₂/V̇O₂</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>1.09±0.05</td>
<td>1.16±0.03</td>
<td>0.226</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>74±3</td>
<td>67±2</td>
<td>0.098</td>
<td>133±6</td>
<td>157±4</td>
<td>0.003</td>
<td>59±7</td>
<td>90±4</td>
<td>0.001</td>
</tr>
<tr>
<td>Stroke volume, mL/beat</td>
<td>59±3</td>
<td>69±2</td>
<td>0.008</td>
<td>79±3</td>
<td>94±2</td>
<td>0.001</td>
<td>19±2</td>
<td>25±3</td>
<td>0.128</td>
</tr>
<tr>
<td>Cardiac output, L/min*</td>
<td>4.4±0.4</td>
<td>4.6±0.2</td>
<td>0.556</td>
<td>10.4±0.8</td>
<td>14.8±0.6</td>
<td>&lt;0.001</td>
<td>6.0±0.7</td>
<td>10.2±0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>a-V̇O₂ (%) mL/100 mL</td>
<td>6±1</td>
<td>6±0.5</td>
<td>0.629</td>
<td>11±1</td>
<td>14±1</td>
<td>0.106</td>
<td>6±1</td>
<td>8±1</td>
<td>0.152</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>123±10</td>
<td>123±4</td>
<td>0.972</td>
<td>165±16</td>
<td>191±9</td>
<td>0.143</td>
<td>42±15</td>
<td>68±8</td>
<td>0.117</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>78±4</td>
<td>76±3</td>
<td>0.751</td>
<td>81±4</td>
<td>93±5</td>
<td>0.123</td>
<td>3±5</td>
<td>15±4</td>
<td>0.109</td>
</tr>
<tr>
<td>Mean arterial pressure, mm Hg</td>
<td>93±5</td>
<td>92±3</td>
<td>0.870</td>
<td>109±7</td>
<td>126±6</td>
<td>0.098</td>
<td>16±8</td>
<td>32±5</td>
<td>0.092</td>
</tr>
<tr>
<td>SVR, dyne/s/cm²</td>
<td>1824±138</td>
<td>1607±82</td>
<td>0.172</td>
<td>906±85</td>
<td>687±36</td>
<td>0.016</td>
<td>−918±73</td>
<td>−933±69</td>
<td>0.886</td>
</tr>
</tbody>
</table>

*Data not obtained in 3 stroke subjects because of technical difficulties. Reserve values were calculated as peak exercise−rest. Data are mean±SEM.

a-vO₂diff indicates systemic arterial–venous O₂ difference.
high VE, which is consistent with the well-correlated V˙CO₂ and V˙E off-kinetics.

V˙O₂ on-kinetics were slower in SP (Figure B), which indicates a slower rate of muscle O₂ consumption. Unfavorable changes in skeletal muscle function related to stroke may account for this observation, because Type I and II muscle fibers may be atrophied in SP. A consequence of the alteration in the Type I muscle fibers is an associated decline in mitochondrial density and oxidative capacity, which may account for the slower V˙O₂ on-kinetics.

Slower V˙O₂ on-kinetics may have been due to a decline in vascular function. Given that endothelial function may be impaired in SP, coupled with findings that VO₂ kinetics and blood flow become impaired with peripheral arterial disease, supports this hypothesis. Further investigation is required to establish the role of blood flow dynamics and mitochondrial function on muscle O₂ consumption in SP to further clarify the mechanisms responsible for our findings.

A limitation of our investigation is that comorbidities such as diabetes, hypertension, and chronic obstructive pulmonary disease may also prolong V˙O₂ kinetics. Additionally, the years poststroke may account for the slower V˙O₂ kinetics simply because of deconditioning secondary to inactivity. However, we matched SP and healthy control subjects on activity levels and the time poststroke and V˙O₂ kinetics were not related. Future investigations are required to establish the impact of comorbid conditions and stroke type on exercise cardiopulmonary function and V˙O₂ kinetics in SP.

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**Disclosures**

None.

**References**


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