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Effects Of Controlled-Whole Body Vibration Training On Reducing Risk Of Falls In People With Multiple Sclerosis

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EFFECTS OF CONTROLLED-WHOLE BODY VIBRATION TRAINING ON REDUCING RISK OF FALLS IN PEOPLE WITH MULTIPLE SCLEROSIS

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DEDICATION

I dedicate this thesis to the best parents in the world: my daddy and mommy! They have always been supportive and helpful with everything. I would not have been able to complete this thesis without their continuous love and encouragement. Thank you for inspiring me to become better and stronger. Of course I want to thank God, because without him I would have never accomplished this goal.

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by

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THESIS

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ABSTRACT

Falls present a serious challenge among people affected by multiple sclerosis (MS). Controlled whole-body vibration (CWBV) training has been recently introduced into the physical therapy field to prevent falls in older adults. The purpose of this study was to examine the effects of an 8-week vibration-training program in reducing the risk of falls in people living with MS. The study adopted a single-group pre-test – post-test longitudinal design. Twenty-five adults with clinically–confirmed MS were enrolled in this study to undergo the 8-week intervention on a side-alternating vibration machine. The training was delivered three times a week for eight weeks a total of 24 training sessions. The vibration frequency was set at 20 Hz and an amplitude of 1.3 mm. Prior to the training course, a battery of fall risk factors, including body balance, functional mobility, muscle strength, ankle joint range of motion, sensation of the feet, fear of falling, and bone density were evaluated. The results revealed that the vibration training program was able to significantly improve almost all the outcome measurements (body balance, functional mobility, muscle strength, range of motion, fear of falling, and bone density) with moderate to large effect sizes varying from 0.3 to 1.2. More importantly, our study, for the first time, discovered that vibration training could improve the range of motion of the ankle joints, fear of falling and bone density among people with MS. The findings from this study could provide guidance to design an optimal CWBV-based fall prevention program for people with MS. Given that the El Paso region is a nationally-recognized MS cluster area, this project holds clinical, medical, and practical significance.

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1. INTRODUCTION

1.1. Multiple Sclerosis

Multiple sclerosis (MS) is a neurological disease in which the body's immune system attacks the central nervous system (CNS) and damages the protective myelin sheath that covers the nerves. Due to the attack, the T lymphocytes (or T-cells) become sensitive to the proteins, producing inflammation and demyelination of the CNS. These T-cells not only affect the myelin sheath, but also cause damage to the nerve fibers. Such damages can lead to the formation of large demyelinated plaques dispersed through the CNS (Pospescu & Lucchinetti, 2015), which interrupts or distorts the nerve impulses traveling to and from the brain and spinal cord, producing various symptoms. One of the key symptoms experienced by people with MS is motor impairments such as balance deficit, muscle weakness, mobility impairment, and sensation loss, which position them at an elevated risk of falls (Matsuda et al., 2011).

There are four pathological courses of MS (Fig.1):

1) Relapsing-remitting MS (RRMS). In this course there are irregular relapses that are followed by completed or partial recovery.
2) Primary Progressive MS (PPMS). This course is characterized by slowly worsening symptoms from the beginning of the disease, without early relapses and no recovery periods.
3) Secondary Progressive MS (SPMS). This course starts by chronic lesions, which are preceded by RRMS. Symptoms worsen more steadily over time with or without relapses.

4) Progressive-Relapsing MS (PRMS). This course is characterized by steadily worsening disease state from the beginning of the disease with occasional acute relapses without recovery.

Approximately 85% of people with MS start with RRMS, which later turns into a SPMS. The other two courses (PPMS and PRMS) are not very common. All four courses can be mild, moderate, or severe. Due to the complexity of this disease, MS can affect different people in various ways (Lublin et al., 1996).

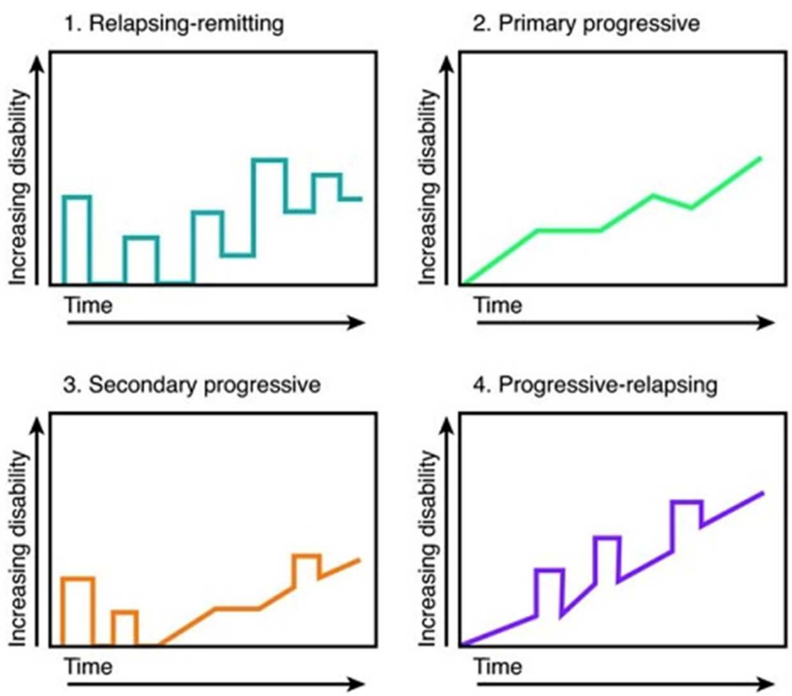

Fig. 1. Courses of MS

Schematic illustration of four courses of MS: (1) relapsing-remitting, (2) primary progressive, (3) secondary progressive, and (4) progressive relapsing; every deviation (shown as a rectangle) represents a relapse with progression (Lublin et al., 1996).

Although MS afflicts approximately 2.5 million people worldwide, its prevalence varies considerably globally. No study has indicated a comprehensive mechanism that explains why certain countries are more prone to having a higher prevalence of MS. The United States has been reported as one of the countries with the highest MS prevalence, having about 150 cases per 100,000 individuals (Valuck et al., 2016) and an estimation of more than 570,000 people affected by MS across the nation (Campbell et al., 2014). In the state of Texas, it was estimated that about 47.2 per 100,000 individuals were affected by MS in 2000 (Noonan, 2010).

However, the situation is worse in the El Paso, Texas region compared to the state and the nation. El Paso was reported as a nationally-recognized MS cluster region after examining the prevalence of MS among school cohorts in El Paso (Henry, 2014). It was reported that Mesita Elementary School was estimated to have a prevalence of 360 per 100,000 persons – almost 1.5 times higher than the national level during the investigated period. The study results also indicated a standardized morbidity ratio of 1.93 [95% Confidence Interval (CI) = 1.06 - 3.24], which illustrates a statistically significant greater risk of MS among this particular cohort (Henry, 2014).

1.2. Falls Among People with MS

Falls are a serious challenge faced by people with MS. It was reported that more than 50% of people with MS fall at least once every two months (Finlayson, Peterson, Cho, 2006; Nilsagard, 2007). People with MS demonstrate a retrospective prevalence of falls between 27.9% and 64.0%, and a prospective prevalence of falls between 35.0% and 43.0%, implying that the incidence of multiple falls in MS is extremely common (Matsuda 2011; Peterson, Cho, von Koch, and Finlayson, 2008). Falls frequently cause severe health, medical, and physical consequences. A study concluded that approximately 23% of all falls result in serious injury or death among people with MS (Matsuda et al., 2011). Injuries can also amplify the fear of falling, which further limits individuals' activity level. This lack of physical activity may result in muscle atrophy and bone loss (Gibson & Summers, 2011), in turn increasing their likelihood of falls and related injuries (Steffensen, Mellgren & Kampman, 2010).

Falls among people with MS also presents a financial burden to society. The fall-induced direct costs, such as the expenses of the treatment and medications, and indirect costs, such as the cost due to unemployment or institutionalization, considerably increase the already-heavy economic burden encumbered by the individual, family, and the health care system (Bell et al., 20017; Grima, 2000). Falls can also limit an individual's mobility level, their involvement in social activities, and reduce their quality of life (Gunn, Newell, Haas, Marsden &, Freeman, 2013). Furthermore, people with MS have an increased risk of fracture relative to non-MS age-matched counterpart and, in particular, an increased risk of fragility fractures, with a hip fracture hazard ratio of 4.08 (95% CI = 2.21 - 7.56) (Bazelier al., 2012). These facts underscore the importance of managing fall risk and identifying measures to reduce the negative consequences of falls. It is crucial to develop effective fall prevention interventions that reduce falls and fall-related fractures for this population.

1.3. Risk Factors of Falls

Knowledge of fall risk factors is essential to guide the development, implementation, design, and evaluation of fall management interventions. MS causes a wide range of motor dysfunctions and impairments, such as balance impairment, mobility deficit, muscle weakness, reduction in range of motion (ROM), sensation disturbance, and bone density decrement (Cameron and Lord, 2010; Finlayson, Peterson, Cho, 2006; Matsuda et al., 2011). For older adults (Ambrose, Paul, & Hausdorff, 2013; Dargent-Molina et al., 1996; Menz, Morris, & Lord,

2006) and other populations with neurological dysfunctions (Allen, Sherrington, Paul, & Canning, 2011; Grimbergen, 2008; Stolze, 2004), these impairments are common risk factors associated with falls (Menz, Morris, and Lord, 2006; Tinetti, Speechley, & Ginter, 1988). Muscle weakness, balance impairment, and functional mobility deficits have also been identified as the main risk factors of falls among people with MS. Moreover, these motor dysfunctions could lead to the development of fear of falling among this population, which is considered another major risk factor of falls (Mazumder et al., 2015; Kasser et al., 2011; van Vliet et al., 2013).

Muscle Weakness. Sufficient muscle strength is necessary for humans to ambulate, transfer, and perform daily activities. In MS, muscle weakness as a symptom is common. Two factors possibly cause the weakness. First, damage to the nerve fibers (i.e., the demyelination) in the CNS that stimulate the muscles can lead to weakness. Due to the disease, the muscles are not receiving the necessary nerve impulses to effectively perform a desired activity (Carroll, Gallagher, Seidle, & Trappe, 2005). Another factor could be that the deconditioning of muscles resulting from the lack of use. People with MS frequently have an overall low activity level due to fatigue, pain, imbalance, or other symptoms (Bakshi, 2003; Gibson, & Summers, 2011). Lack of activity could cause the muscles affected by MS, as well as those that are not affected by the disease, to become weak. Because of muscle weakness many people with MS exhibit poor functional capacity, various problems in gait pattern, balance, level of the physical activity and reduce quality of life (Gutierrez et al., 2005). Kasser and associates examined the relationship between muscle weakness and falls among people with MS and reported that the lack of muscle strength was strongly associated with falls (Kasser, Jacobs, Foley, Cardinal, & Maddalozzo, 2011).

Balance Impairment. Body balance is fundamental to all human daily activities and people with MS are more prone to having impaired balance than healthy older adults. It was found that people with MS exhibit greater body sway compared to their healthy counterparts, indicating impairment in regulating body balance (Kalron, 2013). Studies have reported a significant correlation between balance impairments and high risk of falls for people with MS (Finlayson, Peterson, & Cho, 2006; Nilsagård, Lundholm, Denison, & Gunnarsson, 2009). Another study conducted by Prosperine et al. (2011) confirmed this notation by assessing the connection between balance deficit and accidental falls among people with MS and concluded that poor static standing balance may predispose people with MS to a high probability of accidental falls.

Functional Mobility. Persons with MS commonly experience restrictions in mobility and everyday functional activities. A wide range of factors, such as psychological, physical, and socioeconomic issues may contribute to the limited mobility of people with MS. Mobility limitations have also been identified as one of the greatest challenges for people with MS (Schwid et al., 1997), and have been related to falls (Sosnoff, 2011). A study by Finlayson et al. (2006) examined the risk factors for falling among people with MS and found a significant linkage between the number of falls and the mobility deficit.

Fear of Falling. Fear of falling is a psychological measurement, which assesses to what extent an individual is concerned about falling during daily activities. Previous studies showed a strong link between the fear of falling and an increased risk of falls in people with MS (Coote, Hogan, & Franklin, 2013). Another study reported that 60% of people who reported a fall also reported fear of falling (Finlayson, Peterson, & Cho, 2006).

Bone Mineral Mass Loss. People with MS are more prone to high levels of bone mineral density loss, which elevates the risk of osteoporosis. This bone loss is common with MS due to their lower level of physical activity (Bazelier et al., 2012; Gibson, & Summers, 2011). Consequently, fractures after a fall are more common for people with MS than their age-matched healthy counterparts (Cosman et al., 1998). According to Peterson et al. (2007), a decrement in bone density is strongly associated with fall related injuries. A similar finding, reported by Bazelier et al. (2012), documented a strong connection between fractures after a fall and bone mineral mass loss among people with MS.

1.4. Fall Prevention Among MS

Various types of fall prevention paradigms have been developed aiming at people with MS with different levels of effectiveness. This section reviews several exercise-based training methods that have been applied in people with MS.

Traditional Exercise-based Training. Current fall prevention interventions include balance, strength, and endurance training. Studies have shown that traditional exercise-based training could be a supportive treatment for people with MS to reduce their risk of falls (Cattaneo et al., 2007; Gutierrez et al., 2005; Platta et al., 2016). A recent systematic review reported that conventional exercise-based interventions among people with MS have the potential to improve their balance, functional mobility, muscular strength, and aerobic fitness (Latimer-Cheung et al., 2013). Briken and associates examined the effects of an 8-10 week exercise program using an arm ergometer, and bicycle ergometer among people with MS. Their results indicated that exercise training could present a beneficial effect on aerobic fitness and walking ability (Briken et al., 2013). These results confirmed the finding from a previous study by Motl et al. (2012), which reported an improvement in ambulatory ability after an 8-week intervention of aerobic, resistance, and balance training. Other studies also observed similar results. For instance, it was suggested that an 8-week lower body resistance-training program among people with MS could improve gait pattern, strength (Gutierrez et al., 2005), body balance (Moradi, 2015), and functional mobility (Dalgas, Stenager & Ingemann-Hansen, 2007; Motl & Gosney 2007).

Other Exercise-based Training. Besides the traditional-based training exercises, other exercise-based training methods have been examined as an alternative to improve balance, functional mobility, strength and endurance of people with MS. These alternative training methods include Pilates, Tai chi, and aquatic training. Very few studies have been conducted to inspect the effects of these training paradigms in reducing risk of falls among people with MS. For instance, Ahmadi and colleagues (2010) assessed the effects of an 8-week yoga intervention and detected a significant improvement in balance walking and walking endurance. A study regarding a 12-week Pilates program reported improvement of balance and mobility among people with MS (Freman, Gear and Hough, 2012). Similar results were reported by Maradi et al. (2013) after 12 weeks of Pilates and aquatic exercises. Additionally, Gehlse et al. (1984) reported an increase in muscular strength, endurance, and power after a 10-week aquatic exercise program among people with MS. However, the sample size was small in these studies. The effectiveness and efficacy of these training methods are still largely unknown.

Although the aforementioned fall prevention interventions showed some effects in reducing the risk of falls, some people with MS may be unable or unwilling to undergo the intervention due to some factors that limit the application of traditional exercise-based training paradigms. First, people with MS may experience a fall during exercise due to their inherent higher risk of falls. Second, the lower muscle strength may prevent people with MS from conducting some high intensity physical activities. Third, fatigue and pain, two common symptoms associated with MS, lower the motivation to undergo traditional exercise training among people with MS. Some other limiting factors include the lack of time, lack of information regarding the exercise recommendation, lack of interest, disliking the exercise, and the cost of training (Mayo et al., 2013). Therefore, an easy yet effective alternative intervention is highly needed to prevent falls among people with MS.

Controlled whole-body vibration (CWBV) training has recently been introduced as a relatively novel training modality for older adults and people with neurological disorders primarily because it is safe, easy to use, and requires less intensive physical activity than traditional exercise-based methods. Literature has shown that a short-term (6 to 10 weeks) CWBV training reduced the risk of falls among seniors (Bautmans, Van Hees, Lemper, & Mets, 2005; Yang, King, Dillon, & Su, 2015), people with cerebral palsy (Ahlborg, Andersson, & Julin 2006), Parkinson's disease (Ebersbach, Edler, Kaufhold, & Wisse, 2008), and stroke (Tihanyi, 2007) by improving the body balance, stability, strength, and physical and physiological properties. For example, a study reported that 6 weeks of CWBV training improved body balance, gait functional mobility, and strength of institutionalized elderly people (Sitjà-Rabert, 2015). In another study, after CWBV training, the Timed-Up-and-Go performance improved 13% at normal walking speed and 8% at maximal speed (Bogaerts, 2011). Ahlborg et al. (2008) investigated the effect of CWBV training on strength among people with cerebral palsy and indicated that 8 weeks of CWBV training increased quadriceps strength. A study conducted by Tihanyi and associates (2007) suggested that one bout of CWBV training increased voluntary forces and muscle activation among people affected by a stroke. Moreover, Eberbabach et al. (2008) showed an improvement of equilibrium and gait in patients with Parkinson's disease.

Given the common risk factors of falls shared between older adults, people with other movement disorders and individuals affected by MS, the CWBV training method may be a promising alternative modality for people with MS to reduce the risk of falls.

1.5. Controlled Whole-body Vibration Training

1.5.1. Mechanisms

During CWBV training, trainees usually stand on a vibration platform which oscillates at a given vibration frequency and amplitude. The mechanical vibrations from the platform stimulate the muscle-tendon complex and cause the tonic vibration reflex, which increases the activation of alpha motor neurons and enhances muscle contractions (Cardinale & Bosco, 2003; Cochrane, 2011). Further, physiological and neuromuscular changes, such as muscle strength, body balance, flexibility, sensation level, and mobility, occur on numerous levels within the human body that can improve functional performance and reduce the risk of falls.

The effect of the vibration is dependent on three parameters: frequency, amplitude, and duration. The amplitude of the machine is measured in millimeters (mm), is independent of the vibration frequency, and is determined as the displacement between the neutral and peak positions of the platform during the oscillations. The frequency of the vibration is measured in hertz (Hz), which quantifies how quickly the platform oscillates, particularly the number of cycles completed within one second. The duration is the total amount of time the trainees receiving the vibration stimulus during a single training session (Moezy, Olyaei, Hadian, Razi & Faghihzadeh, 2008).

There are three types of vibrating platforms: side-alternating (oscillating), vertical (linear), and multidimensional (oscillating and linear) (Fig. 2). The side-alternating vibration platform rotates around an anterior-posterior horizontal axis, which operates like a seesaw mimicking a human gait pattern. In this type of vibration if the feet are further from the axis it results in larger vibration amplitude. Intuitively, the vertical vibration platform moves both sides of the body up and down synchronously. The multidimensional platform creates oscillating movements in both vertical and horizontal planes (Pel, 2009). The vertical and multidimensional platforms, which operate mainly in a vertical movement, cause the vibrations to be transmitted up the body towards the head, which may lead to discomfort of the participants as well as excess joint displacement at the cervical spine. It may also create unwanted stress on the joints, tendons and ligaments (Merriman & Jackson, 2010). On the other hand, the pivoting movement of the hip joints during the side-alternating vibration provides an additional movement degree of freedom to the body (Torvinen et al., 2002). As a result, the side-alternating vibration machine has been shown to be safer and more effective than the vertical vibration machine, due to the oscillations being transfer mainly to the lower limbs and causing isolation of the upper body. A side-alternating vibration platform (Galileo Med-L, Germany) was used in this study.

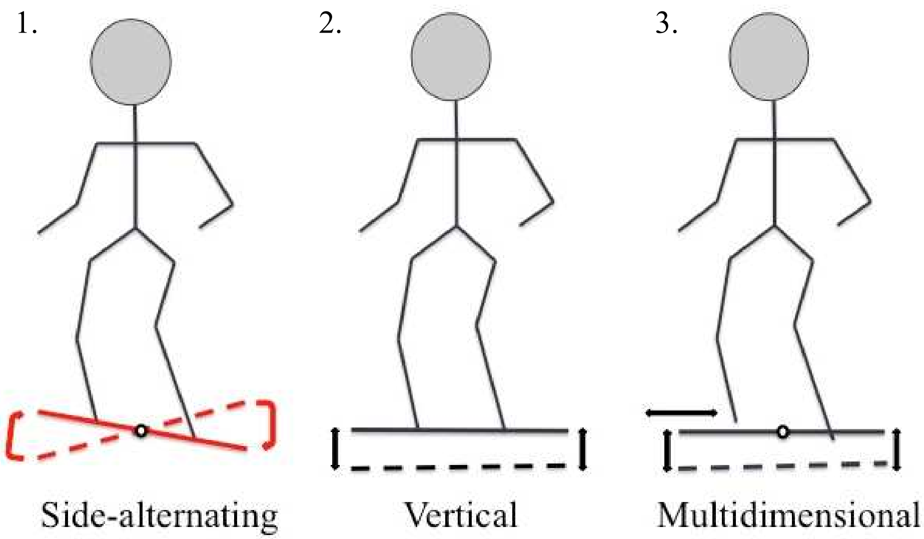

Fig. 2. Types of Vibration Platforms

Schematic illustration of the three types of vibration platforms: (1) the side-alternating (oscillating), (2) vertical vibration (linear), and (3) multidimensional vibration.

1.5.2. CWBV and MS

Although CWBV training has been applied to populations with other neurological dysfunctions, few studies have examined the effect of CWBV training at modifying functional performance and reducing risk of falls among people with MS. The limited studies have shown that CWBV training may result in an increase in neuromuscular activation during and after training (Madou & Cronin, 2008). In total, 11 articles regarding the effects of CWBV training among people with MS were found after searching various major databases (such as PubMed, ScienceDirect, and Google Scholar). All these articles were concerned with the effects of CWBV training on altering some functional activities of people with MS. While the focus of these articles was not directly about fall prevention, those factors investigated could be considered risk factors of falls. The protocols, training parameters, participants, and findings of these studies are summarized in Table 1.

Table 1. Summary of studies applying CWBV training to people with MS

Study	Participants	Design	Vibration parameters	Device	Posture and tasks	Outcome measures	Results
Schuhfried et al., 2005	n = 12 CWBV group: 6 (F = 5, M = 1) Age: 49.3 ± 13.3 yrs EDSS: 3.7 ± 0.8 Placebo group: 6 (F = 4, M = 2) Age: 46.0 ± 12.7 yrs EDSS: 3.7 ± 0.8	Double-blind randomized experiment	*f*: 2.0-4.4 Hz A: 3 mm Training session: 5 series of 1 min each followed by 1 min rest Duration: 2 weeks	Multidimensional (Zeptor-Med system; Scisen Gmbh, Germany)	Static with slightly flexion at the hips, knees, and ankle joints	Balance; Functional mobility	Significant improvements for functional mobility; however, in balance no differences between the two groups.
Jackson et al., 2008	n = 15 CWBV group: 15 (F = 12, M = 3) Age: 54.6 ± 9.6 yrs EDSS: 4.2 ± 2.3	Crossover study: two groups, pre-test and post-test	*f* : 2 and 26 Hz A: 6 mm Training session: 30 s Duration: 1 session	Side alternative (Maxuvibe; Fitgroup BV, Hoogstrat, Holland)	Static with knee flexion at 25	Lower limb muscle strength	No significant improvement; however, the peak the quadriceps and hamstring muscles were higher after every 30 s of CWBV at 26 Hz than at 2 Hz.
Schyns et al., 2008	n = 16 CWBV group 1: 8 (F = 3, M = 5) CWBV group 2: 8 (F = 7, M = 1) Age: 45.8 ± 8.4 yrs	Crossover pilot study	*f* : 40 Hz A: 2 mm Training session: 30 s Duration: 2 weeks	Vertical (VibroGym International BV, The Nerthelands)	Variety of exercises with vibration	Lower limb muscle strength; functional mobility; sensation	No significant improvements in the outcomes however, functional mobility slightly improved.
Broekmans et al., 2010	n = 20 CWBV group: 11 (F = 7, M = 4) Age: 46.1 ± 2.1 yrs EDSS = 4.5 ± 0.4 Control group: 14 (F = 11, M = 3) Age: 49.7 ± 3.3 yrs EDSS = 4.1 ± 0.3	Randomized experiment	*f* : 20 Hz (0 weeks), 35 Hz (10th week), 45 Hz (20th week) A: 2.5 mm Training session: 2.5 to 8.0 to 16.5 s Duration: 20 weeks	Vertical (Alpha Vibe Nijverdal, The Netherlands)	Variety of exercises with vibration	Lower limb muscle strength; functional mobility	No significant improvement in lower limb muscle strength or functional mobility.
Wunderer et al., 2010	n = 3 CWBV group: 3 (F = 2; M = 1) Age: 43-60 yrs	Non experiment design	*f* : 40 Hz A: 2 mm Training session: 30 to 45 min Duration: 4 weeks	Vertical (VibroGym)	Variety of exercises with vibration	Lower limb muscle strength; functional mobility	Significant improvement on both muscle strength and functional mobility.
Claerbout et al., 2012	n = 55 CWBV-full group: 21 (F = 6, M =15) CWBV-light group: 18 (F = 4, M = 14) Control group: 17 (F = 11, M = 6) Age: range from 20 to 65 yrs, EDSS from 1 to 7	Randomized experimental design	*f* : 30-40 Hz, A: 1.6 mm Training session:7 to 13 min. Duration: 3 weeks	Vertical (Vibrafit; Fysiomed NV-SA, Edgem, Belgium)	CWBV-full group: variety of exercises with vibration CWBV-light group: same exercises as full group with a foam mat of 10 cm thickness	Lower limb muscle strength; functional mobility	Significant improvement on both muscle strength and functional mobility in CWBV-full group.

Manson et al. (2012)	<u>*n* = 15</u> CWBV group: 15 (F = 11, M = 4) Age: 50.2 ± 6.9 yrs EDSS: 3.5 ± 0.9	Non experiment al design	*f* : 15-25 Hz A: 2.6 to 6.1 mm Training session: 5 to 8 min Duration: 8 weeks	Side alternative (Galileo XS; Novotec, Pforzheim, Germany)	Static with slightly flexion at the hips, knees, and ankle joints	Functional mobility and balance	Significant improvement on both functional mobility and balance.
Eftekhari et al., 2012	<u>*n* = 24</u> CWBV group: 12 Age = 35.0 ± 6.8 yrs EDSS = 2.8 ± 0.8 Control group: 12 Age = 33.7 ± 5.3 yrs EDSS = 2.7 ± 0.6	Randomize d experiment	*f* : 2-20 Hz A: 2 mm Training session: 6 sets of 30 s Duration: 8 weeks	Multidimensional (Crazy Fit Massage, Fitness Vibration Machine, Power Plate (TQ908) e., China)	Variety of exercises with vibration	Lower limb muscle strength and functional mobility	Significant improvement on both muscle strength and functional mobility.
Hilgers et al., 2013	<u>*n = 30*</u> CWBV group: 30 (F = 22, M = 8) Age: 43.5 ± 10.0 yrs EDSS: 3.5 ± 1.2 Placebo group: 30 (F = 23, M = 7) Age: 43.9 ± 7.5 yrs EDSS: 3.3 ± 1.3	Randomize d controlled study	*f* : 30 Hz A: 1-2 mm Training session: 60 s Duration: 3 weeks	Vertical (Power Plate pro5, Power Plate International, London U.K)	Variety of exercises with vibration	Functional mobility	Significant improvement in functional mobility.
Wolfsegger et al., 2014	<u>*n = 17*</u> CWBV group: 9 (F = 8, M = 1) Age: 43.0 ± 13.4 yrs EDSS = 2.5 ± 1.0 Placebo group: 8 (F = 7, M = 1) Age: 39.3 ± 10.6 yrs EDSS: 2.4 ± 0.8	Randomize d controlled study	Training session: WEEK 1: *f* : 2.5-3.0 Hz, Training ssession: 45 s WEEK 2: *f* : 3.5-4.0 Hz, Training sesion : 60 s WEEK 3: *f* : 4.5-5.0 Hz, Training ssesion : 60 s Duration: 3 weeks	Multidimensional (Zeptoring multidirectional stochastic platform, Scisen GmbH, Germany)	Variety of exercises with vibration	Functional mobility and gait function	No significant improvement in functional mobility and gait function.
Uszynski et al., 2015	<u>*n = 24*</u> CWBV group: 12 Age: 43.5 ± 10.0 yrs EDSS = 3.5 ± 1.2 Placebo group: 12 Age: 43.9 ± 7.5yrs EDSS = 3.3 ± 1.3	Randomize d controlled study	*f* : 40 Hz A: 0-10 mm Training session: Depended on the exercise duration Duration: 12 weeks	Vertical (Crazy Fit)	Variety of exercises with vibration	Functional mobility	No significant improvement in functional mobility.

CWBV: Controlled whole-body vibration
EDSS: Expanded Disability Statues Scale
A: Amplitude (mm)
f: Frequency (Hz)
n: Number of participants
F: females
M: males

The first study applying CWBV training among MS, conducted by Schuhfried et al. (2005), examined the effect of CWBV training on functional mobility and balance among people with MS. The study consisted of 12 individuals of whom 6 participants underwent vibration training (the training group), and 6 had electrical nerve stimulation (the control group). The training group underwent a multidimensional CWBV training with a 3-mm amplitude and various frequencies. The frequency began with 1 Hz and slowly increased until the patient no longer tolerated a further increase. According to the study, the range of the frequency in all participants was between 2.0 and 4.4 Hz. During vibration training the participants were asked to maintain a squat position with slight flexion at the hips, knees, and ankle joints. The control group had a Burst-transcutaneous electrical nerve stimulation application on the non-dominant forearm. The intervention for both groups included five cycles of 1-minute training followed by a 1-minute resting period. The results indicated that functional mobility significantly increased for the training group from pre-training to post-training after two weeks of intervention. In regard to balance improvement, the researchers did not see any difference between the two groups (Schuhfried et al., 2005). This study revealed that CWBV training could improve functional mobility, but not the body balance, among people with MS. One of the reasons why the results did not reach the significant level in body balance was the low vibration frequency, which may not be sufficiently intense to generate desired changes. Another possible explanation of the non-significant difference could be the small sample size.

The first two studies that examined the effects of CWBV training on improving strength among people with MS did not detect any statistically significant results; however, the studies reported that the strength measurement did increase after the vibration training (Jackson et al., 2008; Schyns et al., 2009). The first study by Jackson et al. (2008) investigated the acute effects of CWBV on lower extremity muscle performance among people with MS. The training was delivered on a side-alternating vibration platform at two different frequencies of 2 and 26 Hz and an amplitude of 6 mm. Each training bout lasted 30 s. The participants' strength of the quadriceps and hamstrings was measured before training (or baseline test) and at 10 and 20 min following the vibration exposure. Neither frequency showed any significant improvement in lower extremity muscle strength; however, there was a tendency of improvement on both quadriceps and hamstring muscles, implying that vibration training could modify muscle strength among MS (Jackson et al., 2008).

The second article by Schyns et al. (2009) utilized a longer training period of four weeks. The variables assessed were functional mobility, spasticity, muscle force and sensation among people with MS. Sixteen individuals participated in the study, and were randomly assigned to either group 1 or group 2. Group 1 received an intervention exercise with vibration three times a week for a total of four weeks followed by a two week washout period. The training was performed on a vertical platform and the frequency and amplitude were set at 40 Hz and 2 mm, respectively. Following the washout period, the same protocol with the same amount of training sessions was performed; however, vibration was not included. Group 2 performed the same protocol as group 1 but the order of the treatment was reversed. This group had four weeks of exercise alone, two weeks rest and then four weeks of exercise with vibration. The only significant outcome as a result of the training was a reduction in spasms. Spasms in the group receiving exercise and CWBV were reduced significantly as a result of the vibration training. Researcher reported a tendency of improvement in muscle strength with the addition of whole body vibration training; but did not reach statistical significance. Similarly, functional mobility did improve but did not achieve statistical significance. For sensation there was no improvement for either group (Schyns et al., 2009).

Another study examined the effects of a 3-week CWBV training on changing the functional mobility among people with MS. This study enrolled 30 individuals in the intervention group and 30 in the control group. The intervention involved three series of 60-second moderate squats while standing on a multidimensional vibration platform, three times per week at a frequency of 30 Hz. The training intensity was increased each week by reducing the rest period between sets and increasing the amplitude from 1 to 2 mm. During the exercise series the intervention group had the platform turned on while it was off for the control group. The results indicated significantly greater improvements in the intervention group than the control group after the training program (Hilgers, Mündermann, Riehle, & Dettmers, 2013).

Wolfsegger, Assar, and Topakian (2014) assessed the influence of 3 weeks of CWBV training on gait function and functional mobility among people with MS. In their study, the frequency, vibration duration, and sets of exercises were increased gradually each week. The vibration frequency, duration of each bout, and number of exercise ranged from 2.5 - 5.0 Hz, 45 - 60 seconds, and 5 - 7 sets, respectively. The results did not show any significant improvement in the measurements of interests after the training course (Wolfsegger, Assar, & Topakian, 2014).

All studies reviewed above focused on a relatively short training duration (30 s – 4 weeks) and the findings were mixed. Some other studies have examined the effect of long-term CWBV training program on functional performance among people with MS. For example, Broekmans and associates examined the effects of a 20-week CWBV training intervention on strength performance and functional capacity among 25 people with MS. In the intervention group participants performed static and dynamic leg squats and lunges on a vertical vibration platform (frequency: 25 - 25 Hz, amplitude: 2.5 mm). The results were similar to those reported by Schyns et al. (2009) and Jackson et al. (2008), who examine strength. No significant improvements of the outcomes were observed at week 10 or week 20 of the training course. Therefore, the authors concluded long-term CWBV training did not improve upper leg muscle strength or functional capacity (Broekmans et al., 2010).

In contrast to the findings from Jackson et al. (2008), Schyns et al. (2009) and Broekmans et al. (2010), a study conducted by Wundered, Shabrun and Chipchase examined the effects of six weeks of CWBV training on strength and functional mobility among people with MS. The intervention adopted a vertical vibration platform with a frequency of 30 - 50 Hz, amplitude at 2 or 4 mm, and a variety of exercise activities during vibrations training. The results indicated significant improvements for both knee flexor strength and the functional mobility post-training in comparison with pre-training (Wunderer, Schabrun, & Chipchase, 2010). A similar study measuring the same outcomes also showed significant increases in lower muscle strength and functional mobility (Clerbout et al., 2012). In this study, three weeks of CWBV training were used to investigate its impact on muscle strength and functional mobility among people with MS. The study employed a vertical vibration platform with a frequency ranging from 30 - 40 Hz, amplitude of 1.6 mm and a variety of exercises performed with the vibration training. Although muscle strength improved significantly following training, the functional mobility did not exhibit any significant improvement (Clerbout et al., 2012).

Another similar study demonstrated a significant improvement in functional mobility after eight weeks of vibration training (Manson et al., 2012). The intervention in this study consisted of 5 series of 1-minute vibration training with 1-minute rest period between each series. The training was performed on a side-alternating vibration platform with a frequency ranging from 15 to 25 Hz and amplitude ranging from 2.6 to 6.1 mm (Manson et al., 2012). This study also examined body balance, which displayed significant improvements after the training.

Efekhari et al. (2012) sought to determine if an 8-week progressive resistance training and vibration program affects strength and ambulatory function among people with MS. The study incorporated an exercise program of different workouts for different muscle groups. Additionally, the training consisted of a series of exercises with vibration frequency ranging from 2 to 20 Hz and the amplitude of 2 mm on a multidimensional platform. The results indicated that resistance training along with CWBV training could lead to significant improvement of maximal voluntary contraction and better functional mobility (Efekhari et al., 2012).

Lastly, Uzynski and associates compared the effects of CWBV training to standard exercise among people with MS by measuring strength, functional mobility and balance (Uszynski, Purtill, Donnelly, & Coote, 2015). This study included an intervention group and a control group. Both groups performed various types of exercises for 12 weeks. Specifically, the intervention group performed those exercises on a vertical vibration platform at 40 Hz and amplitude ranging from 0 to 10 mm, whereas the control group did the same type of exercises without the vibration training. The results showed significant differences in all outcome measurements between groups although a slight increase in all outcome parameters for both groups was observed.

1.5.3. Knowledge Gap

As mentioned previously, MS is associated with multiple motor impairments of balance, functional mobility, muscle strength and sensation, all contributing to increased risk of falls. CWBV training could serve as an alternative training method for people with MS to reduce their risk of falls. However, several barriers still exist before the deployment of CWBV training clinically to reduce falls among people with MS. First, the findings from previous studies regarding CWBV and MS are inconclusive. A possible reason is the vastly different training parameters, protocols, and devices used in the previous studies. Second, no study was designed to inspect the potential effect of CWBV training on modifying other risk factors of falls, such as bone density, ROM, or cutaneous sensation of the feet. Last, the assessment instrument or tools were not standardized across previous studies. For example, in the two studies that examined the effects of CWBV training on sensation, one study measured sensation by using the Nottingham Sensory Assessment and the other study used the Neurothesiometer and Verbal analogue scale, which are not reliable tools because they may not be sufficiently sensitive in detecting specific changes in sensation. Thus, a systematic examination of the interactions between CWBV training and more comprehensive fall risk factors under the same training protocols is highly desired.

1.6. Purpose and Hypotheses

The primary purpose of this study was to examine the overall effectiveness of an 8-week CWBV training intervention on reducing the risk of falls among people living with MS. Aligning with the aim, we hypothesized that an 8-week CWBV training would reduce the risk of falls among individuals with MS. The decrease in the risk of falls would be reflected by the improvements in the risk factors of falls, which were quantified by body balance, functional mobility, lower limb muscle strength, ROM, sensation of the feet, fear of falling and bone density.

Fall prevention is of vital importance for persons with MS, their families and caregivers, and our society. If CWBV training could enhance the neuromuscular function and reduce risk of falls among people with MS, it can be implemented alone or in combination with an exercise-based fall prevention paradigms, offering people with MS a convenient extra option. As fall incidence decreases, the cost to individuals and the health care system will also decrease.

2. METHODS

2.1. Participants Recruitment

Participants were mainly recruited from El Paso and its adjacent regions. Recruitment efforts were facilitated via meetings with the MS Association of El Paso. Recruitment tactics involved verbal presentations at local MS events and the distribution of recruitment flyers to individuals at the MS meetings. Other recruitment efforts were made through the University of Texas at El Paso website, local radio stations and news broadcasts.

Those who were interested in participating in the study were contacted via a phone call to collect their full name, home address, and email address (if any). Investigators then contacted them and administered a pre-screening questionnaire to verify their eligibility of participation. The questionnaire consisted of their history of falling, exercise performance, neurological disease, health issues, and consumption of medication, alcohol, or recreational drugs. All participants who met the inclusion criteria (see **Section 2.2** below for details.) were given information about the study and an opportunity to ask questions. Prior to data collection all participants were required to sign an informed written consent form approved by the Institutional Review Board at the University of Texas at El Paso (514810-4). Additionally, participants were given a physician letter, which offered information to their neurologist who verified that the participant has been officially diagnosed with MS

Although no restriction was applied to participants' ethnic background or gender, there were some inclusion and exclusion criteria to avoid any potential impact on our findings from confounding factors, such as health status. The inclusion criteria were:

1) Participants must be between 21 and 75 years of age.

2) They must not have had a significant MS relapse within the past 8 weeks.
3) They must be free from other major general medical or surgical disorders or pregnancy.
4) Their Patient Determined Disease Steps (PDDS) score must be less than 7. People in this range are able to stand and walk independently, with or without assistance, which exposes them to risk of falls (Kalron, 2013). In addition, they have the physical capability to undergo the training and evaluations.
5) They must be medically stable.

The exclusion criteria were comprised of:

1) Participation in whole-body exercise, balance training or resistance exercise within the past 6 months.
2) Any experienced with vibration training.
3) Under 21 years of age or over 75 years of age.
4) Severe pain at the shoulder, knee, cervical region, or back.
5) Surgery of the back, hip, shoulder, or knee in the past two years prior to the study.
6) Other medical conditions or health issues, such as rheumatoid arthritis, broken bones within six months prior to the study, uncontrolled diabetes, neurological diseases besides MS, and practice of recreational drugs.

A total of 37 participants were identified as potential participants for the study; however, 30 individuals were screened for eligibility and 25 participants met the enrollment criteria. All participants were asked to maintain their normal lifestyle during the study term. After the initial evaluation 3 participants withdrew from the intervention due to scheduling conflict or medical issue, not associated with the training. During the evaluation and training, the investigators closely monitored the participants to ensure their safety. They were also, frequently asked if they needed to take a break, if they were feeling fatigued or any other discomfort. Refer to Table 2 for participant demographic information.

Table 2. Demographic information of 25 participants (18 females and 7 males)

Parameter	Mean	SD	Minimum	Maximum	Median
Age (years)	50.3	14.1	21	71	52.0
Height (cm)	165.4	9.2	152.3	186	162.3
Mass (kg)	73.9	14.1	51.4	105.3	73.3
PDDS	3.6	1.8	0	6.5	4
Duration (years)	15.3	10.5	2	43	13
Type of MS	RR = 16	SP = 5	PR = 1	Unknown = 3	

SD: Standard Deviation; PDDS: Patient Determined Disease Steps

RR: Relapsing-remitting; SP: Secondary Progressive; PR: Progressive-Relapsing

2.3. Study Design

The study adopted a single-group pre-test – post-test longitudinal design. All risk factors of falls were evaluated and compared before and after the 8-week intervention. The 8-week CWBV training course consisted of 24 total sessions (i.e. three sessions per week for eight weeks) (Fig. 3a).

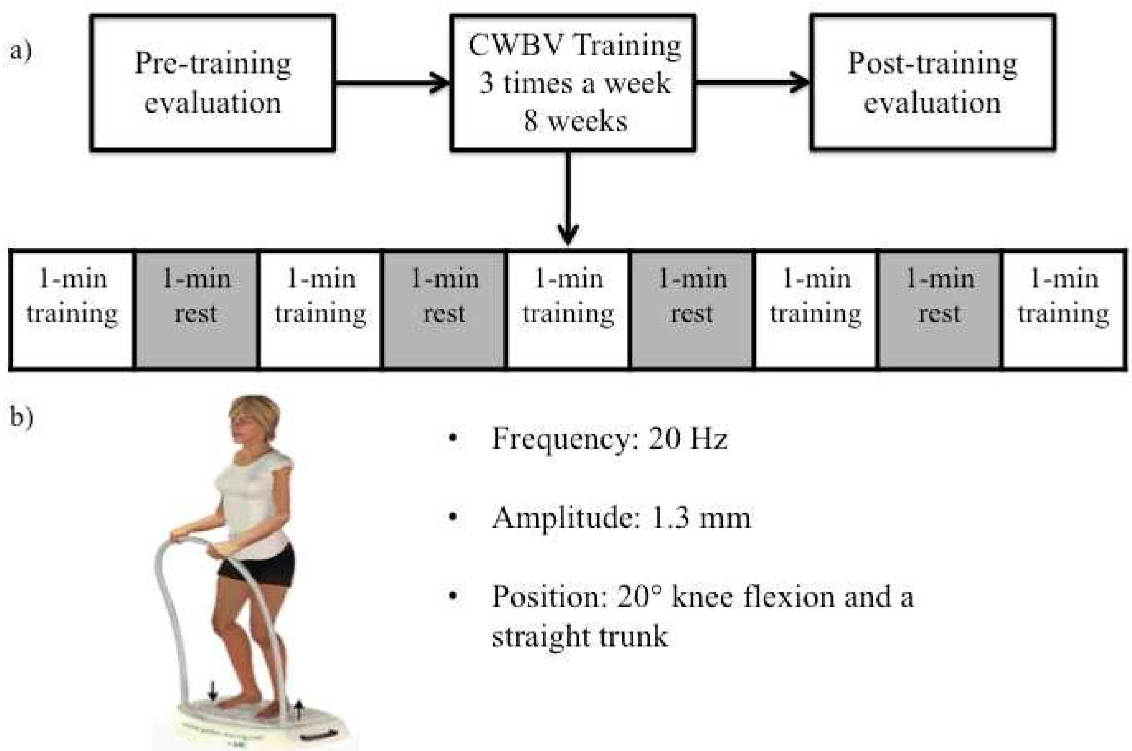

Fig. 3. Study design and experimental protocol

Schematic illustrations of a) the experimental protocol of the 8-week CWBV program and b) the side-alternating vibration platform and body posture during the training. Each training session consisted of five repetitions of 1-min vibration followed by a 1-min rest period. Participants were required to stand barefoot on the platform, holding on to the handlebars, with 20° knee flexion and a straight trunk.

2.4. Vibration Training

A side-alternating vibration platform (Galileo Med-L, Germany) was used for the study. Participants stood on the platform with a straight trunk and knees flexed at 20° to assure their safety and comfort (Fig. 3b). The vibration frequency was set at 20 Hz with an amplitude of 1.3 mm (or peak to peak displacement of 2.6 mm). Training consisted of five cycles of 1-min of vibration and 1-min rest period (Fig. 3a). During the training, the participants were monitored to avoid any undesired deviation in position or any negative side effects of the training.

2.5. Fall Risk Evaluation

Based on the extent to which each risk factor relates to falls, we divided the risk factors into two outcome groups: primary and secondary. Both groups of risk factors were evaluated twice: prior to and following the 8-week training course (Fig. 3a).

2.5.1. Primary Outcomes

The three primary measurements consisted of the body balance, functional mobility, and muscle strength.

Body Balance. Balance impairment has been identified as the attribute most often associated with falls among individuals with MS (Finlayson, Peterson, & Cho, 2006). In this study, participants' balance performance was assessed using the EquiScale Test (Granger, 1990). During the EquiScale test, participants performed a series of 8 functional balance tasks of increasing difficulty. The tasks included standing, transferring, rotating, and reaching. The degree of success in achieving each task was scored from 0 (unable) to 2 (independent), and the final measure was the sum of all of the scores, which range between 0 and 16, was used for analysis. The greater the total score, the better the body balance skill.

Functional Mobility. Functional mobility was evaluated using the Timed-Up & Go (TUG) test (Nilsagard, 2007). In the TUG test, participants stood up from an armed chair, walked forward 3 m at a self-selected pace, crossed a marked line on the floor, turned around, walked back, and then sat back down on the chair (Schuhfried et al., 2005). The chair was fixed on the floor to avoid any unwanted movement during the test. The time required to complete the task was recorded for analysis. The entire procedure was explained to the participants before the actual test.

Muscle Strength. The isometric strength capacity was assessed on the knee extensor and flexor via an isokinetic dynamometer (Biodex System 3, Shirley, NY). Before the strength test, all participants underwent a standardized warm-up on the dynamometer to experience the test conditions (Armstrong, 1983). While participants were seated on the dynamometer chair, their trunk and the tested thigh were stabilized with safety belts to avoid any unwanted movement during the strength test. The rotational axis of the dynamometer was aligned with the transverse knee-joint axis and connected to the distal end of the tibia using a length-adjustable rigid lever arm. The three-dimensional positions of the rotational axis, the position of the chair, and the length of the lever arm were identical for the pre- and post-intervention evaluation sessions. Participants firstly performed maximal voluntary isometric contractions of knee extensors and flexors three times each lower limb. The contractions lasted seven seconds each and were separated by a 2-min rest interval. The greatest torque normalized to body mass (Nm/kg) was recorded as isometric strength performance during each repetition under each contraction condition. The average maximum torque across the three repetitions under each contraction condition was calculated. The side (left or right) producing higher maximum knee extensor strength was identified as the strong side. Therefore, four muscle measurements (extensor or flexor × strong or weak) were collected for each participant for analysis.

2.5.2. Secondary Outcomes

The following variables were considered the secondary outcomes.

Range of Motion. The active and passive plantarflexion and dorsiflexion ROM of the ankle joint was measured bilaterally using a goniometer (Reese & Bandy, 2016). The assessment of the ROM was conducted when participants were in the supine position. Participants were asked to voluntarily push their toes away as far as possible (plantarflexion). Then participants were asked to relax and investigator applied passive force pushing the participant's toes forward. Afterwards, participants were asked to bring their toe towards their body as close as possible (dorsiflexion) and then participants relaxed and investigator applied passive force to assist them with the dorsiflexion movement.

Cutaneous Sensation. Light touch-pressure sensation threshold was assessed using a full Semmes-Weinstein Monofilament test kit (North Coast Medical, San Jose, CA, USA) at the three regions of both soles (first and fifth phalanges and the heel). The sizes of the filament range between 1.65 and 6.65 (Kelleher, Spence, Solomonidis, & Apatsidis, 2010). The smallest (1.65) monofilament was applied firstly. Monofilaments were touched for 1.0 – 1.5 s to the test locations and 1.65 – 3.61 monofilaments were applied three times consecutively. When the participant felt the stimulus correctly in one of the three trials, the filament representing a specific force was noted as the participant's score, 3.84 and higher filaments were applied only once (Jerosch-Herold, 2005).

Fear of Falling. Fear of falling was measured with the Falls Efficacy Scale – International (FES-I) questionnaire. This questionnaire lists 16 daily living activities. Participants were asked to rate how concerned they are about falling when performing these activities. The level of concern for each activity is scored on a four–point scale (1 = not at all concern, 2 = somewhat concern, 3 = quite a lot concern, 4 = very concern). The score from all items were summed which ranges between 16 and 64 (van Vliet, Hoang, Lord, Gandevia, & Delbaere, 2013). The greater the score is, the greater the concern about falling.

Bone Density. Bone density of the calcanei was measured on both sides by a bone ultrosonometer (The Achillies Insight, GE, UK). The heel bone (calcaneus) was measured because it is one of the most important weight–bearing bones in the body and it is a common measurement site due to its accessibility, suitable shape and high trabecular content (Yung et al., 2005). Additionally, Blanchet et al. (2003) showed an association between physical activity and non-radiation quantitative ultrasound measurement on the calcanei, independently of bone mineral density. Therefore, the heel bone could be a suitable outcome measurement by using a bone ultrosonometer. The bone density results were reported as the *T*-score, which was defined as the number of standard deviations (SD) from the average value of healthy young adults, indicating how much the score is diverse, from the desirable value (Kanis, 1994).

2.6. Statistical Analyses

The mean and SD of the participants' demographics and risk factors of falls were calculated. The Shapiro-Wilk test was used to determine the normality for the difference of all the outcome variables between the pre- and post-training evaluations. Paired *t*-tests (for the normally distributed factors) and the Wilcoxon matched-pairs signed rank test (for those factors with non-normal distribution) were used to compare the risk factors between pre-training and post-training evaluations. The risk factors analyzed included body balance, functional mobility, muscle strength, ROM, cutaneous sensation, fear of falling, and bone density. The Bonferroni step-down (Holm) correction was used to minimize the Type I error due to the multiple comparisons. The effect size for all the outcome variables was calculated to illustrate the degree of difference between the pre-test and post-test. For the variables with normal distribution, Cohen's d_z was calculated as the effect size (Field, 2013). For factors, which were not normally distributed, the equation suggested by Pallant (2007) was used to determine the effect size.

$$r = \frac{Z}{\sqrt{n_{pre} + n_{post}}}$$

Where Z is the output from the Wilcoxon matched-pairs signed rank test statistic and n_{pre} and n_{post} respectively represents the number of observations during the pre- and post-training evaluations.

All analyses were conducted using SPSS 22.0 (IBM, Armonk, NY) and graphs and figures were created using GraphPad Prism 7.0. Statistical significance level was set at $p < 0.05$.

3. RESULTS

Three participants withdrew from the study due to scheduling conflict (*n* = 2) or relapsing (*n* = 1). Thus, 22 participants successfully completed the intervention with a compliance rate of 100% (number of training sessions = 24). The vibration training was well accepted by all participants and none of them reported any major discomfort or adverse effects. Some of them experienced itching of their legs or nose, but these effects were mild and subsided soon after approximately 3 – 5 training sessions.

3.1 Normality Analysis

The Shapiro-Wilk normality test indicated that the body balance, the passive dorsiflexion ROM on the weak side, the active plantarflexion ROM on the weak side, the sensation threshold on the strong side, and the sensation threshold at positions 2 and 3 on the weak side were not normally distributed while all other variables met the requirements of the normality tests (Table 3).

Table 3. Shapiro-Wilk normality test for outcome variables

Outcome Variable	*p* value	Normal Distribution	Test Strategy
Body Balance	.005	No	Wilcoxon Test
Functional Mobility	.193	Yes	Paired T –Test
Strength: Extensor, Strong Side	.529	Yes	Paired T –Test
Strength: Flexor, Strong Side	.968	Yes	Paired T –Test
Strength: Extensor, Weak Side	.046	No	Wilcoxon Test
Strength: Flexor, Weak Side	.739	Yes	Paired T –Test
Dorsiflexion ROM: Active, Strong Side	.676	Yes	Paired T –Test
Dorsiflexion ROM: Passive, Strong Side	.130	Yes	Paired T –Test
Plantarflexion ROM: Active, Strong Side	.842	Yes	Paired T –Test
Plantarflexion ROM: Passive, Strong Side	.290	Yes	Paired T –Test
Dorsiflexion ROM: Active, Weak Side	.123	Yes	Paired T –Test
Dorsiflexion ROM: Passive, Weak Side	< .001	No	Wilcoxon Test
Plantarflexion ROM: Active, Weak Side	.034	No	Wilcoxon Test
Plantarflexion ROM: Passive, Weak Side	.937	Yes	Paired T –Test
Sensation: Position 1, Strong Side	.030	No	Wilcoxon Test
Sensation: Position 2, Strong Side	.009	No	Wilcoxon Test
Sensation: Position 3, Strong Side	.002	No	Wilcoxon Test
Sensation: Position 1, Weak Side	.056	Yes	Paired T –Test
Sensation: Position 2, Weak Side	.024	No	Wilcoxon Test
Sensation: Position 3, Weak Side	< .001	No	Wilcoxon Test
Fear of Falling	.462	Yes	Paired T –Test
Bone Density: Strong side	.225	Yes	Paired T –Test
Bone Density: Weak Side	.118	Yes	Paired T –Test

3.2 Primary Risk Factors

Compared to pre-training values, the post-training EquiScale Balance Test significantly increased (11.09 ± 3.99 vs. 12.68 ± 3.18, $p < .0001$, $r = 0.5$, Fig. 4a) after the 8-week CWBV training. The time for completing the TUG test significantly reduced from 14.75 ± 6.60 s during the pre-training assessment to 13.04 ± 5.49 s at post-training evaluation ($p < .01$, $d_z = 0.8$, Fig. 4b). The muscle strength also showed significant improvements on the strong-side knee flexor (0.82 ± 0.23 vs. 0.89 ± 0.31 Nm/kg, $p < .05$, $d_z = 0.6$, Fig. 4c) while the extensor did not exhibit significant improvement (1.16 ± 0.48 vs. 1.20 ± 0.49 Nm/kg, $p > .05$, $d_z = 0.1$, Fig. 4c). In contrast, the value for muscle strength on the weak side knee extensor was significantly improved from pre-training (0.93 ± 0.49 Nm/kg) to post-training (1.07 ± 0.50 Nm/kg) ($p < .01$, $d_z = 0.7$, Fig. 4d). The strength on the weak side knee flexor also showed significant improvements (0.72 ± 0.33 vs. 0.81 ± 0.35 Nm/kg, $p < .05$, $d_z = 0.6$, Fig. 4d).

3.3 Secondary Risk Factors

The dorsiflexion active ROM demonstrated significant improvements on the strong side (-3.09 ± 13.49° vs. -0.09 ± 11.70°, $p < .05$, $d_z = 0.5$, Fig. 5a); so did the passive ROM (0.80 ± 10.50° vs. 4.55 ± 7.46°, $p < .05$, $d_z = 0.7$, Fig. 5a). Likewise the dorsiflexion active ROM (-5.86 ± 15.3° to -2.6 ± 14.4°, $p < .001$, $d_z = 0.9$, Fig. 5b) and dorsiflexion passive ROM (-0.5 ± 11.8° to 1.1 ± 11.5°, $p < .05$, $r = 0.3$, Fig. 5b) dorsiflexion ROM was significantly improved after training on the weak side. The plantarflexion active ROM for the strong side was significantly improved from the pre-training test to the post-training test (56.6 ± 10.0° vs. 59.5 ± 8.0°, $p < .05$, $d_z = 0.5$, Fig. 5c), though the passive one showed a marginal improvement (61.8 ± 9.2° vs. 63.8 ± 8.4°, *p*

= .059, $d_z = 0.4$, Fig. 5c). Similarly, the plantarflexion ROM was significantly improved during the active motion on the weak side (54.0 ± 11.4° vs. 59.2 ± 7.8°, $p < .01$, $r = 0.4$, Fig. 5d), whereas passive motion only exhibited a marginal training-related improvement on the same side (61.0 ± 9.0° vs. 63.7 ± 7.9°, $p = .050$, $d_z = 0.4$, Fig. 5d).

All the participants were able to detect the monofilaments at each of the 3 location contact sites of both feet at pre- and post-training assessments. The sensation threshold for the 3 locations on the strong and weak sides did not show any significant improvements after the training (strong side: location #1: 4.5 ± 0.9 vs. 4.2 ± 0.3, $p > .05$, $r = 0.2$, location #2: 4.1 ± 0.7 vs. 4.0 ± 0.4, $p > .05$, $r = 0.1$, location #3: 5.0 ± 1.0 vs. 4.8 ± 1.0, $p > .05$, $r = 0.3$, Fig. 6a; weak side: location #1: 4.4 ± 0.8 vs. 4.2 ± 0.7, $d_z = 0.3$, $p > .05$, location #2: 4.2 ± 0.9 vs. 3.8 ± 0.5, $p > .05$, $r = 0.3$, location #3: 5.0 ± 1.0 vs. 4.9 ± 0.9, $p > .05$, $r = 0.1$, Fig. 6b).

The fear of falling score was significantly improved at the-post-training evaluation compared with the pre-training test (39.0 ± 10.4 vs. 35.1 ± 11.3, $p < .05$, $d_z = 0.5$, Fig. 6c). Bone density on the strong side was significantly increased after the training (-0.6 ± 1.2 vs. -0.4 ± 1.18, $p < .0001$, $d_z = 1.2$, Fig. 6d), likewise for the weak side (-0.7 ± 1.2 vs. -0.5 ± 1.2, $p < .05$, $d_z = 0.6$, Fig. 6d).

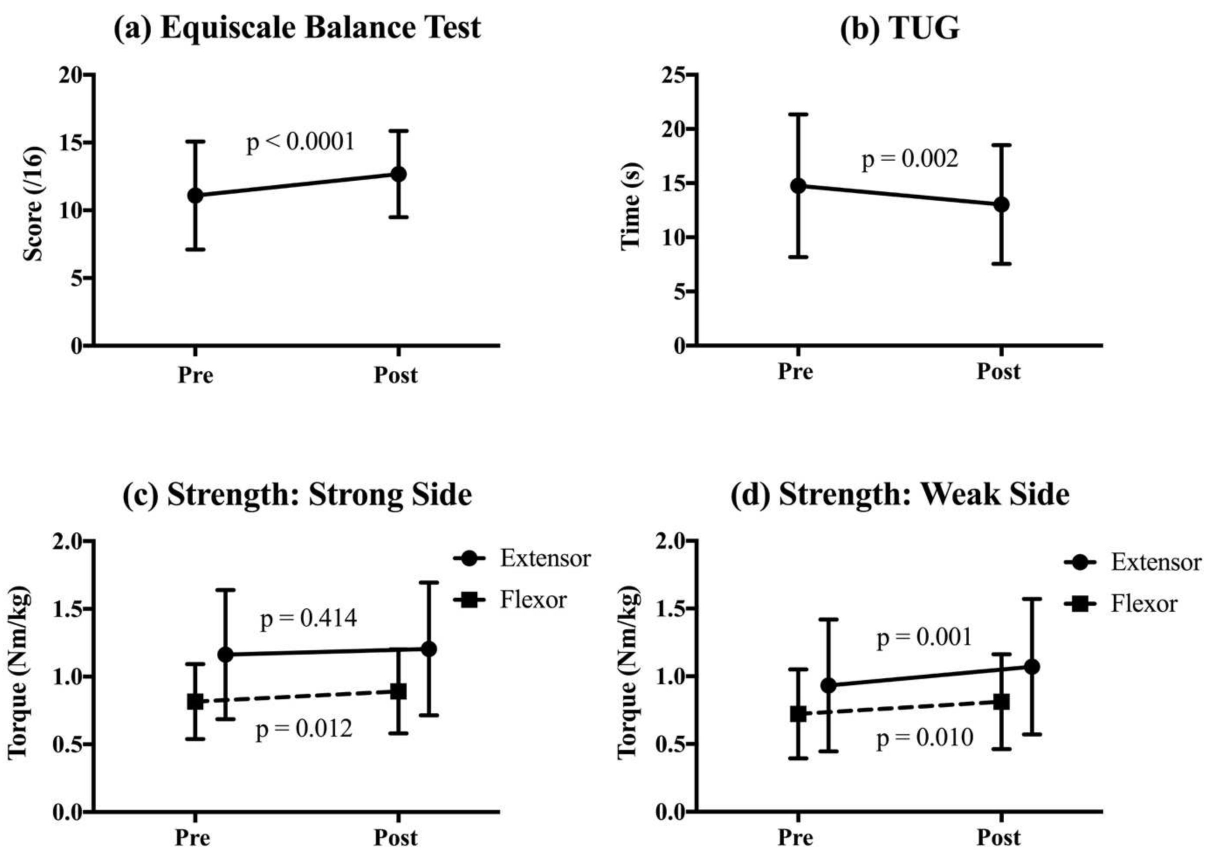

Fig. 4. Primary outcomes: Balance, mobility, and strength

Comparisons of (a) EquiScale balance score, (b) the Time-Up-and-Go (TUG) test, the maximum isometric voluntary muscle strength of knee joint in Nm/kg on (c) the strong side and (d) weak side between pre- (Pre) and post-training (Post) evaluations. The strong side was determined as the one which produces greater knee extensor strength capacity.

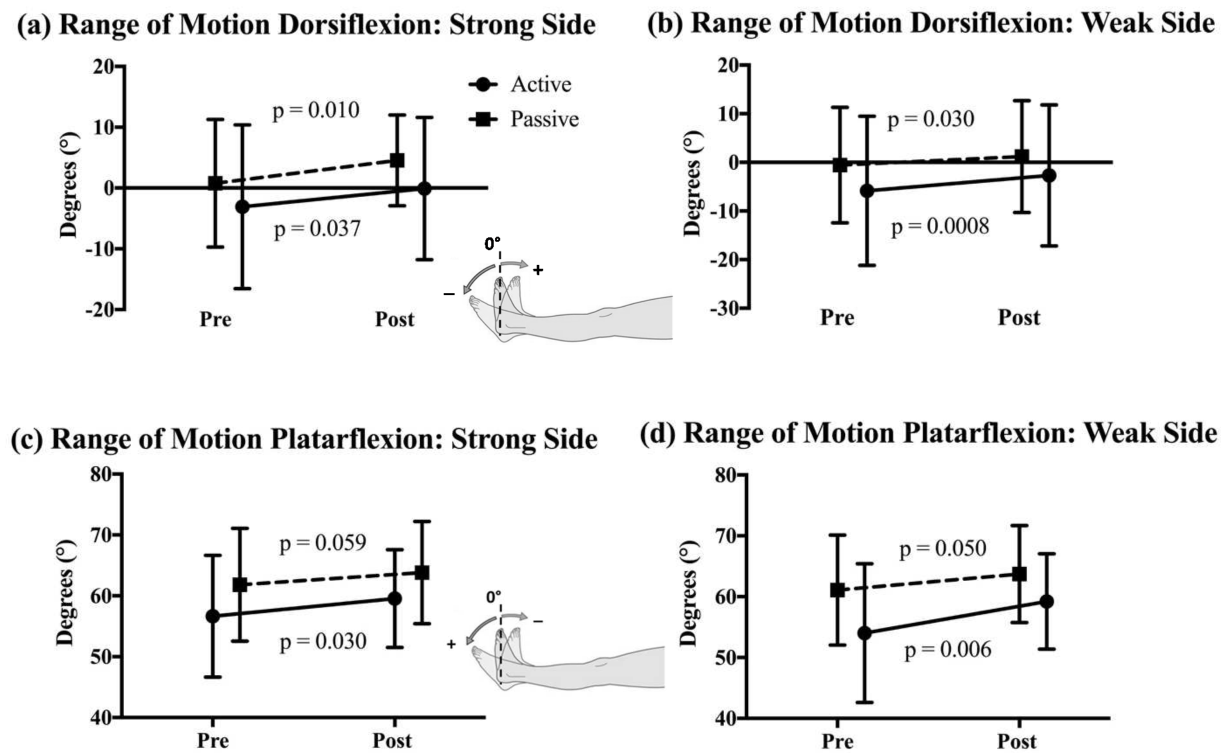

Fig. 5. Secondary outcome: Active and passive ROM

Comparisons of the dorsiflexion range of motion (ROM) on (a) the strong and (b) the weak sides, the plantarflexion ROM on (c) the strong side and (d) the weak side between pre-training (Pre) and post-training (Post) evaluations.

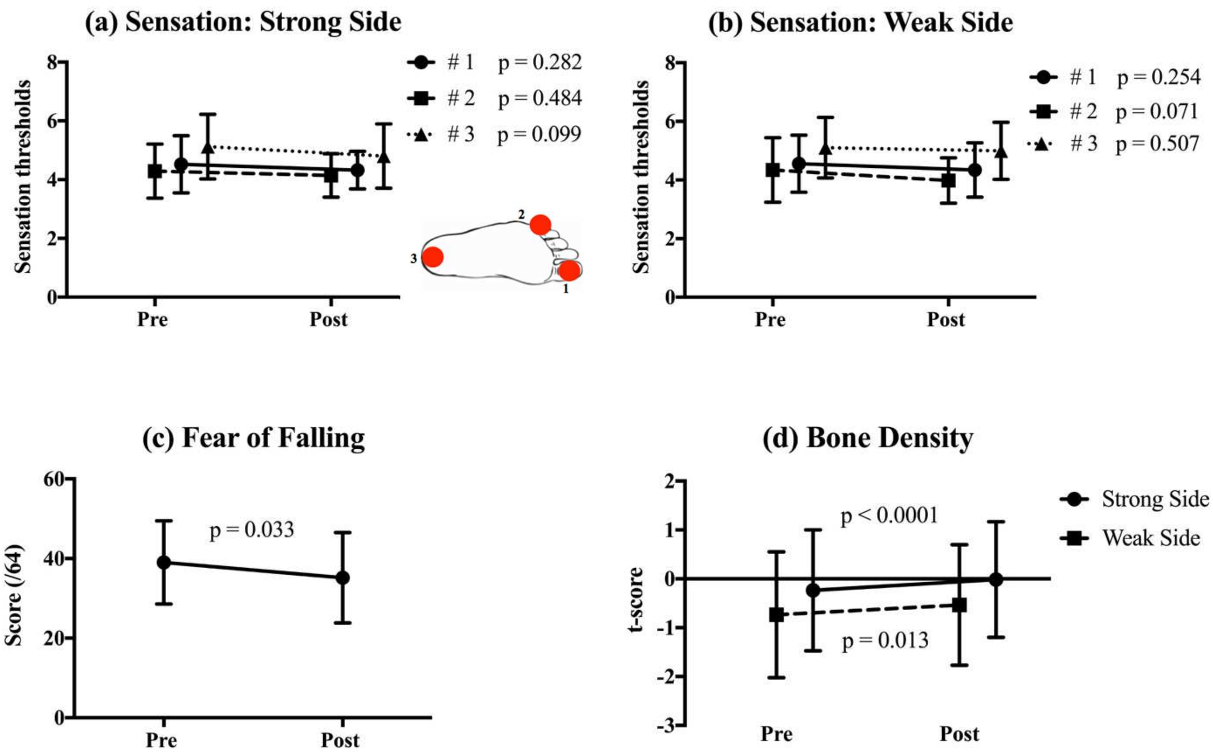

Fig. 6. Secondary outcomes: Cutaneous sensation, fear or falling, and bone density

Comparisons of the sensation threshold of the sole on (a) the strong side and (b) the weak side, (c) fear of falling, and (d) T-score quantifying the calcaneus bone density between pre-training (Pre) and post-training (Post) evaluations.

4. DISCUSSION

This study investigated whether an 8-week CWBV intervention improves the risk factors of falls among people with MS. Our results indeed support our hypothesis that an 8-week CWBV training program reduces the risk of falls among people with MS. Specifically, the vibration intervention improved body balance, functional mobility, muscle strength, ROM, cutaneous sensation of the feet, fear of falling and bone density. To our knowledge, this is the first study to investigate the impact of CWBV training on ROM of the ankle, fear of falling, and bone density among people with MS.

4.1 Primary Outcomes

Body balance was improved after the training in the present study (Fig. 4a). This finding confirms that of Manson et al. (2012) who reported that after 8 weeks of CWBV training body balance improved among people with MS and is similar to results observed for fragile elderly population (Bautmans et al., 2005), people with Parkinson's (Eberbach et al., 2008), and stroke patients (van Ness et al., 2006).

Regarding functional mobility, the present study found significant reduction in time to complete the TUG test (Fig. 4b). Our findings are consistent with previous studies, which also showed significant improvements of the TUG test for people with MS following vibration training (Schuhfried et al., 2005, Wunderer et al., 2010, Claerbout et al., 2012, Manson et al., 2012, Eftekhari et al., 2012, & Hilgers et al., 2013). Likewise, Chan et al., reported significant reduction in time for the TUG test after a single session of CWBV training among stroke patients.

These significant improvements of body balance and functional mobility may have been possibly related to the increased lower limb muscle strength, given reports correlating muscle strength with body balance and mobility for stroke patients (Karatas et al., 2004), people suffering from Parkinson's disease (Nallegowda et al., 2004), and elderly population (Ringsberg et al., 1999). Owing that balance and functional mobility are common motor impairments observed with those at increased risk of falls, our findings could be critical in preventing falls among this population.

There was significant improvement in all the strength measurements except for the knee extensor strength on the strong side. As illustrated in Table 2, the initial disability level determined by the PDDS indicated an average of 3.6, which denotes that there was a rather mild baseline ambulatory impairment among these participants. Thus, it could be possible that the stimulation of the weak side could have been grater than the stimulation on the strong side. This could have led to the weak side having more potential to in generating a larger amount of motor units and force production. This explanation could be indirectly reinforced by the significant improvements of all the weak side knee extensor/flexor strength and strong side knee flexor strength; after the intervention the values were still lower than the maximum knee extensor of the strong side. It has been implied that CWBV training can possibly result in neurological and morphological adaptations; however, among people with MS this adaptation may take a longer period to develop (Delecluse, Roelants & Verschueren, 2003). Therefore, on the other hand, the strong side knee joint extensor may have needed a longer period of training, higher intensity or exercises added to the vibration training to show significant improvement.

It is impossible to directly compare our results with the mixed finding from previous studies regarding CWBV training and MS, due to the variety of parameters. For instance, in the article by Clarbout et al. (2012), a significant improvement of quadriceps strength was reported after 3 weeks of exercises and vibration training. Another study by Eftekhari et al. (2012) reported significant improvements of the knee extensors after 8 weeks of vibration training with exercises. Before these two studies Wunderer et al. (2010), showed significant results after a variety of exercises with vibration training on the knee joint extensors; however, this article only consisted of a single participant experimental design (*n* = 3). Thus, their results are not conclusive since it is difficult to determine whether that exercise was causing the improvement or the vibration training. In contrast to the present study, Jackson et al. (2008), Schyns et al. (2008), and Broekmans et al. (2010), did not observe significant improvement in muscle strength the intervention. The discrepancy between these studies may be attributed to the vibration parameters, the exercises added while standing on the platform, the type of vibration machine, and the duration of the whole intervention.

4.2 Secondary Outcomes

Ankle ROM is required in daily activities such walking (Cornwall & McPoil, 1999) and limited ankle ROM is a common risk factor associated with falls (Whipple, Wolfson, & Amerman, 1987). Dropped foot is a common problem among MS due to their lack of ROM of the ankle (Esnouf et al., 2010). It has been suggested that vibration training may have beneficial effects for improving flexibility and ROM among several populations (Dolny & Reyes, 2008). Moreover, it could improve dorsiflexion and plantarflexion ROM in the frail elderly population (Rees, Murphy, & Watsford, 2007). Our study provided important findings in regards to the ROM of the ankle joint. To our knowledge this is the first study to assess the effect of vibration training on the ROM of the ankle. Our data indicated an improvement in both active/passive

ROM during dorsiflexion and plantarflexion of both lower limbs. However, only active and passive dorsiflexion significantly improved, whereas plantarflexion was only significantly improved for the active movement on both sides (strong and weak). Given that ROM of the ankle is an important factor for walking (Cornwall & Mcpoil, 1999) CWBV training could be essential to improve dorsiflexion and plantarflexion for walking, which may reduce the risk of falling.

The cutaneous receptors of the soles of the feet are one of the main components of the somatosensory system (Citaker et al., 2011). These receptors are important because it provokes the cutaneous afferents of the sole to provide useful information to the CNS to maintain human balance during standing and walking (Meyer, Oddsson, & De Luca, 2004). Studies have reported that during walking the body will move the center of pressure to areas of greater sensitivity of the foot. Thus, it has been proposed that sensory feedback from the feet has an important role during dynamic foot movement (Nurse & Nigg, 1999). Additionally, reduced feedback from the receptors in the foot may contribute to gait abnormalities and increased sway (Nurse & Nigg, 2001). Among MS loss of signal of the cutaneous afferent to the CNS is very common, which in result leads to poor balance. The sensation levels on the plantar surface among people with MS vary substantially, but in general the MS population tends to have sensory problems of the feet (Citaker et al., 2011). In the present study, the cutaneous sensation thresholds of these sites of both strong (Fig. 6a) and weak side (Fig. 6b) feet did not show any significant improvements; however, there was a tendency towards improvement in all measurements.

These results are in accordance with two past studies, which measured sensation of the feet and did not find significant improvements after the intervention (Schyns et al., 2008;

Uszynski et al., 2015). However, these studies used equipment, which are not eminent instruments to measured sensation on people with MS. The measurement that were used in the study were Nottingham Sensory Assessment, Neurothesiometer with Verbal analogue scale, respectively, which are not reliable tools because they may not be sufficiently sensitive in detecting changes in sensation in MS.

It has been reported that people suffering of MS have reported high levels of fear of falling, due to their motor impairments (Finlayson, Peterson, & Cho, 2006). To our best knowledge this study is the first of its kind to analyze the effects of CWBV training on fear of falling among people with MS. Our results indicated that CWBV training could significantly reduce the fear of falling among people with MS (Fig. 6c). This reduction could have been related to the improvements of the motor impairments (muscle strength, balance, functional mobility, ROM, sensation, and bone density). This finding implied that CWBV training could be a promising intervention to reduce the fear of falling by improving motor impairments among people with MS.

It is widely recognized that the risk of fractures is associated with the decline in bone mineral mass during the ageing process (Gomez-Cabello et al., 2012). However, among people with MS bone mineral mass is significantly reduced, which elevates them to a high risk of fractures and falls (Nieves et al., 1994). It has been reported that bone density among MS is significantly lower than healthy individuals (Ozgocmen et al., 2004). CWBV training has been categorized as a new non-pharmacological approach to counteract the decrement of bone density (Stengel et al., 2011). The possible mechanism for the improvement in bone density could be due to the high-frequency loading of the skeleton, which is linked to the activation of the mechanotransduction by increasing fluid flow in bone and stimulation of osteogenesis (Stengel et al., 2011).

Another possible mechanism could be that vibration training might indirectly provoke the regulation of bone remodeling via an acute change in testosterone and growth hormone levels (Kim, Lee, Yoo, & Hwang, 2014). However, these mechanisms still remain unclear. Additionally, studies have reported that CWBV training increases bone mineral mass among elderly population (Verschueren et al., 2011; Stengel et al., 2011). Our study is the first known to examine the effects of CWBV training on bone density among people with MS. The data indicated significant improvements in calcanei bone of both the strong and weak side of our participants (Fig. 6d). These results are vital to people with MS due to their high levels of bone mineral loss and falls. Given that vibration training can improve bone density, CWBV training can be a potential device to prevent fractures among people suffering from MS.

4.3 Limitations

This study has several limitations. First, the sample size in the present study does not allow us to utilize a randomized controlled design. Not having a placebo group caused less homogeneous disability status, MS type, gender, and disease duration; all these could have influenced the response to the vibration training. Second, our ability to comparing the effectiveness of CWBV training on reducing falls with other types of training methods is limited since we did not have an active control group (like aerobic or resistance training). Third, we did not systematically record whether the participants experienced any subjective improvement of spasticity, fatigue, depression, or quality of life. Forth, given the nature of vibration training, there are countless combinations of vibration frequency, amplitude, body posture, duration, and volume. We only explored one combination in this study. The optimal training dosage to maximize the training effects needs to be determined. Fifth, clinical significance was not evaluated; all findings were based on statistical significance. The clinical significance could have determined the practical effects of the intervention. It remains unknown to what extent the finding from this study could be practically applied to clinical settings. Sixth, the outcome variables were measured immediately after the last session; acute effects could have influenced the results. Last, this intervention can improve the risks on falls; however, it remains unknown weather vibration training can indeed prevent falls during everyday living among people with MS. All these issues warrant further studies based on a larger scale sample size with a more rigorous study design (like a randomized controlled trial).

4.4 Significance

Despite the limitations, our findings demonstrated the potential for CWBV training to reduce the risk of falls among people with MS. More importantly, our study indicated that side-alternating CWBV training performed 3 days/week for 8 weeks could be a well-accepted and safe intervention treatment for this population. The impose intervention had a positive effect on improving all the main risk factors of falls, which could influence the quality of life among this population.

The findings of the present support the use of CWBV training as a safe and effective exerciser intervention to improve common motor impairments (balance, mobility, strength, ROM, sensation, and bone density) that may lead to falls and by reducing the fear of falling. Given all the positive effects, this type exercise could positively be promoted/recommended intervention so that clinicians may advocate it as a home setting training method for people with

MS. This intervening could improve and maintain physical function activities, which could potentially reduce service cost for the health system because of the improvements of the main risk factors of falls balance, mobility, strength, ROM, sensation fear of falling and bone density.

4.5 Summary

In conclusion, our findings demonstrated that an 8-week CWBV training is a promising alternative intervention for people with MS because it improves the risk factors of falls. More importantly, our study demonstrated that an 8-week CWBV training could increase ROM, fear of falling and bone density. Although these factors could considerably contribute to falls among people with MS (Benedetti, 1999; Coote, Hogan, and Franklin, 2013; Marrie, Cutter, Tyry, & Vollmer, 2009), the possible influence of CWBV training on modifying them has not been examined previously. Side-alternating CWBV training appears to be a safe and effective exercise intervention for people with MS to reduce falls by improving their risk of falls. The reduced falls would have the potential to lower the cost incurred by falls and injuries among MS, to improve the mobility and thus the quality of life among people with MS. Therefore, this study carries medical, socioeconomic, and practical significances.

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6. VITA

Maria Cristal Sanchez was born in El Paso, Texas on May 5, 1992. She is the third daughter out of 5 siblings of Eleuterio Sanchez and Maria Sanchez. She graduated from The University of Texas at El Paso (UTEP) with her Bachelors in Kinesiology in 2014. During her last semester of her Bachelor's Degree, Maria got involved in research and started to work at the Stanley E. Fulton Biomechanics Laboratory. Since then she has been working as a research assistant for the past two years and half. After obtaining the bachelor degree, Maria became more interested in the field of Kinesiology and enrolled in the graduate program at UTEP to pursue a Master's Degree in Kinesiology.

Maria has presented her research projects at various national or international conferences. She was awarded the 3rd place of a research competition at the Texas Chapter of the American College of Sports Medicine (ACSM) conference in February 2016, and was recognized at the 2016 ACSM conference at Boston, MA, where she presented her findings about fall prevention in people with multiple sclerosis. She was the only winner of "The 1st UTEP 3-minute Thesis Competition" in April 2016. She has also received numerous travel awards or summer research assistantship from the UTEP Graduate School. In addition she published 11 journal articles or abstracts in the past two years.

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