Research Article

The effects of whole body vibration on pulse wave velocity in men with chronic spinal cord injury

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Objective: A pilot study to evaluate the therapeutic potential of 40 weeks of passive standing with whole body vibration (PS-WBV) on central and peripheral arterial stiffness among men with chronic spinal cord injury (SCI).

Methods: Consenting participants were pre-screened to ensure safe participation. Fifteen individuals with chronic SCI were enrolled to participate in PS-WBV sessions three times per week for 40 weeks on a modified WAVE platform custom-fitted with an EASYStand 5000. Knee angle was set at 160°, and vibration parameters were 45Hz frequency and 0.7mm displacement. Each 45-minute session of PS-WBV training was intermittent (60 seconds on and 120 seconds off). Aortic and leg pulse wave velocity (PWV) was measured at baseline, mid-point (20 weeks) and exit (40 weeks).

Results: Nine males (age 41 ± 11 years, American Spinal Injury Association Impairment Scale A-D, neurological level of injury T4-T10, years post-injury 12 ± 8 years) completed the intervention. Aortic PWV was collected on $n=7$ at exit, and leg PWV was collected on $n=6$ at exit. No changes over time were found for either aortic PWV ($P = 0.46$) or leg PWV ($P = 0.54$). One possible study-related serious adverse event occurred during study intervention: the development of a grade III pressure sore on the right proximal anterior shin ($n=1$).

Conclusion: Forty weeks of PS-WBV in adults with SCI did not result in an observable change in arterial stiffness.

Keywords: Arterial stiffness, Exercise, Pulse wave velocity, Spinal cord injury, Whole body vibration

Introduction

Historically, pulmonary and renal conditions were the leading causes of death among individuals with chronic spinal cord injury (SCI). However, in recent years cardiovascular disease (CVD) has emerged as the leading cause of mortality.¹ Individuals with chronic SCI have a higher incidence of hyperlipidemia, abdominal obesity, diabetes, coronary artery disease, and ischemic stroke when compared to their age- and sex-matched able-bodied counterparts.^{2,3} The primary etiology of elevated CVD risk in chronic SCI is considered to be autonomic imbalance that perturbs cardiovascular homeostasis via blood pressure abnormalities (orthostatic hypotension, autonomic dysreflexia, AD),

rhythm disturbances (bradyarrhythmias, reduced heart rate variability), and blunted cardiovascular responses to exercise.⁴ Typically CVD risk is determined based on traditional metabolic disorder risk factors of abdominal obesity, elevated triglycerides, low high-density lipoprotein cholesterol, high blood pressure (BP), and elevated fasting glucose.⁵ Over the past decade, however, models based on traditional risk factor assessment fail to predict CVD in ~50% of cases among able-bodied persons,⁶ nor do they fully explain the increased CVD risk in the SCI population.⁷

Arterial plaque accumulation and subsequent rupture is the cause of ~70% of fatal acute myocardial infarction and/or sudden coronary death.⁶ Cardiovascular events may be better predicted by factors that render individuals susceptible to plaque formation, such as vascular structure.^{8,9} Arterial stiffness measured by pulse

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wave velocity (PWV) has been shown to be a strong independent risk factor for CVD in the able-bodied population.^{10,11} Aortic PWV measures the speed of the arterial pulse between the carotid and femoral arteries,¹² and is considered to be the best indicator of atherosclerotic burden.¹³ Peripheral PWV is assessed between the femoral and posterior tibial arteries (leg PWV). PWV is calculated as: $D/\Delta t$ where D is the distance between measurement sites in meters, and Δt is the pulse transit time in seconds. PWV has shown high repeatability in the SCI population using both Doppler¹⁴ and photoplethysmography¹⁵ methods of data collection, and PWV values have been reported as higher among persons with SCI when compared to matched able-bodied individuals.^{15,16} A recent study among a cohort of 87 persons with SCI suggests cardiovascular consequences among individuals with SCI and higher PWV.¹⁷

Regular physical activity decreases the risk of CVD,¹⁸ and in the general population aerobic training has been shown to improve arterial stiffness.¹⁹ Recently, studies have begun to show exercise training-induced vascular adaptations in the SCI population.^{20,21} A cross sectional study reported lower central PWV in wheelchair athletes vs. sedentary persons with SCI, suggesting long-term exercise might improve arterial health.²² Further, one case study in an individual with acute paraplegia assessed the effects of exercise on regional artery stiffness and reported that 6 weeks of wheelchair ergometry improved arm and leg PWV.²³

Individuals with SCI have far less choice of physical activity and lower capacity for physical activity than their able-bodied counterparts. Whole body vibration (WBV) is a new exercise modality that has been shown to emulate both resistance training^{24,25} and aerobic training.^{26–29} WBV generates vibration of the plate that activates both monosynaptic and polysynaptic neural pathways adequate to generate a tonic vibration reflex,^{30,31} similar to the stretch reflex generated from traditional physical activity. The type of WBV plate, magnitude, frequency, and duration of WBV applied, and the individual device user's posture, are key parameters of the vibration stimulus that determine physiological response.³² Several studies have reported reduced PWV following WBV interventions among able-bodied persons.^{33–37}

Individuals with SCI are typically unable to independently stand. Passive standing (PS)-WBV has been shown to induce muscle activation in the absence of voluntary muscle contraction among individuals with motor complete SCI,³⁸ and can therefore be used as a potential surrogate for conventional exercise among

individuals with SCI. Further, since physical activity participation restrictions include the inability to voluntarily contract skeletal muscles, PS-WBV may be a means for reducing arterial stiffness among individuals with chronic SCI. This pilot study tests the potential efficacy of 40 weeks of PS-WBV training for reducing PWV among men with chronic SCI.

Methods

Participants

Participants were recruited from the greater Toronto area. Screening, informed consent, data collection, and the study intervention implementation took place at Lyndhurst Center, Toronto Rehabilitation Institute – University Health Network in Toronto, Ontario, Canada. Inclusion criteria were: adult males aged 20–60 years with paraplegia (NLI T2–T10, AIS A–D) of traumatic etiology and a stable neurological deficit. Participants were excluded if they had any condition that made prolonged PS unsafe, such as severe hip or knee flexion contractures $>30^\circ$, untreated orthostatic hypotension, heterotopic ossification, and/or uncontrolled autonomic dysreflexia. Participants were excluded for contraindications to WBV therapy, including kidney or bladder stones, spondylolisthesis, venous thromboembolism, joint implants, epilepsy, or a pacemaker. To ensure staff safety during transfers throughout the 40 week intervention, participant weight >113 kg and height >189 cm were additional exclusion criteria. Toronto Rehabilitation Institute Research Ethics Board approved study procedures (REB#08-051), and all participants written informed consent.

Following pre-screening to ensure safe participation in the intervention, basic anthropometric measures of mass (kg), body mass index (kg/m^2) and waist circumference (cm) were determined.

Pulse Wave Velocity

Participants were instructed to abstain from caffeine, nicotine, alcohol, and food for ≥ 8 hours, and physical activity for a minimum of 24 hours prior to PWV testing sessions. PWV assessments were conducted in a quiet, temperature controlled room ($22\text{--}24^\circ\text{C}$) between 0900 and 1300, with two trained technicians performing data collection. Participants lay supine for 10–15 minutes prior to data collection to ensure stability of resting measures. Heart rate was assessed using an automated heart rate monitor (UA-767 Digital blood pressure monitor; Omron, Inc., Tokyo, Japan), and blood pressure was measured using a mercury sphygmomanometer. Two consecutive heart rate and blood

pressure measures separated by one minute were averaged.

Blood vessel waveforms were acquired via two identical transcutaneous Doppler flow meters (Smartdop50, Hadeco, Inc., Kanagawa, Japan). Signals were band-pass filtered to remove frequencies below 2Hz and above 30Hz to improve detection of the onset of the waveform using LabChart software (LabChart 7; ADInstruments Inc., Colorado Springs, CO, USA). The filter portrayed the onset of the waveform as a minimum value that corresponded with end diastole. The time delay between the filter minimum values was considered the pulse transit time. A minimum of 20 simultaneously recorded waveforms was analyzed to determine the pulse transit time between the measurement sites. Recent expert consensus advises that 80% of the direct carotid-femoral distance be used as the most accurate distance estimate³⁹; therefore aortic PWV was calculated as $(0.8 \times D)/\Delta t$. Leg PWV between the femoral and posterior tibial arteries was calculated using $D/\Delta t$. All the distances were determined using a flexible non-elastic Gulick II tape measure (Country Technology Inc, Gay Mills, WI, USA) to the nearest 0.001m. Aortic PWV and leg PWV were measured prior to the first week of PS-WBV exposure (baseline), halfway through the intervention (midpoint; 20 weeks), and post-intervention measurements were conducted within a week of completing the 40-week intervention.

Intervention

A customized WBV platform (WAVE® Manufacturing Inc., Windsor, ON, Canada) was developed that incorporated an EasyStand™ 5000 frame (Altimate Medical Inc., Morton, MN, USA) to allow individuals with SCI to stand passively on the platform (PS-WBV). Participants underwent PS-WBV therapy for 45 minutes three times weekly for 40 weeks.

Table 1 Baseline participant characteristics

Parameter	Mean ± SD	Median	Range
Age, years	41 ± 11	42	24–58
Mass, kg	79.7 ± 17.7	82.1	55–105
Height, m	1.75 ± 0.08	1.71	1.68–1.91
BMI, kg/m ²	26.1 ± 5.3	25.1	19.9–36.8
WC, cm	92.6 ± 17.3	93.0	65.5–119.0
Injury			
T4-T10 AIS A-B	7		
T4-T10 AIS C-D	2		
Years Post Injury	12 ± 8	8	3–25

Values are mean ± SD, or n(%).

Abbreviations: BMI = body mass index; WC = waist circumference; AIS = American Spinal Injury Association Impairment Scale; NLI = neurological level of injury; YPI = years post injury.

Adherence to the training program was calculated based on the percentage of completed sessions out of a maximum of 120 sessions. Participants were required to complete 9 WBV sessions per month; if less than 9 sessions were completed in a month for three consecutive months, participants were withdrawn from the study due to non-adherence. Additionally, if participants missed 10 or more consecutive sessions, they were withdrawn from the study.

The WBV protocol was intermittent (60 seconds on and 120 seconds off) at 45 Hz with a displacement of 0.7mm at a knee angle of 160° of flexion. These vibration parameters were chosen based on research from our laboratory assessing the effectiveness of various postures, frequencies, and amplitudes on subject tolerance and vibration propagation.⁴⁰ Heart rate and blood pressure were measured during each session to monitor for orthostatic hypotension and/or autonomic dysreflexia.

Statistics

Baseline characteristics are presented as mean ± SD, median, and range in Table 1. PS-WBV intervention

Table 2 Pulse Wave Velocity and Hemodynamics during Passive Standing-Whole Body Vibration Intervention

Parameter	Baseline	20 weeks	40 weeks
Aortic PWV, m/s	7.20 ± 1.04; 5.90–8.63	7.45 ± 1.43; 5.69–9.40	7.50 ± 1.08; 6.34–9.55
Age <30 y (2)	5.97 ± 0.01; 5.90–6.03	5.91 ± 0.03; 5.69–6.12	6.58 ± 0.33; 6.35–6.81
Age 30–39 y (2)	8.03 ± 0.03; 7.80–8.25	8.61 ± 1.11; 7.82–9.40	7.01 ± 0.19; 6.87–7.15
Age 40–49 y (3)	6.88 ± 0.92; 5.90–7.73	7.41 ± 1.33; 6.10–8.76	7.90 ± 0.37; 7.64–8.16
Age 50–59 y (2)	8.10 ± 0.75; 7.57–8.63	7.88 ± 1.90; 6.54–9.22	---
Leg PWV, m/s	11.43 ± 0.88; 9.64–12.53	12.09 ± 1.27; 10.18–13.55	11.62 ± 0.82; 10.25–12.50
HR, bpm	67 ± 5; 60–75	64 ± 7; 56–72	64 ± 7; 54–76
SBP, mmHg	119 ± 19; 90–158	113 ± 11; 94–128	123 ± 21; 98–160
DBP, mmHg	78 ± 15; 58–108	73 ± 7; 60–84	82 ± 8; 70–96
MAP, mmHg	91 ± 15; 74–125	86 ± 7; 76–95	96 ± 12; 79–115

Values are mean ± SD, range.

Abbreviations: PWV = pulse wave velocity; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure.

data at baseline, 20 and 40 weeks are presented in Table 2. Intention-to-treat analyses of variance (ANOVA) with repeated measures were used to determine any interaction effects (baseline, mid-point, exit). Shapiro-Wilk was used to test for normality, and Mauchly's was used to test for sphericity. If the distribution violated the assumption of sphericity, the Greenhouse–Geisser correction was used. The last available observation was carried forward in the case of missing data. Statistical analyses were performed using SPSS 20.0 software (IBM Corp., Armonk, NY, USA) with a level of significance of $P < 0.05$.

In clinical practice it is necessary to determine if the change observed is clinically meaningful, and is due to 'real' change and not to change in variation or measurement error using a smallest real difference (SRD) value.⁴¹ A recent paper from our group suggests a SRD change of 11.2% and 8.8% for aortic and leg PWV, respectively, to describe 'real' changes in PWV (14). Further, due to multiple factors influencing PWV throughout the lifespan causing a 6–8% increase in PWV with each decade of life, age-adjusted PWV values may provide additional insight into identifying individuals who are at risk.^{42,43} Abnormal aortic PWV was defined as a value above the age-specific 90th percentile of healthy, able-bodied subjects^{17,42}: <30 years: 7.1 m/s, 30–39 years: 8.0 m/s, 40–49 years: 8.6 m/s, 50–59 years: 10.0 m/s, 60–69 years: 13.1 m/s, >70 years: 14.6 m/s.

Results

Fig. 1 describes the participant flow through the study; there was approximately a 4:1 screening to recruitment ratio due to the strict inclusion criteria. Recruitment and training took place from April 2009 to July 2012. Fifteen persons participated in the intervention. One participant withdrew from the intervention after six sessions, but agreed to continue the outcome assessments.

At baseline only one participant had an aortic PWV value above the age-specific 90th percentile of healthy, able-bodied subjects.⁴² Aortic PWV data was collected on $n=9$ males at baseline (7.20 ± 1.04 m/s) and at 20 weeks (mid-point) (7.45 ± 1.43 m/s), and $n=7$ males at 40 weeks (exit) (7.50 ± 1.08 m/s). Leg PWV data was collected on $n=8$ males at baseline (11.43 ± 0.88 m/s) and at 20 weeks (mid-point) (12.09 ± 1.27 m/s), and $n=6$ males at 40 weeks (exit) (11.62 ± 0.82 m/s) (Table 2). In one case, neither aortic PWV nor leg PWV assessments could be acquired, and in another case, leg PWV could not be acquired. In two instances, signals could not be acquired due to a faulty cable creating electrical background noise, limiting the ability to

Figure 1 Participant Flow Diagram.

filter the data. In another instance, the participant had an abdominal pannus that limited the ability to obtain a clear signal through the adipose tissue. As a result, $n=7$ and $n=6$ males were included in the aortic and leg PWV data analysis, respectively. When assessing differences in PWV, change from baseline to exit between AIS A-B and AIS C-D, no differences were observed.

Participants attended an average of 2.0 ± 0.5 (range 0.6–2.6) sessions per week, and an average of 70 ± 32 (range 6–106) sessions over the course of 40 weeks. For participants included in the aortic PWV analysis at study exit (the $n=7$), adherence to the intervention was 72% (87 ± 10 sessions). The most common reasons for participants missing study sessions were illness and competing commitments. The most frequently reported adverse events determined to be possibly or probably related to study participation ($n=9$) were dizziness, headache, autonomic dysreflexia, low back pain, and orthostatic hypotension. Only one participant reported a serious adverse event that occurred

Figure 2 Pulse wave velocity at baseline, midpoint (20 weeks) and exit (40 weeks) whole body vibration training. Mean and individual data are presented. Error bars represent standard deviation.

during the training period of a grade III pressure sore overlying a pre-existing 3rd degree burn (incurred midway through the study, in the community setting, external to study participation). It is possible that the pressure sore developed as a result of the participant's interface with the standing frame.

Neither aortic ($F(1,143,6.859)=0.672$, $P = 0.460$) nor leg PWV ($F(2,10)=0.656$, $P = 0.540$), differed between time points. Visually, there appears to be a trend towards an increase in leg PWV from baseline to 20 weeks (Fig. 2). None of heart rate ($F(2,14)=0.471$, $P = 0.634$), systolic blood pressure ($F(2,14)=1.853$, $P = 0.193$), diastolic blood pressure ($F(2,14)=2.598$, $P = 0.110$) or mean arterial pressure ($F(2,14)=2.514$, $P = 0.117$) differed between time points.

Discussion

Contrary to the main theory of using WBV training as an exercise modality that results in increased muscular activity, subsequent increased blood flow, and theoretically improved arterial stiffness, we did not observe improved PWV or hemodynamics (heart rate, blood pressure) following 40 weeks of PS-WBV training in persons with SCI. When looking at age-categorized PWV cut-off values, one subject (30–39 years) had

abnormal aortic PWV at baseline that persisted to 20 weeks, but decreased to normal at 40 weeks. One subject (40–49 years) had normal aortic PWV at baseline that became abnormal at 20 weeks; unfortunately the 40-week time point was missing. When looking at average change in PWV from baseline to exit, aortic and leg PWV was $7.4 \pm 15.5\%$ and $3.6 \pm 10.2\%$, lower than the SRD of 11.2% and 8.8%, respectively, suggested to reveal 'real' changes in PWV.¹⁴ Therefore our findings did not approach statistical (difficult with the small sample size) or clinical significance. Possible rationale for unchanged PWV following PS-WBV could be: 1) insufficient exercise intensity; 2) elevated systemic oxidative stress; and/or 3) lack of sympathetic nervous system activity.

To our knowledge, no previous research has been conducted assessing the impact of WBV training on PWV among individuals with SCI. Previous literature reported improved leg PWV but unchanged aortic PWV following 8 weeks³³ and 12 weeks^{34,37} of dynamic exercise on WBV platforms among obese post-menopausal women. Another study among $n=38$ middle-aged and elderly persons suggested that 3 months of WBV exposure may reduce brachial-ankle PWV in the WBV group, but no interaction effect with the control group.³⁵ Participants in three of these studies had high blood pressure at the onset of the intervention,^{33,34,37} and the methodology for PWV assessment and WBV training were different from the present study,^{33–35,37} perhaps contributing to the lack of agreement between study findings.

A recent meta-analysis showed improved arterial stiffness following moderate-high intensity exercise among able-bodied persons⁴⁴; WBV may result in different intensities and variable cardiovascular responses when different vibration parameters are applied. Previous work in able-bodied persons have reported increases in skin blood flow^{45,46} and blood volume in the gastrocnemius and quadriceps muscles²⁶ following exposure to WBV of various frequencies (26–50 Hz) and amplitudes (3 mm), and one study in $n=8$ complete SCI (AIS A) reported increased femoral peak blood velocity following WBV exposure (30 Hz and 5 mm displacement).⁴⁷ It appears that higher frequencies may be more beneficial among able-bodied persons (more rapid increase in blood flow and no vasoconstriction during recovery).⁴⁶ Our chosen vibration parameters were selected for their tolerance by individuals with SCI and their potential to modify muscle activation based on evidence from our lab.⁴⁰ We observed variable PWV responses to PS-WBV, and a closer look at participant characteristics of those who responded positively vs. negatively to the

PS-WBV training intervention revealed no particular pattern for age, level or severity of injury, blood pressure, smoking, anthropometrics, or baseline aortic PWV. It is possible that the PS-WBV stimulus was of insufficient intensity to increase blood flow and elicit improvements in arterial stiffness.

Other possible rationales for the lack of improvement in PWV could be related to the altered physiology that occurs post-SCI. Increased systemic oxidative stress occurring secondary to the primary injury⁴⁸ can reduce the bioavailability of nitric oxide and consequently impair vascular stiffness (i.e. PWV).⁴⁹ Previous research has observed increases in nitric oxide concentrations following WBV.⁵⁰ It is possible that higher basal oxidative stress levels could cancel out WBV-induced increases in nitric oxide, resulting in unchanged PWV among individuals with SCI in the present study. Further, individuals with SCI experience attenuated sympathetic tone in sublesional arteries⁵¹ resulting from a parasympathetic-dominant resting state and smooth muscle denervation below the level of lesion. It is possible that decreased sympathetic tone contributed to lower resting PWV values. Recent expert consensus guidelines state that aortic PWV of ≥ 10 m/s represents an increased risk for morbidity and mortality³⁹; all participants had aortic PWV values below the cut off of 10 m/s at baseline. All but one participant had aortic PWV values below the age-adjusted PWV cut-off at baseline⁴²; this ceiling effect leaves little room for improvement. Lastly, although not statically or clinically significant, a visible trend is evident towards a negative effect of PS-WBV on leg PWV (Fig. 2). The prognostic value of leg PWV is unclear, and the time course of leg PWV responses to exercise is unknown. While vascular function (e.g. endothelial function) changes are thought to precede structural changes (e.g. PWV) in able-bodied persons in response to exercise,⁵² it is unknown how autonomic [dys]function influences the time course of vascular adaptations to exercise (i.e. following SCI). The observed trend of increased leg PWV at 20 weeks highlights the lack of knowledge regarding underlying mechanisms, and how they may differ in the presence of altered autonomic function among patients with lesions above the T5 neurological level of injury.

Limitations

Several limitations need to be addressed. We did not include EMG to assess the quantity of muscular activity occurring during the WBV exercise bouts. However, a previous study reported increased leg EMG activity among individuals with AIS A SCI during WBV

exposure,⁴⁷ so it is plausible that participants in this study (AIS A-D) experienced some degree of neuromuscular activity. Further, there were no differences in PWV change from baseline to exit between AIS A-B and C-D (i.e. between those with none and those with some voluntary muscle activation); this pilot data may suggest completeness of injury does not influence PWV responses to WBV. We did not assess blood flow during WBV exposure; observing blood flow in response to WBV may provide insight into subsequent arterial stiffness changes. We did not have a control group, and we had a small heterogeneous sample. Lastly, we did not control for lifestyle factors and did not measure or control diet, factors that are important determinants of vascular health.⁵³

Summary and future directions

Forty weeks of PS-WBV did not improve aortic or leg PWV. The visual trend towards a negative effect of PS-WBV on leg PWV at 20 weeks highlights the lack of knowledge regarding underlying mechanisms; future studies must incorporate candidate biomarkers (e.g. nitric oxide) to further our understanding of the time course for peripheral arterial modifications.

It is important to note that the present study is a pilot study consistent with case series methodology: “a group of patients with similar diagnoses or undergoing the same procedures followed over time”.⁵⁴ The findings from the present pilot study provide preliminary results that are hypothesis generating and may help inform longitudinal study design in a larger cohort. Although there were no differences in aortic PWV changes from baseline to exit between AIS A-B and C-D in this study, an alternate comparison of those who are “autonomic complete” versus “autonomic incomplete”⁵⁵ with a larger sample size may provide insight into the mechanisms of potential arterial stiffness improvements. Future prospective studies should explore the use of WBV therapy among a larger sample with elevated PWV at baseline, and monitor potential autonomic, metabolic, and neural responses to specific WBV stimuli.

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