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 (VO₂) 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 VO₂, carbon dioxide production, ventilation (tidal volume; breathing frequency; minute ventilation), and cardiac output. VO₂, 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 VO₂ 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. VO₂ off-kinetics were 29% slower in SP (P<0.001) and related to peak VO₂ (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. VO₂ on-kinetics were 29% slower (P=0.031) during low-level exercise in SP.

**Conclusions**—The impaired peak VO₂ in SP is secondary to a decline in peak and reserve cardiac output and ventilation. Prolonged VO₂ kinetics in SP are associated in part with deconditioning and may be mediated by reduced O₂ availability and/or the rate of muscle O₂ use. (Stroke. 2008;39:3102-3106.)

**Key Words:** cardiac output ■ exercise ■ oxygen uptake kinetics ■ stroke
where \( Y \) is the parameter at any time \( t \), \( \text{peak} \) is the greatest 30-s value of \( Y \), and \( \text{rest} \) is the value of \( Y \) over 1 minute before exercise onset. \( A \) is the amplitude change in \( Y \), \( T_{1/2} \) is the time to reach a 63\% change in \( Y \), and \( TD \) is the time delay before the exponential change in \( Y \).

Phase II \( \dot{V}O_2, \dot{V}CO_2 \), and \( \dot{V}E \) 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 \( \dot{V}O_2, \dot{V}CO_2, \dot{V}E, \) 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 reduced peak and reserve \( Q_\dot{\text{O}}_2 \) and \( V_\dot{\text{E}} \); (2) prolonged \( V_\dot{\text{O}}_2 \) off-kinetics in SP related to a reduced peak \( V_\dot{\text{O}}_2 \) and \( Q_\dot{\text{O}}_2 \); and (3) SP have slower \( V_\dot{\text{O}}_2 \) on-kinetics during low-level exercise.

We demonstrate that impaired \( V_\dot{\text{O}}_2 \) in SP is secondary to a lower peak and reserve \( Q_\dot{\text{O}}_2 \). The impaired \( Q_\dot{\text{O}}_2 \) reserve was secondary to an impaired HR reserve, because SV reserve was not different between groups (Table 2). Our finding of a similar SV reserve despite a higher systemic vascular resistance in SP (Table 2) is likely due to an enhanced preload or contractile reserve. This is plausible given that peak exercise end systolic volume likely increased secondary to an increased afterload. Additionally, systolic peak velocity is inversely related to afterload. Thus, the lower peak and reserve HR (Table 2) in our SP would lead to a greater diastolic filling time, preserving preload and SV reserve.

Peak and reserve VE was lower in SP secondary to an impaired peak and reserve VT, because peak and reserve breathing frequency were not different between groups (Table 2). Electromyographic activity is reduced in ventilatory muscles contralateral to the brain lesion side in SP and may be exacerbated during increases in VT. Lanini and colleagues reported no asymmetrical effect of resting breathing on VT, which is consistent with our findings (Table 2). However, VT of the paretic chest wall may be reduced during hyperventilation. Peak and reserve VT was lower in our SP, suggesting the normal increase in breathing frequency throughout exercise exacerbated asymmetrical ventilation, thus contributing to an overall lower peak and reserve VT.

\( V_\dot{\text{O}}_2 \) remained elevated throughout recovery in SP (Figure A), reflecting a slower rate of skeletal muscle energy restoration. This is determined in part by the oxidative capacity and maximal rate of oxidative adenosine triphosphate synthesis of skeletal muscle, which may be mediated by aerobic fitness and the availability of \( O_2 \) for phosphocreatine regeneration. Indeed, a lower peak \( V_\dot{\text{O}}_2 \) was associated with prolonged \( V_\dot{\text{O}}_2 \) off-kinetics in our SP. Consistent with the hypothesis that \( O_2 \) availability may be rate-limiting for \( V_\dot{\text{O}}_2 \) recovery, peak \( Q_\dot{\text{O}}_2 \) and \( V_\dot{\text{O}}_2 \) off-kinetics were well correlated.

\( V_\dot{\text{O}}_2 \) and VE off-kinetics were prolonged in SP (Figure A). \( V_\dot{\text{O}}_2 \) and VE off-kinetics were correlated \((R=0.80, P<0.001)\) and \( V_\dot{\text{O}}_2 \) off-kinetics related to peak \( V_\dot{\text{O}}_2 \) \((R=-0.72, P<0.001)\) and peak \( Q_\dot{\text{O}}_2 \) \((R=-0.75, P<0.001)\).

The power output was lower during low-level exercise \((26\pm3 \text{ versus } 59\pm5 \text{ W}; P<0.001)\) and \( V_\dot{\text{O}}_2 \) on-kinetics slower in SP (Figure B). \( V_\dot{\text{O}}_2 \) \((66\pm10 \text{ versus } 62\pm6 \text{ s}; P=0.800)\), VE \((65\pm11 \text{ versus } 66\pm6 \text{ s}; P=0.764)\), and HR \((45\pm9 \text{ versus } 32\pm8 \text{ s}; P=0.307)\) on-kinetics were not different between SP and healthy control subjects, respectively. There was no relation between time poststroke and \( V_\dot{\text{O}}_2 \) on-kinetics \((R=-0.60, P=0.064)\).
high VE, which is consistent with the well-correlated V̇CO₂ and V̇E off-kinetics.

V̇O₂ 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 V̇O₂ on-kinetics.

Slower V̇O₂ 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 V̇O₂ 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 V̇O₂ kinetics. Additionally, the years (≈7.5) poststroke may account for the slower V̇O₂ kinetics simply because of deconditioning secondary to inactivity. However, we matched SP and healthy control subjects on activity levels and the time poststroke and V̇O₂ kinetics were not related. Future investigations are required to establish the impact of comorbid conditions and stroke type on exercise cardiopulmonary function and V̇O₂ kinetics in SP.

Acknowledgments
We thank the participants of this study for their time. We also thank the staff at the Steadward Centre and the Community...
Rehabilitation Interdisciplinary Program (CRIS) for their assistance in identifying participants.

Sources of Funding
This study was funded by a grant to P.J.M. from the EFF Support for Advancement of Scholarship Fund. C.R.T. is a Canadian Institutes of Health Research (CIHR) Strategic Training Fellow in TORCH (Tomorrow’s Research Cardiovascular Health Professionals) and is supported by a doctoral Canada Graduate Scholarship from the Natural Sciences and Engineering Research Council of Canada. M.J.H. is a CIHR New Investigator.

Disclosures
None.

References


Cardiac Reserve and Pulmonary Gas Exchange Kinetics in Patients With Stroke
Corey R. Tomczak, Anwar Jelani, Robert G. Haennel, Mark J. Haykowsky, Robert Welsh and Patricia J. Manns

Stroke. 2008;39:3102-3106; originally published online August 14, 2008;
doi: 10.1161/STROKEAHA.108.515346
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2008 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/39/11/3102

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/