

## Cardiovascular Stress Induced by Whole-Body Vibration Exercise in Individuals With Chronic Stroke

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**Background.** Although whole-body vibration (WBV) has sparked tremendous research interest in neurorehabilitation, the cardiovascular responses to WBV in people with stroke remain unknown.

**Objective.** The aim of this study was to determine the acute effects of different WBV protocols on oxygen consumption ( $\dot{V}O_2$ ), heart rate (HR), rate of perceived exertion (RPE), blood pressure (BP), and rate-pressure product (RPP) during the performance of 6 different exercises among people with chronic stroke (time since onset  $\geq 6$  months).

**Design.** A repeated-measures design was used.

**Methods.** Each of the 48 participants experienced all 3 WBV protocols in separate sessions: (1) no WBV, (2) low-intensity WBV (peak acceleration = 0.96 unit of gravity of Earth [g]), and (3) high-intensity WBV (1.61g). The order in which they encountered the WBV protocols was randomized, as was the order of exercises performed during each session. Oxygen consumption, HR, and RPE were measured throughout the study. Blood pressure and RPP were measured before and after each session.

**Results.** Low-intensity and high-intensity WBV induced significantly higher  $\dot{V}O_2$  by an average of 0.69 and 0.79 mL/kg/min, respectively, compared with the control condition. These protocols also increased HR by an average of 4 bpm. The 2 WBV protocols induced higher RPE than the control condition during static standing exercise only. Although the diastolic and systolic BP and RPP were increased at the end of each exercise session, the addition of WBV had no significant effect on these variables.

**Limitations.** The results are generalizable only to ambulatory and community-dwelling people with chronic stroke.

**Conclusions.** Addition of high- and low-intensity WBV significantly increased the  $\dot{V}O_2$  and HR, but the increase was modest. Thus, WBV should not pose any substantial cardiovascular hazard in people with chronic stroke.



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Stroke is one of the most common debilitating conditions worldwide. People who survive a stroke may already have had poor cardiorespiratory health prior to the stroke event, as cardiovascular disease and poor cardiorespiratory fitness are known risk factors for stroke.<sup>1</sup> Additionally, individuals after stroke often sustain various physical impairments that involve multiple body systems and adversely affect mobility, thereby further encouraging a physically inactive lifestyle.<sup>2</sup> Cardiorespiratory fitness in individuals with stroke, which often is reflected by the rate of peak oxygen consumption ( $\dot{V}O_{2\text{peak}}$ ), has been found to be as low as 50% to 80% of values reported among age- and sex-matched physically inactive individuals<sup>3</sup> and is far below the threshold for independent living (around 20 mL/kg/min).<sup>4</sup> Benefits of endurance exercise training to improve cardiovascular health outcomes in patients after stroke have been reported.<sup>3,5-7</sup> Exercising at 60% to 80% of heart rate reserve (HRR) for 20 to 40 minutes per day, 3 to 5 days a week, has been recommended for patients with mild to moderate stroke for improving cardiovascular fitness and walking endurance.<sup>7</sup>

Whole-body vibration (WBV) therapy has sparked tremendous research interest in the field of geriatric rehabilitation. As WBV can augment muscle activity,<sup>8</sup> it has been used to train different aspects of neuromuscular function, such as muscle strength and power, postural control, and mobility, in the elderly population.<sup>9,10</sup> Cardiovascular responses to WBV also have been studied in young healthy adults,<sup>11-16</sup> older adults,<sup>17,18</sup> women who are overweight,<sup>19</sup> and people with spinal cord injury.<sup>20</sup> It has been demonstrated that among young healthy adults, the addition of WBV during exercise induced a significant

increase in oxygen consumption ( $\dot{V}O_2$ ) and heart rate (HR).<sup>14,21</sup> On the other hand, Hazell et al<sup>11</sup> demonstrated minimal cardiovascular stress (HR, blood flow, or mean arterial pressure) with the addition of WBV to a static semisquat exercise. The choice of exercise mode (static versus dynamic) and intensity may partially explain the discordance in results. There also is evidence that the cardiovascular response is influenced by the intensity of WBV.<sup>15</sup> The increased  $\dot{V}O_2$  and HR responses during WBV have led to its potential use as an adjunct intervention in cardiovascular exercise training. Indeed, in a randomized controlled trial involving 220 older adults, Bogaerts et al<sup>18</sup> found that a 1-year WBV training program resulted in significantly more gain in  $\dot{V}O_{2\text{peak}}$  compared with the control group without WBV.

Over the past few years, there has been an increasing interest in using WBV to improve neuromuscular function in people after stroke.<sup>22,23</sup> However, no studies have explored cardiovascular responses to WBV in the stroke population. As the integrity of the cardiovascular system and exercise capacity in people with stroke may be very different from those measures in people without stroke,<sup>3,24</sup> their cardiovascular responses to WBV also may differ. Examining the effects of WBV on acute cardiovascular responses is clinically important for 2 reasons. First, many individuals with stroke have a positive cardiovascular history and are at risk for recurrent stroke and cardiovascular event.<sup>24</sup> For safety reasons, it is essential to know the level of cardiovascular stress experienced as the patients are engaging in WBV exercises. Second, for those who are deemed safe to undergo cardiovascular exercise training, an understanding of the  $\dot{V}O_2$  and HR changes during WBV would help determine whether WBV is a useful adjunct treatment for cardio-

vascular exercise training. The specific objective of the current study was to determine the acute effect of different WBV protocols on  $\dot{V}O_2$ , HR, rate of perceived exertion (RPE), blood pressure (BP), and rate-pressure product (RPP) during the performance of various static and dynamic exercises among people with chronic stroke. We hypothesized that the WBV intensity, exercises performed, and their interactions would significantly influence the above cardiovascular variables of interest.

## Method

### Study Design

This study used a repeated-measures design to compare cardiovascular responses during exposure to different WBV conditions.

### Participants and Sample Size Calculation

As no study had previously investigated cardiovascular response during WBV in individuals with stroke, research in healthy adults was used to estimate the sample size required for this study. In a study involving a sample of 8 healthy men, Hazell and Lemon<sup>21</sup> found that WBV (frequency=45 Hz, peak-to-peak displacement=2 mm) significantly increased  $\dot{V}O_2$  by an average of 2.08 L/min (SD=0.40) compared with the same exercises without WBV (mean difference=1.69 L/min, SD=0.27) during various static exercises. The mean difference between the 2 groups equated to a large effect size (Cohen  $d=1.10$ ). A more conservative effect size, represented by  $F$  score in analysis of variance (ANOVA), was estimated for this study because the WBV intensities used were lower and the study population was disabled. Based on the ANOVA (3 WBV conditions and 6 exercises), assuming a medium effect size (convention:  $F=0.25$ ) with an alpha of .05, power of 0.9, and attrition rate of 10%, a minimum

of 40 participants would be required.

Participants were recruited through stroke self-help groups in the local community from January 2011 to June 2012. Inclusion criteria were chronic stroke (diagnosis of a hemispheric stroke with onset  $\geq 6$  months), community dwelling, Abbreviated Mental Test score  $\geq 6$ ,<sup>25</sup> and having hemiparesis in the lower extremity, as indicated by a composite leg and foot motor score of 13 or lower on the Chedoke-McMaster Stroke Assessment (CMSA).<sup>26</sup> Exclusion criteria were cerebellar or brainstem stroke, neurological conditions in addition to stroke, serious heart conditions, vestibular dysfunctions, other serious illnesses that affected performance of daily activities, and having a cardiac pacemaker or stent. All participants gave written informed consent prior to data collection.

### WBV Protocol

All experiments were conducted in a research laboratory at Hong Kong Polytechnic University. A platform that generated vertical vibrations (Danil SMC Co Ltd, Seoul, Korea) was used for all experiments. The device had an adjustable frequency range between 20 and 55 Hz with corresponding preset amplitudes.<sup>22,23</sup> The peak acceleration ( $a_{\text{peak}}$ ), which represented the WBV intensity, was related to the amplitude ( $A$ ) and frequency ( $f$ ) and was calculated as:  $a_{\text{peak}} = (2\pi f)^2 A$ .<sup>27</sup> It is usually represented in units of gravity of Earth ( $g$ ,  $9.8 \text{ ms}^{-2}$ ) for easy comparison across studies. The peak acceleration values generated by the machine were validated using a triaxial accelerometer (model 7523A5, Dytran Instruments Inc, Chatsworth, California).

As WBV frequencies lower than 20 Hz may cause destructive resonance effects to the body, and previous

studies showed that frequencies higher than 30 Hz caused discomfort and fatigue in some individuals with stroke,<sup>22,23</sup> a frequency range of 20 to 30 Hz was chosen in the current study. Each participant, while performing different exercises, underwent 3 different WBV conditions for measuring cardiovascular responses: (1) no WBV, (2) a low-intensity WBV protocol (amplitude=0.60 mm, frequency=20 Hz, peak acceleration=0.96g) (ie, subgravity), and (3) a high-intensity WBV protocol (amplitude=0.44 mm, frequency=30 Hz, peak acceleration=1.61g) (ie, supragravity). The 3 WBV conditions were tested separately in 3 different days, with a minimum of one rest day between sessions. To avoid an order effect, the sequence of WBV conditions was decided randomly by drawing lots at the beginning of the first session.

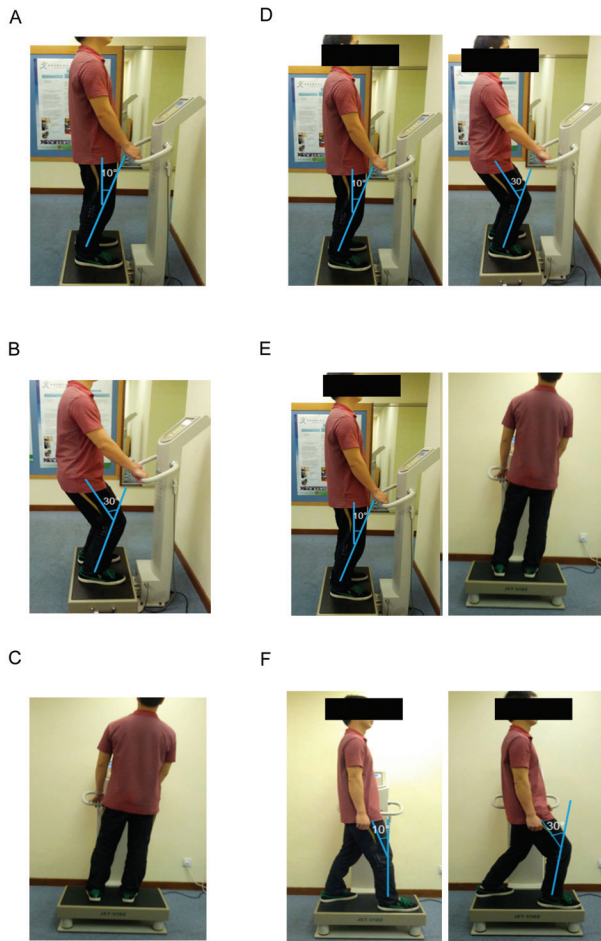
### Exercise Protocol

In each session, the participants were instructed to perform 6 different exercises (Fig. 1). Three of these exercises were static: (1) static standing exercise (Fig. 1A), (2) static semisquat (Fig. 1B), and (3) static standing with weight shifted to paretic leg (Fig. 1C). The other 3 exercises were dynamic: (1) dynamic semisquat (Fig. 1D), (2) dynamic side-to-side weight shifting (Fig. 1E), and (3) dynamic forward lunge (Fig. 1F). The exercises chosen were commonly used in previous WBV trials in different populations.<sup>9,10,22,23</sup> The sequence of exercises performed was randomized by drawing lots from a box at the beginning of each session. There was a total of 6 lots, with each lot containing the name of one of the 6 exercises. Therefore, the number of possible exercise sequences was 720. Figure 2 illustrates the path of testing.

In a previous study,<sup>14</sup> a steady state of  $\dot{V}_{\text{O}_2}$  was reached in the third minute in most young healthy partici-

pants during these exercises. Most people also would feel fatigue if a longer period was used and no change in posture was allowed.<sup>15</sup> It has been reported that  $\dot{V}_{\text{O}_2}$  would reach a plateau within 3 minutes in people with stroke at a given workload.<sup>28</sup> Thus, the duration of 3 minutes was chosen for each exercise in the current study. The dynamic exercises (Figs. 1D, 1E, and 1F) were performed in cycles of 3 seconds (ie, 20 repetitions per minute). A metronome was used to guide the people with stroke in performing the exercises at the desired rhythm. This exercise rhythm was selected based on our pilot study and was designed to balance between sufficient stimulus to increase  $\dot{V}_{\text{O}_2}$  and HR, as well as the individual's ability to maintain the required exercise pace for 3 minutes of exercise. After each exercise, participants were instructed to sit down and rest until the  $\dot{V}_{\text{O}_2}$  and HR returned to baseline values before the commencement of the next exercise.

To familiarize the participants with the exercises, a practice trial was given before actual data collection. A manual goniometer (Baseline HiRes plastic 360° ISOM goniometer, Fabrication Enterprises, White Plains, New York) was used to monitor the knee joint angle to ensure that each participant was performing the required exercises properly. Verbal feedback was given to the participants as necessary to ensure consistent performance of the exercises. All participants were instructed to gently hold on to the handrail of the WBV device for maintaining standing balance to ensure safety. Throughout the experimental session, the condition of each participant was monitored closely. The participants were informed of their option to terminate exercises at any time they experienced adverse symptoms. Overall, it took approximately 50 to



**Figure 1.**

Exercise protocol. (A) Static standing exercise: standing on the platform with feet placed apart at shoulder width and knees slightly flexed at 10° and hold for 3 minutes. (B) Static semisquat: standing on the platform with feet placed apart at shoulder width and knees flexed at 30° and hold for 3 minutes. (C) Static standing with weight shifted to paretic leg: standing with body weight shifted to the paretic leg as much as possible and hold for 3 minutes. (D) Dynamic semisquat: starting position same as in static standing exercise (left), then bending knees to achieve the semisquat position (right) and return to starting position; repeat at a rate of 20 cycles per minute for 3 minutes. (E) Dynamic side-to-side weight shifting: starting position same as in static standing exercise (left), then shifting body weight onto paretic leg (right) and return to starting position and shifting weight onto the nonparetic leg. Repeat at a rate of 20 cycles per minute for 3 minutes. (F) Dynamic forward lunge: standing in a forward lunge position with the paretic leg placed in front of the nonparetic leg and with paretic knee flexed at 10° (left), then leaning forward and shifting body weight onto the paretic leg as much as possible with knee flexed at 30° (right), and then moving back to the starting position. Repeat at a rate of 20 cycles per minute for 3 minutes.

60 minutes to complete a data collection session.

### Measurement of Cardiovascular Response

The primary outcome variables in this study were diastolic and systolic

blood pressure (DBP and SBP, in mm Hg) and RPP, RPE,  $\dot{V}O_2$ , and HR. A full-face mask and HR monitor (Polar, Tampere, Finland) were worn by participants throughout the testing sessions, as  $\dot{V}O_2$  and HR were continuously measured using a por-

table metabolic system (FitMate Pro, COSMED, Rome, Italy). Previous research showed that the FitMate system is a reliable and valid system for measuring  $\dot{V}O_2$  during graded exercise.<sup>29</sup> In addition, our pilot study showed that the reliability of the FitMate system was good when used in people with stroke, with intraclass correlation coefficients (ICC [3,1]) of .80 for static exercise and .91 for dynamic exercise. The system was calibrated according to the manufacturer's guidelines prior to each testing session. The last 30 seconds of  $\dot{V}O_2$  and HR data during the 3-minute exercise period was averaged to obtain the mean value for analyses.<sup>18,21</sup> A similar data processing approach was used by Cochrane et al.<sup>17</sup>

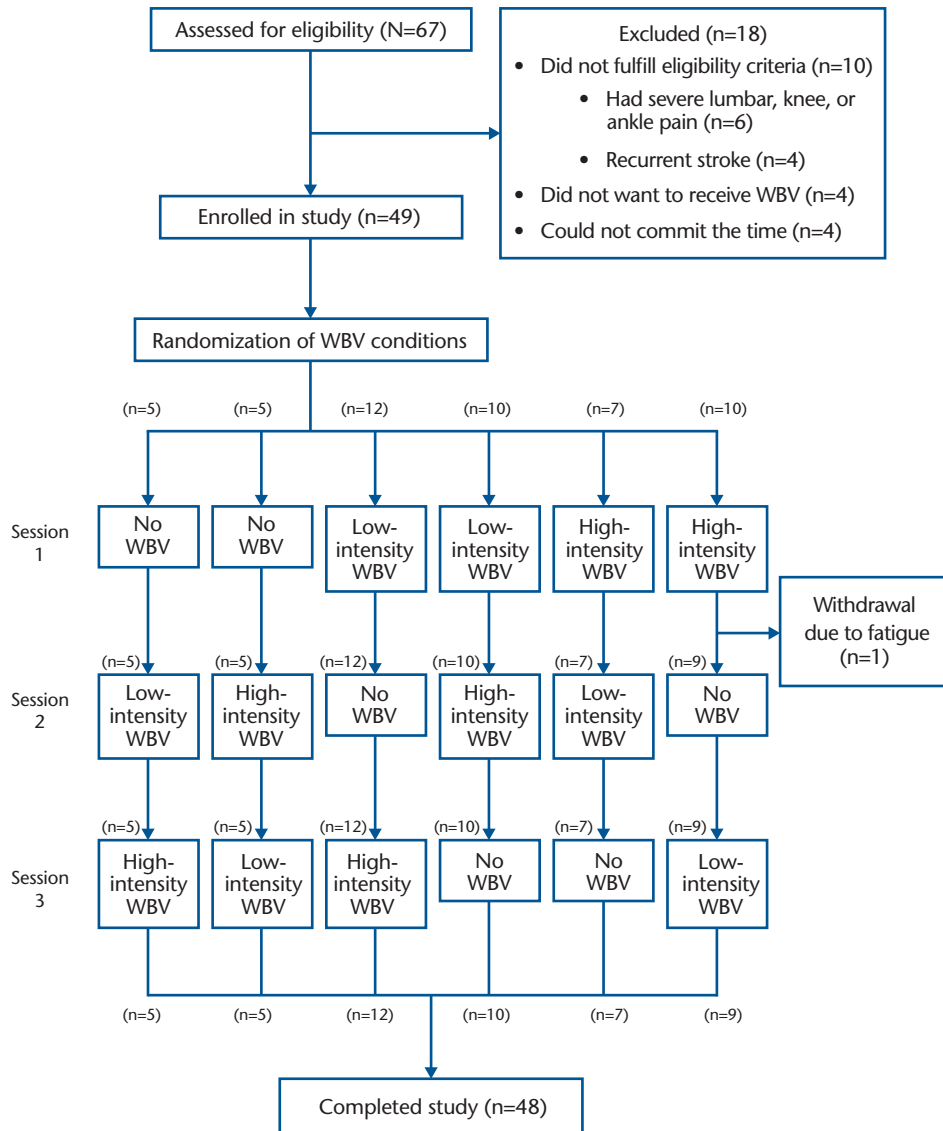
Systolic blood pressure and DBP were recorded (BPM I, Manning, Hong Kong) before and at the end of each session. The RPP was calculated as:  $(HR \times SBP)/100$ .<sup>30</sup> Verbal RPE (from 6 to 20 according to the Borg's Scale)<sup>31</sup> also was asked at the beginning and at 1-minute intervals during each set of exercises. The highest RPE value reported in each trial was noted and used for analysis. Measures of RPP and RPE together might provide an indication of an individual's physiological tolerance to submaximal activity.<sup>31</sup>

At the beginning of the second and third sessions, the participants were asked whether they were experiencing fatigue or other symptoms that may have resulted from the previous testing session. If the answer was positive, the assessment session was postponed until the suspected carry-over effect from the previous session had subsided.

### Data Analysis

Statistical analysis was performed with IBM SPSS Statistics software (version 20.0, IBM Corp, Armonk, New York). The duration of the





**Figure 2.**

Study flowchart. Each participant underwent 3 experimental sessions. The sequence of whole-body vibration (WBV) conditions was decided randomly by drawing lots once at the beginning of the first session. At the beginning of each session, the order of exercise also was randomized by drawing lots. A total of 48 participants with chronic stroke completed all assessment procedures.

washout period (measured in number of days) between testing sessions 1 and 2 was compared with that between testing sessions 2 and 3 using a paired *t* test. A two-way ANOVA with repeated measures (within-subject factors: intensity [no WBV, low- and high-intensity WBV] and time [before and after session]) was used to assess the difference in mean DBP, SBP, and RPP between pre-session and post-session performance within each of the 3 sessions

and at corresponding times between the 3 sessions. The intensity × time interaction term determined whether changes observed between the beginning and end of each session were consistent among the 3 sessions, that is, whether the 3 WBV protocols were associated with different within-session responses.

Another two-way ANOVA with repeated measures model (within-subject factors: intensity [no WBV,

low- and high-intensity WBV] and 6 exercises) was used to assess the mean  $\dot{V}O_2$  and HR between exposure to the 3 WBV protocols and among the 6 exercises. The intensity × exercise interaction effect determined whether the changes in  $\dot{V}O_2$  and HR responses induced by WBV were exercise dependent. The Greenhouse-Geisser epsilon adjustment was used if the sphericity assumption was violated. If significant results were found, contrast

analysis with Bonferroni adjustment was performed. For each exercise, the comparisons of RPE (ordinal data) among the 3 WBV protocols were tested using the Friedman test, followed by pair-wise comparisons using Wilcoxon signed rank tests.

Additional analyses were done to examine whether the cardiovascular responses were related to the baseline values. For BP and RPP data, the within-session change score was calculated by subtracting the baseline score from the postsession score. For  $\dot{V}O_2$  and HR data, the change score (before and after each exercise) was obtained by subtracting the baseline score from the post-exercise score (ie, average of the last 30 seconds of the trial). Pearson product moment correlations were then used to determine the degree of association between the change score and the baseline value for each variable.

A level of significance of  $P \leq .05$  was set, except for post hoc analysis where the alpha was adjusted according to the number of comparisons made. We did not formally test for order effects related either to protocol or to exercise but relied on randomization to minimize order effects.

### Role of the Funding Source

The work described in this report was substantially supported by a grant from the Research Grants Council of the Hong Kong Special Administrative Region, China (General Research Fund, Project No. 524511).

## Results

### Characteristics of Participants

A total of 48 participants (36 men and 12 women; mean age=56.3 years, SD=10.1) completed all assessments (Fig. 2). Participant characteristics are presented in Table 1. The median composite leg

**Table 1.**  
Characteristics of Study Participants (n=48)<sup>a</sup>

Variable	Value
<b>Basic demographics</b>	
Age (y), $\bar{X}$ (SD)	56.3 (10.1)
Sex, men/women, n	36/12
Body mass index (kg/m <sup>2</sup> ), $\bar{X}$ (SD)	24.8 (3.2)
Required walking aid for indoor mobility, none/cane/quad, n	43/3/2
Required walking aid for outdoor mobility, none/cane/quad, n	17/26/5
<b>Stroke characteristics</b>	
Poststroke duration (y), $\bar{X}$ (SD)	4.7 (3.2)
Type of stroke, hemorrhagic/ischemic/ischemic+hemorrhage/unknown, n	16/23/3/6
Side of paresis, left/right, n	19/29
CMSA lower extremity composite score (out of 14), median (IQR)	8 (7–9)
Abbreviated mental test score (out of 10), $\bar{X}$ (SD)	9.3 (0.9)
<b>Comorbid conditions</b>	
Hypertension, n	14
Diabetes mellitus, n	9
High cholesterol, n	20
<b>Medications</b>	
Antihypertensive agents, n	
Beta-blockers	11
Calcium channel blockers	5
Angiotensin converting enzyme inhibitors	8
Angiotensin II receptor antagonists	1
Adrenergic receptor blockers	1
Others	8
Hypolipidemic agents, n	20
Antidiabetic agents, n	9
<b>Baseline <math>\dot{V}O_2</math> and HR data</b>	
Baseline $\dot{V}O_2$ (mL/kg/min), $\bar{X}$ (SD)	
No-WBV session	4.03 (0.70)
Low-intensity WBV session	4.08 (1.06)
High-intensity WBV session	3.99 (0.86)
Baseline HR (bpm), $\bar{X}$ (SD)	
No-WBV session	76.3 (11.7)
Low-intensity WBV session	77.6 (13.3)
High-intensity WBV session	76.9 (13.6)

<sup>a</sup> Mean (SD) presented for continuous variables. CMSA=Chedoke-McMaster Stroke Assessment, IQR=interquartile range, HR=heart rate,  $\dot{V}O_2$ =oxygen consumption, WBV=whole-body vibration.

motor score (CMSA) was 8 out of 14 (interquartile range=7–9), indicating moderate motor impairment. There was no significant between-session difference in baseline  $\dot{V}O_2$  ( $P=.69$ ) and HR ( $P=.93$ ). Thus, the

baseline HR values of the 3 sessions were averaged to obtain the mean resting HR for each participant. We found that 13 (27.1%) of our participants had a mean resting HR of  $\geq 77$  bpm, whereas only 6 (12.5%) had a

mean resting HR of  $\leq 64$  bpm. A previous study in people with stroke showed that a resting HR of  $\geq 77$  bpm was significantly associated with increased rate of vascular death compared with their counterparts with a resting HR of  $\leq 64$  bpm.<sup>32</sup>

**Washout Period**

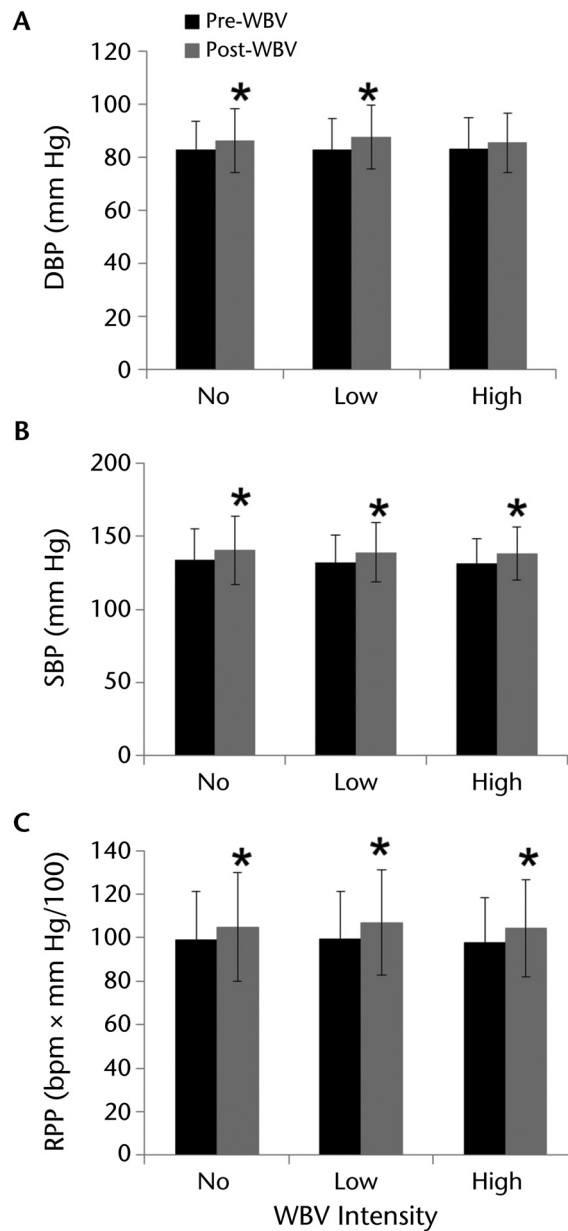
On average, the washout period between sessions 1 and 2 was 1.4 days (SD=0.6, range=1-3), which was similar to that between sessions 2 and 3 (mean=1.3 days, SD=0.6, range=1-3) ( $P=.73$ ). None of the participants reported any carryover effects that may have resulted from the previous testing session that required postponement of testing.

**DBP, SBP, RPP, and RPE changes.** The DBP ( $F_{1,47}=24.10$ ,  $P\leq .001$ ), SBP ( $F_{1,47}=29.91$ ,  $P\leq .001$ ), and RPP ( $F_{1,47}=17.19$ ,  $P\leq .001$ ) immediately after the exercise session were significantly higher than their respective values at baseline (Fig. 3), except that in the high-intensity WBV condition, the DBP postexercise was not significantly different from that at baseline after Bonferroni adjustment ( $P>.017$ ) (Tab. 2, Fig. 3A). The main effect of WBV intensity and intensity  $\times$  time interaction were not statistically significant for DBP, SBP, and RPP ( $P>.05$ ).

The pooled RPE data are shown in Figure 4A. Out of the 288 exercise trials for each WBV protocol (6 exercises  $\times$  48 participants), only 2% (2 participants, 6 trials), 6% (3 participants, 17 trials), and 5% (4 participants, 15 trials) reported an RPE of  $>15$  for no-WBV and low- and high-intensity WBV sessions, respectively. The low-intensity WBV protocols ( $Z=-4.43$ ,  $P<.001$ ) and high-intensity WBV protocols ( $Z=-3.70$ ,  $P<.001$ ) significantly induced higher perceived effort than the no-WBV condition during static standing exercise. For the rest of the exer-

cises, the RPE value demonstrated no significant differences among the 3 WBV protocols ( $P>.05$ ). Other than the one participant who dropped out after the first session

due to fatigue (Fig. 2), no adverse effects were reported, and none of the participants requested to stop the exercises during any of the testing sessions.



**Figure 3.**

Effect of whole-body vibration (WBV) on systolic and diastolic blood pressure (SBP and DBP) and rate-pressure product (RPP). The average DBP (A), SBP (B), and RPP (C) recorded at baseline (black bars) and immediately after each exercise session (gray bars). The error bars represent 1 SD from the mean. The within-session differences in DBP, SBP, and RPP did not themselves differ among the 3 WBV protocols, as evidenced by the nonsignificant time  $\times$  intensity interaction. \*Significant difference from baseline.

Table 2.

Effect of Whole-Body Vibration (WBV) Intensity on Outcome Measurements<sup>a</sup>

Variable	WBV Intensity × Time Interaction Effect		Main Effect of WBV Intensity		Main Effect of Time		Post Hoc Analysis (Within-Session Difference for Each WBV Protocol)					
	F	P	F	P	F	P	No WBV Pretest vs Posttest		Low-Intensity WBV Pretest vs Posttest		High-Intensity WBV Pretest vs Posttest	
							Mean Difference <sup>b</sup> (95% CI)	P	Mean Difference (95% CI)	P	Mean Difference (95% CI)	P
DBP	0.95	.39	0.46	.61	24.10	≤.001 <sup>c</sup>	3.3 (1.1, 5.5)	.01 <sup>d</sup>	4.6 (2.0, 7.2)	≤.001 <sup>d</sup>	2.3 (1.1, 4.6)	.04
SBP	0.05	.95	0.90	.41	29.91	≤.001 <sup>c</sup>	6.4 (2.8, 10.1)	≤.001 <sup>d</sup>	7.2 (3.3, 11.1)	≤.001 <sup>d</sup>	6.6 (3.0, 10.3)	≤.001 <sup>d</sup>
RPP	0.24	.76	0.56	.57	17.79	≤.001 <sup>c</sup>	5.9 (2.0, 9.9)	.01 <sup>d</sup>	7.6 (2.9, 12.3)	.01 <sup>d</sup>	6.8 (2.4, 11.1)	.01 <sup>d</sup>
Variable	WBV Intensity × Exercise Interaction Effect		Main Effect of WBV Intensity		Main Effect of Exercise		Contrast Analysis (Main Effect of Intensity)					
	F	P	F	P	F	P	No WBV vs Low-Intensity WBV		No WBV vs High-Intensity WBV		Low-Intensity vs High-Intensity WBV	
							Mean Difference (95% CI)	P	Mean Difference (95% CI)	P	Mean Difference (95% CI)	P
$\dot{V}O_2$	0.25	.25	16.98	≤.001 <sup>c</sup>	29.85	≤.001 <sup>c</sup>	0.7 (0.4, 1.0)	≤.001 <sup>c</sup>	0.8 (0.5, 1.2)	≤.001 <sup>c</sup>	0.1 (-0.3, 0.5)	1.00
HR	2.94	.01 <sup>c</sup>	4.63	.01 <sup>c</sup>	32.67	≤.001 <sup>c</sup>	4 (1, 7)	.01 <sup>c</sup>	4 (0, 7)	.05	0 (-4, 4)	1.00

<sup>a</sup> SBP=systolic blood pressure, DBP=diastolic blood pressure, RPP=rate-pressure product, 95% CI=95% confidence interval,  $\dot{V}O_2$ =oxygen consumption, HR=heart rate.

<sup>b</sup> A positive mean difference indicates that the mean value of the latter group was higher than that of the former group.

<sup>c</sup> Statistically significant ( $P \leq .05$ ).

<sup>d</sup> Statistically significant ( $P \leq .017$ ).

**$\dot{V}O_2$  changes.** Overall, significant main effects of WBV intensity ( $F_{2,94}=16.98$ ,  $P \leq .001$ ) and exercise ( $F_{5,235}=29.85$ ,  $P \leq .001$ ) were found (Fig. 4B). The intensity × exercise interaction effect, however, was not significant ( $F_{10,470}=1.32$ ,  $P=.25$ ). Contrast analysis revealed that, across all 6 exercises, both the low- and high-intensity WBV protocols induced significantly higher  $\dot{V}O_2$  than the control condition, by an average of 0.69 mL/kg/min (95% confidence interval [95% CI]=0.35, 1.03;  $P \leq .001$ ) and 0.79 mL/kg/min (95% CI=0.45, 1.14;  $P \leq .001$ ) respectively (Tab. 2). Analysis further showed that the increase in  $\dot{V}O_2$  induced by the 2 WBV protocols remained statistically significant after Bonferroni adjustment, except the dynamic weight shifting to paretic leg and dynamic forward lunge exercises during low-intensity WBV. The difference in  $\dot{V}O_2$  value between the low- and high-intensity WBV proto-

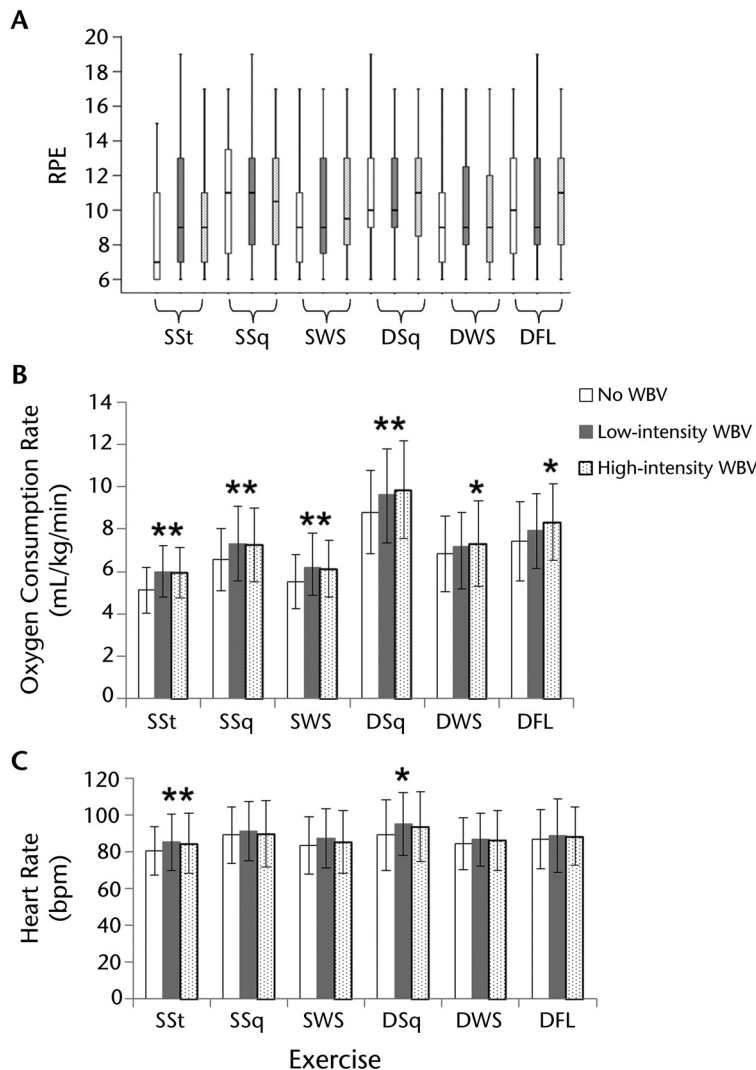
cols was not significant in any of the exercises after Bonferroni adjustment ( $P=1.00$ ) (Tab. 2). Contrast analysis of the effect of exercises showed that static standing and static standing with weight shifted to the paretic leg resulted in significantly lower  $\dot{V}O_2$  than that measured during other exercises ( $P < .01$ ). On the other hand,  $\dot{V}O_2$  during dynamic semisquat and dynamic forward lunge was significantly higher than that during other exercises ( $P < .01$ ) (Fig. 4B).

**HR changes.** Overall, significant main effects of WBV intensity ( $F_{2,94}=4.63$ ,  $P=.01$ ) and exercise ( $F_{5,235}=32.67$ ,  $P \leq .001$ ) were found (Fig. 4C). The intensity × exercise interaction effect also was significant ( $F_{10,470}=2.94$ ,  $P=.01$ ). Contrast analysis revealed that overall, low-intensity WBV induced significantly higher HR than the control condition by an average of 4 bpm (95% CI=1,

7;  $P=.01$ ). The HR also was increased by the addition of high-intensity WBV (mean difference=4 bpm; 95% CI=0, 7), but the result was marginally significant ( $P=.05$ ) (Tab. 2). The difference in HR was not significant between the low- and high-intensity WBV protocols ( $P=1.00$ ) (Tab. 2). The increase in HR induced by low-intensity WBV remained significant for static standing ( $P \leq .001$ ), and dynamic semisquat ( $P \leq .001$ ) exercises only after Bonferroni adjustment. Regarding the main effect of exercise, static standing induced significantly lower HR than other exercises ( $P < .01$ ) whereas the HR response during the dynamic semisquat exercise was significantly higher than that during other exercises ( $P < .01$ ) (Fig. 4C).

To determine the exercise intensity during different WBV conditions, the age-predicted maximal heart rate (HR<sub>max</sub>) formula was used to esti-





**Figure 4.** Effect of whole-body vibration (WBV) on rate of perceived exertion (RPE), oxygen consumption, and heart rate. Figure 4A shows the box plot for the RPE data. The highest RPE value reported in each exercise trial was used for analysis. The thick line inside each box represents the median, and the upper and lower borders of each box define the interquartile range. The vertical bars represent data up to 1.5 times the interquartile range extending from the upper and lower borders of the box. The oxygen consumption (Fig. 4B) and heart rate (Fig. 4C) data obtained during the last 30 seconds of each 3-minute exercise trial were averaged for subsequent analyses. The error bars represent 1 SD from the mean. The RPE level was significantly higher in the low- and high-intensity WBV conditions than the no-WBV condition during static exercise only. Whole-body vibration induced a significant increase in oxygen consumption. Adding WBV also led to significant increases in heart rate in static standing exercise (SSt) and dynamic side-to-side weight shifting exercise (DWS). \*Significant difference from the no-WBV condition. SSq=static semisquat, SWS=static standing with weight shifted to paretic leg, DSq=dynamic semisquat, DFL=dynamic forward lunge.

predicted HRmax at 64% (ie, moderate intensity)<sup>7</sup> or above for the no-WBV, low-intensity WBV, and high-intensity WBV conditions, respectively.

**Association With Baseline Values**

Baseline SBP ( $r = -.57, P < .001$ ), DBP ( $r = -.42, P = .01$ ), and RPP ( $r = -.50, P < .001$ ) were significantly correlated with their corresponding within-session change scores for the high-intensity protocol. The baseline SBP ( $r = -.43, P = .01$ ) and RPP ( $r = -.39, P = .01$ ) also were correlated with their respective change scores for the low-intensity protocol.

Out of 18 different WBV intensity and exercise combinations (3 protocols  $\times$  6 exercises), baseline  $\dot{V}O_2$  was significantly correlated only with the change score during static semisquat exercise ( $r = -.43, P = .01$ ) and static standing with weight shifted to the paretic leg exercise ( $r = -.33, P = .02$ ) when receiving low-intensity WBV. No significant correlations were identified with the HR data.

**Discussion**

This is the first study to examine the cardiovascular response to WBV in individuals with chronic stroke. The principal finding of this study was that addition of high- and low-intensity WBV significantly increased the  $\dot{V}O_2$  and HR, but the increases were modest.

**Is WBV Exercise Training Safe for Individuals With Stroke?**

Whole-body vibration is gaining popularity in stroke rehabilitation for enhancing neuromuscular function.<sup>22,23</sup> Studying the cardiovascular stress imposed by WBV during exercises can provide important information for rehabilitation practitioners to establish exercise intensity and safety. Our results showed that WBV induced only modest increases in DBP ( $< 5$  mm Hg) and SBP ( $< 8$  mm Hg) (Tab. 2). The upper bound of the

mate each individual's HRmax (220 - age); for participants taking beta-blockers (n=11), the formula was modified to 70% (208 - [0.7  $\times$  age]).<sup>33</sup> The results of this study showed that, of the 288 exercise trials for each WBV protocol, only 23%, 29%, and 25% achieved the age-

95% CI for these variables did not even exceed 8 and 12 mm Hg, respectively. These increases were much lower than the increases in BP after walking on a treadmill at a self-selected speed for 20 minutes previously reported in people with stroke (mean increase in SBP=46.7 mm Hg and DBP=21.0 mm Hg).<sup>34</sup> Thus, our results generally agree with the finding in previous studies in young and older adults that WBV did not induce major changes in BP.<sup>11,17</sup>

Rate-pressure product is an estimate of myocardial  $\dot{V}_{O_2}$  and gives an indication of the amount of oxygen demanded by the heart.<sup>30</sup> Although the RPP was significantly increased at the end of each exercise session, the WBV intensity  $\times$  time interaction effect was not significant, indicating that the myocardial oxygen demand during different exercises was similar regardless of whether WBV was added.

Rimmer et al<sup>35</sup> reported that if the RPP is higher than 200, the patient is not suited to exercise. In the current study, the mean postexercise RPP values for the low- and high-intensity WBV sessions were 107 and 104, respectively, compared with 105 for the no-WBV session. We also recorded the RPE to monitor exercise intensity during different WBV conditions.<sup>36</sup> Even when low- and high-intensity WBV were added, the median RPE values were below 12 for all exercise conditions (Fig. 4A). Overall, the level of myocardial exertion (RPP) and RPE during WBV exercises did not exceed their corresponding values during the Six-Minute Walk Test (mean RPP=144, SD=33; mean RPE=11.6, SD=3.2) in people with chronic stroke previously reported by Eng et al.<sup>30</sup> With the exception of one participant who withdrew from the study due to fatigue after WBV exercise, no other adverse signs and symptoms were reported, and none of the partici-

pants requested to terminate the exercise sessions, suggesting that the WBV protocols used in the current study were safe and well tolerated.

We found that higher baseline BP and RPP values had fair to moderate relationships ( $r=-.4$  to  $-.6$ ), with smaller increases in the same variables after the WBV exercise sessions. Thus, WBV exercise did not pose disproportionately higher cardiovascular stress to participants with higher baseline resting BP and RPP (the higher-risk group).

### Do WBV Exercises Have Potential to Provide a Positive Cardiovascular Training Effect?

Another question pertains to whether WBV exercises have any potential in inducing a positive cardiovascular training effect. We found that WBV induced a significant, but modest, increase in  $\dot{V}_{O_2}$  (by 0.7–0.8 mL/kg/min, upper bound of 95% CI=1.2 mL/kg/min) and HR (by 4 bpm, upper bound of 95% CI=7 bpm), likely because of the increased exercise intensity resulting from the WBV-induced increase in skeletal muscle activity.<sup>8</sup> Thus, our results concurred with previous studies, which also showed that the increases in  $\dot{V}_{O_2}$  and HR during WBV exercise were modest in younger adults<sup>13,14,21</sup> and older adults.<sup>17,18</sup>

The WBV intensity  $\times$  exercise interaction effect for  $\dot{V}_{O_2}$  was not significant, as the WBV-induced increase in  $\dot{V}_{O_2}$  was quite consistent across all exercises tested, regardless of whether the exercise was static or dynamic (Fig. 4B). On the other hand, the intensity  $\times$  exercise interaction effect was significant for the HR response, indicating that the WBV-induced increase in HR at various intensities was dependent on the exercise. Adding WBV led to significant increases in HR during static standing and dynamic semisquat but not other exercises (Fig. 4C),

thereby contributing to the interaction effect. The discordance between the results on  $\dot{V}_{O_2}$  and HR may indicate that the increase in  $\dot{V}_{O_2}$  could not be solely explained by the increase in HR. Possible mechanisms may include increase in stroke volume, muscle blood flow velocity and volume, and increased utilization of oxygen by exercising muscles<sup>37</sup> and will warrant further investigation.

The exercise intensities of most WBV trials were generally low (<64% of HRmax) and were similar to those reported during standing, stepping, basic walking, and advanced walking activities in a typical physical therapy session for people with stroke (below 60% of HRmax or 40% of HRR).<sup>38</sup> They were considered to be ineffective in inducing a cardiovascular training effect.<sup>7,38–40</sup> The training intensities, even after addition of WBV, were much lower than those reported in aerobic exercise training using a treadmill,<sup>40,41</sup> a cycle ergometer,<sup>42–44</sup> or a combination of strengthening and aerobic activities, which often involved a training intensity of 60% to 80% of HRR.<sup>7,45–47</sup> The training intensities achieved during WBV exercises also were considerably lower than that during the Six-Minute Walk Test among people with chronic stroke, which could reach 80% to 85% of the  $\dot{V}_{O_2}$  peak.<sup>48</sup> Thus, our finding is in accordance with Cochrane et al,<sup>17</sup> who found that the estimated percentage of  $\dot{V}_{O_2}$  peak achieved during static squat exercise with WBV was only at 24% and would not be sufficient to enhance aerobic capacity.<sup>17</sup> However, it is acknowledged that using age to predict the HRmax may not be ideal. It has been reported that the HRmax achieved during a symptom-limited exercise test is significantly lower than the age-predicted HRmax in people with stroke.<sup>49</sup>

Interestingly, Bogaerts et al<sup>18</sup> showed that their 1-year WBV training protocol had significantly improved  $\dot{V}O_{2\text{peak}}$  in older adults (by 18.2%), which was comparable to that following a conventional aerobic fitness exercise program (21.0%). However, the intensity of their WBV protocol was much higher (frequency=35–40 Hz, high amplitude=5 mm, low amplitude=2.5 mm), which may partially explain why they were able to raise the HR to about 62% to 80% of HRR (moderate to high aerobic exercise intensity). We did not choose a higher WBV intensity, as our pilot study revealed an increased incidence of discomfort with higher WBV frequencies. Furthermore, use of WBV with high peak accelerations warrants caution for patients with stroke, as they often have fragile bones.<sup>50,51</sup> The fact that we did not use WBV of higher intensities also may partially explain the lack of difference in  $\dot{V}O_2$  and HR between the low- and high-intensity WBV protocols (Tab. 2).

Based on the resting HR data, the cardiovascular health of 27% of our participants could be considered poor, as Böhm et al<sup>32</sup> showed that people with stroke who had a resting HR of  $\geq 77$  bpm had a significantly higher risk of vascular death compared with those with resting HR in the lowest quintile ( $\leq 64$  bpm). However, we did not identify any relationship between baseline HR and the change scores in any of the exercise trials. Of the very few significant correlations between baseline  $\dot{V}O_2$  and change in  $\dot{V}O_2$ , the relationship was only fair ( $r < .5$ ). Taken together, the HR and  $\dot{V}O_2$  responses to our exercise protocols, with or without WBV, were generally similar regardless of the cardiovascular health status of the participants.

### Limitations and Future Directions

First, because all of our participants were ambulatory and community dwelling, the results are generalizable only to people with characteristics similar to those of our participants. Second, we studied the effects of the overall intensity of WBV (indicated by peak acceleration) on cardiovascular parameters. Other variables (eg, WBV frequency, amplitude) may exert independent cardiovascular effects. We also did not measure BP before and after each exercise. Third, only a rhythm of 20 repetitions per minute was used during the dynamic exercises. Although higher movement frequencies may elicit more impressive  $\dot{V}O_2$  and HR changes, it may not be feasible for people with stroke to sustain such rhythms for prolonged periods. In addition, a substantial proportion of participants were taking long-term medications, including beta-blockers, for various reasons, which may attenuate the cardiovascular response to exercise. However, we feel that our sample is a good representation of the general chronic stroke population, in which administration of long-term medications is very common. Determining the cardiovascular responses during WBV exercise is important, regardless of whether an individual is taking medications. A symptom-limited exercise test was not conducted, and actual HRmax and  $\dot{V}O_{2\text{peak}}$ , and thus appropriate target exercise HR (or  $\dot{V}O_2$ ), were not determined. Finally, the study was not designed to assess the long-term effects of WBV. Whether the WBV protocols used in this study can induce long-term changes in cardiovascular fitness among people with stroke warrants further investigation.

In conclusion, this study suggested that in individuals with chronic stroke,  $\dot{V}O_2$  and HR increased modestly with the addition of either low- or high-intensity WBV. The impact of

WBV on BP and myocardial oxygen demand was not significant, suggesting that WBV imposes no threats to cardiovascular function for people with stroke.

All authors provided concept/idea/research design and consultation (including review of manuscript before submission). Mr Liao, Dr Jones, and Dr Pang provided writing. Mr Liao provided data collection. Mr Liao, Dr Ng, and Dr Jones provided data analysis. Dr Pang provided project management and fund procurement.

The study was approved by the Human Research Ethics Subcommittee, The Hong Kong Polytechnic University. All experimental procedures were conducted according to the Declaration of Helsinki.

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### References

- 1 Agabiti-Rosei E, Muiesan ML. Carotid atherosclerosis, arterial stiffness and stroke events. *Adv Cardio*. 2007;144:173–186.
- 2 Michael KM, Allen JK, Macko RF. Reduced ambulatory activity after stroke: the role of balance, gait, and cardiovascular fitness. *Arch Phys Med Rehabil*. 2005;86:1552–1556.
- 3 Pang MY, Eng JJ, Dawson AS. Relationship between ambulatory capacity and cardiorespiratory fitness in chronic stroke: influence of stroke-specific impairments. *Chest*. 2005;127:495–501.
- 4 Letombe A, Cornille C, Delahaye H, et al. Early post-stroke physical conditioning in hemiplegic patients: a preliminary study. *Ann Phys Rehabil Med*. 2010;53:632–642.
- 5 Pang MY, Eng JJ, Dawson AS, Gylfadóttir S. The use of aerobic exercise training in improving aerobic capacity in individuals with stroke: a meta-analysis. *Clin Rehabil*. 2006;20:97–111.
- 6 Pang MY, Eng JJ. Determinants of improvement in walking capacity among individuals with chronic stroke following a multi-dimensional exercise program. *J Rehabil Med*. 2008;40:284–290.
- 7 Pang MY, Charlesworth SA, Lau RW, Chung RC. Using aerobic exercise to improve health outcomes and quality of life in stroke: evidence-based exercise prescription recommendations. *Cerebrovasc Dis*. 2013;35:7–22.
- 8 Liao LR, Lam FM, Pang MY, et al. Leg muscle activity during whole-body vibration in individuals with chronic stroke. *Med Sci Sports Exerc*. 2014;46:537–545.



- 9 Lau RW, Liao LR, Yu F, et al. The effects of whole body vibration therapy on bone mineral density and leg muscle strength in older adults: a systematic review and meta-analysis. *Clin Rehabil*. 2011;25:975-988.
- 10 Lam FM, Lau RW, Chung RC, Pang MY. The effect of whole body vibration on balance, mobility and falls in older adults: a systematic review and meta-analysis. *Maturitas*. 2012;72:206-213.
- 11 Hazell TJ, Thomas GW, Deguire JR, Lemon PW. Vertical whole-body vibration does not increase cardiovascular stress to static semi-squat exercise. *Eur J Appl Physiol*. 2008;104:903-908.
- 12 Hazell TJ, Lemon PW. Synchronous whole-body vibration increases  $\dot{V}_{O_2}$  during and following acute exercise. *Eur J Appl Physiol*. 2012;112:413-420.
- 13 Rittweger J, Beller G, Felsenberg D. Acute physiological effects of exhaustive whole-body vibration exercise in man. *Clin Physiol*. 2000;20:134-142.
- 14 Rittweger J, Schiessl H, Felsenberg D. Oxygen uptake during whole-body vibration exercise: comparison with squatting as a slow voluntary movement. *Eur J Appl Physiol*. 2001;86:169-173.
- 15 Rittweger J, Ehrig J, Just K, et al. Oxygen uptake in whole-body vibration exercise: influence of vibration frequency, amplitude, and external load. *Int J Sports Med*. 2002;23:428-432.
- 16 Rittweger J, Moss AD, Colier W, et al. Muscle tissue oxygenation and VEGF in VO-matched vibration and squatting exercise. *Clin Physiol Funct Imaging*. 2010;30:269-278.
- 17 Cochrane DJ, Sartor F, Winwood K, et al. A comparison of the physiologic effects of acute whole-body vibration exercise in young and older people. *Arch Phys Med Rehabil*. 2008;89:815-821.
- 18 Bogaerts AC, Delecluse C, Claessens AL, et al. Effects of whole body vibration training on cardiorespiratory fitness and muscle strength in older individuals (a 1-year randomised controlled trial). *Age Ageing*. 2009;38:448-454.
- 19 Vissers D, Baeyens JP, Truijien S, et al. The effect of whole body vibration short-term exercises on respiratory gas exchange in overweight and obese women. *Phys Sports Med*. 2009;37:88-94.
- 20 Yazar-Fisher C, Pascoe DD, Gladden LB, et al. Acute physiological effects of whole body vibration (WBV) on central hemodynamics, muscle oxygenation and oxygen consumption in individuals with chronic spinal cord injury. *Disabil Rehabil*. 2014;36:136-145.
- 21 Hazell TJ, Lemon PW. Synchronous whole-body vibration increases  $\dot{V}_{O_2}$  during and following acute exercise. *Eur J Appl Physiol*. 2012;112:413-420.
- 22 Lau RW, Yip SP, Pang MY. Whole-body vibration has no effect on neuromotor function and falls in chronic stroke. *Med Sci Sports Exerc*. 2012;44:1409-1418.
- 23 Pang MY, Lau RW, Yip SP. The effects of whole-body vibration therapy on bone turnover, muscle strength, motor function, and spasticity in chronic stroke: a randomized controlled trial. *Eur J Phys Rehabil Med*. 2013;49:439-450.
- 24 Hardie K, Hankey GJ, Jamrozik K, et al. Ten-year risk of first recurrent stroke and disability after first-ever stroke in the Perth Community Stroke Study. *Stroke*. 2004;35:731-735.
- 25 Lam SC, Wong YY, Woo J. Reliability and validity of the abbreviated mental test (Hong Kong version) in residential care homes. *J Am Geriatr Soc*. 2010;58:2255-2257.
- 26 Gowland C, Stratford PW, Ward M, et al. Measuring physical impairment and disability with the Chedoke-McMaster Stroke Assessment. *Stroke*. 1993;24:58-63.
- 27 Kiiski J, Heinonen A, Jarvinen TL, et al. Transmission of vertical whole body vibration to the human body. *J Bone Miner Res*. 2008;23:1318-1325.
- 28 Tomczak CR, Jelani A, Haennel RG, et al. Cardiac reserve and pulmonary gas exchange kinetics in patients with stroke. *Stroke*. 2008;39:3102-3106.
- 29 Nieman DC, Austin MD, Benezra L, et al. Validation of Cosmed's FitMate in measuring oxygen consumption and estimating resting metabolic rate. *Res Sports Med*. 2006;14:89-96.
- 30 Eng JJ, Chu KS, Dawson AS, et al. Functional walk tests in individuals with stroke: relation to perceived exertion and myocardial exertion. *Stroke*. 2002;33:756-761.
- 31 Borg G. Perceived exertion as an indicator of somatic stress. *Scand J Rehabil Med*. 1970;2:92-98.
- 32 Böhm M, Cotton D, Foster L, et al. Impact of resting heart rate on mortality, disability and cognitive decline in patients after ischaemic stroke. *Eur Heart J*. 2012;33:2804-2812.
- 33 Tesch PA. Exercise performance and beta-blockade. *Sports Med*. 1985;2:389-412.
- 34 Yoo J, Lim KB, Lee HJ, Kwon YG. Cardiovascular response during submaximal underwater treadmill exercise in stroke patients. *Ann Rehabil Med*. 2014;38:628-636.
- 35 Rimmer JH, Riley B, Creviston T, Nicola T. Exercise training in a predominantly African-American group of stroke survivors. *Med Sci Sports Exerc*. 2000;32:1990-1996.
- 36 Sage M, Middleton LE, Tang A, et al. Validity of rating of perceived exertion ranges in individuals in the subacute stage of stroke recovery. *Top Stroke Rehabil*. 2013;20:519-527.
- 37 Lythgo N, Eser P, de Groot P, Galea M. Whole-body vibration dosage alters leg blood flow. *Clin Physiol Funct Imaging*. 2009;29:53-59.
- 38 Kuys S, Brauer S, Ada L. Routine physiotherapy does not induce a cardiorespiratory training effect post-stroke, regardless of walking ability. *Physiother Res Int*. 2006;11:219-227.
- 39 MacKay-Lyons MJ, Makrides L. Cardiovascular stress during a contemporary stroke rehabilitation program: is the intensity adequate to induce a training effect? *Arch Phys Med Rehabil*. 2002;83:1378-1383.
- 40 Macko RF, Ivey FM, Forrester LW, et al. Treadmill exercise rehabilitation improves ambulatory function and cardiovascular fitness in patients with chronic stroke: a randomized, controlled trial. *Stroke*. 2005;36:2206-2211.
- 41 Globas C, Becker C, Cerny J, et al. Chronic stroke survivors benefit from high-intensity aerobic treadmill exercise: a randomized control trial. *Neurorehabil Neural Repair*. 2012;26:85-95.
- 42 Potempa K, Lopez M, Braun LT, et al. Physiological outcomes of aerobic exercise training in hemiparetic stroke patients. *Stroke*. 1995;26:101-105.
- 43 Lee MJ, Kilbreath SL, Singh MF, et al. Comparison of effect of aerobic cycle training and progressive resistance training on walking ability after stroke: a randomized sham exercise-controlled study. *J Am Geriatr Soc*. 2008;56:976-985.
- 44 Lennon O, Carey A, Gaffney N, et al. A pilot randomized controlled trial to evaluate the benefit of the cardiac rehabilitation paradigm for the non-acute ischaemic stroke population. *Clin Rehabil*. 2008;22:125-133.
- 45 Duncan P, Studenski S, Richards L, et al. Randomized clinical trial of therapeutic exercise in subacute stroke. *Stroke*. 2003;34:2173-2180.
- 46 Pang MY, Eng JJ, Dawson AS, et al. A community-based fitness and mobility exercise program for older adults with chronic stroke: a randomized, controlled trial. *J Am Geriatr Soc*. 2005;53:1667-1674.
- 47 Mead GE, Greig CA, Cunningham I, et al. Stroke: a randomized trial of exercise or relaxation. *J Am Geriatr Soc*. 2007;55:892-899.
- 48 Salbach NM, Brooks D, Romano J, et al. Cariorespiratory responses during cardiorespiratory responses during the 6-minute walk and ramp cycle ergometer tests and their relationship to physical activity in stroke. *Neurorehabil Neural Repair*. 2014;28:111-119.
- 49 Tang A, Sibley KM, Thomas SG, et al. Maximal exercise test results in subacute stroke. *Arch Phys Med Rehabil*. 2006;87:1100-1105.
- 50 Pang MY, Cheng AQ, Warburton DE, Jones AY. Relative impact of neuromuscular and cardiovascular factors on bone strength index of the hemiparetic distal radius epiphysis among individuals with chronic stroke. *Osteoporos Int*. 2012;23:2369-2379.
- 51 Pang MY, Ashe MC, Eng JJ. Tibial bone geometry in chronic stroke patients: influence of sex, cardiovascular health, and muscle mass. *J Bone Miner Res*. 2008;23:1023-1030.