Title: Different Whole-Body Vibration Intensities in Stroke: Randomized Controlled Trial

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ABSTRACT

Purpose: Whole body vibration (WBV) has become an increasingly common adjunct treatment in rehabilitation of people with chronic neurological conditions. No study, however, has compared the effects of different WBV training intensities in people with stroke. A single-blinded randomized controlled study was conducted to investigate the effects of different WBV intensities on body functions/structures, activity and participation in individuals with stroke. **Methods:** 84 people with chronic stroke (mean age: 61.2 years, SD: 9.2) were randomly assigned to the low-intensity WBV, high-intensity WBV, or control groups. Outcome measurements included knee muscle strength (isokinetic dynamometry), spasticity at the knee and ankle joints (Modified Ashworth Scale, MAS), balance (Mini Balance Evaluation Systems Test, Mini-BESTest), mobility (Timed-Up-and-Go test, TUG), endurance (6-Minute Walk Test, 6MWT), balance self-efficacy (Activities specific Balance Confidence scale, ABC), participation in daily activities (Frenchay Activity Index, FAI), perceived environmental barriers (Craig Hospital Inventory of Environmental Factors, CHIEF), and quality of life (Short-Form 12 Health Survey, SF-12). The assessments were performed at baseline, and immediately after the 10-week intervention period. **Results:** Intention-to-treat analysis revealed a significant time effect for muscle strength, TUG, distance and oxygen consumption rate achieved during 6MWT, Mini-BESTest, ABC, and the SF-12 physical composite score domain in all three groups after the 10-week treatment period ($P<0.05$). However, the time by group interactions effects were not significant for any of the outcome measures ($P>0.05$). **Conclusions:** The addition of the 10-week WBV paradigm to the leg exercise protocol was no more effective in enhancing body functions/structures, activity and participation than leg exercises alone in community-dwelling people with stroke who sustained mild to moderate motor impairments.

Key Words: cerebrovascular accident; whole body vibration; rehabilitation; exercise; hemiparesis

INTRODUCTION

Paragraph Number 1 Stroke is one of the most common leading causes of long-term disability and is a major public health issue (9). Stroke can result in problems across multiple functional domains, such as body functions/structures (e.g., muscle weakness, spasticity, balance deficit, etc.), activity (e.g., walking, transfers), and participation (engagement in community activities) according to the International Classification of Functioning, Disability and Health (ICF) (40). Therefore, considerable research efforts have been made to identify effective intervention strategies to counteract the deleterious health consequences after stroke.

Paragraph Number 2 Whole-body vibration (WBV) therapy, in which vibratory signals are delivered to the human body through a vibration platform, has gained increasing attention in neurorehabilitation. WBV has been consistently shown to augment muscle activity during exercise in healthy adults (1). There is also some evidence that it could improve muscle strength and certain balance and mobility functions in older adults (17,18). Considering that people with neurological conditions have similar problems with physical functioning, it has been postulated that WBV could also benefit people with neurological disorders. Indeed, some preliminary studies have investigated the potential therapeutic value of WBV in people with various neurological conditions, including spinal cord injury, multiple sclerosis, Parkinson's disease, and cerebral palsy (6). Recent studies have demonstrated that adding WBV can increase the level of muscle activation during exercise in individuals with stroke, as measured by surface electromyography (EMG) (21,23). A number of research studies have examined the efficacy of WBV in people with stroke, with mixed results (5,19,26,31,35). A recent systematic review of randomized controlled trials (RCTs) suggested that there was limited evidence to support or refute the notion that adding WBV to exercise confers additional benefits, mainly due to the limited number of studies (nine trials only) and their methodological weaknesses (only two of the trials provided level 1 evidence) (20). Moreover, the studies used diverse WBV protocols, and none of them compared the effects of the different WBV protocols, making it difficult to make meaningful comparisons across studies. For example, it remains uncertain which WBV intensities are more effective in improving various health outcomes post-stroke (17,18). Another major limitation of the previous WBV trials is the relative lack of activity and participation outcomes. As mentioned, the health consequences of stroke are multi-dimensional, which should be taken into consideration when selecting outcome measures (36). Therefore, the framework of this study was constructed based on the ICF model (40) by incorporating outcomes at the body functions/structures, activity and social participation levels so as to provide a more comprehensive picture of the therapeutic value of the experimental intervention.

Paragraph Number 3 The objective of this RCT was to investigate the effects of different WBV intensities on body functions/structures, activity and social participation in community-dwelling individuals with chronic stroke. It was hypothesized that 1) adding WBV to exercise training would lead to significantly greater improvements in body functions/structures, activity and perceived participation compared with the same exercise training without WBV; and 2) the high-intensity protocol would induce significantly more gain in the same outcomes compared with the low-intensity protocol.

METHODS

Design

Paragraph Number 4 The present investigation was a single-blinded RCT, in which the assessor was blinded. The study was registered at ClinicalTrials.gov (NCT01822704).The reporting of this WBV clinical trial is in accordance with the recommendations of the International Society of Musculoskeletal and Neuronal Interactions (34).

Participants and sample size

Paragraph Number 5 The study was conducted at a research laboratory at the University. The inclusion criteria were: diagnosis of hemispheric stroke with onset more than 6 months at the time of enrolment, age ≥ 18 years, community-dwelling, a score of 6 or above on the Abbreviated Mental Test (AMT) (2), and the ability to stand with or without aid for more than 90 seconds. Patients were excluded if any of the following conditions were present: brainstem or cerebellar stroke; other neurological disorders (e.g., spinal cord injury), neoplasms, severe cardiovascular diseases (e.g., a pacemaker, uncontrolled hypertension), pain that affected the ability to participate in physical activities, pregnancy, vestibular conditions, recent fractures or metal implants in the lower limbs, or other serious medical problems.

Paragraph Number 6 The sample size was estimated based on evidence from previous WBV studies that investigated the leg extensor EMG activity during WBV in individuals with stroke (21), using G Power 3.1 software (Universitat Dusseldorf, Germany). Liao et al. (21) demonstrated that WBV training induced significantly higher levels of muscle activity in the paretic leg, with effect sizes (f) of 0.46-0.93 (i.e., large effect sizes). To be more conservative, a medium effect size was assumed (convention: f=0.25). Based on a 2 × 3 analysis of variance (ANOVA) model with repeated measures, with an alpha value of 1% and power of 80%, the minimum sample size required to detect a significant group by time interaction effect would be 21 subjects in each group (total of 63 participants). We used a more stringent alpha value because of the inflated probability of making a type I errors due to multiple testing. To account for a 15% attrition rate, we aimed to recruit a minimum of 75 participants (25 subjects per group).

Paragraph Number 7 Written informed consent was obtained from all subjects. The principles of the Declaration of Helsinki were followed, and the study was approved by the Human Research Ethics Review Subcommittee of the Hong Kong Polytechnic University.

Recruitment and randomization

Paragraph Number 8 The recruitment of participants took place from February 2013 to February 2014 in the Hong Kong Stroke Association. After the eligibility was confirmed, the participants were then randomized into the low-intensity WBV group (LWBV), high-intensity WBV group (HWBV), or control group (CON) using a 1:1:1 allocation ratio (Figure 1). To ensure concealed allocation, the subjects were randomly assigned to the groups using sealed opaque envelopes distributed by an 'off-site' researcher who was not involved in the recruitment of participants, provision of exercise training, or measurement of outcomes. The last participant completed the post-intervention assessment on May 20, 2014.

Interventions

Paragraph Number 9 All participants were given WBV exercise training 3 times a week for 10 weeks (i.e., 30 sessions). A minimum one-day rest period was scheduled between training sessions. Extra sessions for missed appointments were arranged to ensure that all participants completed all 30 sessions. All exercise training took place in the same research laboratory of the University. The exercise sessions for the 3 groups took place at different times of the day, so that the participants from one treatment group could not observe what the other groups were engaging in. Each exercise session began with 10 minutes of warm-up exercises and ended with 10 minutes of cool-down exercises (general stretching exercises in a sitting position and exercise using a cycle ergometer).

Paragraph Number 10 Participants in the LWBV group (n = 28) and HWBV group (n = 28) received their exercise training on a WBV platform that delivered synchronous WBV (Gymna Fitvibe Medical System, Gymna Uniphy Pasweg, Bilzen, Belgium). The choice of WBV and exercise protocols (Table 1) was adapted from a previous study that examined muscle activity during WBV exposure among individuals with stroke (21). In that study, WBV intensities similar to our LWBV protocol induced significantly higher leg muscle activity compared with the control condition (21). The highest level of muscle activity was attained during deep-squat, semi-squat, forward and backward weight-shift exercises in the leg muscles (21). Therefore, these exercises were chosen in this study to optimize the activation of major leg muscle groups in our participants (Table 1). A combination of dynamic and static exercises was included in the training protocol (Table 1), as daily activities involve both static (isometric) and dynamic muscle work. Similar exercises have been used in previous WBV studies in people with stroke or other patient populations (19,31,35,38).

Paragraph Number 11 The dynamic exercises (Exercises 1-3 in Table 1) were performed in cycles of 3 seconds with 20 repetitions per minute. A metronome was used to pace the participants in performing the exercises at the desired rhythm. A rhythm of 20 repetitions per minute was selected based on our pilot study, which demonstrated that most individuals were able to perform the exercises at this pace for 1.5 minutes without experiencing excessive fatigue, while finding it sufficiently challenging. For the static exercise (Exercise 4 in Table 1), the participants were asked to sustain the semi-squat position for 1.5 minutes in each repetition. The training protocol was a progressive design with a gradual increase in the duration of exercise (from 12 to 18 minutes per session) over the course of the treatment period (10 weeks) as the exercise tolerance increased. The WBV settings were validated by a tri-axial accelerometer (Model 7523A5; Dytran Instruments Inc., Chatsworth, CA). The frequency of the WBV signals used was 20 Hz and 30 Hz, as a number of WBV trials in older adults have demonstrated that therapeutic effects on neuromuscular performance could be induced using these frequencies (10). Frequencies higher than 30 Hz and amplitudes higher than 1 mm were not used in this study, due to the very high peak acceleration values generated (15). It has also been shown that signal distortion is more severe with high-amplitude vibration signals (15). WBV frequencies below 20 Hz were not used because they may induce a considerable resonance effect, resulting in amplification of the vibration signals and possible adverse effects (12). Our pilot work also showed that the high-intensity protocol demanded substantial exercise effort from the stroke participants without causing excessive fatigue.

Paragraph Number 12 The CON group completed the same movements while standing on the same WBV platform, but no WBV was delivered (i.e., WBV device was turned off). The treatment sessions for all three groups were supervised by a researcher (researcher: participant ratio = 1:2). The participants performed four exercises while standing on the WBV platform (Table 1). The training instructions and exercise progression pattern were the same for all three groups.

Outcome measures

Paragraph Number 13 Outcome measurements were performed between February 2013 and May 2014. Demographics and other relevant information (i.e., medications, medical history) were collected at the baseline assessment. The level of impairment of the leg and foot was evaluated using the Chedoke McMaster Stroke Assessment (11). The rating for each body part was based on a seven-point ordinal scale, with higher scores indicating better motor recovery. The ratings for the leg and foot were summed to yield an overall CMSA motor score for the paretic lower limb. The Functional Ambulation Category (score range: 0-5; 0=non-ambulatory, 5: independent) was used to indicate walking ability (14). The following outcomes were measured at baseline (within one week before the commencement of the exercise training), and post-intervention (within one week after the termination of the 10-week intervention) by the same blinded assessor.

Primary outcome

Muscle strength

Paragraph Number 14 The knee extension and flexion muscle strength of both the paretic and the non-paretic leg were measured by a dynamometer (NUMAC® NORMTM Testing & Rehabilitation System, Computer Sports Medicine, Inc., Stoughton, MA). Isometric, isokinetic concentric and eccentric muscle strength were tested. After a practice trial, each participant performed a maximal voluntary isometric contraction of knee flexion and extension at two knee joint angles, 30° and 70° of knee flexion, respectively. The peak torque value (in Nm) was registered. Isokinetic knee concentric and eccentric flexion/extension contractions through a range of movement between 70° and 10° of knee flexion at a fixed angular velocity of 60°/s were also measured. An angular speed of 60°/s was chosen, as it has commonly been used in previous stroke studies on patients with stroke (3,5,19,31,35). It is also known that a good proportion of stroke survivors could not perform at higher angular velocities, due to factors such as spasticity (3). The peak power value (Watts, W) was recorded. For all test conditions, three trials were performed with a 2-minute rest period between trials. The data were then averaged and normalized by the participant's body weight to yield the mean isometric strength (Nm/kg), and concentric and eccentric strength (W/kg) of knee flexion and extension in each leg. Muscle strength measurements using isokinetic dynamometry have been shown to be highly reliable in individuals with chronic stroke (5,19,31).

Secondary outcomes

Spasticity

Paragraph Number 15 Spasticity in the knee extensors and ankle plantarflexors was assessed using the 6-point Modified Ashworth scale (MAS) (0 = no spasticity, 4 = affected part rigid). The MAS is a widely used tool to evaluate muscle tone in stroke research and has acceptable reliability (Kendall's tau correlation = 0.847) (29).

Balance

Paragraph Number 16 The 14-item Mini Balance Evaluation Systems Test (Mini-BESTest) was used to evaluate participant's balance performance in everyday functional activities (8). The total score on this test ranges from 0 to 28, with higher scores indicating better balance ability. The Mini-BESTest has good psychometric properties when used in individuals with stroke, with excellent internal consistency (Cronbach's alpha = 0.89-0.94), intra-rater reliability (intraclass correlation coefficient (ICC) = 0.97), and inter-rater reliability (ICC = 0.96) (39).

Walking endurance

Paragraph Number 17 The 6-Minute Walk Test (6MWT) was administered while oxygen consumption (VO_2) was continuously recorded using the FitMate™ metabolic system (Cosmed, Rome, Italy) (27). At the beginning of each testing session, the system was calibrated according to the manufacturer's guidelines. The total distance covered (in meters) and the mean VO_2 rate (ml/kg/min) during the last 30 seconds of the 6MWT (a measure that is moderately associated with peak VO_2 in stroke) were used for subsequent analysis (30). Both the VO_2 measured during the 6MWT and the distance covered have shown high test-retest reliability in individuals with stroke (ICC >0.95) (7).

Functional mobility

Paragraph Number 18 Functional mobility was measured with the Timed-Up-and-Go (TUG) test (32). The TUG test was carried out twice, with an interspersed 1-minute rest period. The time taken to perform the test was averaged to obtain the mean value (in seconds).

Balance self-efficacy

Paragraph Number 19 Balance self-efficacy was evaluated using the Activities-specific Balance Confidence (ABC) scale (25). The participants were instructed to rate their level of confidence in performing each activity without losing their balance using a numerical rating scale from 0 to100, with higher scores denoting better balance confidence. The scores for each item were summed and then averaged to obtain the total ABC score. The ABC scale has been demonstrated to be a reliable and valid tool for evaluating self-perceived balance confidence in individuals with stroke (4).

Participation in daily activities

Paragraph Number 20 The Frenchay Activity Index (FAI) was used as a measure of participation (13). The FAI records the frequency of participating in social activities and performing more complex activities of daily living (e.g., domestic chores, outdoor mobility, leisure). Each of the 15 items was rated on a scale from 0 to 3, yielding a total score of 15 to 60 (15-29: inactive or restricted participation; 30-44: active; 45-60: highly active) (13). The construct validity and reliability of the FAI have been established (ICC= 0.87) (13).

Perceived environmental barriers

Paragraph Number 21 The participants also rated their perception of environmental barriers using the 25-item Craig Hospital Inventory of Environmental Factors (CHIEF) (22). The score for each of the 25 items was calculated by multiplying the magnitude score (small problem, 1; big problem, 2) by the frequency score (range: daily, 4; never, 0) to yield a product or overall "impact" score. Items relating to work or school, when the respondent was neither working nor in school, were considered "not applicable" and were not scored (Craig Hospital Research Department, 2001). The total CHIEF score is the mean of up to 25 overall impact scores. Liao et al. (22) demonstrated that CHIEF is a reliable and valid tool for evaluating the perceived environmental barriers experienced by individuals with chronic stroke.

Quality of life

Paragraph Number 22 Quality of life (QOL) was assessed using the Short-Form 12 Health Survey, version 2 (SF-12, Chinese version) (16). A mental health composite score (MCS) and a physical composite score (PCS) were generated (range: 0-100), with higher scores denoting better health-related QOL.

Statistical analysis

Paragraph Number 23 All statistical analyses were performed using IBM SPSS software (version 20.0, IBM, Armonk, NY, USA). A more stringent significance level at $P < 0.01$ was set due to the many outcomes involved.

Paragraph Number 24 Descriptive statistics (e.g., mean and standard deviation) were used to indicate the central tendencies and variability of the data. One-way analysis of variance (ANOVA) (for continuous variables), Chi-square tests (for nominal variables), and Kruskal-Wallis tests (for ordinal variables) were used to compare the baseline characteristics of the three groups. Intention-to-treat analysis was performed. For those who dropped out from the study, the results of the baseline assessment were carried over to the subsequent assessments using the last observation carried forward (LOCF) method (33). The Kolmogorov-Smirnov test was used to check the normality of the data. Analysis of variance (ANOVA) (mixed design; between-subject factor: group; within-subject factor: time) was used to compare the outcome variables across the two time points (i.e. baseline and post-intervention). Contrast analysis was performed within each group post-hoc when appropriate (28). As the MAS was an ordinal variable, between-group comparisons of the post-intervention scores were made using the Kruskal-Wallis test, followed by post-hoc Mann-Whitney tests as indicated. The above analyses based on the intention-to-treat (ITT) principle were repeated after excluding the drop-outs (i.e., on-protocol analysis).

Paragraph Number 25 Secondary analysis was done to explore the factors that may be related to better treatment outcomes after WBV training. The change scores (post-intervention score minus the pre-intervention score) of the LWBV and

HWBV groups for each outcome were correlated with the corresponding baseline scores, and relevant characteristics of the participants (e.g. age, CMSA motor recovery score, time taken to finish the 30 sessions of exercise training, baseline outcome measure scores, etc.) using either Spearman's rho or Pearson's correlation, depending on whether the assumptions for parametric analysis were fulfilled.

RESULTS

Paragraph Number 26 One hundred and thirteen individuals with stroke were screened for eligibility, and 84 of them fulfilled all selection criteria (see the CONSORT flow diagram in Figure 1). Twenty-eight participants were randomly allocated to each of the LWBV (8 women), HWBV (10 women) and CON (4 women) groups, respectively. One participant from the HWBV group dropped out after the initial (baseline) assessment due to other engagements, and another nine participants (five from the LWBV group, three from the HWBV group, and one from the CON group) dropped out during the period of the study, yielding an attrition rate of 11.9%. A total of 74 participants completed the training programs and post-intervention assessments (Figure 1).

Demographics

Paragraph Number 27 The demographic information is summarized in Table 2. All of the participants were ambulatory; 75 of them did not require any walking aid indoors. The overall CMSA motor score for the paretic lower limb (median =9, interquartile range = 7-11.8) revealed that the stroke motor impairment level was mild to moderate. There was no significant between-group difference in any of the demographic (Table 2) or outcome variables at baseline ($P > 0.05$) (Table 3 & 4). The on-protocol analysis with the removal of dropouts yielded similar results.

Training duration

Paragraph Number 28 Among those who completed all of the post-intervention assessments, the mean number of days taken to complete the 30 sessions of exercise training showed no significant difference among the three groups ($P=0.729$) (Table 2). The maximum time interval (mean number of days) between two training sessions was also similar among the three groups ($P=0.474$)(Table 2).

Adverse events

Paragraph Number 29 One participant from the LWBV group reported mild knee pain after WBV therapy and four reported fatigue (two each from the LWBV and HWBV groups) (Figure 1). These five participants eventually dropped out of the study.

Outcome measures

ITT analysis

Paragraph Number 30 In the ITT analysis, there was a significant time effect for several muscle strength measures on the paretic side (i.e. isometric flexion and extension at 70°, and concentric flexion) ($P < 0.01$; Table 3), TUG, 6MWT distance,

VO_2 during 6MWT, Mini-BESTest, ABC, and the PCS domain of the SF-12 ($P < 0.01$; Table 4). However, none of the variables showed significant time × group interaction effect ($P > 0.01$). No significant difference was identified in the knee MAS ($\chi^2 = 0.230$; $P = 0.891$) or ankle MAS scores ($\chi^2 = 0.642$; $P = 0.725$) post-intervention among the three groups. A separate analysis was also performed after removal of the dropouts (i.e., on-protocol analysis), and similar results were found (not shown).

Secondary analysis

Paragraph Number 31 In the secondary analysis, an attempted was made to determine whether there was any significant association between the change score of each outcome measure and their respective baseline values and other relevant factors (e.g., training duration).

LWBV group

Paragraph Number 32 A significant negative correlation was found between the baseline scores and change scores for knee flexion eccentric strength ($r = -0.509$, $P = 0.006$) in the paretic leg, indicating that the participants with poorer neuromuscular function tended to have greater improvement in this outcome.

HWBV group

Paragraph Number 33 There were significant negative correlations between the change scores and their respective baseline scores for concentric flexion ($r = -0.510$, P = 0.006) and extension strength (r = -0.832, P < 0.001), eccentric flexion (r = -0.554, P = 0.002) and extension strength (r = -0.554, P = 0.002) of the paretic knee, and isometric extension strength at 30° (r = -0.500, P = 0.007) and flexion concentric strength (r = -0.490, P = 0.008) of the non-paretic knee. Thus, the participants with poorer neuromuscular function tended to have greater improvements in these outcomes.

DISCUSSION

Paragraph Number 34 This is the first randomized control trial (RCT) to specifically evaluate the efficacy of different WBV intensities on body functions/structures, activity, and participation in individuals with chronic stroke. The key finding was that the addition of the 10-week WBV paradigm (i.e., LWBV and HWBV protocols) to the leg exercise protocol (i.e., the CON protocol) was no more effective in enhancing body functions/structures, activity and participation than leg exercises alone in community-dwelling people with chronic stroke.

Does WBV stimulation alone confer any additional benefits?

Paragraph Number 35 The first hypothesis of the present study was not supported. The findings of this study revealed that certain leg muscle strength variables showed significant time effects, indicating significant improvement after the training period. However, the group × time interaction effects were not significant, indicating that adding WBV to the leg exercise protocol did not confer additional therapeutic effects on the strength outcomes.

Paragraph Number 36 This is in contrast with the results reported in a number of studies that reported beneficial effects of WBV in older adults (18) and stroke (20,31,35). Among the various outcomes, those related to muscle strength were the most studied in previous WBV trials in older adults (18). A systematic review and meta-analysis by Lau et al. (18) concluded that WBV significantly improved certain aspects of leg muscle strength, including leg extension isometric strength, knee extension dynamic strength, jumping height, and sit-to-stand performance. Muscle strength was also the most studied variable among the various outcomes in previous stroke WBV exercise trials (5,19,31). However, the efficacy of WBV training on muscle strength in individuals with stroke remains controversial (20). While some RCTs found positive effects of WBV on neuromotor outcomes (35,37), others reported no significant effects (5,19,31).

Paragraph Number 37 Although there may be many reasons for the discrepancies in results between the current study and previous ones, one key issue may be related to the design of the control group. Among the three studies that involved a comparison group that performed exactly the same exercises as the WBV group (5,19,31), all reported no significant between-group differences in muscle strength outcomes after the intervention period. In contrast, the other studies that reported results in favor of WBV involved a comparison group that engaged in different activities (35, 37). Specifically, Tankisheva et al. (35) found a significantly greater increase in isometric and isokinetic knee extension torque (240°/s) in the paretic leg for the WBV group than the comparison group that engaged in habitual physical activities. It is thus possible that the better outcomes in the WBV group were related to the leg exercises performed while standing on the WBV device rather than the WBV stimulation. In Tihanyi et al. (37), the WBV group (WBV plus conventional rehabilitation) experienced a significantly greater improvement in eccentric and isometric knee extension torque in both legs compared with the comparison group that received conventional rehabilitative treatment only. The better improvement in muscle strength reported in the WBV group could be attributable to the leg exercises and the increased total treatment time rather than the WBV stimulation. Considering the available evidence overall, no study has convincingly demonstrated any positive effect of WBV alone on muscle strength in individuals with stroke. The results of this study further showed that the WBV protocols used here did not confer additional therapeutic effects on leg muscle strength above and beyond that induced by the prescribed leg exercises.

Paragraph Number 38 An alternative explanation of the lack of significant effects on muscle strength is that the intensity of the WBV stimulation may not be high enough. However, the intensity used here in the HWBV group (3.62*g*) was already much higher than that used in a previous stroke WBV trial that showed no significant effect (1.61*g*). Adding WBV of similar intensity to our LWBV protocol during the performance of various leg training has been shown to augment the EMG activity of major leg muscle groups by approximately 10-25% (21,23). Presumably, the HWBV protocol used in this study would have induced a greater EMG response. Perhaps the augmentation in muscle activation induced by WBV is not substantial enough to induce a positive training effect on top of that induced by the leg exercises. Higher intensities were not used in this study, as the high peak accelerations generated may pose potential hazards (1,15).

Paragraph Number 39 Another potential explanation of the non-significant results is that the duration of the treatment program may have been too short at only 10 weeks. This duration was chosen based on previous studies in older adults that showed strength gains after 6-10 weeks of WBV training (24). Perhaps individuals with stroke, due to their more severe physical impairments, may require a longer treatment duration before significant treatment effects can be detected.

Paragraph Number 40 Finally, the overall non-significant results may be related to the heterogeneity of the sample, and to the observation that WBV may be beneficial only for a highly select group of individuals. The secondary analysis indeed revealed that those with more severe deficits tended to gain more improvement from WBV training. Perhaps future WBV studies should use a more homogeneous group of people with more severe stroke deficits so that the effects of WBV can be better delineated.

Paragraph Number 41 Significant time effects were also detected for body functions/structures (Mini-BESTest, ABC, and VO_2), activity (TUG, 6MWT distance), and participation levels (physical health domain of SF-12), indicating that all three groups experienced improvement in these outcomes after the 10-week training period. However, the lack of a group × time interaction effect on these outcomes indicated that the WBV stimulation itself did not confer any additional effects. As WBV did not pose any significant effect on the muscle strength and balance variables (body functions/structures), a significant treatment effect on the related outcomes at the activity and participation levels, which often have multiple determinants, would not be expected. Another possible explanation of the non-significant treatment effect on the mobility outcomes may be that the WBV therapy did not involve any walking-related activities. Only four studies have previously investigated the influence of WBV on mobility function (TUG, 6MWT) (5,19,26), and only Merkert et al. (26) reported better performance in the TUG test in the WBV group. However, their control group engaged in conventional rehabilitation whereas the WBV group received additional WBV training. Thus, the additional treatment time may be confounding. Only one study has investigated the effect of WBV therapy on social participation, using the Stroke Impact Scale, and found no significant effect compared with sham vibration (5). Taken together, the present results generally concurred with previous studies in showing that WBV itself does not induce improvement in mobility and participation outcomes.

Comparison between low-intensity and high-intensity protocols

Paragraph Number 42 The second hypothesis of this study was also not supported. Previous studies in patients with stroke found that increasing WBV intensity led to increased neuromuscular activation of the leg muscles, as measured by surface EMG (21). Based on these results, we postulated that the HWBV protocol would lead to significantly better outcomes than those for the other two groups after 10 weeks of exercise training. However, the lack of a significant group × time interaction indicated that the two WBV intensities had no differential effects on the measured outcomes. It is possible that the difference in WBV intensity between the LWBV and HWBV protocols was not large enough. While the absolute difference in intensity (expressed in units of Earth's gravity) was 2.01*g*, which was quite substantial, it may not necessarily translate into a proportional difference in muscle activation during training. As shown in a recent study on people with chronic stroke, the relationship between WBV intensity and EMG response is not a linear one (23). Further increasing the WBV intensity beyond a certain point may no longer effectively increase EMG activity. In their study, it was shown that the increase in WBV-induced EMG activity was disproportionally greater when the WBV intensity increased from 0 g to 0.96 g. Further increasing the intensity to 1.61 g induced only a modest increase in EMG activity (21).

Limitations

Paragraph Number 43 This study has several limitations. First, the findings should not be generalized to patients who are in the acute/subacute stage of recovery or who have severe motor impairments, because the participants in the present study were all in the chronic stage (onset more than 6 months) and had mild to moderate impairments post-stroke. Second, the participants and the trainer were not blinded to the group allocation, but it was difficult to achieve these in exercise trials. However, all efforts were made to minimize any possible bias (e.g., assessor blinding, separate exercise periods for the three groups, etc.). Third, no long-term follow-up assessment was performed. The potential long-term beneficial or harmful effects of WBV remain uncertain.

Conclusion

Paragraph Number 44 In summary, while WBV therapy is safe and feasible for patients with chronic stroke, the addition of the 10-week WBV paradigm (LWBV and HWBV protocols) to the leg exercise protocol was no more effective in enhancing body functions/structures, activity and participation than leg exercise training alone in community-dwelling individuals with mild to moderate chronic stroke impairments. Further studies are needed to investigate some fundamental questions, such as the transmissibility of WBV signals, and how it varies with different WBV parameters and exercises performed. Further studies should also explore the use of WBV in patients with more severe stroke deficits.

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FIGURE LEGENDS

Figure 1. CONSORT Flow Chart