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ORIGINAL ARTICLE

Sclerostin and parathyroid hormone responses to acute whole-body vibration and resistance exercise in young women

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Abstract

Whole-body vibration (WBV) has been shown to improve bone mineral density, and muscle strength and power. No studies to date have examined sclerostin and parathyroid hormone (PTH) responses to WBV combined with resistance exercise (RE). This randomized crossover study compared acute serum sclerostin and PTH responses to RE and WBV + RE in young women ($n = 9$) taking oral contraceptives. Participants were exposed to 5 1-min bouts of vibration (20 Hz, 3.38 peak–peak displacement, separated by 1 min of rest) before high intensity resistance exercise. Fasting blood samples were obtained before (PRE), immediately after WBV (POSTWBV), immediately post RE (IP) and 30 min post RE (30P). Pre-exercise sclerostin and PTH levels were not significantly different between conditions. Sclerostin levels significantly ($p < 0.05$) increased from PRE to IP for the WBV + RE condition, then decreased back to the pre-exercise level. PTH significantly decreased from PRE to 30P ($p < 0.05$) and IP to 30P ($p < 0.01$) for both conditions. Correcting for hemoconcentration eliminated the significant sclerostin responses, but the significant decrease in PTH remained ($p < 0.05$). There were no significant relationships found between sclerostin and PTH. In conclusion, sclerostin concentrations increased in response to the WBV + RE condition, which may have been mediated by plasma volume shifts. There was no transient PTH increase, but it showed a large decrease at 30P for both conditions. Based on these findings, the addition of WBV exposures prior to high intensity RE did not alter sclerostin and PTH responses to RE in young women.

Keywords Bone turnover markers · Mechanical loading · Vibration · Resistance exercise

Introduction

Mechanical loading is essential for the maintenance of a healthy skeleton throughout the lifespan. In addition to high impact weight-bearing exercise and resistance exercise, whole-body vibration (WBV) has potential as a non-pharmacological intervention for improving bone mineral density (BMD). During WBV, mechanical oscillations are transmitted through the body, activating mechanotransduction in bone directly by stimulating bone cells and indirectly by increasing muscle contraction forces placed upon the skeleton [1]. In vivo animal models have demonstrated that bone accrual increases in response to low acceleration (< 1 g) [2, 3] and high acceleration (> 1 g) [4] vibration protocols. Recent studies reported that vibration stimuli decreased sclerostin expression in young healthy mice [4] and in a stem cell derived osteocyte cell culture model [5].

Meta-analyses of human studies [6, 7] have shown that WBV interventions result in significant improvements in areal BMD (aBMD) at the lumbar spine and proximal femur sites. In addition, short-term (8–12 weeks) WBV interventions elicited beneficial alterations in bone turnover markers (BTM), such as increases in the bone formation marker, N-terminal propeptide of type I procollagen (PINP) [8] or decreases in the bone resorption marker, C-terminal telopeptide of type I collagen (CTX-I) [9]. The efficacy of the WBV intervention depends on the characteristics of the vibration stimulus with low frequency (≤ 20 Hz) high magnitude (≥ 1 g) protocols significantly increasing lumbar spine and trochanter aBMD, whereas high frequency (> 20 Hz) low acceleration (< 1 g) protocols improved aBMD at the lumbar

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spine but not at the hip [6]. Also, side alternating vibration platforms and a semi-flexed knee posture were more effective for increasing aBMD than synchronous platforms or standing with knees extended on the platform [6].

The increase in muscle force production through WBV performed in conjunction with traditional high-intensity resistance exercise may provide an additive effect on skeletal responses [1]. Findings that WBV combined with exercise elicits significantly greater improvements in muscular strength and power than exercise alone supports an additive effect [10]. Previously, we tested this hypothesis by comparing acute BTM responses to two protocols; high intensity resistance exercise (RE) only and RE performed after 5 intermittent bouts of WBV (WBV + RE) in young women and men [11, 12]. Both studies showed significant decreases in CTX-I, for the WBV + RE condition with no changes in the bone formation marker (bone-specific alkaline phosphatase, bone ALP).

Sclerostin is a potent inhibitor of the Wnt signaling pathway; thus, it inhibits bone formation and stimulates bone resorption [13]. Sclerostin is highly expressed in osteocytes and its expression is downregulated in response to mechanical loading [14] and upregulated during conditions of unloading in animal models [15] and in humans [16]. Although sclerostin acts in a paracrine manner, circulating sclerostin concentrations may reflect changes in bone cell activities that are partly regulated by osteocytes [17]. Despite the known importance of osteocytes in mechanotransduction, there have been relatively few human studies to date examining sclerostin responses to acute exercise; however, the majority of the existing studies reported increases in sclerostin after exercise. Circulating sclerostin significantly increased after acute bouts of treadmill running in young women [18], high impact jumping in young men [19], walking in postmenopausal women [20] and WBV in premenopausal women [21]. None of these studies measured plasma volume changes, which could partially explain the sclerostin increases post exercise. Plasma volume shifts occur during exercise due to changes in oncotic and hydrostatic pressures at the capillary bed [22]. It is important to assess plasma volume shifts to determine whether circulating BTM changes reflect true metabolic bone responses to the exercise protocol or are the result of hemoconcentration [23].

Parathyroid hormone (PTH) plays a key role in the regulation of calcium metabolism. Although continuous increases in PTH stimulate bone resorption, intermittent increases in PTH are anabolic for bone [17]. It has been postulated that transient increases in PTH occurring during exercise bouts may stimulate bone formation similar to what is observed with intermittent PTH treatment [24]. Recently, PTH treatment enhanced trabecular and cortical bone volume compared to exercise alone in mice, suggesting that PTH signaling contributes to bone adaptation to loading [24]. PTH regulates sclerostin as evidenced by decreased sclerostin expression in rodent bone tissue [25], and serum sclerostin concentrations in humans [26] in response to PTH treatment. PTH responses to acute exercise stimuli in humans show variable patterns depending on the type of exercise. Circulating PTH increased immediately post aerobic exercise [27–31] and jumping [19] protocols, although several studies [19, 27–29] documented a significant PTH decrease below baseline several hours after exercise. The transient increase in PTH did not occur after acute resistance exercise, but a PTH decrease by 2 h post exercise was observed [32, 33]. The underlying mechanisms for the PTH exercise response patterns are not well understood. Alterations in serum ionized calcium during exercise would be expected to mediate PTH responses [30–32]. Some of the exercise studies [19, 29, 32] did not account for the effects of hemoconcentration on the PTH responses. The post-exercise decrease in PTH may be influenced by its circadian rhythm, which reaches its nadir mid-morning [34]. However, the PTH decrease may not be completely explained by circadian rhythm since PTH concentrations after a treadmill running trial were reported to be significantly lower than the control trial performed at the same time of day [29].

Currently, the acute effects of exercise protocols on circulating sclerostin and PTH concentrations are unclear. Previous results may have been confounded by pre-analytical factors, such as circadian rhythm and diet, as well as hemoconcentration, if these variables were not controlled. The purpose of this study was to compare acute serum sclerostin and PTH responses to RE and WBV + RE in young women. Based on our observations about the acute bone turnover response to exercise [11, 12], and previous studies related to sclerostin and PTH, we hypothesized that RE would cause transient increases in circulating sclerostin and PTH, followed by decreases, and that the addition of a vibration stimulus to RE would amplify these response patterns.

Materials and methods

Participants

This study presents findings from an analysis of a subset of the previously collected blood samples in our study by Sherk et al. [11] that compared acute BTM responses to two exercise protocols; RE only and WBV + RE conditions in young women. One participant from that study was omitted because of a missing serum sample, thus, there were 9 healthy and recreationally active women, aged 20–30 years included in the present analysis. Other inclusion criteria were: (1) women who were not resistance or endurance trained within the previous 12 months; and (2) women who

were taking oral contraceptives (OC) for at least 6 months prior to the study. We chose women taking OC to minimize the effects of menstrual cycle phase on BTM concentrations [35]. Written informed consent was obtained prior to participation. Exclusion criteria for this study included: (1) current smokers; (2) women with irregular menstrual cycles prior to OC use; (3) women taking hormonal contraceptives other than OC; (4) women engaging in aerobic exercise more than 2 h per week or more than 2 times per week within the past 6 months; (5) women taking medications that affect bone metabolism; and (6) contraindications to resistance exercise (e.g., current musculoskeletal injuries, hypertension) and/or WBV exposures (conditions recommended as unsafe by the vibration platform manufacturer). This study was approved by the University of Oklahoma Institutional Review Board for Human Subjects.

Research design

This study utilized a randomized, repeated measures crossover design where all participants completed two exercise protocols (RE and WBV + RE) in random order. Participants completed four visits. During the first visit, they completed the written informed consent form, medical screening questionnaires (PAR-Q and HSQ), menstrual history questionnaire, calcium intake [36], and BPAQ [37]. A total body scan was used to assess body composition and total body areal bone mineral density (aBMD) and bone mineral content (BMC) using dual-energy X-ray absorptiometry (DXA). Areal bone density variables also were measured for the lumbar spine (L1–L4) and dual proximal femur (data are shown in Sherk et al. [11]). Following this, participants were familiarized with the resistance training machines and WBV platform. In visit 2, muscular strength for 7 lower body and 2 upper body resistance exercises was assessed by standardized one repetition maximum (1RM) procedures to determine 80% 1RM loads for the RE protocols. The two exercise conditions, RE and WBV + RE, were performed in random order in visits 3 and 4 by all participants. The specific tasks for each condition are described below in the exercise protocol section.

Body composition

Body composition was assessed by a total body scan using DXA (GE Lunar Prodigy, enCORE software, version 13.31.016, GE Healthcare, Madison, WI, USA). Height and weight were measured by a wall stadiometer (Novel Products, Rockton, IL, USA) and a digital scale (Tanita Corporation of America, Inc., Arlington Heights, IL, USA), respectively. Participants were instructed to remove all attenuating materials and to lie in a supine position on the DXA table with knees and ankles secured by the Velcro straps. The anteroposterior thickness of the subject was determined by DXA software. Similarly, scanning speeds were determined by the thickness of the subject at the navel, as determined by the DXA software (thick = > 25, standard = 12–25 and thin = > 13 cm. The in vivo precision for the body composition variables (% coefficient of variation % CV) was less than 3%; 2.5% for fat, 2.74% for fat mass, and 1.39% for the bone-free lean body mass (BFLBM). The same technician performed both DXA scan acquisition and analyses.

Muscular strength testing

Muscular strength assessment was done by 1RM procedures for leg press, hip extension (right and left), hip abduction (right and left), hip adduction (right and left), seated row, and shoulder press resistance exercises (Cybex International, Inc., Medway, MA, USA). Participants completed a 5-min warm-up on a stationary bike, then completed 1 set of 10 repetitions at about 50% of their estimated 1RM. A 2-min rest was given between each 1RM attempt, and 1RM was obtained within 5 attempts using progressively heavier weight. In our laboratory, the reliability for muscular strength assessment with intraclass correlation coefficients was > 0.90.

Exercise protocols

All participants completed two exercise protocols in random order in the early morning (08:00 h) following an overnight fast, separated by 2 weeks to eliminate potential 48–72 h last-bout effects (Fig. 1). Subjects were instructed to remain well hydrated and to eat a good meal no later than 22:00 h the night prior to the testing day. Also, the exercise protocols were not performed during the OCs placebo week. The specific tasks for the RE protocol included the following: (1) a 5 min cycling warmup at a light intensity; (2) 9 isotonic resistance exercises (leg press, right and left hip extension, right and left hip abduction, right and left hip adduction, seated row, shoulder press) performed using Cybex weight machines (Cybex International, Inc., Medway, MA, USA). Participants performed 3 sets of 10 repetitions of each exercise at 80% 1RM with 2 min rest between sets; (3) a 30 min passive recovery. This high-intensity resistance exercise protocol was based on the American College of Sports Medicine's recommendations for strength and hypertrophy gains [38].

The WBV + RE protocol involved the RE protocol described above preceded by 5 1-min intermittent exposures of WBV at 20 Hz frequency with 3.38-mm peak-to-peak displacement using a Vibraflex Vibration Platform (Orthometrix, Inc., Naples, FL, USA) with the load stimulus of approximately 2.7 g. 1 min rest periods between vibration bouts were used based on animal data showing a greater

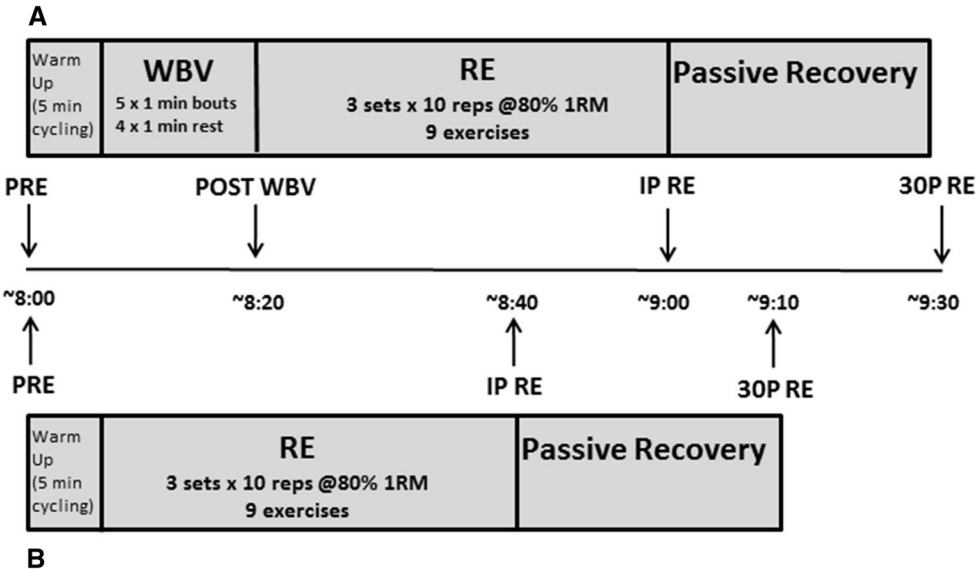

Fig. 1 Blood sampling timeline for WBV + RE (**a**) and RE (**b**) protocols

osteogenic response when recovery periods between loading cycles were employed compared to continuous bouts of loading [39]. Participants were instructed to stand barefoot on the vibration platform with the second toe in line with the dot between the foot positions of 1 and 2 with knees bent at a 30° angle. We chose this low-frequency high acceleration WBV protocol using a side-alternating vibration platform based on the previous literature showing these characteristics were more effective for stimulating bone responses [6]. The semi-flexed knee posture was selected because it was more effective for improving aBMD [6] and it minimizes the transmission of the vibration stimulus to the neck and head reducing the risk of repetitive brain injury [40, 41].

Blood sampling and biochemical assays

Blood samples were obtained in the morning after an overnight fast for both exercise conditions starting at 08:00 h and ending about 10:00 h. Venipuncture blood samples were collected from an antecubital vein by a registered nurse. Four blood samples were collected during WBV + RE condition; at rest before WBV (PRE), immediately post WBV (POSTWBV), immediately post-resistance exercise (IP), and 30 min post RE (30P). The PRE blood draw was obtained about 25 min prior to the start of the RE for this condition. Three blood samples were collected for RE only condition; at rest before resistance exercise (PRE), immediately post RE (IP), and 30 min post RE (30P). The PRE blood draw was obtained about 10 min prior to the start of RE for this condition. The timing of the blood draws is depicted in Fig. 1. Blood samples were allowed to clot then were centrifuged and the serum was transferred into microtubes, and stored at − 84 °C in the freezer until the assays were performed. All the samples were thawed only once before performing the assays.

Lactate was measured at PRE and IP for both protocols using a Lactate Plus Portable Lactate Analyzer (Nova Biomedical, Waltham, MA, USA). Hematocrit was measured in duplicate using a microhematocrit centrifuge (StatSpin, Norwood, MA, USA) to estimate the plasma volume changes (%ΔPV) using the following equation: $\%\Delta PV = (100/(100 - \text{Hct Pre}) \times 100$ ((Hct Pre-Hct post)/Hct post) [42]. Acute exercise causes plasma volume shifts resulting in hemoconcentration, which could affect the measurement of circulating concentrations of sclerostin and PTH. It is recommended that blood-borne substances, such as hormones and bone markers, be corrected for the effects of hemoconcentration to determine whether the response is a true metabolic response or is caused by plasma volume shifts [22, 23]. The following formula was used to adjust sclerostin and PTH concentrations for hemoconcentration: corrected concentration = uncorrected concentration × ((100 + %ΔPV)/100).

Serum sclerostin concentrations were determined in duplicate by Teco Medical kits (Quidel Corporation, San Diego, CA, USA). PTH concentrations were determined in duplicate by intact PTH kits (DRG International, Inc., USA). Intra-assay %CVs ranged from 3.5 to 6.0% and inter-assay %CVs ranged from 2.5 to 5% for sclerostin. Intra-assay %CVs ranged from 1.1 to 1.8% and inter-assay %CVs ranged from 3.0 to 8.4% for PTH. Bone ALP, CTX-I, and TRAP5b assessments were conducted using ELISA kits as previously described [11].

Data analyses

All the descriptive data are reported as mean ± standard error (SE). IBM SPSS Statistics 23 (SPSS Inc., Chicago, IL, USA)

was used for the statistical analyses. All the descriptive statistics were calculated for the dependent variables at each condition and time point. The Kolmogorov–Smirnov procedure was used to determine the normality of the data. Two (condition) × 3 (time) repeated measures ANOVA was used to determine hematocrit, sclerostin and PTH responses to the resistance exercise protocols. When a significant time × condition interaction occurred, one way (time) repeated measures ANOVA with a least significant difference post hoc test was performed within each condition. Two (condition) × 2 (time) repeated measures ANOVA was used for lactate and %Δ PV responses and for percent change sclerostin and PTH variables. Paired *t* tests were used to compare PRE and POSTWBV time points for the effect of the vibration condition for the dependent variables. Zero-order Pearson Product Moment Correlation Coefficients were utilized to examine relationships between sclerostin and PTH concentrations, and sclerostin and PTH concentrations with bone and BTM variables. The level of significance was set at $p \leq 0.05$.

Results

Participant characteristics

Table 1 shows the physical characteristics and BPAQ scores for the participants. As previously reported [11], all the women met the criterion (*Z*-score > −2.0) for normal aBMD at all sites [43].

Biochemical responses

There were no significant differences observed between the two conditions for lactate and hematocrit responses (Table 2). Both protocols showed significant increases in lactate at IP compared to PRE ($p < 0.05$). There was a significant time effect ($p = 0.002$) for hematocrit, which was higher at IP vs. PRE ($p = 0.035$) and 30P ($p = 0.001$). Hematocrit also significantly increased ($p < 0.05$) from PRE to POSTWBV. No significant differences were observed between two conditions for % PV changes ($p > 0.05$).

Table 2 shows the uncorrected sclerostin and PTH responses. Pre-exercise sclerostin concentrations were not significantly different between conditions. There was a significant ($p < 0.01$) condition × time interaction for uncorrected concentrations of sclerostin. For WBV + RE, sclerostin levels ($p < 0.05$) increased from WBVPRE to WBVIP and decreased from WBVIP to WBV30P ($p < 0.01$). There was a trend ($p = 0.07$) for sclerostin to increase from PRE to POSTWBV. Sclerostin % change showed a significant ($p < 0.01$) condition × time interaction as it increased 16.9 ± 5.1% from PRE to IP then decreased by 30P for the WBV + RE condition (Fig. 2a). No significant sclerostin responses were found for RE only condition. Correcting

Table 1 Participant characteristics ($n = 9$)

Variables	Mean ± SE
Age (years)	20.66 ± 0.22
Weight (kg)	69.01 ± 6.08
Height (cm)	166.16 ± 2.03
% Body fat	37.82 ± 2.76
Fat mass (kg)	26.97 ± 4.26
Bone-free LBM (kg)	38.73 ± 1.95
Calcium intake (mg/day)	956 ± 91
BPAQ scores	
Current	2.10 ± 0.76
Past	125.90 ± 29.08
Total body BMD (g/cm^2)	1.159 ± 0.029
Total body BMC (kg)	2.61 ± 0.14

LBM lean body mass, *BPAQ* Bone-Specific Physical Activity Questionnaire, *BMD* bone mineral density, *BMC* bone mineral content

Table 2 Sclerostin, PTH, hematocrit, and lactate responses ($n = 9$; mean ± SE)

Variables	WBV + RE	RE
Hematocrit (%)[a]		
PRE	40.5 ± 1.0	41.6 ± 1.0
POSTWBV	41.8 ± 0.7*	–
IP	43.4 ± 0.9*,††	42.6 ± 1.0*,††
30P	40.5 ± 1.1	40.8 ± 1.0
%PVΔ PRE to POSTWBV	−5.0 ± 2.2	–
%PVΔ PRE to IP	−10.6 ± 3.6	−3.6 ± 3.0
%PVΔ PRE to 30P	2.0 ± 3.5	3.3 ± 1.9
Lactate (mmol/L)[a]		
PRE	0.9 ± 0.1	1.1 ± 0.2
POSTWBV	1.4 ± 0.1	–
IP	5.3 ± 0.5**	5.4 ± 0.6**
Uncorrected sclerostin (ng/mL)[b]		
PRE	0.276 ± 0.015	0.297 ± 0.016
POSTWBV	0.302 ± 0.011	–
IP	0.324 ± 0.025*,††	0.289 ± 0.016
30P	0.268 ± 0.021	0.288 ± 0.016
Uncorrected PTH (pg/mL)[a]		
PRE	44.3 ± 6.3†	42.2 ± 5.9†
POSTWBV	44.6 ± 5.7††	–
IP	43.2 ± 4.3††	42.2 ± 6.7††
30P	25.1 ± 2.5	29.9 ± 4.2

RE resistance exercise, *WBV* whole-body vibration, *%PVΔ* percent plasma volume change, *PRE* before exercise, *POSTWBV* immediately after WBV, *IP* immediately after RE, *30P* 30 min after RE

[a]Significant time effect; [b]significant condition × time interaction

*$p \leq 0.05$ significant vs. PRE; **$p \leq 0.01$ significant vs. PRE; †$p \leq 0.05$ significant vs. 30P; ††$p \leq 0.01$ significant vs. 30P

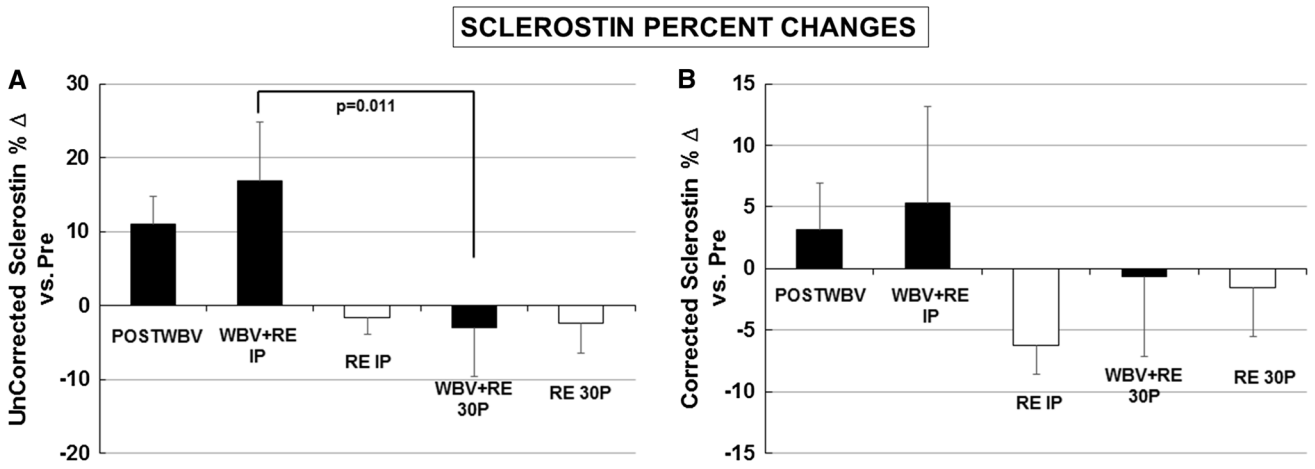

Fig. 2 Uncorrected sclerostin (**a**) and corrected sclerostin (**b**) percent changes (mean ± SE) to the WBV + RE and RE protocols ($n = 9$). *RE* resistance exercise, *WBV* whole-body vibration, *PRE* before exercise, *POSTWBV* immediately after WBV, *IP* immediately after RE, *30P* 30 min after RE

for hemoconcentration eliminated all the significant sclerostin responses. Figure 2b depicts the percent changes for corrected sclerostin concentrations vs. PRE. There was a significant condition × time interaction ($p < 0.05$), however, no time or condition differences were detected in the post hoc analysis. Sclerostin concentrations were not significantly correlated with aBMD variables or BTM concentrations.

PTH responses (uncorrected) were similar for the two conditions (Table 2). Pre-exercise PTH concentrations were not significantly different between conditions. Also, PTH did not change significantly at POSTWBV compared to PRE. There was a significant time effect for uncorrected PTH concentrations, which significantly decreased from PRE to 30P ($p < 0.05$) and from IP to 30P ($p < 0.01$). Correcting for hemoconcentration did not affect the PTH responses, with the significant decreases ($p < 0.05$) still observed at 30P. PTH % changes also showed significant time effects, with both uncorrected (Fig. 3a, $p = 0.002$) and corrected (Fig. 3b, $p = 0.032$) % changes being lower at 30P vs. IP. PTH concentrations were not significantly correlated with aBMD, BTM concentrations or sclerostin.

Discussion

In this study, we report sclerostin and PTH responses to acute high-intensity resistance exercise protocols performed with and without WBV. Uncorrected sclerostin

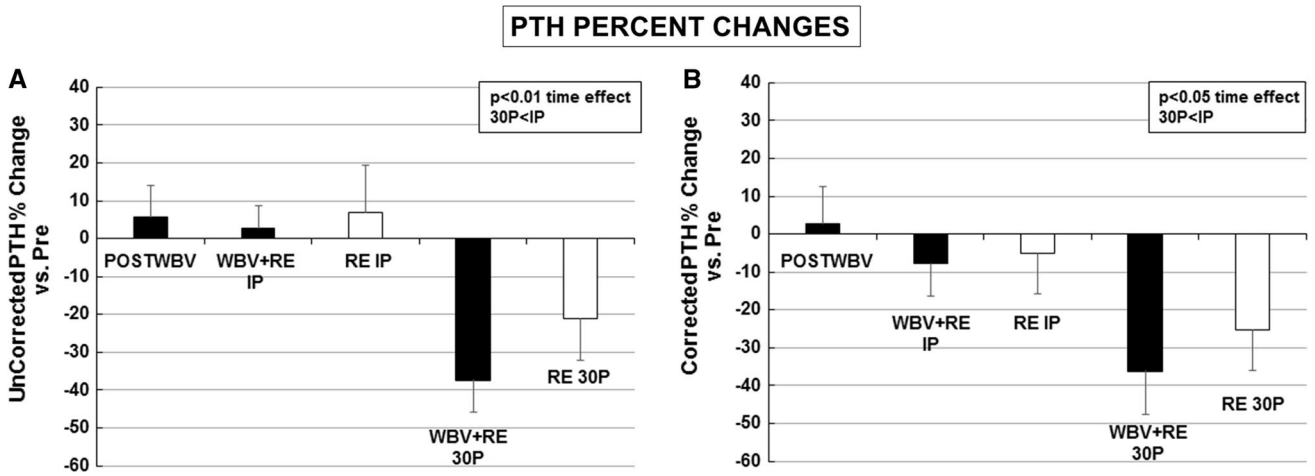

Fig. 3 Uncorrected PTH (**a**) and corrected PTH (**b**) percent changes (mean ± SE) to the WBV + RE and RE protocols ($n = 9$). *PTH* parathyroid hormone, *RE* resistance exercise, *WBV* whole-body vibration, *PRE* before exercise, *POSTWBV* immediately after WBV, *IP* immediately after RE, *30P* 30 min after RE

concentrations increased (~ 17%) immediate post RE only for the WBV + RE condition; however, this was accompanied by ~ 11% decrease in plasma volume, resulting in non-significant changes after correcting for hemoconcentration. We also found a significant decrease (− 29%) in PTH concentrations from PRE to 30P for both conditions, and this finding remained after adjusting for plasma volume changes. We did not observe the negative relationship between resting sclerostin and PTH serum concentrations previously reported in studies with larger age ranges and sample sizes [19, 44]. Also, sclerostin and PTH were not significantly correlated with aBMD variables or BTM concentrations.

Mechanical loading of the skeleton downregulates sclerostin expression in bone, a response purported to play an important role in the osteogenic response to loading by reducing Wnt signaling inhibition in osteoblasts and decreasing osteoclastic resorptive activity [45]. While animal studies consistently document decreases in sclerostin with loading [5, 14, 46], the majority of acute exercise studies in humans found that circulating sclerostin significantly increased within 10 min post loading [18–21]. There are several methodological explanations for the unexpected direction of sclerostin responses in humans. None of these studies adjusted serum sclerostin concentrations for the effects of hemoconcentration, therefore, the sclerostin increase may have been the result of plasma volume shifts rather than a true metabolic bone response. Differences in loading protocols, timing of the sclerostin measurements, and the type of sample also could explain discrepant results. Robling et al. [14] used a loading regimen of 360 cycles/day and measured sclerostin in bone tissue 24 h later, whereas we measured short-term responses to loading up to 30 min post exercise. It may require more time for sclerostin responses to be detected in the blood; although, Falk et al. [19] found that sclerostin concentrations were not significantly different from pre-exercise by 60 min and 24 h after the acute jumping protocol.

We previously reported that Bone ALP responses to these two protocols were not significant; however, CTX-I (uncorrected and corrected) serum concentrations significantly decreased only for the WBV + RE protocol [11]. This finding suggests the addition of the WBV to RE stimulated osteoclasts but not osteoblasts. The current work now extends to the response by osteocytes via changes in sclerostin, thus providing a more complete understanding of how WBV influences mechanical adaptations to mechanical loading. Circulating sclerostin showed a significant time effect (increase) for uncorrected concentrations only, and sclerostin was not significantly correlated with bone variables, or BTM concentrations. The lack of correlation results contradict previous reports of significant positive correlations between resting sclerostin and aBMD [47, 48] and negative correlations between resting sclerostin and serum BTM concentrations [47, 48] in larger studies of older women and men. The young age of our participants may explain the discrepant correlation results as Modder et al. [47] found no significant correlations between sclerostin, aBMD, or BTM in their young women cohort (20–39 years). Also, Ardawi et al. [44] reported significant negative correlations between sclerostin, aBMD and BTM variables in premenopausal women (35–45 years) who were older than our participants. The small sample size in our study limits our ability to detect meaningful relationships between sclerostin and bone variables.

There are only a handful of human studies that have investigated the effects of WBV on serum sclerostin concentrations, and to our knowledge, there are no studies that have utilized WBV combined with resistance exercise. Cidem et al. [21] reported a 91% increase in plasma sclerostin concentrations after acute WBV exposures (2.7 g, 30 s bouts × 2) using a synchronous vibration platform in premenopausal women, although this response may have been influenced by pre-analytical factors (e.g., circadian rhythm, fasting) and plasma volume changes. They also found that the acute sclerostin response was attenuated after 5 continuous days of the WBV protocol; a finding confirmed with longer duration WBV training (5 days per week × 4 weeks) at accelerations of 2.7 and 5.1 with a synchronous vibration platform [49]. It is still unclear if there is any advantage to combining WBV with RE for bone adaptations in humans; however, animal models have reported that WBV + RE hindlimb loaded rats had significantly higher bone formation markers compared to control rats [50].

Our decreased PTH responses 30 min post each exercise condition agrees with the findings of Ashizawa et al. [32] and Rogers et al. [33] who reported that circulating PTH did not increase after acute resistance exercise; rather it decreased (− 30 to 38%) below resting levels 2 h post exercise. It is difficult to discern the role of circadian rhythm in these PTH responses. PTH has its nadir mid-morning [34], but the magnitude of the decrease varies depending on the age, sex, ethnicity, and clinical status of the participants [51–53]. The magnitude of the diurnal variation in PTH between 08:00 and 10:00 was about − 25% in premenopausal women [51]. Rogers et al. [33] conducted their resistance exercise protocols in the morning similar to ours (when the nadir is expected); however, Ashizawa et al. [32] tested their participants in the late afternoon (15:45–20:00 h); therefore, circadian rhythm may not completely account for the changes in circulating PTH in these exercise studies. Another factor that affects PTH responses to acute exercise bouts are serum-ionized calcium concentrations, which have been reported to significantly decrease immediately post both aerobic [29, 30], and resistance exercise [32]. The decrease in serum calcium in the resistance exercise protocol was followed by an increase above resting levels by 2 h

post-exercise [32]. The effects of the serum calcium changes would be expected to cause opposite response patterns in PTH but that relationship is not consistently supported in the literature. Sherk et al. [31] found that serum calcium changes were negatively correlated with PTH changes after aerobic exercise in male cyclists. Scott et al. [29] reported significant alterations in serum PTH after 60 min of treadmill running (transient increase followed by a decrease) that were not accompanied by significant changes in albumin-adjusted serum calcium. However, PTH and calcium concentrations were not adjusted for plasma volume shifts in that study. The physiological importance of transient exercise-induced increases in serum PTH for bone metabolism is not clear. Increased serum PTH concentrations may stimulate bone resorption, an effect supported by positive correlations in % changes in PTH and CTX-I reported by Sherk et al. [31]. Although we also found positive correlations between % changes in PTH and CTX-I (data not shown), closer examination of the data indicated that the correlation in our small sample size was largely influenced by the responses of two participants.

In this study, we attempted to control for as many of the known sources of biological variability in sclerostin and PTH as possible, including circadian rhythm, pre-exercise food intake, last exercise bout effect, plasma volume changes and physical activity status [34, 54]. However, there are several limitations to this study. We utilized a randomized crossover design; however, no control group or control condition was included, therefore, we cannot determine directly the circadian rhythm effect on the PTH responses. Also, we did not measure serum-ionized calcium levels, which would have been useful for the interpretation of the PTH responses. The timing of the post-exercise blood draws may not have been long enough to fully capture the sclerostin and PTH responses to the exercise protocols. As previously mentioned, all participants were OC users to control for the potential effects of the menstrual cycle on BTM concentrations. Estrogen status affects circulating sclerostin concentrations as reflected by higher concentrations with estrogen deficiency (e.g., higher concentrations in postmenopausal women vs. premenopausal women), and lower concentrations in estrogen-treated postmenopausal women [17]. Endogenous variations in estrogen during the menstrual cycle do not appear to affect sclerostin concentrations [55, 56]. While the effects of OC on sclerostin are not clear, OC decrease BTM concentrations [57], thus, it is possible that sclerostin responses may be different in women OC and non-OC users.

In conclusion, we compared sclerostin and PTH responses to WBV + RE and RE only in young women. We found that increases in sclerostin concentrations occurred only in the WBV + RE condition; however, these responses were mediated by plasma volume shifts. PTH decreased by 30 min post-exercise for both protocols, even when adjusted for hemoconcentration. Based on these findings, the addition of WBV exposures prior to high-intensity RE did not alter sclerostin or PTH responses to RE alone in young women OC users. Our results highlight the importance of measuring plasma volume changes for interpreting circulating biomarker responses to acute exercise. Further research is needed to elucidate the impact of acute WBV training on sclerostin and PTH responses in a variety of populations.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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