Research article

The effect of low-magnitude whole body vibration on bone density and microstructure in men and women with chronic motor complete paraplegia

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Objective: To examine the effect of low-magnitude whole body vibration on bone density and microstructure in women and men with chronic motor complete paraplegia.

Methods: We studied nine subjects (four women and five men) with motor complete paraplegia of 2 years duration or more, age 20–50 years. Subjects were instructed to stand on a low-magnitude vibration plate within a standing frame for 20 minutes per day, 5 days a week, and for 6 months. Bone density at the proximal femur by dual-energy X-ray absorptiometry and bone microstructure at the distal tibia by high-resolution peripheral quantitative computed tomography were assessed at four timepoints over 12 months (baseline, at 3 months and 6 months while on intervention, and after 6 months off intervention).

Results: Standing on the low-magnitude vibration plate with a standing frame was well tolerated by participants. However, most subjects did not show an improvement in bone density or microstructure after 6 months of intervention, or any relevant changes 6 months following the discontinuation of the low-magnitude vibration.

Conclusion: We were unable to identify an improvement in either bone density or microstructure following 6 months use of a low-magnitude vibration plate in women or men with chronic motor complete paraplegia. Longer duration of use may be necessary, or it is possible that this intervention is of limited benefit following chronic spinal cord injury.

Keywords: Bone density, Bone microstructure, Paraplegia, Spinal cord injuries, Low-magnitude vibration

Introduction

Bone loss is a universal complication of spinal cord injury (SCI), with increased bone resorption beginning soon after injury[1] resulting in an accelerated loss of bone density, particularly in the first 2 years.[2–5] Acutely, the rate of bone loss is greater than that observed following exposure to microgravity or bedrest alone.[4,6,7] Although the pathogenesis for bone loss following SCI is considered multifactorial, and includes disruption of neuronal control of bone metabolism as well as hormonal and nutritional deficiencies,[8] the loss of gravity-loaded mechanical strain on bone is considered a key mechanism.[9,10] Bone loss following SCI increases the risk for fracture, notably in the lower extremities.[11,12] The incidence of fracture increases with longer duration of injury[13] and fracture prevalence is reported as being as high as 21%.[14] Lower limb fractures can be a serious complication in persons with chronic SCI, resulting in joint stiffness, loss of range of motion of the limb, pressure ulcers, pain, and increased spasticity in some cases.[12]

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There is no clear consensus or standard of care for the treatment of low bone density in persons with either acute or chronic SCI. Interventions to both preserve and improve bone health are needed. In both, the acute and chronic setting following SCI, bisphosphonates have been reported to be effective for bone health.[15–19] However, there have been recent questions raised on the possible risks of long-term bisphosphonate therapy for osteoporosis,[20] which may be particularly relevant in this population whose average age at injury is currently in the fourth decade (http://www.NSCISC.UAB.edu). There have been some non-pharmacological interventions, such as passive standing and functional electrical stimulation, that have shown promise for bone health if implemented in the acute phase following SCI.[21–24] However, similar interventions have not demonstrated consistent improvement in bone density when studied in individuals who have chronic SCI.[25–29] Additional treatment options for improving bone health in women and men living with chronic SCI are therefore needed.

Given the recognized importance of loading on bone metabolism, even in the general population, there is growing interest in identifying different delivery forms of mechanical stimulation that will improve bone health. One form of mechanical stimuli that has shown some benefit for bone density is low-magnitude whole body vibration. Mechanical stimuli that affect bone metabolism are transmitted to bone cells through alterations in fluid flow or sheer forces and changes in intramedullary pressure within the lacuna-canalicular network, the porous spaces of bone.[30,31] Low-magnitude vibration provides mechanical stimuli to bone in the form of vertical oscillation, which is sufficient to increase fluid flow in bone and produce an osteogenic signal.[32,33] Indeed, in animal studies, low-magnitude whole body vibration is anabolic to bone.[34] Clinical studies using low-magnitude whole body vibration during weight bearing, administered as 10 or 20 minute sessions in a day, have reported improvement of bone mass in children and adolescents,[35,36] although in studies involving post-menopausal women, the effects have been conflicting.[37,38]

The mechanical stimuli of a low-magnitude vibration plate combined with passive standing regimens using a standing frame may provide a promising non-pharmacological strategy for preventing bone loss and potentially improving bone density in the lower extremities of women and men following chronic SCI. Thus, the primary goal of this study was to examine the effect of low-magnitude whole body vibration in persons with chronic motor complete paraplegia on bone density, microstructure, and metabolism.

Methods

Study participants

The study was approved by the Institutional Review Board and all subjects provided written informed consent. Women and men between the ages of 20 and 50 years with traumatic, complete motor paraplegia (American Spinal Injury Association Impairment Scale (AIS) A or B)[39] for at least 2 years were recruited from the clinical practice of an academic SCI center and with assistance from the EasyStand company. Study participants were unable to come to a stand without bracing or a standing frame. Persons with a history of long bone fracture since onset of SCI, existing pressure ulcer greater than stage 2, lower extremity contractures, or inability to tolerate passive standing for any reason were excluded. The subjects could have been previously using a standing frame regularly. None of the women studied were post-menopausal and none of the participants were on chronic oral glucocorticoids or receiving osteoporosis management, other than calcium and/or vitamin D supplementation.

Study protocol

All participants had baseline bone mineral density (BMD) measurements at the proximal femur by dual-energy absorptiometry (DXA) and bone microstructure at the distal tibia by high-resolution peripheral quantitative computed tomography (HRpQCT). Measurements of bone turnover were also assessed at baseline. Subjects were then provided a low-magnitude vibrating platform (Juvent Medical, Somerset, NJ, USA; model Juvent 1000) for home use during the study and were instructed to stand on the vibrating platform with the aid of a standing frame, for 20 minutes per day, 5 days per week, and for 6 months. All were also asked to maintain a log of the duration of time they were able to stand per day on the machine, which was reviewed at each study visit. Subjects were advised by a rehabilitation physical therapist on proper positioning while in the standing frame, with hips and knees extended and bare feet flat on the vibrating plate surface (Fig. 1). Foot plates of the standing frames were removed to accommodate the vibrating plate. For subjects not accustomed to standing, abdominal binding, and compressive leg wraps were applied as deemed necessary by the study participant and therapist to ensure orthostatic homeostasis during the intervention. Subjects then had follow-up bone density, microstructure, and turnover markers measured at 3 and 6 months while on intervention, and then again 6 months after stopping the intervention.

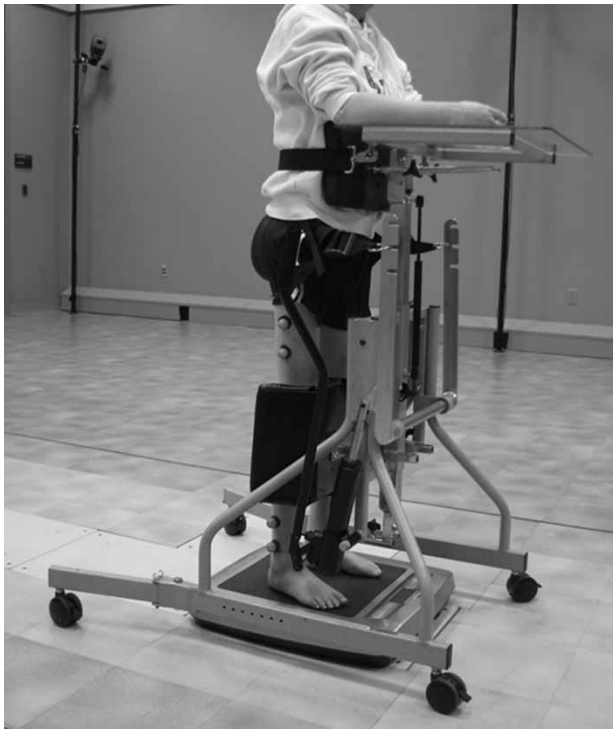

Figure 1 Subject standing on a low-magnitude vibrating plate using a standing frame. (Reproduced with permission).[40]

Low-magnitude whole body vibration

The Juvent 1000 is a commercially available vibrating plate that provides a 0.3 g, 34 Hz vertical sinusoidal movement of ~50 μm. We previously determined that women and men with chronic motor complete paraplegia bear the majority of their weight (86 ± 10% body weight) through their lower limbs when using a standing frame and that supporting their arms on the tray reduces the ground reaction forces by only ~10% body weight.[40] We also observed that low-magnitude vibration provided additional oscillation of the load-bearing forces and was proportionally similar regardless of arm position.[40] Subjects were instructed to stand in their standing frames on the Juvent device without shoes. It was recommended that they keep their arms at their side to maximize ground reaction forces; however, most subjects preferred resting their arms on the tray for stability and comfort.

DXA and HRpQCT measurements

We measured areal BMD (aBMD) at the proximal femur (total hip and femoral neck) by DXA using the Lunar Prodigy system (GE Healthcare, Madison, WI, USA). The short-term coefficients of variation (CV) for the total hip and femoral neck measurements were 0.9 and 2.7%, respectively.

We evaluated the non-dominant distal tibia by HRpQCT (XtremeCT, Scanco Medical AG, Brüttisellen, Switzerland) for total, trabecular, and cortical volumetric BMD (vBMD) (CV: 0.3, 0.4, and 0.4%, respectively) and microstructure. As described elsewhere,[41] trabecular bone volume/total volume (BV/TV) fraction (CV: 0.4%) was derived from trabecular vBMD. A thickness-independent structure extraction was used to identify three-dimensional ridges (centers of the trabeculae), and trabecular number (Tb.N) (CV: 4.7%) was then taken as the inverse of the mean spacing of the ridges.[42] Analogous with standard histomorphometry,[43] trabecular thickness (Tb.Th) (CV: 4.0%) was calculated as (BV/TV)/Tb.N, and trabecular spacing (Tb.Sp) (CV: 4.1%) as (1 − BV/TV)/Tb.N. Validation studies show excellent correlation ($R \geq 0.96$) of these parameters with gold standard *ex vivo* μCT.[44] The distal tibia cortex was segmented from the gray-scale image with a Gaussian filter and threshold.[42] Cortical vBMD and area were measured directly and the periosteal circumference calculated from the contour; cortical thickness (Ct.Th) (CV: 0.5%) was then calculated as area/circumference. Excellent correlation ($R = 0.98$) has also been shown with Ct.Th measurements by μCT.[45]

Bone turnover markers

A serum bone resorption marker, C-terminal telopeptide of type I collagen (CTX), was measured by a two-site immunoenzymatic sandwich assay on the Roche Cobas e411 (Roche Diagnositics, Indianapolis, IN, USA). Intra-assay CVs are 7.8, 2.7, 3.2, and 1.9% at 0.046, 0.292, 0.709, and 2.94 ng/ml, respectively. Inter-assay CVs are 7.7, 8.5, and 7.8% at 0.291, 0.679, and 2.77 ng/ml, respectively. A serum bone formation marker, amino-terminal pro-peptide of type I collagen (PINP) was measured by a double antibody radioimmunoassay (Orion Diagnostica, Espoo, Finland; distributed by Diasorin, Stillwater, MN, USA). Intra-assay CVs are 2.3% at 44.5 μg/l and 12.7% at 103 μg/l. Inter-assay CVs are 3.8% at 28.0 μg/l and 9.2% at 165 μg/l. Serum sclerostin, an antagonist of bone formation, was measured using a validated enzyme-linked immunosorbent assay (Biomedica, Wien, Germany; distributed in USA by ALPCO, Salem, NH, USA). Intra-assay CVs are 5% at 54 pmol/l and 5% at 154 pmol/l. Inter-assay CVs are 6% at 44 pmol/l, 3% at 127 pmol/l, and 3% at 150 pmol/l.

Body composition measurements

We assessed body composition longitudinally also using the Lunar Prodigy instrument. Total body lean mass (kg) and total body fat mass (kg) was determined from the whole body scan (CV: 1.6 and 2.6%, respectively).

From these scans, separate assessments of the lean and fat mass of the lower extremities could be determined.

Body mass index (BMI) (kg/m^2) was calculated from the height and weight of each subject. Each subject with SCI was weighed in their wheelchair, and then the wheelchair alone was weighed, with the difference being the body mass (kg) of the subject. Self-reported height prior to their injury was recorded for subjects with paraplegia.

Statistical analyses

Trends over time using the repeated measurements were analyzed with a linear mixed effects model. Means and standard deviations were used to summarize values at each timepoint and plots were used to show the changes over time for each subject. We also determined the minimal detectable change (MDC) for the parameters being studied, based on CVs, in order to determine the proportion of subjects with relevant changes that could be detected over follow-up. Analyses were performed using SAS 9.3 and R 2.14 and the significance level was set at 0.05.

Results

For our intervention study, we enrolled six women and six men with traumatic, motor complete paraplegia, all of whom were white, non-Hispanic; however, two women and one man withdrew before their first follow-up visit. Drop-out was reported by subjects as due to inability to commit the time to the study, and not due to any adverse effects. We therefore studied four women and five men who had at least one follow-up visit while using the low-magnitude vibrating platform, of whom, four women and four men returned for all study visits. Individual SCI characteristics of the nine subjects who had at least one follow-up visit are presented in Table 1. At baseline, the mean ± SD for age, BMI, weight, and height of subjects (and for women and men, respectively) was 42 ± 8 years (41 ± 5 years and 43 ± 10 years), 22.3 ± 4.1 kg/m^2 (21.2 ± 5.2 and 23.4 ± 3.3 kg/m^2), 71.0 ± 13.3 kg (61.6 ± 13.0 and 78.5 ± 8.0 kg), and 177.2 ± 10.5 m (169.0 ± 5.7 and 183.8 ± 8.6 m). The results did not ultimately differ by sex, so results in Table 2 are shown for women and men combined.

Of subjects who returned for their study visits, they self-reported standing between 20–60 minutes per day, 5 days per week. Although some stood on the plate for longer than 20 minutes, the vibrating plate would shut off at 20 minutes. Overall, the low-magnitude whole body vibration was well tolerated by participants who completed the study. One subject noted a mild increase in neuropathic pain, but did not require a change in medication regimen, nor did he stop the study. Several others noted slight increases in spasticity following standing, but again, did not change their medication regimen, nor stop the study protocol. One subject, who only completed the first 3 months of the study, did subsequently undergo revision surgery due to loose hardware in the spine. It is unknown if this was study related or not, as he had neither follow-up for his SCI nor imaging to assess his hardware in recent years and was followed up elsewhere.

There was no significant change in aBMD at the proximal femur sites in subjects following either 6 months on intervention or 6 months off (Table 2 and Fig. 2A). Although our number of subjects limited statistical power, after 6 months on intervention, only three of the subjects had an increase in total hip aBMD that was greater than the MDC, while the remainder had no detectable changes. None had any changes in femoral neck aBMD that were greater than the MDC at 6 months on intervention. Similarly, when we examined tibia vBMD and bone microstructure parameters by HRpQCT, there were again no significant differences noted over follow-up in either the trabecular or cortical compartments (Table 2 and Fig. 2B and C). Almost all subjects either had no changes or worsening of tibia vBMD and bone microstructure parameters that were greater than the MDC by 6 months on intervention. There was one female subject who, at baseline, had a considerable loss of trabecular bone at the distal tibia, resulting in very low trabecular microstructure estimates which were considered outlier values, and contributed to the large standard deviations observed around means for some parameters; however, these values were consistent over the study period. We did not observe any relevant trends in the CTX, PINP, or sclerostin measurements over follow-up that would have suggested a beneficial change in bone metabolism over the period of intervention, or any detrimental changes once it was discontinued (Table 2). Finally, we did not observe any clinically relevant changes in total, or lower extremity, lean mass or fat mass over follow-up (Table 2).

Discussion

This is the first study to examine the effects of combining passive standing and low-magnitude whole body vibration on bone density, microstructure, and metabolism in persons with chronic motor complete paraplegia. Although well tolerated, we did not observe any relevant improvement in bone density or microstructure after 6 months of combined standing and low-magnitude vibration. Nor did we note any significant

Table 1 Characteristics of nine subjects (four women and five men) with motor complete paraplegia who had at least one follow-up visit

Subjects	Age (years)	Level of injury	AIS*	Spastic/flaccid	Duration of injury (years)
Women					
	34	T3	A	Spastic	17
	41	T11	A	Flaccid	2
	43	T12	A	Spastic	23
	44	T7	A	Flaccid	3
Men					
	25	T5	A	Spastic	7
	45	T9	A	Flaccid	6
	46	T6	A	Spastic	27
	48	T11	B	Spastic	3
	50	T5	A	Spastic	15

*American Spinal Injury Association Impairment Scale (AIS).[39]

changes in bone density or microstructure 6 months following completion of the intervention. There were no clinically relevant changes in bone turnover markers observed over follow-up. Total, and lower extremity, lean and fat mass were also unchanged.

Although we did not see any improvement in bone density with low-magnitude vibration in our study subjects with chronic SCI, it has shown beneficial effects in other populations, although not all. In a clinical trial by Gilsanz *et al.*[35] of young women ages 15–20 years with

Table 2 Baseline (visit 1) and follow-up results (mean ± SD) at 3 months (visit 2) and 6 months (visit 3) on intervention and after 6 months off intervention (visit 4) for the subjects with motor complete paraplegia who had at least one follow-up visit

Characteristics	Baseline	Visit 2	Baseline*	Visit 3	Baseline*	Visit 4
No. of Subjects	9	9	8	8	8	8
Total hip aBMD (g/cm^2)	0.71 ± 0.22	0.71 ± 0.22	0.68 ± 0.22	0.69 ± 0.21	0.68 ± 0.22	0.70 ± δ0.20
Femur neck aBMD (g/cm^2)	0.75 ± 0.20	0.74 ± 0.19	0.73 ± 0.20	0.74 ± 0.18	0.73 ± 0.20	0.75 ± 0.16
Tibia total vBMD (mg/cm^3)	167.69 ± 64.73	163.02 ± 61.45	168.39 ± 69.16	163.25 ± 64.18	168.39 ± 69.16	159.98 ± 59.32
Tibia trabecular vBMD (mg/cm^3)	67.53 ± 54.58	66.17 ± 51.83	69.13 ± 58.12	64.66 ± 52.68	69.13 ± 58.12	63.99 ± 49.95
Tibia cortical vBMD (mg/cm^3)	809.84 ± 52.87	788.81 ± 73.43	811.18 ± 56.36	804.23 ± 66.80	811.18 ± 56.36	793.51 ± 62.48
Tibia trabecular number (1/mm)	1.09 ± 0.51	1.10 ± 0.53	1.10 ± 0.54	1.04 ± 0.48	1.10 ± 0.54	1.02 ± 0.51
Tibia trabecular separation (mm)	1.15 ± 0.82	1.25 ± 1.12	1.18 ± 0.87	1.27 ± 1.05	1.18 ± 0.87	1.36 ± 1.15
Tibia: trabecular thickness (mm)	0.04 ± 0.03	0.04 ± 0.03	0.04 ± 0.03	0.04 ± 0.03	0.04 ± 0.03	0.04 ± 0.04
Tibia cortical thickness (mm)	0.80 ± 0.28	0.78 ± 0.29	0.79 ± 0.30	0.78 ± 0.31	0.79 ± 0.30	0.76 ± 0.31
Tibia cortical area (mm^2)	86.47 ± 30.49	83.63 ± 31.40	83.44 ± 31.11	81.98 ± 31.76	83.44 ± 31.11	80.53 ± 32.17
C-terminal peptide (CTX) (ng/ml)	0.27 ± 0.16	0.34 ± 0.19	0.25 ± 0.15	0.26 ± 0.12	0.25 ± 0.15	0.23 ± 0.17
Procollagen type 1 (P1NP) (μg/l)	56.90 ± 25.55	54.57 ± 26.00	52.86 ± 24.05	48.38 ± 20.53	52.86 ± 24.05	54.95 ± 23.00
Sclerostin (pmol/l)	28.27 ± 12.52**	30.69 ± 15.81**	27.04 ± 13.24**	29.43 ± 10.88**	27.04 ± 13.24**	31.98 ± 16.98**
Total body fat mass (kg)	27.0 ± 12.4	26.9 ± 12.4	27.7 ± 13.1	28.0 ± 12.0	25.2 ± 11.9***	25.4 ± 10.5***
Lower extremity fat mass (kg)	9.1 ± 4.3	9.0 ± 3.9	9.4 ± 4.5	9.5 ± 4.0	8.0 ± 2.2***	8.1 ± 1.9***
Total body lean mass (kg)	39.6 ± 10.9	39.7 ± 10.5	38.3 ± 11.0	38.8 ± 11.3	39.5 ± 11.3***	39.8 ± 11.8***
Lower extremity lean mass (kg)	10.1 ± 3.4	10.2 ± 3.3	9.6 ± 3.3	9.7 ± 3.5	9.7 ± 3.5***	10.2 ± 4.0***

None of the differences were statistically significant.
*Baseline results for the eight corresponding subjects available at follow-visits.
**Sclerostin measurements were available for seven subjects at baseline, so baseline vs. visit 2 values correspond to seven subjects, while baseline vs. visits 3 and 4 values correspond to six subjects.
***Body composition variables were available for seven subjects instead of eight at visit 4, so baseline values are for the corresponding seven subjects.

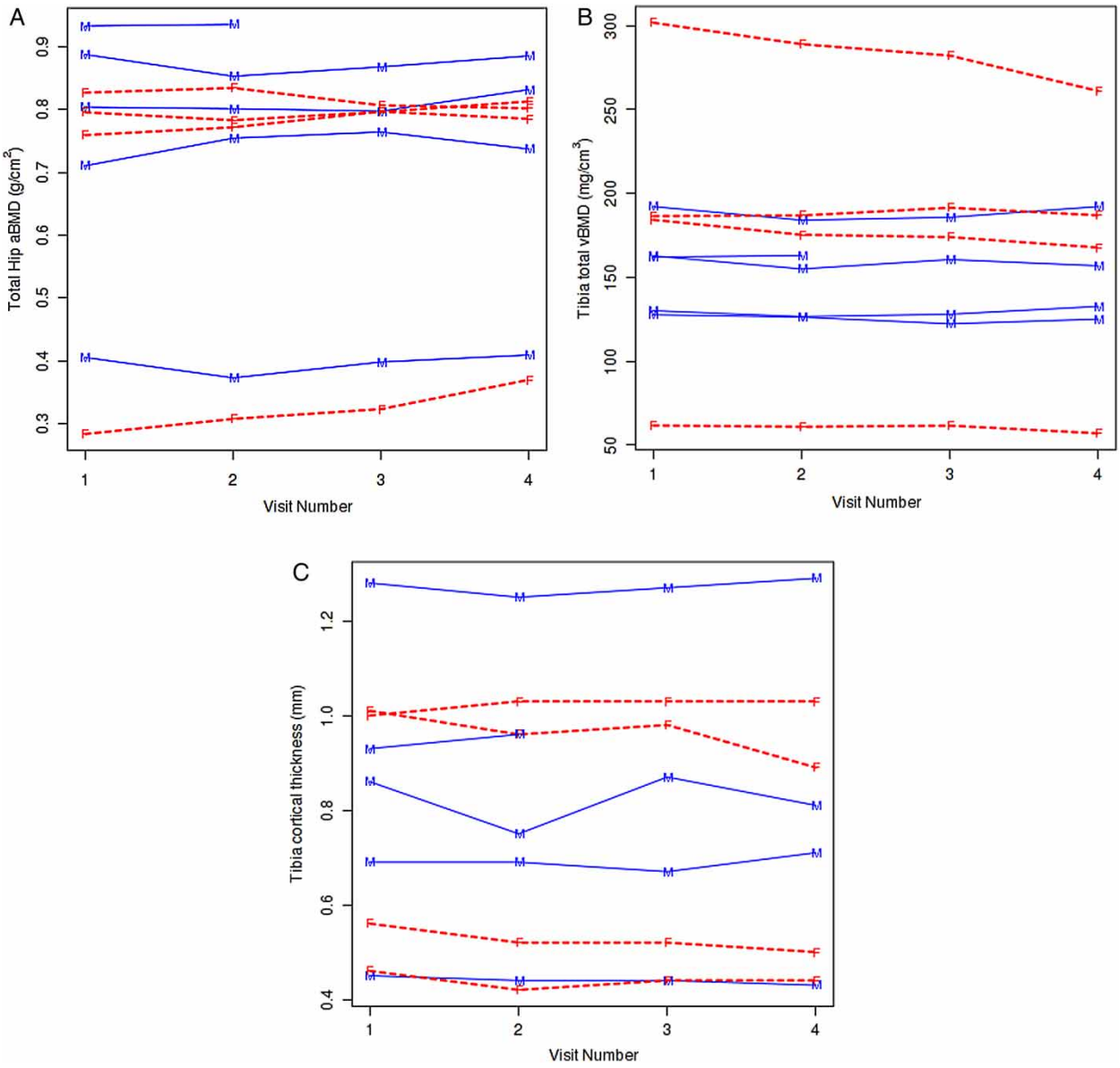

Figure 2 This figure shows individual values for each subject at baseline (visit 1), 3 month (visit 2), 6 month (visit 3), and 12 month (visit 4) timepoints for (A) total hip aBMD, (B) total tibia vBMD, and (C) cortical thickness. The first 6 months (up to visit 3) were on intervention, and the last 6 months (visits 3–4) were off intervention. The men are indicated with solid lines with an "M" for each measured value and the women are indicated with dashed lines with an "F" for each measured value.

low bone mass who were randomized to using vertical oscillation 10 minutes per day for 1 year or no intervention, there was a statistically significant increase in bone density at the femoral midshaft and lumbar spine for women on intervention. Furthermore, the young women who were compliant with utilizing the device showed a 3.9% greater increase in lumbar spine trabecular density and a 2.9% greater increase in femoral shaft cortical area when compared with the pooled group of controls and women who were non-compliant with the intervention. Ward *et al.*[36] reported that non-ambulatory children with cerebral palsy, who were randomized to standing on a low-magnitude vibrating plate for 10 minutes per day, 5 days per week, and for 6 months, had an increase in volumetric tibial bone density by a mean of 6.3%, while the control group, who stood on a placebo device, experienced a mean decrease in bone density of 11.9% ($P = 0.003$). These significant differences were noted despite compliance at 44% (standing on the device 4.4 minutes per day instead of the prescribed 10 minutes per day).[36] These studies suggest that low-magnitude whole body vibration may be effective at improving bone density when bone accrual is actively occurring, such as in the growing skeleton. On

the other hand, studies involving post-menopausal women using low-magnitude vibration have not demonstrated a clear benefit. Rubin *et al.*[37] studied 70 early post-menopausal women randomized to either receiving vertical oscillation from a low-magnitude vibrating plate or placebo while standing for two 10 minute sessions, three times per week, and for 1 year. In the intention-to-treat analysis, there was no significant difference observed in bone density between the two groups.[37] However, in *post hoc* analyses of women who were in the highest quartile of compliance with standing on the vibrating platform or placebo (86% compliant), the intervention group showed little change in bone density at the hip or spine, while the control group demonstrated a 2.13% loss at the hip and a 1.6% loss at the lumbar spine ($P = 0.06$ and $P = 0.09$, respectively, for difference between the groups).[37] In a more recent randomized trial involving 202 post-menopausal women by Slatkovska *et al.*[38] daily low-magnitude whole body vibration, at either of two frequencies, had no measurable benefit on bone density when compared with controls receiving no intervention.

In our own study, even though the intervention was well tolerated and study participants self-reported they were compliant, the majority of our subjects did not show an improvement in lower extremity bone density or microstructure after 6 months of using the vibrating plate. It is possible that the duration of the intervention was not long enough to produce an increase in bone density. On the other hand, since we did not have a control group, it may be that low-magnitude vibration prevented greater than anticipated losses of bone in our subjects with chronic motor complete paraplegia, even though it could not reverse the loss already present. However, there are two recent longitudinal studies of 30 and 60 months duration in individuals with chronic SCI, measuring bone density and/or microstructure at the lower extremities, that have tended to suggest that bone turnover may reach a new steady state following the acute accelerated loss observed in the first few years after injury, with minimal annualized change in either bone density or bone microstructure parameters in the chronic phase, and for some, there may even be an increase in lower extremity bone density.[46,47] We believe, therefore, that it is unlikely that vibration was efficacious in the prevention of bone loss, but this is difficult to say with any degree of certainty because of the absence of a well-matched control group; this is especially the case with regard to prevention of bone loss for those subjects who were injured within 3 years of being recruited for study. We also evaluated the distal tibia using HRpQCT in order to determine whether there were positive trends in bone microstructure that would suggest a potential beneficial effect of low-magnitude whole body vibration, but we observed none. Finally, we measured markers of bone turnover as well as sclerostin levels over follow-up. Sclerostin is an inhibitor of bone formation through its effect as a Wnt signaling antagonist.[48] It is produced by osteocytes, cells which are considered mechanosensors responsible for signaling the adaptive response of bone to mechanical stimuli.[49] In acute unloading, such as following SCI, sclerostin levels are increased, although in chronic SCI, levels are decreased, likely reflecting the severity of bone loss and reduction in osteocyte number.[50] Sclerostin expression is downregulated by mechanical stimuli and is reported to be an obligatory step in mechanotransduction inducing osteogenesis.[49] If low-magnitude vibration were producing a sufficient mechanical stimuli that would induce bone formation through an effect of Wnt signaling, we would expect sclerostin levels to decrease over 6 months of intervention, but we observed no relevant trends in either sclerostin or bone turnover markers in our study population.

It may be that mechanical stimuli as an intervention for improving bone density in chronic SCI is of limited efficacy, especially once significant bone mass is already lost. Among studies examining other loading strategies to bone, such as passive standing and functional electronic stimulation of muscles, many have failed to show a beneficial effect to bone when evaluated in those with chronic SCI[25–29] even though similar interventions have shown promise in the acute setting.[21–24] Education and modalities for maintaining bone health after SCI need to become a priority acutely, as there may be a window of time where treatment has the best opportunity in preserving bone mass. Use of low-magnitude vibration and passive standing may prove to have benefits in the acute phase following SCI, but further study is necessary; currently, a clinical trial is underway (http://www.clinicaltrials.gov; NCT00886145).[51] If beneficial, timing the use of vibration after any surgical fusions with instrumentation would need to be considered. More recently, ambulation with exoskeleton systems offer new treatment modalities for mechanical loading through the lower extremities of persons with complete paraplegia[52]; however, the effect of exoskeleton use for bone preservation has yet to be reported.

Our study was limited by the small number of subjects, which precluded our ability to see significant changes over follow-up. Nevertheless, we saw no apparent trends over time when we plotted the data, suggesting there was little relevant change in bone density or microstructure either on or off intervention. Our study was

initially designed to include a control group, but due to challenges in recruitment, we were required to change our design. Our lack of a control group limits our ability to determine if the intervention was completely ineffective. It remains possible that it helped to prevent greater than anticipated bone loss over the 6 months on intervention, although we believe this may be less likely based on the more recent literature available on longitudinal bone density changes in those with chronic SCI, as discussed earlier.[46,47] Furthermore, based on these longitudinal data that are now available, we estimate that 72 subjects per group would have been needed to detect a difference of 0.0137 over the baseline total hip bone density value of 0.684, which is a 2% difference, at a significance level of 0.05 and 80% power. Nonetheless, a robust conclusion on the lack of benefit of low-magnitude whole body vibration in chronic paraplegia is not possible. The intervention was only 6 months, with standing compliance self-reported by study subjects. It remains possible that longer duration of use, with a larger cohort, may yield different findings. Compliance was self-reported, but because most of our participants had a strong desire to stand as part of their therapy, this inclination was probably the reason why their logs reported a level of compliance that was so markedly better than that previously observed in which children and ambulatory post-menopausal women were studied with a similar vibratory intervention. While we did not limit recruitment other than by age, our SCI population was entirely white, non-Hispanic, reflecting the local community population. However, we did study women as well as men with SCI, and findings were similar for both sexes. It is not known how low-magnitude vibration would affect bone density and microstructure in children or older age groups, including post-menopausal women, with chronic motor complete paraplegia.

Conclusion

In summary, we found that use of low-magnitude vibration is tolerable, low risk, and relatively easy to use with standing frames for persons with chronic motor complete paraplegia. However, 6 months of this intervention did not appear to improve their bone density or microstructure. A larger and controlled study, with potentially a longer intervention timeframe, would be required to determine if low-magnitude vibration is effective in improving bone density and structure following chronic SCI.

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Disclaimer statements

Contributors All authors have made a substantial contribution to either the concept and design, acquisition of data or analysis and interpretation of data. All authors have either drafted the article or revised it critically for important intellectual content. All authors approved the version to be published.

Conflicts of interest All other authors state that they have no conflicts of interest with respect to this work.

Ethics approval The study was approved by the Institutional Review Board and all subjects provided written informed consent.

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