Title: Cardiovascular Stress Induced by Whole-Body Vibration Exercise in Individuals with Chronic Stroke

Authors:

Lin-Rong Liao (MPT)[1,2], Gabriel Y.F. Ng (PhD)[2], Alice Y.M. Jones (PhD)[3], Marco Y.C. Pang (PhD)[2*]

Affiliations:

[1]Department of Physiotherapy, Guangdong Provincial Work Injury Rehabilitation Hospital, Guangzhou, CHINA

[2]Department of Rehabilitation Sciences, Hong Kong Polytechnic University, Hong Kong, CHINA

[3]School of Allied Health Sciences, Griffith University, AUSTRALIA

Running head: Whole body vibration and stroke

***Corresponding author:**

Marco Y.C. Pang

Department of Rehabilitation Sciences,
Hong Kong Polytechnic University,
Hung Hom, Hong Kong, China
Tel: +852-2766-7156
Fax: +852-2330-8656
E-mail: Marco.Pang@polyu.edu.hk

This is a pre-copyedited, author-produced version of an article accepted for publication in Physical Therapy following peer review. The version of record Lin-Rong Liao, Gabriel Y.F. Ng, Alice Y.M. Jones, Marco Y.C. Pang, Cardiovascular Stress Induced by Whole-Body Vibration Exercise in Individuals With Chronic Stroke, Physical Therapy, Volume 95, Issue 7, 1 July 2015, Pages 966–977 is available online at: https://doi.org/10.2522/ptj.20140295.

Funding: This study is substantially supported by the General Research Fund provided by the Research Grants Council (no. PolyU 5245/11E).

Conflict of interest: All authors declare no conflict of interest.

Abstract

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

Objective. To determine the acute effect of different WBV protocols on oxygen consumption (VO_2), heart rate (HR), rate of perceived exertion (RPE), blood pressure (BP), and rate-pressure product (RPP) during the performance of six different exercises among people with **chronic stroke (time since onset ≥6 months).**

Design. Repeated measures design.

Methods. Each of the 48 participants experienced all three WBV protocols in separate sessions: (1) no WBV, (2) low-intensity WBV [peak acceleration: 0.96 unit of gravitational constant (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.** VO_2, HR and RPE were measured throughout. BP and RPP were measured before and after each session.

Results. Low-intensity and high-intensity WBV induced significantly higher VO_2 by an average of 0.69 and 0.79ml/kg/min respectively ($P \leq 0.001$) than the control condition. These protocols also increased HR by an average of 4 beats per minute ($P \leq 0.05$). The two WBV protocols induced higher RPE than the control condition during static standing exercise only ($P \leq 0.001$). While the diastolic and systolic BP and RPP were increased at the end of each exercise session ($P \leq 0.001$), the addition of WBV had no significant effect on these variables ($P > 0.05$).

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

Conclusions. Addition of high- and low-intensity WBV significantly increased the VO_2 and HR, but the increase was modest. WBV thus should not pose any substantial cardiovascular hazard in people with chronic stroke.

Word count: 4421

Stroke is one of the most common debilitating conditions worldwide. People who survived a stroke may already have poor cardiorespiratory health prior to the stroke event, as cardiovascular disease and poor cardiorespiratory fitness are known risk factors for stroke.[1] 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.[2] Cardiorespiratory fitness in individuals with stroke, which is often reflected by the peak oxygen consumption rate (VO_{2peak}), has also been found to be as low as 50-80% of values reported among the age- and sex-matched physically inactive individuals,[3] and is far below the threshold for independent living (around 20 ml/kg/min).[4] Benefits of endurance exercise training to improve cardiovascular health outcomes in patients after stroke have been reported.[3,5-7] Exercising at 60-80% heart rate reserve (HRR) for 20-40 minutes per day for 3-5 days a week has been recommended for patients with mild to moderate stroke for improving cardiovascular fitness and walking endurance.[7]

Whole-body vibration (WBV) therapy has sparked tremendous research interest in the field of geriatric rehabilitation. As WBV can augment muscle activity,[8] it has been used to train different aspects of neuromuscular function, such as muscle strength/power, postural control, and mobility in the elderly.[9,10] The cardiovascular responses to WBV have also been studied in young healthy adults,[11-16] older adults,[17,18] women who are overweight[19] and people with spinal cord injury.[20] It has been demonstrated that among young healthy adults, the addition of WBV during exercise induced a significant increase in VO_2 and heart rate (HR).[14,21] On the other hand, Hazell et al.[11] demonstrated minimal cardiovascular stress (HR, blood flow, or mean arterial pressure) with the addition of WBV to a static semi-squat exercise. The choice of exercise mode (static Vs dynamic) and intensity may partially explain the discordance in results. There is also evidence that the cardiovascular response is influenced by the intensity of WBV.[15] The increased VO_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.[18] found that a 1-year WBV training program resulted in significantly more gain in VO_{2peak}, 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.[22,23] 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 the able-bodied group,[3,24] their cardiovascular responses to WBV may also differ. Examining the effects of WBV on acute cardiovascular responses is clinically important for two reasons. First, many individuals with stroke have a positive cardiovascular history, and are at risk of recurrent stroke and cardiovascular event.[24] 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 VO_2 and HR changes during WBV would help determine whether WBV is a useful adjunct treatment for cardiovascular exercise training. The specific objective of the current study was to determine the acute effect of different WBV protocols on the VO_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. It was hypothesized that the WBV intensity, exercises performed, and their interactions would significantly influence the above cardiovascular variables of interest.

Methods

Study design

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

Participants and sample size calculation

As no study had previously investigated the 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[21] reported that WBV (frequency: 45 Hz, peak-to-peak displacement: 2 mm) significantly increased VO_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 two groups had translated into a large effect size (Cohen's 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 ANOVA analysis (3 WBV conditions and 6 exercises), assuming a medium effect size (convention: f=0.25), with an alpha of 0.05, power of 0.9, an 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 ≥ 6 months), community-dwelling, Abbreviated Mental Test score ≥6,[25] and having hemiparesis in the lower extremity, as indicated by a composite leg and foot motor score of 13 or lower according to the Chedoke-McMaster Stroke Assessment (CMSA).[26] Exclusion criteria were cerebellar or brainstem stroke, neurological conditions in addition to stroke, serious heart conditions, vestibular dysfunctions, or other serious illnesses that affected performance of daily activities, having a cardiac pacemaker or stent.

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. All participants gave written informed consent prior to data collection.

WBV Protocol

All experiments were conducted in a research laboratory in the 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 20-55Hz with corresponding preset amplitudes.[22,23] The peak acceleration (a_{peak}), which represented the WBV intensity, was related to the amplitude (A) and frequency (f), and was calculated as: $a_{peak} = (2\pi f)^2 A$.[27] It is usually represented in units of gravitational constant (G) for easy comparison across studies. The peak acceleration values generated by the machine were validated by a tri-axial accelerometer (Model 7523A5, Dytran Instruments Inc., CA, USA).

As WBV frequencies of 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,[22,23] a frequency range of 20-30 Hz was chosen in the current study. Each participant underwent three different WBV conditions for measuring cardiovascular responses: (a) no WBV, (b) low-intensity WBV protocol (amplitude: 0.60mm, frequency: 20 Hz, peak acceleration: 0.96 G) (i.e. sub-gravity), and (c) high-intensity WBV protocol (0.44mm, 30 Hz, 1.61 G) (i.e., supra-gravity) while performing different exercises. **The three WBV conditions were tested separately on three different sessions, with a minimum of one rest day in between each session. To avoid order effect, the sequence of WBV conditions was decided randomly by drawing lots once at the beginning of the first session.**

Exercise protocol

In each session, the participants were instructed to perform six different exercises (Fig. 1). **Three of these exercises were static: (1) Static standing exercise (SSt) (Fig. 1A), (2) Static semi-squat (SSq) (Fig. 1B), (3) Static standing with weight shifted to paretic leg (SWS) (Fig. 1C). The other three were dynamic: (4) Dynamic semi-squat (DSq) (Fig.1D), (5) Dynamic side-to-side weight shifting (DWS)(Fig. 1E), and (6) Dynamic forward lunge (DFL) (Fig. 1F).** The exercises chosen were commonly used in previous WBV trials in different populations.[9,10 22,23] **The sequence of exercise performed was randomized by drawing lots from a box at the beginning of each session. There were six lots in total, with each lot containing the name of one of the six exercises. Therefore, the number of possible exercise sequences was 720. Figure 2 illustrates the flow of participants and path of testing.**

A steady state of VO_2 was reached in the third minute in most young healthy participants during these exercises.[14] Most people would also feel fatigue if a longer period was used and no change in posture was allowed.[15] It has also been reported that VO_2 would reach a plateau within 3 minutes in people with stroke at a given workload.[28] Thus, the duration of 3 minutes was chosen for each exercise in the current study. The dynamic exercises (Fig.1D-F) were performed in cycles of 3 seconds (i.e., 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 VO_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 VO_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 360º ISOM Goniometer, Fabrication Enterprises, White Plains, New York, USA) 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 patients 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 50-60 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 mmHg) and rate-pressure product (RPP), rate of perceived exertion (RPE), VO_2 (ml/kg/min), and HR (beats per minute or bpm). A full-face mask and HR monitor (Polar®, Tampere, Finland) were worn by participants throughout the testing sessions, as VO_2 and HR were continuously measured by a portable metabolic system (FitMate™ Pro, Cosmed, Rome, Italy). Previous research showed that the FitMate system was a reliable and valid system for measuring VO_2 during graded exercise.[29] In addition, our pilot study found that the reliability of the FitMate system was good when used in people with stroke [intraclass correlation coefficients ($ICC_{3,1}$) = 0.80 (static exercise), and 0.91 (dynamic exercise)]. The system was also calibrated according to the manufacturer's guidelines prior to each testing session. **The last 30 seconds of VO_2 (ml/kg/min) and HR (beats per minute) data during the 3-minute exercise period was averaged to obtain the mean value for analyses.[18,21]** A similar data processing approach was also used by Cochrane et al.[17]

SBP and DBP (in mmHg) were recorded (BPM I, Manning, Hong Kong) before and at the end of each session. The RPP was calculated as: (HR × SBP)/100.[30] Verbal RPE (from 6 to 20 according to the Borg's Scale)[31] was also asked at the beginning and at 1-minute intervals during each set of exercise. **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.[31]

At the beginning of the second and third session, 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 carryover effect from the previous session had subsided.

Statistical Analysis

Statistical analysis was performed with IBM SPSS Statistics software (version 20.0, IBM, Armonk, NY, USA). **The duration of the washout period (measured in number of days) between testing session 1 and 2 was compared with that between testing session 2 and 3 using paired t-test. Two-way ANOVA with repeated measures [within-subject factors: 1. intensity (no WBV, low- and high-intensity WBV); and 2. time (before and after session)]**

was used to assess the difference in mean DBP, SBP, and RPP between pre- and post-session performance within each of the three sessions, and at corresponding times between the three sessions. The intensity × time interaction term determined whether changes observed between the beginning and end of each session were consistent among the three sessions, that is, whether the three WBV protocols were associated with different within-session responses.

Another two-way ANOVA with repeated measures model [within-subject factors: 1. intensity (no WBV, low- and high-intensity WBV); and 2. six exercises] was used to **assess the mean VO_2 and HR between exposure to three different WBV protocols and among the six exercises. The intensity × exercise interaction effect determined whether the changes in VO_2 and HR responses induced by WBV were exercise-dependent.** 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 three WBV protocols were tested using the Friedman test, followed by pairwise 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 post-session score. For VO_2 and HR data, the change score (before and after each exercise) was obtained from subtracting the baseline score from the post-exercise score (i.e., average of the last 30 seconds of the trial). Pearson's 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.**

Results

Characteristics of participants

A total of 48 participants (36 men and 12 women; mean age: 56.3 ±10.1 years) completed all assessments (Fig.2). Participant characteristics are presented in Table 1. The median composite leg 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 VO_2 ($P=0.69$) and HR ($P=0.93$). **The baseline HR values of the three sessions were thus averaged to obtain the mean resting HR for each participant. It was found that 13 (27.1%) of our participants had a mean resting HR of ≥77 bpm, whereas only six (12.5%) had a mean resting HR of ≤64 bpm. A previous study in stroke found that a resting HR of ≥77 bpm was significantly associated with increased rate of vascular death, compared with those with their counterparts with resting HR of ≤64 bpm.[32]**

Washout period

On average, the washout period between session 1 and 2 was 1.4 days (SD=0.6 days, range =1-3 days), which was similar to that between session 2 and 3 (mean=1.3 days, SD=0.6 days, range=1-3 days) (*P*=0.73). 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, $P \leq 0.001$), SBP ($F_{1,47}$=29.91, $P \leq 0.001$) and RPP ($F_{1,47}$=17.19, $P \leq 0.001$) 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 post-exercise was not significantly different from that at baseline after Bonferroni adjustment (P>0.017) (Table 2, Figure 3A).** The main effect of WBV intensity, and intensity × time interaction were not statistically significant for DBP, SBP and RPP ($P>0.05$).

The pooled RPE data are shown in Figure 4A. Out of the 288 exercise trials for each WBV protocol (6 exercises × 48 participants), only 2% (2 participants, 6 trials), 6% (3 participants, 17 trials), and 5% (4 participants, 15 trials) reported a RPE >15 for no-WBV, low- and high-intensity WBV sessions, respectively. **The low-intensity WBV protocols (Z =-4.43, $P<0.001$) and high-intensity WBV protocols (Z =-3.70, $P<0.001$) significant induced higher perceived effort than no WBV condition during static standing exercise. For the rest of the exercises, the RPE value demonstrated no significant differences among the three WBV protocols ($P>0.05$).**

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.

VO_2 changes

An overall significant main effect of WBV intensity ($F_{2,94}$=16.98, $P \leq 0.001$) and exercise ($F_{5,235}$=29.85, $P \leq 0.001$) was found (Fig.4B). The intensity × exercise interaction effect, however, was not significant ($F_{10,470}$=1.32, P =0.25). **Contrast analysis revealed that overall, both the low-intensity and high-intensity WBV protocols induced significantly higher VO_2 than the control condition, by an average of 0.69 ml/kg/min (95%CI: 0.35, 1.03; $P \leq 0.001$) and 0.79 ml/kg/min (95%CI: 0.45, 1.14; $P \leq 0.001$) respectively (Table 2).** Post-hoc analysis further showed that the increase in VO_2 induced by the two 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 VO_2 value between the low- and high-intensity WBV protocols was not significant in any of the exercises after Bonferroni adjustment (P=1.00) (Table 2). *Post hoc* analysis of the effect of exercises showed that the static standing and static standing with weight-shifted to the paretic leg resulted in significantly lower VO_2 than that measured during other exercises (P<0.01). On the other hand, VO_2 during dynamic semi-squat and dynamic forward lunge was significantly higher than that during other exercises (P<0.01) (Fig.4B).

HR changes

There was an overall significant main effect of WBV intensity ($F_{2,94}$=4.63, P=0.01) and exercise ($F_{5,235}$=32.67, $P \leq 0.001$) (Fig.4C). The intensity × exercise interaction effect was also significant ($F_{10,470}$=2.94, P=0.01). **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=0.01). The HR was also increased by the addition of high-intensity (mean difference: 4 bpm; 95%CI: 0, 7), but the result was marginally significant (P=0.05)(Table**

2). The difference in HR was not significant between the low- and high-intensity WBV protocols (*P*=1.00) (Table 2). The increase in HR induced by low-intensity WBV remained significant for static standing (*P*≤0.001), and dynamic semi-squat (*P*≤0.001) exercises only after Bonferroni adjustment. Regarding the main effect of exercise, static standing induced significantly lower HR than other exercises (*P* <0.01) while the HR response during the dynamic semi-squat exercise was significantly higher than that during other exercises (*P* <0.01) (Fig.4C).

To determine the exercise intensity during different WBV conditions, the age-predicted maximal HR (HR_{max}) formula was used to estimate of the individual's HR_{max} [220 – age]; for participants on beta-blockers (n=11), the formula was modified to 70% [208 - (0.7× age)].[33] Results of this study showed that, of the 288 exercise trials for each WBV protocol, only 23%, 29%, and 25% achieved the age-predicted HR_{max} at 64% (i.e., moderate intensity)[7] or above for the no-WBV, low-intensity WBV, and high-intensity WBV conditions respectively.

Association with baseline values

Baseline SBP (r=-0.57, P<0.001), DBP (r=-0.42, P=0.01) and RPP (r=-0.50, *P*<0.001) were significantly correlated with their corresponding within-session change scores for the high-intensity protocol. The baseline SBP (r=-0.43, *P*=0.01) and RPP (r=-0.39, *P*=0.01) were also correlated with their respective change scores for the low-intensity protocol.

Out of 18 different WBV intensity and exercise combinations (3 protocols × 6 exercises), baseline VO_2 was only significantly correlated with the change score during SSq (r =-0.43, P=0.01) and SWS exercises (r=-0.33, P=0.02) 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 VO_2 and HR, but the increase was modest.

Is WBV exercise training safe for individuals with stroke?

WBV is gaining popularity in stroke rehabilitation for enhancing neuromuscular function.[22,23] 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 increase in DBP (<5mmHg) and SBP (<8mmHg) (Table 2). The upper bound of the 95%CI for these variables did not even exceed 8mmHg and 12mmHg respectively. This was much lower than the increase 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 mmHg, DBP: 21.0mmHg).[34]** Our results thus generally agree with previous studies in young and older adults that WBV did not induce major changes in BP.[11,17]

RPP is an estimate of myocardial oxygen consumption and gives an indication of the amount of oxygen demanded by the heart.[30] While the RPP was significantly increased at the end of each exercise session, the WBV intensity × time interaction effect were not significant, indicating that the myocardial oxygen demand during different exercises was similar regardless of whether WBV was added.

Rimmer et al.[35] reported that if the RPP is higher than 200, the patient is not suited to exercise. In the current study, the mean post-exercise RPP for the low- and high-intensity WBV sessions was 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.[36] Even when low- and high-intensity WBV was 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 (RPP: mean=144, SD=33; RPE: mean=11.6, SD=3.2) in people with chronic stroke previously reported by Eng et al.[31] 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 participants requested to terminate the exercise sessions, suggesting that the WBV protocols used in the current study were safe and well tolerated.

It was found that higher baseline BP and RPP values had fair to moderate relationships (r=-0.4 -0.6) with ***smaller*** **increase in the same variables after the WBV exercise sessions. WBV exercise thus did not pose disproportionally higher cardiovascular stress to those 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 VO_2 (by 0.7-0.8 ml/kg/min, upper bound of 95%CI=1.2ml/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.[8] **Our results thus**

concurred with previous studies, which also reported that the increase in VO_2 and HR during WBV exercise was modest in younger adults,[13,14,21] and older adults.[17,18]

The WBV intensity × exercise interaction effect for VO_2 was not significant, since the WBV-induced increase in VO_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 and exercise interaction effect was significant for the HR response, indicating that the WBV-induced increase in HR at various intensities was dependent upon the exercise. Adding WBV led to significant increase in HR during static standing and dynamic semi-squat but not other exercises (Fig.4C), thereby contributing to the interaction effect. The discordance between the results on VO_2 and HR may indicate that increase in VO_2 could not be solely explained by increase in HR. Possible mechanisms may include increase in stroke volume, muscle blood flow velocity and volume, increased utilization of oxygen by exercising muscles,[37] and will require further investigation.

The exercise intensities of most WBV trials were generally low (<64% 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%HRmax or 40% HR reserve),[38] which were considered to be ineffective in inducing a cardiovascular training effect.[7,38-40] The training intensities, even after addition of WBV, were much lower than those reported in aerobic exercise training using a treadmill[40,41], cycle ergometer[42-44], or a combination of strengthening and aerobic activities, which often involved a training intensity of 60-80% HR reserve.[7,45-47] The training intensities achieved during WBV exercises were also considerably lower than that during the Six Minute Walk Test among people with chronic stroke, which could reach 80%- 85% of the VO_{2peak}.[48] Our finding is thus in accord with Cochrane et al.,[17] who found that the estimated percentage VO_{2peak} achieved during static squat exercise with WBV was only at 24%, and would not be sufficient to enhance aerobic capacity.[17] However, it is acknowledged that using the age to predict the maximal HR may not be ideal. In fact, it has been reported that the maximal HR achieved during a symptom-limited exercise test is significantly lower than the age-predicted maximal HR in people with stroke.[49]

Interestingly, Bogaerts et al.[18] showed that their 1-year WBV training protocol had significantly improved the peak VO_2 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, amplitude: high 5mm/low 2.5mm), which may partially explain why they were able to raise the HR to about 62%-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.[50,51] The fact that we did not use WBV of higher intensities may also partially explain the lack of difference in VO_2 and HR between the low-intensity and high-intensity WBV protocols (Table 2).

Based on the resting HR data, the cardiovascular health of 27% of our participants could be considered poor, as **Bohm et al.[32] showed that people with stroke who had a resting HR of ≥77 bpm had a significantly higher risk of vascular death compared to those with resting HR in the lowest quintile (≤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 VO_2 and change in VO_2, the relationship was only fair**

(r<0.5). Taken together, the HR and VO_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

Firstly, since all of our participants are ambulatory and community dwelling, the results are **only** generalizable to people with similar characteristics as our participants. Secondly, we studied the effects of the overall intensity of WBV (indicated by peak acceleration) on cardiovascular parameters. Other variables (e.g. WBV frequency, amplitude) may exert independent cardiovascular effects. We also did not measure BP before and after each individual exercise. Thirdly, only a rhythm of 20 repetitions per minute was used during the dynamic exercises. While higher movement frequencies may elicit more impressive VO_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 patients 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 the individual was on medications. A symptom-limited exercise test was not conducted, the individual's actual HR_{max} and VO_{2peak}, and thus appropriate target exercise HR (or VO_2), was 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 will require further investigation.**

Conclusions

This study suggested that in individuals with chronic stroke, VO_2 and HR increased modestly with 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.

Acknowledgment The work described in this paper was substantially supported by a grant from the Research Grants Council of the Hong Kong Special Administrative Region, China (Project No. PolyU 5245/11E).

References

1 Agabiti-Rosei E, Muiesan ML. Carotid atherosclerosis, arterial stiffness and stroke events. *Adv Cardio*. 2007;l 44:173-186.

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 MYC, 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 MYC, 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 MYC, 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 MYC, Charlesworth SA, Lau RWK, Chung RCK. 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 FMH, Pang MYC, Jones AYM, Ng GYF. Leg muscle activity during whole-body vibration in individuals with chronic stroke. *Med Sci Sports Exerc*. 2014;46:537-545.

9 Lau RWK, Liao L-R, Yu F, Teo T, Chung RCK, Pang MYC. 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 FMH, Lau RWK, Chung RCK, Pang MYC. 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 VO_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, Mutschelknauss M, Kirsch KA, Felsenberg D. 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, Stewart C, Degens H. 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, Stannard SR, Narici MV, Rittweger J. 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, Troosters T, Boonen S, Verschueren SM. 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, Truijen S, Ides K, Vercruysse CC, Van Gaal L. 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 Yarar-Fisher C, Pascoe DD, Gladden LB, Quindry JC, Hudson J, Sefton J. 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 and Lemon PW. Synchronous whole-body vibration increases VO_2 during and following acute exercise. *Eur J Appl Physiol*. 2012;112:413-420.

22 Lau RWK, Yip SP, Pang MYC. Whole-body vibration has no effect on neuromotor function and falls in chronic stroke. *Med Sci Sports Exerc*. 2012;44:1409-1418.

23 Pang MYC, Lau RWK, 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, Broadhurst RJ, Anderson C. 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 P, 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, Kannus P, Sievanen H. 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, Haykowsky MJ, Welsh R, Manns PJ. 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, Kim CM, Hepburn KE. 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, im K-B, Lee H-J, Kwon Y-G. 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, Sibley KM, Brooks D, McIlroy W. 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;11219-27.

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, Zeman B, Lord SR, Raymond J, Davis GM: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, Stephenson J, Blake C. 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, McKay HA, Dawson AS. 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;5:892-899.

48 Salbach NM, Brooks D, Romano J, Woon L, Dolmage TE. 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, McIlroy WE, Brooks D. Maximal exercise test results in subacute stroke. *Arch Phys Med Rehabil*. 2006;87:1100-1105.

50 Pang MYC, Cheng AQ, Warburton DE, Jones AYM. 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.

Table 1. Characteristics of study participants (n=48)

Variable	**Value**[*]
Basic demographics	
Age, years, mean (mean±SD)	56.3 ±10.1
Sex, men/women (n)	36/12
Body mass index (kg/m^2) (mean±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
Stroke characteristics	
Post-stroke duration, years (mean±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) (mean±SD)	9.3±0.9
Co-morbid conditions	
Hypertension (n)	14
Diabetes mellitus (n)	9
High cholesterol (n)	20
Medications	
Antihypertensive agents	
Beta-blockers (n)	11
Calcium channel blockers (n)	5
Angiotensin converting enzyme inhibitors (n)	8
Angiotensin II receptor antagonists (n)	1
Adrenergic receptor blockers (n)	1
Others, n	8
Hypolipidemic agents (n)	20
Antidiabetic agents (n)	9
Baseline VO_2 and HR data	
Baseline VO_2 (ml/kg/min) (mean±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 (beats per minute) (mean±SD)	
No-WBV session	76.3±11.7
Low-intensity WBV session	77.6±13.3
High-intensity WBV session	76.9±13.6

[*] Mean±SD presented for continues variables.

[†] CMSA: Chedoke-McMaster Stroke Assessment; HR: heart rate; IQR: interquartile range; n: number count; SD: standard deviation; VO_2: oxygen consumption; WBV: whole-body vibration

Table 2. The effect of whole-body vibration (WBV) intensity on outcome measurements

	WBV intensity × time interaction effect		Main Effect of WBV intensity		Main effect of time		Post-hoc analysis (within-session difference for each WBV protocol)					
							No WBV condition Pre-test Vs Post-test		Low-intensity WBV Pre-test Vs Post-test		High-intensity WBV Pre-test Vs Post-test	
Variable	**F**	**p-value**	**F**	**p-value**	**F**	**p-value**	**Mean difference[‡] (95% CI)**	**p-value**	**Mean difference (95% CI)**	**p-value**	**Mean difference (95% CI)**	**p-value**
DBP[§]	0.95	0.39	0.46	0.61	24.10	≤0.001*	3.3 (1.1, 5.5)	0.01[†]	4.6 (2.0, 7.2)	≤0.001[†]	2.3 (1.1, 4.6)	0.04
SBP	0.05	0.95	0.90	0.41	29.91	≤0.001*	6.4 (2.8, 10.1)	≤0.001[†]	7.2 (3.3, 11.1)	≤0.001[†]	6.6 (3.0, 10.3)	≤0.001[†]
RPP	0.24	0.76	0.56	0.57	17.79	≤0.001*	5.9 (2.0, 9.9)	0.01[†]	7.6 (2.9, 12.3)	0.01[†]	6.8 (2.4, 11.1)	0.01[†]
	WBV Intensity × exercise interaction effect		**Main Effect of WBV intensity**		**Main effect of exercise**		**Post-hoc contrast analysis (main effect of intensity)**					
							No WBV Vs Low-intensity WBV		**No WBV Vs High-intensity WBV**		**Low-intensity Vs High-intensity WBV**	
Variable	**F**	**p-value**	**F**	**p-value**	**F**	**p-value**	**Mean difference (95% CI)**	**p-value**	**Mean difference (95% CI)**	**p-value**	**Mean difference (95% CI)**	**p-value**
VO$_2$	0.25	0.25	16.98	≤0.001*	29.85	≤0.001*	0.7 (0.4, 1.0)	≤0.001*	0.8 (0.5, 1.2)	≤0.001*	0.1 (0.3, 0.5)	1.00
HR	2.94	0.01*	4.63	0.01*	32.67	≤0.001*	4 (1, 7)	0.01*	4 (0, 7)	0.05	0 (-4, 4)	1.00

*Statistically significant ($P \leq 0.05$)

[†] Statistically significant ($P \leq 0.017$)

[‡] A positive mean difference indicates that the mean value of the latter group is higher than that of the former group.

[§] HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; RPP: rate-pressure product; VO$_2$: oxygen consumption

Legends

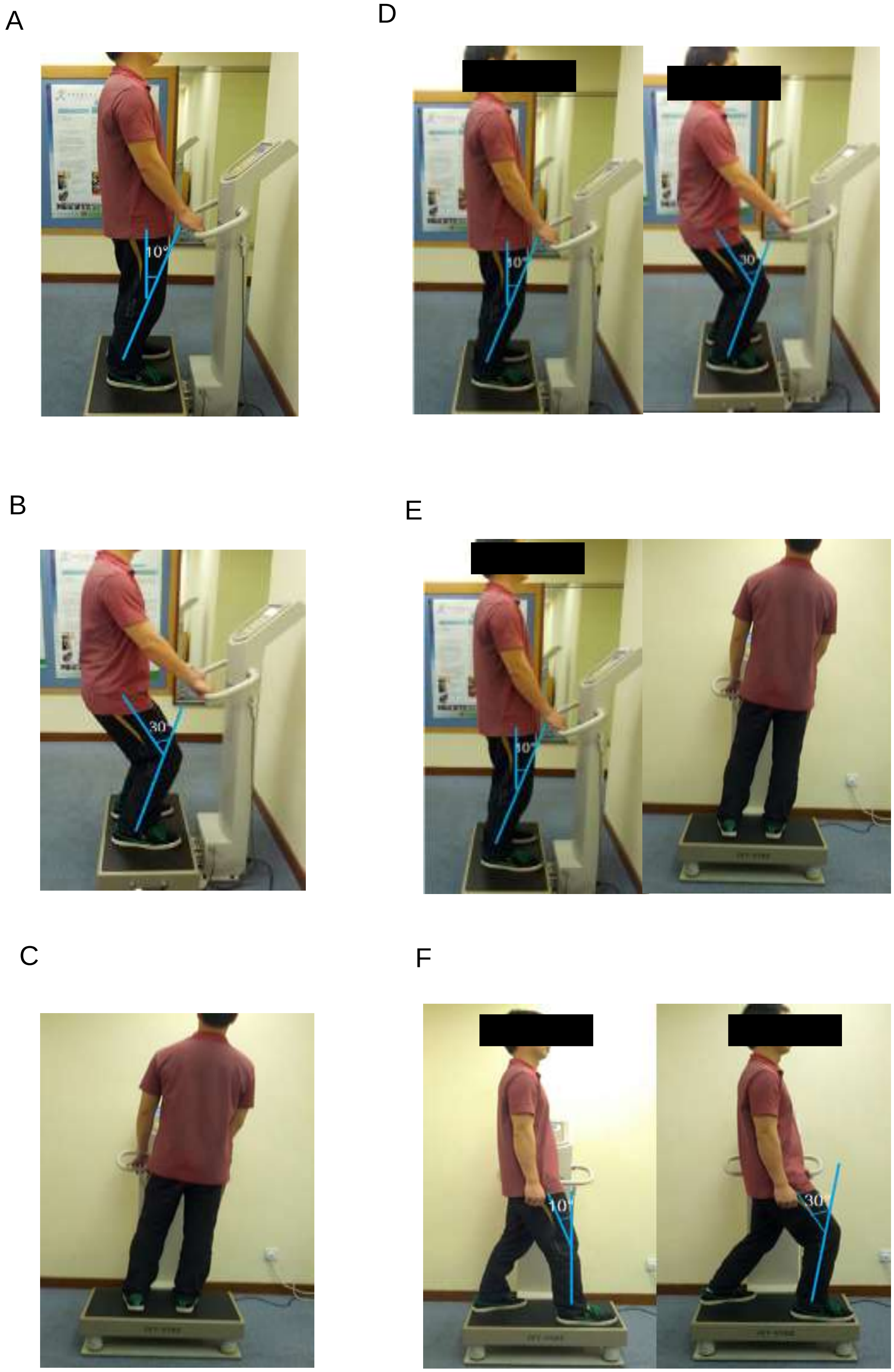
Figure 1. Exercise protocol. (A) Static standing exercise (SSt): standing on the platform with feet placed apart at shoulder width and knees slightly flexed at 10º, and hold for 3 minutes. (B) Static semi-squat (SSq): Standing on the platform with feet placed apart at shoulder width and knees flexed at 30º, and hold for 3 minutes. (C) Static standing with weight shifted to paretic leg (SWS): Standing with body weight shifted to the paretic leg as much as possible and hold for 3 minutes. (D) Dynamic semi-squat (DSq): Starting position same as in static standing exercise (left), then bending knees to achieve the semi-squat position (right), and return to starting position, and repeat at a rate of 20 cycles per minute for 3 minutes. (E) Dynamic side-to-side weight shifting (DWS): 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 non-paretic leg. Repeat at a rate of 20 cycles per minute for 3 minutes. (F) Dynamic forward lunge (DFL): Standing in a forward lunge position with the paretic leg placed in front of the non-paretic leg with paretic knee flexed at 10º, then learning forward and shifting body weight onto the paretic leg as much as possible with knee flexed at 30 º, and then moving back to the starting position. Repeat at a rate of 20 cycles per minute for 3 minutes

Figure 2. Study flow chart. Each participant underwent 3 experimental sessions. **The sequence of 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 was also randomized by drawing lots.** A total of 48 participants with chronic stroke completed all assessment procedures.

Figure 3. Effect of whole-body vibration on blood pressure and rate-pressure product. The average systolic blood pressure (DBP) (Fig.3A), systolic blood pressure (SBP) (Fig.3B) and rate pressure product (RPP) (Fig.3C) recorded at baseline (black bars) and immediately after each exercise session (gray bars). The error bars represent 1 SD from the mean. Significant difference from baseline was indicated by *. **The within-session differences in DBP, SBP and RPP did not themselves differ between the three WBV protocols, as evidence by the non-significant time × protocol interaction.**

Figure 4. Effect of whole-body vibration on rate of perceived exertion, oxygen consumption and heart rate. **Fig. 4A shows the boxplot 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, whereas the upper and lower borders of the box define the interquartile range. The vertical bars represent data up to 1.5 times the interquartile range extending from the upper and lower border of the box. The VO_2 (Fig. 4B) and HR (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 no-WBV, low-intensity WBV and high-intensity WBV exercise sessions is represented by white, gray, and dotted boxes/vertical bars, respectively. Significant difference from the no-WBV condition was indicated by *. **The RPE level was significantly higher in the low-intensity and high-intensity WBV conditions than the no-WBV condition during static exercise only.** WBV induced a significant increase in VO_2. Adding WBV also led to significant increase in HR in static standing and dynamic semi-squat exercises.

Fig. 1 Exercise protocol.



[redacted]
[redacted]
[redacted]
[redacted]
[redacted]

Fig. 2 Study flow chart.

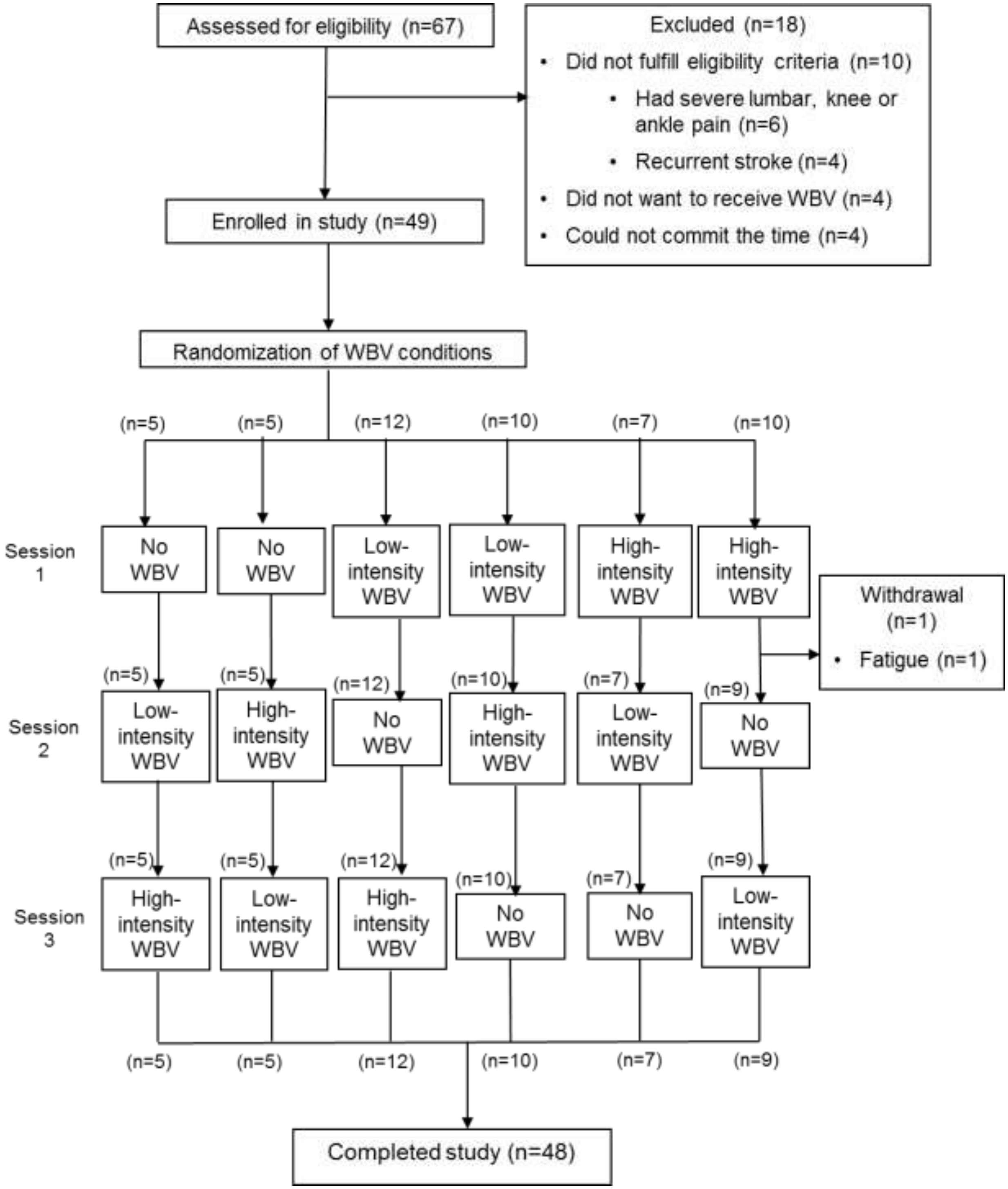


Fig. 3 Effect of whole-body vibration on blood pressure and rate-pressure product.

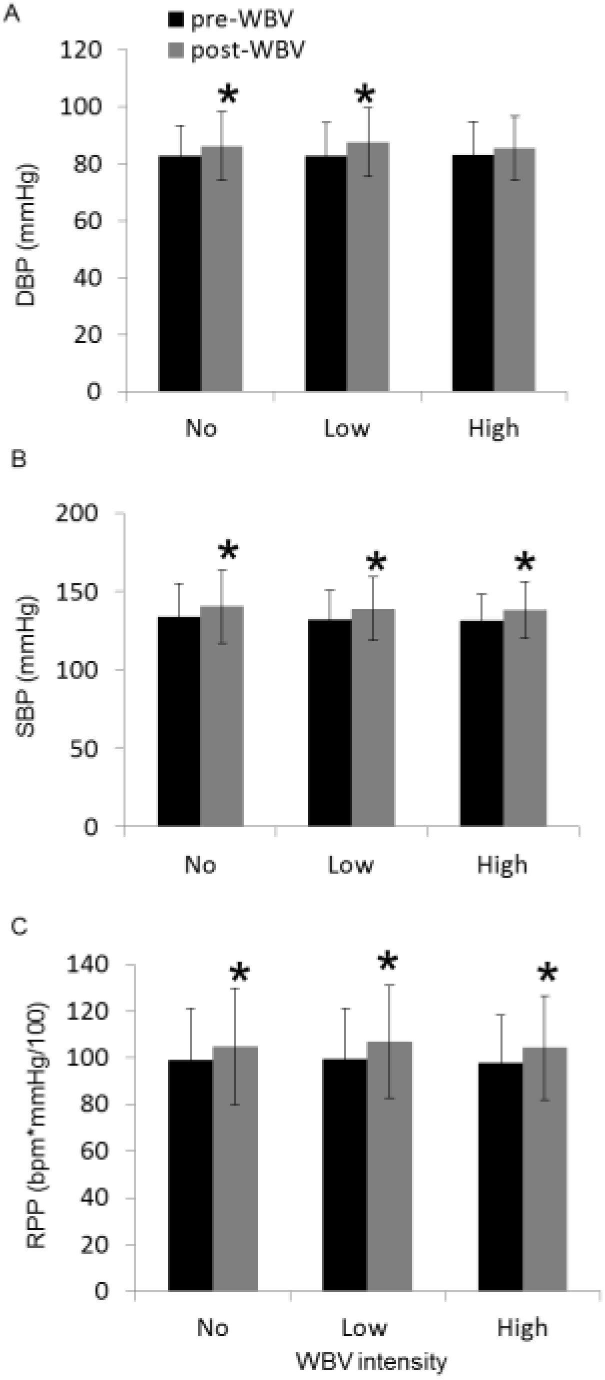


Fig. 4 Effect of whole-body vibration on rate of perceived exertion, oxygen consumption and heart rate.