<u>The effect of an exercise intervention during early lactation on bone mineral density during the first year postpartum</u>

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Abstract:

Background: During lactation, women may lose up to 10% of bone mineral density (BMD) at trabecular-rich sites. Previous studies show that resistance exercise may slow BMD; however, the long-term effects of exercise on BMD during lactation have not been reported. Objective: To evaluate the effect of two 16-week exercise interventions (4- to 20-wk postpartum) in lactating women at 1-year postpartum on lumbar spine, total body, and hip BMD. Methods: To increase sample size at 1-year postpartum, two 16-week exercise interventions were combined for analysis. At 4-week postpartum, 55 women were randomized to intervention group (weight bearing aerobic exercise and resistance exercise) or control group (no exercise) for 16-week, with a 1-year postpartum follow-up. BMD was measured by dual-energy X-ray absorptiometry. Repeated-measures analysis of covariance was used to test for time and group differences for BMD controlling for prolactin concentration and dietary calcium at 1-year postpartum. Results: Change in lumbar spine BMD was significantly different over time and between groups from 4week to 1-year postpartum, when controlling for prolactin concentration and dietary calcium. There were no significant differences between groups in total body and hip BMD. Conclusion: These results suggest that resistance exercise may slow bone loss during lactation, resulting in higher BMD levels at 1-year postpartum.

Keywords: vitamin D | diet | breastfeeding

Article:

Lactation is a critical period of rapid bone turnover. During lactation, infant suckling stimulates prolactin, the hormone responsible for breast milk production. Prolactin initiates the release of parathyroid hormone-related peptide from the mammary tissue into the bloodstream.¹ The presence of parathyroid hormone-related peptide along with the low estradiol concentration in the bloodstream upregulates maternal bone resorption.¹ Calcium from bone is then released into the bloodstream, which will be transferred into breast milk for the infant.¹ This increase in bone remolding results in losses of up to 10% of maternal bone mineral density (BMD) at the trabecular-rich sites (lumbar spine, hip, and femur).² Once resumption of menses and weaning occurs, most women return to their baseline BMD levels; however, adolescent mothers, women with short intervals between pregnancies, and older women who give birth close to menopausal

age may not see complete bone recovery, increasing the risk of osteoporosis and osteopenia later in life.³

In previous studies, using weight-bearing exercise in nonpregnant, nonlactating women with normal estrogen status has shown to increase BMD in the lumbar spine and hip or femoral neck by increased mechanical stress on bones.^{4–7} A recent meta-analysis of studies examining the effect of weight loss on BMD found that energy restriction decreased lumbar spine and hip in premenopausal and postmenopausal women, whereas exercise-induced weight loss had no adverse effect on BMD.⁸

We previously reported the results of 2 randomized trials examining the effects of exercise on BMD in lactating women. The "Be Hip Mom" (Be Hip 1) study⁹ examined the effects of resistance and aerobic exercise on BMD in postpartum normal and overweight breastfeeding women for 16 weeks. The "Be Hip Mom Too!" (Be Hip 2) study¹⁰ examined the effects of a similar 16-week resistance and aerobic exercise combined with energy restriction on BMD in overweight and obese postpartum breastfeeding women. After the 16-week intervention, the exercise group in the Be Hip 1 lost significantly less lumbar spine BMD compared with those who were leading sedentary lifestyles (-4.8% [0.6%] vs -7.0% [0.3%]); however, in Be Hip 2, lumbar spine BMD losses were similar in each group, (intervention group [IG]: -3.4% [2.5%] vs control group [CG]: -3.7% [3.3%]).

This study reports the results of the women from the 2 previous studies who returned for followup measurements at 1-year postpartum. The objective of this study was to determine the effect of exercise during early lactation on BMD at 1-year postpartum. We hypothesized that women who exercised during early lactation would lose less lumbar spine and total hip BMD at 1-year postpartum compared with those who remained sedentary, controlling for hormonal status and dietary intake at 1-year postpartum.

Subjects and Methods

Study Design

Data from participants enrolled in our intervention studies, Be Hip 1⁹ and Be Hip 2,¹⁰ were combined for this analysis. Laboratory measurements for both studies were conducted before (baseline, 3 [2] wk postpartum) and after the intervention (endpoint, 21 [2] wk postpartum). Results from the 16-week intervention have been reported elsewhere.^{9,10} Participants returned for laboratory measurements at 1-year postpartum (52 [2] wk postpartum).

As previously described,^{9,10} participants were recruited through prenatal and parenting classes. Women were eligible if they were fully breastfeeding (<4 oz of formula given to the infant only on occasion), healthy, nonsmoking, sedentary for at least 3 months, and had a self-reported body mass index (BMI) between 20 and 35 kg/m². Women were not eligible if they delivered by cesarean section or had a preexisting condition that disrupted hormonal levels or made them unable to participate in an exercise intervention. The University of North Carolina at Greensboro Institutional Review Board approved the study, and written informed consent was obtained from all study participants. The study was registered with ClinicalTrials.gov (NCT00966381).

Randomization was stratified by parity to control for prolactin levels, and assignment to either group was made after baseline measurements were completed. All participants were given a year's supply of a multivitamin supplement containing 10 μ g of vitamin D.

Laboratory Measurements

BMD and Anthropometrics. Bone density was measured using a different dual-energy X-ray absorptiometry machine for each study (Delphi A Version 12.3; Hologic Inc, Bedford, MA for the Be Hip 1 study and Lunar Prodigy Adv.; Lunar Radiation Corp, Madison, WI; QDR enCORE software version 11.20.068 for the Be Hip 2 study; GE Healthcare). However, all 3 time points for each participant were done on the same machine. The same trained technician scanned each participant; this ensured accuracy and precision of the scans. Quality control was performed with a phantom spine. All participants lay flat in the supine position on the X-ray table while a total of 3 scans were performed: total body; lumbar spine; and total left hip (femoral neck, trochanter, and Ward's triangle).

Participant's height was measured using a standardized stadiometer (235 Heightronic Digital Stadiometer, QuickMedical, Snoqualmie, WA), and weight was measured using a digital scale (Tanita BWB-800S; Tanita Corp, Arlington Heights, IL). Participants removed shoes and wore light clothing during measurements.

Cardiovascular Fitness and Strength. Predicted maximal oxygen consumption (VO₂max) was assessed by a submaximal treadmill test using a modified Balke protocol as outlined in previous publications.^{9,10} The participants wore heart rate monitors (Polar Inc, Woodbury, NY or Polar Electro Oy, Kempele, Finland) for the duration of the treadmill test, and the test was terminated once participants achieved 85% of predicted maximal heart rate. Predicted VO₂max was calculated using the following formulas obtained from American College of Sports Medicine¹¹:

Walking: 3.5 mL/kg/min + speed in $m/min \times 0.1$ $m/min + grade \times m/min \times 1.8$ Jogging: 3.5 mL/kg/min + speed in $m/min \times 0.2$ $m/min + grade \times m/min \times 0.9$

Predicted maximal oxygen consumption (VO₂max) was determined using a linear regression equation; heart rate was defined as the independent variable, and the dependent variable was the predicted VO_2max .

One-repetition maximum testing was used to assess muscular strength.¹¹ Exercises included squats, bench press, seated or standing military press, stiff-leg deadlifts, and bent-over dumbbell row. Handheld adjustable weights were used, and participants were instructed on proper form and technique for each exercise. Each exercise began at 40% to 60% (Be Hip 1) or 50% to 70% (Be Hip 2) of perceived maximum weight capacity with 5 to 10 repetitions. The adjustable weights increased in total increments of 5-, 10-, 20-lb weights until the participant could no longer complete the full repetition. The heaviest weight lifted without breaking proper form was recorded as the 1-repetition maximum.

Dietary Intake. Dietary intake was assessed by 24-hour dietary recalls, collected in person or by telephone using nutrition data system for research (University of Minnesota) software, using a multiple pass system. This method has been validated against doubly labeled water and has proven accurate for assessing dietary intake in groups.^{12–14}

Hormones and Vitamin D Status. A trained technician drew blood samples at the same time each morning, after an overnight fast to control for diurnal variation. Serum samples were then frozen at -70°C until analyzed. Serum prolactin and estradiol were quantified by enzyme-linked immunosorbent assays (Alpco Diagnostics, Salem, NH). All samples used were thawed once and analyzed in triplicate. Samples for baseline and endpoint for each participant were analyzed in the same assay to eliminate interassay variability; however, 1-year samples were analyzed separately. Serum 25(OH)D status was also measured using enzyme-linked immunosorbent assays (450 nm absorbency; DRG International Inc, Springfield, NJ).

Intervention Group. Women in IG from either study completed a 16-week home-based exercise program focusing on resistance training and aerobic exercise 3 days per week. Both studies had similar intervention protocols designed to increase core strength of the body, the area from the gluteal muscles and hip up to the scapula, with the intent of increasing bone formation at lumbar spine and hip. Detailed methods have been previously published.^{9,10}

Control Group. The CGs in both studies were asked not to participate in any structured exercise or make any changes in their diet. They were allowed to walk their infants in strollers at a leisurely pace (no faster than 2 mph).

After Intervention. After the 16-week intervention, participants in the IG were encouraged to continue their exercise program. Research assistants did not monitor exercise after the intervention had ceased. The CG was offered the intervention program, including all exercise equipment, exercise protocol, and instructions. However, research assistants did not visit the home to monitor exercise. Dietary counseling was also offered to the CG in the Be Hip 2 study. All women were contacted monthly to inquire about breastfeeding status and physical activity until their 1-year follow-up visit.

Statistical Analysis

Data were analyzed with JMP software (version 9.0.0; SAS, Cary, NC). Characteristics of each group were compared using analysis of variance and Pearson's chi-squared test. Repeated-measures analysis of variance was used to test for time and group differences in body weight; BMI; strength (1-repetition maximum); cardiovascular fitness (VO₂max); dietary intake (energy, protein, calcium, and vitamin D); and serum vitamin D, prolactin, and estradiol concentrations. The main outcome of interest in this study was the effect of exercise on BMD at 1-year postpartum. The conceptual model (Figure 1) illustrates what factors may influence BMD at 1-year postpartum. Those covariates identified were serum concentrations of vitamin D, prolactin, and estradiol; calcium intake; and weight change from baseline to 1-year postpartum. Prolactin was used for control for variation of breastfeeding status at 1-year postpartum. Prolactin Although estradiol was included in our model, it is not included in our data analysis because we

did not record the phase of the participant's menstrual cycle when serum samples were collected. Repeated-measures analysis of covariance was used to test for time and time by group differences for bone (density, mineral content, and area) controlling for these covariates: percentage of weight change from baseline to 1-year postpartum; and prolactin concentration, calcium intake and vitamin D concentration at 1-year postpartum. Statistical significance was set at $P \le .05$.







Figure 2. Random assignment and 1-year follow-up of the study participants in the Be Hip Mom and Be Hip Mom Too! studies.

Results

A total of 55 women were randomly assigned to IG or CG between the 2 studies at baseline (4-wk postpartum) and 47 completed the 16-week intervention. In total, 8 women (IG = 5 and CG = 3) dropped out of the study before 16 weeks, 7 due to personal reasons, and 1 moved out of state. The remaining women fully breastfed for the first 5-months postpartum. After the 16-week intervention, 2 women became pregnant, and 4 were unable to schedule the 1-year follow-up

measurements in the IG. One woman became pregnant, and 4 were unable to schedule 1-year measurements in the CG. A total of 36 women (18 in each group) returned for the 1-year postpartum measurements. Of these, 31 were white, non-Hispanic (IG = 15, CG = 16); 3 black, non-Hispanic (IG = 1, CG = 2); 1 Asian (IG); and 1 Hispanic (IG). The results reported in this study are from the 36 participants who completed measurements at all 3-time points (Figure 2).

There were no differences in mean age between groups (IG: 32.0 [2.8] y, CG: 30.8 [3.5] y). A total of 13 women in IG and 10 women in CG were multiparous. The percentage of women in IG was 44%, and 41% in CG that resumed their menses by 1-year postpartum, with the mean return of menses at 34 (13) week postpartum in IG and 28 (14) week postpartum in CG. The percentage of the women who were still breastfeeding at 1-year postpartum was 44% in the IG and 67% in the CG; frequency was not recorded. The average weeks postpartum that women terminated breastfeeding was 42 (11) and 46 (11) weeks postpartum in IG and CG, respectively. There were 9 women in IG and 10 women in CG who reported beginning birth control around 14-week postpartum. Types of birth control included intrauterine devices, progesterone only pill, and a combination of progesterone and estrogen pill. Of the 19 women on birth control, 3 terminated birth control usage by 1-year postpartum (IG, n = 2; CG, n = 1).

	Intervention group (n = 18)			Control grou		
	Baseline	Endpoint	1 y	Baseline	Endpoint	1 y
Total body						
% Change from baseline	_	-1.22 (2.53)	-0.93 (1.04)	_	0.70 (1.95)	0.29 (1.95)
BMD, g/cm^2	1.179 (0.093)	1.164 (0.094)	1.168 (0.088)	1.129 (0.109)	1.122 (0.118)	1.127 (0.119)
BMC, g	2554 (483)	2494 (455)	2529 (459)	2402 (574)	2274 (393)	2289 (494)
Area, cm ²	2154 (294)	2123 (268)	2160 (278)	2106 (317)	2007 (167)	2025 (283)
Lumbar spine						
% Change from baseline	_	-3.59 (2.11)	-1.05 (3.15)	_	-5.17 (3.28)	-2.64 (4.41)
BMD, ^{a,b} g/cm ²	1.172 (0.126)	1.130 (0.128)	1.159 (0.128)	1.134 (0.156)	1.075 (0.149))	1.102 (0.149)
BMC, g	64 (9)	61 (9)	64 (9)	60 (10)	56 (9)	59 (9)
Area, cm ²	55 (5)	54 (6)	55 (5)	53 (7)	52 (7)	53 (7)
Total hip						
% Change from baseline	_	-2.58 (1.96)	1.40 (3.14)	_	-2.57 (2.22)	-3.00 (3.11)
BMD, ^a g/cm ²	1.022 (0.133)	0.995 (0.131)	1.007 (0.131)	1.019 (0.146)	0.992 (0.137)	0.988 (0.143)
BMC, g	32 (5)	31 (4)	32 (4)	31 (5)	30 (5)	30 (5)
Area, cm^2	31 (2)	31 (2)	32 (3)	30 (3)	31 (3)	31 (2)

Table 1. Average and P	ercentage Change	s in Total E	Body, Hip, a	and Lumbar	Spine BME	From
Baseline to 1-Year Post	partum					

Abbreviations: BMC, bone mineral content; BMD, bone mineral density; RMANCOVA, repeated-measures analysis of covariance; RMANOVA, repeated-measures analysis of variance. Note: All values are presented as means (SDs) for group outcomes. Significant differences between variables were determined using RMANOVA and RMANCOVA.

^aSignificantly different over time, RMANOVA, P < .05. ^bSignificantly different between groups, RMANCOVA, P < .05.

Changes in total body, hip, and lumbar spine BMD are presented in Table 1. Total body BMD did not change significantly over time or by group. Total hip BMD changed significantly over time. Both groups lost total hip BMD from baseline to the endpoint, then the IG regained BMD from endpoint to 1-year postpartum, whereas the CG continued to lose BMD; however, the

difference was not significant. Lumbar spine BMD changed significantly over time for both groups, but there was no significant difference between the 2 groups (Figure 3). However, when only dietary calcium intake and prolactin concentrations for at 1-year postpartum were added as covariates to the analysis to control for breastfeeding status, the differences between groups over time became significant. IG lost significantly less lumbar spine BMD from baseline to 1-year postpartum compared with CG (-1.1% vs -2.6%, respectively). Estradiol was not used as a covariate in the analysis because the phase of the menstrual cycle was not controlled for when serum samples were collected. No differences between groups in total body or hip BMD were observed when analyzing with covariates.





Significantly different over time, RMANOVA, P < .05. Significantly different between groups, RMANCOVA, P < .05, when controlled for prolactin concentrations and dietary calcium at 1-year postpartum. BMD indicates bone mineral density; RMANCOVA, repeated-measures analysis of covariance; RMANOVA, repeated-measures analysis of variance.

Women in IG significantly increased muscular strength over time in all exercises compared with CG (Table 2). Compliance for resistance exercises was assessed by how many resistance-training sessions were completed (total of 48 d). Women were able to complete an average of 44 resistance-training sessions (92%).^{9,10}

	Interventio	Intervention group			Control group			
	Baseline	Endpoint	1 y	Baseline	Endpoint	1 y		
VO ₂ , ^{a,b} mL/kg/min ⁻¹	32.5 (4.5)	36.0 (5.5)	35.7 (6.4)	32.3 (4.6)	34.6 (6.0)	37.1 (6.1)		
VO ₂ , L/min	2.5 (0.5)	2.6 (0.6)	2.5 (0.7)	2.3 (0.5)	2.3 (0.5)	2.4 (0.5)		
Squats, ^{a,b} lbs	78 (21)	108 (24)	98 (24)	75 (19)	86 (23)	94 (24)		
Bench press, ^{a,b} lbs	47 (12)	63 (13)	60 (13)	50 (16)	52 (17)	58 (17)		
Bent-over row, ^{a,b} lbs	48 (18)	70 (14)	62 (17)	46 (13)	50 (13)	57 (15)		
Deadlift, ^{a,b} lbs	77 (19)	109 (19)	100 (26)	73 (21)	81 (24)	89 (25)		
Military press, ^{a,b} lbs	39 (10)	48 (8)	47 (10)	39 (10)	39 (10)	42 (10)		

Table 2. Cardiovascular Fitness and Muscular Strength of the Participants in the Intervention

 and Control Groups

Abbreviation: RMANOVA, repeated-measured analysis of variance. Note: Values are presented as means (SDs). ^aSignficantly different over time, RMANOVA, P < .05. ^bSignficantly different over time between groups, RMANOVA, P < .05. Both groups experienced significant increases in predicted relative VO₂max (mL/kg/min) over time (Table 2). CG had higher measurements of predicted relative VO₂max compared with IG; however, absolute VO₂ (L/min) did not differ between groups or by time. Compliance for aerobic activity was assessed for the Be Hip 1 study (n = 7) by how many aerobic training days were completed (total of 48 d). Women were able to complete an average of 41 aerobic training days (86%). In the Be Hip 2 study (n = 11), average daily steps were recorded to monitor compliance. The average daily steps were 5385, which equated to 54% of our goal of 10,000 steps.

No monitoring of exercise was completed after the intervention period for either resistance or aerobic exercise, until workout logs were turned in at the 1-year postpartum laboratory measurement. In IG, 10 women reported continuing exercising after the 16-week study period. A total of 5 women in CG reported beginning an exercise regimen after the 16 week. The average estimated duration of exercise after intervention to 1-year postpartum was 28 weeks. Types of exercises performed by both groups after the intervention period included running, biking, and resistance exercises. All exercises were at a lower intensity and frequency compared with the exercises conducted during the intervention.

	Intervention group (n = 18)			Control group (n = 18)		
	Baseline	Endpoint	1 y	Baseline	Endpoint	1 y
Dietary intake						
Energy intake, ^a kcal/d	2220 (503)	1842 (399)	1706 (360)	2131 (571)	1829 (556)	1750 (498)
Protein, g	88.7 (19.0)	76.0 (21.3)	76.0 (18.1)	78.9 (22.7)	79.4 (21.7)	80.2 (22.4)
Calcium, mg	1366 (477)	1124 (423)	1031 (500)	1091 (374)	990 (292)	1111 (526)
Vitamin D, µg	5.3 (2.6)	4.9 (3.1)	4.8 (3.5)	4.4 (2.5)	4.5 (2.2)	5.6 (3.7)
Anthropometrics						
Prepregnant weight, kg	70.7 (12.8)	_	_	65.2 (14.2)	-	-
Weight, ^b kg	77.0 (12.6)	71.6 (12.6)	69.8 (14.6)	71.6 (13.0)	69.1 (15.5)	65.8 (16.2)
Percentage return prepregnant weight	_	25.0%	30.6%	-	16.7%	33.3%
BMI, ^a kg/m ²	28.5 (4.3)	26.5 (4.4)	25.9 (5.5)	26.4 (3.3)	25.5 (4.1)	24.2 (4.3)
Height, cm	164.3 (5.9)	_	_	164.1 (7.8)	-	-
Hormone concentration						
Prolactin, ^a µg/L	142 (72)	61 (24)	17 (15)	156 (99)	75 (44)	23 (17)
Estradiol, ^a pmol/L	139 (89)	108 (63)	176 (156)	195 (105)	125 (82)	161 (122)
Serum 25(OH)D, ng/mL	26.6 (1.97)	_	26.1 (1.51)	26.1 (2.26)	-	25.3 (1.94)

Table 3. Dietary Intake, Anthropometrics, and Hormone Concentrations Over the First Year

 Postpartum

Abbreviations: ANOVA, analysis of variance; BMI, body mass index; RMANOVA, repeated-measured analysis of variance. Note: All values are means (SDs) for group outcomes. Data reported do not include supplements. Significant differences between groups at baseline were determined using ANOVA. Significant differences between variables were determined using RMANOVA. To convert values from kilocalories to kilojoules, multiply by 4.184. ^aSignificantly different over time, RMANOVA, P < .05. ^bSignificantly different over time between groups, RMANOVA, P < .05.

Energy (measured in kcal) intake in both groups significantly decreased from baseline to 1-year postpartum but was not significantly different between groups (Table 3). Dietary protein, calcium, and vitamin D intakes did not change from baseline to 1-year postpartum or between groups. The percentage of participants meeting the estimated average requirement for calcium

(800 mg) at baseline, endpoint, and 1-year postpartum was 81%, 75%, and 71%, respectively; 8%, 6%, and 9% of participants met the estimated average requirement for vitamin D (10 μ g) from diet at the 3 time points. In addition, 3 women (CG, n = 2; IG, n = 1) reported taking calcium supplements (amount unknown) at 20-week postpartum. At 1-year postpartum, 3 women in each group reported supplementing their diets with calcium.

Weight at baseline, endpoint, and 1-year postpartum were significantly greater in IG compared with CG (Table 3). Weight and BMI significantly decreased over time in both groups, with the pattern of weight lost significantly different between groups. IG lost more during the intervention period, and the CG lost more after the intervention period. At 1-year postpartum, approximately one-third of women in both groups returned to their prepregnant weight. Change in BMI was not correlated with change in BMD.

From baseline to 1-year postpartum, prolactin and estradiol concentrations in both groups changed significantly (Table 3). Serum 25(OH)D concentrations did not differ by group at baseline and 1-year postpartum. No correlations were observed between serum and dietary vitamin D; however, serum 25(OH)D concentrations at baseline correlated with serum 25(OH)D concentrations at 1-year postpartum (r = .53).

Variable	Returned (n = 9)	Did not return (n = 27)
Group, n (%)		
Exercise	7 (78)	11 (41)
Control	2 (22)	15 (59)
Age, y	30 (3.7)	32 (3.0)
Weight, kg		
BMI at baseline, kg/m ²	29.2 (4.5)	26.9 (3.6)
Percentage change in weight from baseline to 1 y	-10.4 (7.2)	-8.8 (8.3)
Calcium intake at 1 y, mg/d	914 (450)	1116 (521)
Hormone concentration at 1 y		
Prolactin, µg/L	23.7 (21.2)	18.8 (14.4)
Estradiol, pmol/L	148.8 (125.2)	175.1 (144.7)
Menses returned (wk postpartum)	27.7 (12.4)	32.8 (14.1)
Percentage change in lumbar spine BMD baseline to endpoint ^a	-2.2 (2.2)	-5.1 (2.6)
Percentage change in lumbar spine BMD endpoint to 1 y ^a	5.2 (2.4)	1.8 (3.1)
Breastfeeding status at 1 y, n (%)		
Yes	3 (33)	17 (63)
No	6 (67)	10 (37)
Parity, n (%)		
Primiparous	5 (56)	8 (30)
Multiparous	4 (44)	19 (70)

Table 4. Characteristics of Participants Who Returned to Baseline Lumbar Spine BMD

Abbreviations: BMD, bone mineral density; BMI, body mass index. Note: All values are presented as means (SDs) for group outcomes.

^aSignificantly different between groups, analysis of variance, P < .05.

Only 25% of participants returned to baseline lumbar spine BMD levels at 1-year postpartum (Table 4). They lost significantly less lumbar spine BMD from baseline to endpoint and gained significantly more lumbar spine BMD from endpoint to 1-year postpartum. In addition, the

majority of those who returned were in IG. Only 5 participants (14%) returned to baseline hip BMD at 1-year postpartum. Only 2 participants returned to both their baseline lumbar spine and total hip BMD at 1-year postpartum (n = 1, each group).

Discussion

The results of this study suggest that exercise during the first 5-months postpartum slows BMD losses in lactating women. Few studies have examined the effects of exercise on BMD in breastfeeding women. In the Be Hip 1 study, the exercise group lost significantly less lumbar spine BMD compared with those leading sedentary lifestyles (-4.8% [0.6%] vs -7.0% [0.3%]).⁹ However, in the Be Hip 2 study, exercise did not have a significant effect on lumbar spine BMD (IG: -3.4% [2.5%] vs -3.7% [3.3%]).¹⁰One possible explanation for the results in the second study may be due to control participants having a higher average BMI in the Be Hip 2 study compared with the former study (27.9 vs 24.7 kg/m²). This heavier weight may be a contributing factor that reduced bone loss during lactation. Previous studies have shown that BMI is positively correlated with BMD.¹⁵ In this study, mean baseline BMI for all participants was 27.5 kg/m²; however, we did not observe a correlation between BMI and changes in BMD in this analysis.

Little and Clapp¹⁶ compared changes in BMD of breastfeeding women engaging in self-selected, nonsupervised exercise (3 d/wk, at least 20 min/d) to nonexercising breastfeeding women. Over the 3-month study period, both groups lost similar amounts of BMD at the femoral neck (IG: -2.8 vs CG: -2.9) and lumbar spine (IG: -4.1 vs CG: -5.4). The authors theorized that the variability in exercises (mode, intensity, frequency, and duration) was not as effective as a standardized, structured exercise program.

Drinkwater and Chestnut¹⁷ followed 6 female athletes during lactation and compared their BMD changes to exercising, nonpregnant, nonlactating women. Femoral neck BMD decreased in the breastfeeding athletes; however, decreases in lumbar spine BMD were not observed. Although the study had the limitations of a lack of structured exercise and nonexercise lactating CG, the authors hypothesized that the exercise done by the lactating mothers may have been protective against lumbar spine bone loss.

The usual bone turnover cycle occurs over 4 to 8 months; however, during lactation, this cycle is shortened to 3 to 4 months.¹⁸ It is possible that the study duration used by Little and Clapp¹⁶ and Drinkwater and Chestnut¹⁷ may not have been long enough to see significant changes in BMD. The 16-week intervention completed in both of our studies was appropriate to allow time for bone turnover. In addition, the resistance exercise in both of our studies targeted the core body and lumbar spine.

At 1-year postpartum, only 9 (25%) participants returned to their baseline lumbar spine BMD and only 5 (16%) returned to baseline hip BMD. These results are different than previous studies that reported the majority of participants returning to baseline BMD.^{19,20} The small number of women returning to baseline BMD may be due to the number of women still breastfeeding in both groups (IG: 44%, CG: 67%, P = .18). Moller et al²¹ investigated changes in BMD during pregnancy and the postpartum period and reported that at 9-months postpartum, women still

breastfeeding had a decreased BMD at the lumbar spine and hip, compared with women who never became pregnant. The 9 women who returned to baseline BMD values lost significantly less lumbar spine BMD from baseline to the 16-week endpoint (-2.2% vs -5.1%) and gained significantly more from endpoint to 1-year (5.2% vs 1.8%) than those who did not return to baseline lumbar spine BMD values. Forty-one percent had regained their lumbar spine BMD and 24% regained their hip BMD to prepregnant levels. At one-year postpartum, 74% returned to prepregnant lumbar spine and hip BMD (n = 31).

The 9 women who returned to baseline BMD values lost significantly less lumbar spine BMD from baseline to the 16-week endpoint (-2.2% vs -5.1%) and gained significantly more from endpoint to 1-year (5.2% vs 1.8%) than those who did not return to baseline lumbar spine BMD values. In addition, there were significantly more women in the IG that returned to baseline BMD, suggesting that exercise had a significant effect.

Prolactin and estradiol concentration changes were similar to those reported by Krebs et al.² Both this study and that of Krebs et al² reported an average lumbar spine BMD loss for all participants at 20-week postpartum of approximately 4%. In their study, estradiol was positively associated with change in lumbar spine BMD after menses had returned; we did not see this in this study. However, we did not record the phase of the participant's menstrual cycle when serum samples were collected. This may be a reason why we did not see a relationship.

Calcium and vitamin D may play a role in BMD during lactation. In addition, supplementation with calcium may not prevent bone loss during lactation but may enhance bone formation after weaning.²² The Recommended Dietary Allowance (RDA) for calcium for lactating and nonlactating women is 1000 mg.²³ Although mean dietary calcium was adequate at all 3 time points, the range of dietary calcium revealed that not all participants were consuming the recommendation. Calcium was included in our analysis because of the correlation between intake and BMD seen in previous studies. Krebs et al² reported that adequate dietary calcium was positively associated with lumbar spine BMD at 6 months after the return of menses. Our 1-year measurements of calcium intake and BMD are approximately 6 months after the return of menses for most women, similar to that observed by Krebs et al.² It is possible that adequate calcium intake did not correlate with BMD at any time point, it was a significant covariate in repeated-measures analysis of covariance of lumbar spine BMD.

The RDA for vitamin D during lactation is 15 μ g/d.²³ Based on our results; the mean dietary vitamin D of all study participants was significantly lower than the RDA but was similar to those reported in previous studies.^{24,25} Serum 25(OH)D concentration associated with the RDA for vitamin D is 50 nmol/L.²³ All participants at baseline and 1-year postpartum had sufficient serum concentrations of 25(OH)D, greater than 50 nmol/L. Mean concentrations of our participants (65 nmol/L) are similar to those reported in lactating women from South Carolina (55 or 71 nmol/L,²⁴ depending on the study group) and from California (52 nmol/L).²⁵ However, Hollis et al²⁶reported higher serum vitamin D concentrations in white (105 nmol/L) and black (70 nmol/L) exclusively breastfeeding women at 4 to 6 weeks postpartum. Using stable isotopes, O'Brien et al²⁵ found a positive relationship between calcium deposition during the early

postpartum period and serum concentrations of 25(OH)D and dietary calcium, while breastfeeding was negatively associated with calcium deposition in the bone.

There are a number of strengths to this study. We combined 2 similar studies to increase our sample size at 1-year postpartum. Both studies had a supervised, randomized exercise intervention as opposed to having participants report exercise completed over time. By doing so, we were able to confirm exercise compliance. The exercise program also targeted the core body, essential in stimulating bone growth at the lumbar spine. Covariates were also addressed and controlled for during statistical analysis. Although the 2 studies used a different dual-energy X-ray absorptiometry, the same dual-energy X-ray absorptiometry was used for each participant from baseline to endpoint to the 1-year postpartum measurement. Despite combining 2 studies, the limitation of this study is the number of dropouts due to pregnancy, personal reasons, and moving away from the area. After adjusting for those who did not have BMD measurements at 1-year postpartum, our sample size decreased from 55 to 36. In addition, most of the women resumed their menses at 1-year postpartum; however, we did not record the phase of the participant's menstrual cycle when serum hormone levels were collected.

Conclusions

Women who participated in a 16-week resistance and aerobic exercise intervention lost significantly less lumbar spine BMD during the first 20-week postpartum, resulting in higher lumbar spine BMD levels at 1-year postpartum as compared with women who did not exercise during the first 16-week of the postpartum period. Additional research is needed to determine the effects of exercise and diet on BMD during the postpartum period, given the low percentage of women who returned to their baseline BMD levels at 1-year postpartum.

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References

1. Kovacs CS. Calcium and bone metabolism during pregnancy and lactation. J Mammary Gland Biol Neoplasia. 2005;10(2):105–118. PubMed ID: <u>16025218</u> doi:10.1007/s10911-005-5394-0

2. Krebs NF, Reidinger CJ, Robertson AD, Brenner M. Bone mineral density changes during lactation: maternal, dietary, and biochemical correlates. Am J Clin Nutr. 1997;65(6):1738–1746. PubMed ID: <u>9174469</u> doi:10.1093/ajcn/65.6.1738

3. National Institute for Health Osteoporosis and Related Bone Disease National Resource Center. Osteoporosis. 2015. <u>https://www.bones.nih.gov/health-info/bone/osteoporosis</u>. Accessed April 20, 2018.

4. Bassey E, Rothwell M, Littlewood J, Pye D. Pre- and Postmenopausal women have different bone mineral density responses to the same high-impact exercise. J Bone Miner Res. 1998;13(12):1805–1813. PubMed ID: <u>9844097</u> doi:10.1359/jbmr.1998.13.12.1805

5. Vainionpaa A, Korpelainen R, Leppaluoto J, Jamsa T. Effects of high-impact exercise on bone mineral density: a randomized controlled trial in premenopausal women. Osteoporos Int. 2005;16:191–197. PubMed ID: <u>15221206</u> doi:10.1007/s00198-004-1659-5

6. Singh JA, Schmitz KH, Petit MA. Effect of resistance exercise on bone mineral density in premenopausal women. Joint Bone Spine. 2009;76(3):273–280. PubMed ID: <u>19217817</u> doi:10.1016/j.jbspin.2008.07.016

7. Winters-Stone KM, Snow CM. Site-specific response of bone to exercise in premenopausal women. Bone. 2006;39(6):1203–1209. PubMed ID: <u>16876495</u> doi:10.1016/j.bone.2006.06.005

8. Soltani S, Hunter GR, Kazemi A, Shab-Bidar S. The effects of weight loss approaches on bone mineral density in adults: a systematic review and meta-analysis of randomized controlled trials. Osteoporos Int. 2016;27(9):2655–2671. PubMed ID: <u>27154437</u> doi:10.1007/s00198-016-3617-4

9. Lovelady CA, Bopp MJ, Colleran HL, Mackie HK, Wideman L. Effect of exercise training on loss of bone mineral density during lactation. Med Sci Sports Exerc. 2009;41(10):1902–1907. PubMed ID: <u>19727023</u> doi:10.1249/MSS.0b013e3181a5a68b

10. Colleran HL, Wideman L, Lovelady CA. Effects of energy restriction and exercise on bone mineral density during lactation. Med Sci Sports Exerc. 2012;44(8):1570–1579. PubMed ID: <u>22460469</u> doi:10.1249/MSS.0b013e318251d43e

11. Franklin BA. American College of Sports Medicine's Guidelines for Exercise Testing and Prescription, 6th ed. Philadelphia, PA: Lipponcott Williams & Wilkins; 2000:60–86.

12. Weber JL, Reid PM, Greaves KA, et al. Validity of self-reported energy intake in lean and obese young women, using two nutrient databases, compared with total energy expenditure assessed by doubly labeled water. Eur J Clin Nutr. 2001;55(11):940–950. PubMed ID: <u>11641742</u> doi:10.1038/sj.ejcn.1601249

13. Moshfegh AJ, Rhodes DG, Baer DJ, et al. The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes. Am J Clin Nutr. 2008;88(2):324–332. PubMed ID: <u>18689367</u> doi:10.1093/ajcn/88.2.324

14. Blanton CA, Moshfegh AJ, Baer DJ, Kretsch MJ. The USDA Automated Multiple-Pass Method accurately estimates group total energy and nutrient intake. J Nutr. 2006;136(10):2594–2599. PubMed ID: <u>16988132</u> doi:10.1093/jn/136.10.2594

15. Asomaning K, Bertone-Johnson ER, Nasca PC, Hooven F, Pekow PS. The association between body mass index and osteoporosis in patients referred for a bone mineral density examination. J Womens Health. 2006;15(9):1028–1034. PubMed ID: <u>17125421</u> doi:10.1089/jwh.2006.15.1028

16. Little KD, Clapp JF. Self-selected recreational exercise has no impact on early postpartum lactation-induced bone loss. Med Sci Sports Exerc. 1998;30(6):831–836. PubMed ID: <u>9624639</u>

17. Drinkwater BL, Chesnut CH. Bone density changes during pregnancy and lactation in active women: a longitudinal study. Bone Miner. 1991;14(2):153–160. PubMed ID: <u>1912763</u> doi:10.1016/0169-6009(91)90092-E

 Kalkwarf HJ, Specker BL, Ho M. Effects of calcium supplementation on calcium homeostasis and bone turnover in lactating women. J Clin Endocrinol Metab. 1999;84(2):464– 470. PubMed ID: <u>10022402</u>

19. Sowers M, Corton G, Shapiro B, et al. Changes in bone density with lactation. JAMA. 1993;269(24):3130–3135. PubMed ID: <u>8505816</u> doi:10.1001/jama.1993.03500240074029

20. Polatti FM, Capuzzo EM, Viazzo FM, Colleoni RM, Klersy CM. Bone mineral changes during and after lactation. Obstet Gynecol. 1999;94(1):52–56. PubMed ID: <u>10389717</u>

21. Moller UK, vio Streym S, Mosekilde L, Rejnmark L. Changes in bone mineral density and body composition during pregnancy and postpartum. A controlled cohort study. Osteoporos Int. 2012;23(4):1213–1223. PubMed ID: <u>21607805</u> doi:10.1007/s00198-011-1654-6

22. Kalkwarf HJ, Specker BL, Bianchi DC, Ranz J, Ho M. The effect of calcium supplementation on bone density during lactation and after weaning. N Engl J Med. 1997;337(8):523–528. PubMed ID: <u>9262495</u> doi:10.1056/NEJM199708213370803

23. Institute of Medicine. Food and Nutrition Board. Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: National Academy Press, 2010.

24. Basile LA, Taylor SN, Wagner CL, Horst RL, Hollis BW. The effect of high-dose vitamin D supplementation on serum vitamin D levels and milk calcium concentration in lactating women and their infants. Breastfeed Med. 2006;1(1):27–35. PubMed ID: <u>17661558</u> doi:10.1089/bfm.2006.1.27

25. O'Brien KO, Donnangelo CM, Ritchie L, Gildengorins G, Abrams S, King JC. Serum 1, 25dihydroxyvitamin D and calcium intake affect rates of bone calcium deposition during pregnancy and the early postpartum period. Am J Clin Nutr. 2012;96:64–72. PubMed ID: <u>22648718</u> doi:10.3945/ajcn.111.029231 26. Hollis BW, Wagner CL, Howard CR, et al. Maternal versus infant vitamin D supplementation during lactation: a randomized controlled trial. Pediatrics. 2015;136(4):625–634. PubMed ID: <u>26416936</u> doi:10.1542/peds.2015-1669