The effects of hormone replacement therapy and resistance training on spine bone mineral density in early postmenopausal women

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Abstract

This study evaluated the additive effects of hormone replacement therapy (HRT) and a 1-year site-specific resistance-training (RT) program involving two free weight exercises (i.e., squat and deadlift) 2 days/week as a strategy to reverse or attenuate bone loss at the lumbar spine in early postmenopausal women. Participants from a group of self-selected HRT or non-HRT (N=141) users were randomly assigned to RT (exercise) or no training, creating four groups: 1) non-HRT plus RT [NHRT plus exercise (n=35)]; 2) HRT plus RT [HRT plus exercise (n=37)]; 3) HRT no resistance training [HRT no exercise (n=35)]; or 4) control [non-HRT no resistance training group (n=34)]. Mean age and months past menopause did not differ between groups (52.1±3.0 years and 52.8±9.9 months, respectively). Post-menopausal status was confirmed by follicle-stimulating hormone levels ≥40 mIU/mL. Bone mineral density (BMD) of the spine was assessed by Dual Energy X-ray Absorptiometry (Hologic), at baseline and month 12. Data were analyzed using a 4 (experimental condition)×2 (time) repeated measures multivariate analysis of variance to determine the effects of RT on HRT and non-HRT in early postmenopausal women. The main effects for group (P<0.007), time (P<0.001), and the group by time interaction (P<0.001) were each significant. Control participants experienced an average of −3.6% reduction of BMD at the spine. HRT treatment with no exercise showed bone loss of −0.66%. One year of RT produced increases in spine BMD of +0.43% and +0.70%, respectively for the NHRT plus exercise, and HRT plus exercise groups with no differences between the NHRT and HRT exercise groups. In conclusion, RT alone was as effective as HRT in preventing bone loss at the spine and was more effective than HRT alone in attenuating bone loss at the spine. Moreover, there was no additional benefit in combining HRT with RT for preventing bone loss at the spine in this group of early postmenopausal women.

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Introduction

Age-related changes to the musculoskeletal system are a major health concern worldwide. In the United States alone, low bone density and muscle loss that compromises bone and muscle strength (i.e., osteopenia and sarcopenia, respectfully) affects over 26 million people, predominantly postmenopausal women, and results in excess of 1.5 million fractures a year [12]. Women are at a particular risk for osteoporosis due to an accelerated bone loss of 2.0–6.5% per year within the first 3 to 5 years after menopause [28]. Evidence suggests that the loss of ovarian function and decreased circulating 17beta-estradiol levels accelerate the rate of bone loss. The loss of ovarian function may also be involved in declines in muscle strength and lean mass, as Walsh et al. [38] recently reported that 50% of osteoporotic postmenopausal women have sarcopenia. Clearly, menopause heralds the onset of changes that have far-reaching consequences on women’s future health [2].

Hormone replacement therapy (HRT) has been prescribed to post-menopausal women to offset bone loss and to minimize the symptoms of menopause, while anti-resorptive agents have been accepted as the mainstay for osteoporosis treatment. However, the pharmacological approach also has limitations,
including side effects and limited efficacy [8]. For example, the Women’s Health Initiative Randomized Trial reported significant adverse affects resulting from hormone replacement therapy [37]. Currently, ultra-low-dose estrogens are being explored and they appear to have affects on bone turnover and bone mass consistent with active antiresorptive methods of treatment for bone loss after menopause [25].

There is also evidence that physical activity of sufficient loading can stimulate bone and muscle formation enough to reduce or attenuate age related osteoporosis and sarcopenia [17,40]. Identifying high compliance, low-risk exercise programs that improve bone mineral density (BMD), bone and muscle strength, and physical function could add many quality years to the lives of older adults.

In a recent meta-analysis of 19 studies, Martyn-St James and Carroll [23] concluded that high intensity resistance training has beneficial effects on lumbar spine BMD in postmenopausal women. However, the potential interactive effects of hormone replacement therapy (HRT) and resistance training as a method of reversing bone loss in early postmenopausal women is not well understood. Additionally, only a few studies, often with limited sample sizes, have attempted to evaluate this topic and they have yielded conflicting results [13,26,31,32]. Furthermore, positive change in BMD at the hip associated with exercise plus HRT has only been reported in one study [13].

We recently reported that at the lumbar spine, men performing high-intensity free-weight resistance exercise had significant increases in BMD compared to men in the moderate-intensity resistance exercise group (1.9% vs. −0.52%). For women, neither high, nor moderate-intensity resistance training resulted in significant changes in lumbar spine BMD, although there was a trend for maintenance of spine BMD in the free weight, high intensity group [22].

Based on these findings we hypothesized that two exercises, the squat and deadlift played a central role in reducing bone resorption at the hip and spine. Performing these two exercises, forces at the hip and spine approach 90% of one repetition maximum (1RM) [14,15] thus providing sufficient mechanical stress to increase lean muscle mass and BMD.

Table 1
Baseline characteristics of women who completed the study (N=125), reported as Mean±S.D.

<table>
<thead>
<tr>
<th></th>
<th>NHRT plus Ex (n=29)</th>
<th>HRT plus Ex (n=33)</th>
<th>HRT no Ex (n=34)</th>
<th>Control (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.3±3.3</td>
<td>52.1±3.1</td>
<td>51.8±2.9</td>
<td>52.5±3.0</td>
</tr>
<tr>
<td>Months post-menopausal</td>
<td>25.3±9.4</td>
<td>27.5±10.5</td>
<td>27.8±10.2</td>
<td>23.4±8.7</td>
</tr>
<tr>
<td>Months on HRT</td>
<td>0.0</td>
<td>25.0±9.4</td>
<td>25.7±8.6</td>
<td>0.0</td>
</tr>
<tr>
<td>Calcium (g)</td>
<td>1089±521</td>
<td>1269±589</td>
<td>1205±598</td>
<td>1296±558</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>57.1±17.1</td>
<td>62.4±21.3</td>
<td>58.3±21.3</td>
<td>58.8±20.2</td>
</tr>
<tr>
<td>Energy expenditure (Mets)</td>
<td>87.5±55.4</td>
<td>107.8±49.3</td>
<td>80.9±46.9</td>
<td>93.8±61.2</td>
</tr>
</tbody>
</table>

Twelve-month follow-up results are not reported for calcium, protein consumption, or energy expenditure since no significant differences was observed (all P>0.05).

To investigate the independent and combined effects of resistance training and estrogen, we examined the bone response to two site specific free weight exercises (squat and deadlift) performed 2 days per week plus HRT in early postmenopausal women (Table 1).

Materials and methods

Study participants

Prior to the commencement of the study, sample size estimates were determined from formal power calculations. With a desired power ≥ 0.8, alpha = 0.05, and an expected difference between groups of 4% increase in muscle mass and a 1% increase in spine BMD, 25 subjects per group were needed.

Early postmenopausal women (self selected HRT or non-HRT) were recruited from a group of subjects who had previously participated in a one-year follow-up observational study [21]. The Institutional Review Board at Oregon State University approved the study. All subjects provided written consent after being fully informed of the nature of the study. Following consent, the self selected HRT and non-HRT users were randomly assigned to either 1) non-HRT plus RT [NHRT plus exercise (n=35)]; 2) HRT plus RT [HRT plus exercise (n=37)]; 3) HRT no resistance training [HRT no exercise (n=35)]; or 4) control [non-HRT no exercise group (n=34)].

Acceptance into the original study [21] was based on the following inclusion and exclusion criteria. Criteria for inclusion: (1) Women who had experienced the menopause within the previous 0–36 months from the time of baseline testing as determined retrospectively from questionnaire reports, (2) No menstrual cycles within the previous 12 months without being pregnant, but not longer than 36 months (based on questionnaire recall phone screening interview), (3) Folic-stimulating hormone levels ≥ 40 mIU/mL (obtained from the subjects physician), (4) Body mass index 19–30 kg m², (5) 36 months or less of being diagnosed as being post-menopausal by their general physician, and (6) either taking HRT 0.625 mg conjugated equine estrogen, (Premarin®) or non HRT use. Criteria for exclusion: (1) Non-HRT users who had taken HRT for 12 consecutive months prior to applying to the study, (2) Hypertension, (3) Metabolic disease that may affect bone or muscle metabolism (including diabetes and thyroid disease), (4) statin medications for hypercholesterolemia, multiple sclerosis, and (4) osteoarthritis or other musculoskeletal disorders that prevented participation in this study.

Participants were self selected as either HRT or non-HRT replaced. Non-HRT replaced participants consisted of women who had never taken HRT either prior to or during the study. HRT participants were women who began taking HRT at the onset of menopause as determined by their personal physicians and continued taking HRT for the duration of the study. No significant differences were observed at baseline on any variable except for spine BMD. Prior to randomization, significant differences were observed at the lumbar spine BMD of 1.00±0.12 and 0.96±0.12 g/cm² for the HRT and non-HRT groups. We previously reported that this group of non-HRT replaced women lost 1.2±3.0% at the spine following a one-year observational study that preceded the present study [21]. Mean scores (±S.D.) at baseline for the two study conditions (HRT group and non-HRT group) are presented in Table 2.

All participants were given a log book and asked to record any changes to their medication routine. The HRT groups were also asked to record compliance of their HRT medication. Participants in the non-exercise groups were requested quarterly to return their log books to our laboratory, at which time new log books were issued to the participants via US mail. Participants in the exercise groups dropped off their log books during one of their regular exercise sessions each quarter of the study.

Measures and procedures

Assessment time line

After assignment into one of four groups, strength measurements were obtained at baseline, 6 and 12 months (±7 days). Only participants who completed all three assessments were included in analysis. Participants who withdrew from the study were not invited back for follow-up analyses.
Bone mineral density and body composition

Dual-energy X-ray absorptiometry (DXA, Hologic QDR-4500 Elite A Waltham, MA) was used to measure bone area (cm²), and bone mineral density (BMD, g/cm²) of the lumbar spine (L1–L4), proximal femur (total hip, femoral neck, and greater trochanter) and whole body composition. All scans were performed and analyzed by a trained laboratory technician using Hologic software version 9.80 D (Hologic, Inc., Waltham, MA). All follow-up scans were analyzed using the compare option. The coefficient of variation (CV) for repeated DXA scans at the Oregon State University Bone Research Laboratory are 1.0% for BMD of the hip and lumbar spine and 1.5% for whole body.

Isokinetic muscular strength

Peak force (kg) of the hip abductors and knee extensors and flexors, chest and upper back was assessed by isokinetic dynamometry (KinCom 500H, Chattanooga Corp.). Participants were seated in an adjustable chair and the upper body was stabilized using straps secured across their hips and shoulders. All tests were conducted at a speed of 30° per second and were corrected for gravitational forces. Following a brief warm-up, subjects performed 3–5 maximal efforts, the highest of which was recorded as peak force. Maximal efforts were separated by approximately 60 s of rest. Protocols employed previously in our laboratory have revealed good reliability with this population. The coefficient of variation for muscle strength assessments in our laboratory is between 4% and 8%. For analyses a mean total strength composite of dependent variables was calculated for lower body strength [quadriceps+ hamstrings+ hip abduction]+total lower body strength score] and upper body strength [chest+ upper back force]/mean total upper body strength score] (Table 3).

One repetition maximum (1RM)

1RM for the squat and deadlift was defined as the maximum amount of weight each subject could lift once with proper technique. After two warm-up sets of 10–12 repetitions using light weights, each participant performed a single repetition with a weight she could lift through a complete range of motion. At the conclusion of each successful lift, 5–20 lbs were added for the next attempt. This procedure was repeated until the participant could no longer lift the weight (generally achieved in 4–6 attempts), and the highest weight lifted successfully was recorded as the 1RM. New 1RM values, re-testing and load adjustments were conducted every 8 weeks. The 1RM results were used to determine the amount of weight to be used by each participant during their exercise session.

Mean training volume

Total mean training volumes of work for both exercise groups were calculated by multiplying the amount of weight lifted by the number of sets and repetitions performed for each exercise and then summed for each workout (Weight×set×sets×repetitions) [3]. These were then averaged for each month over the course of the 12 month study.

Resistance training protocols

Both exercise groups performed free weight back squat and free weight deadlift exercises. All exercise group participants were asked to perform repetitions at a speed of 1–2 s for the concentric (lifting) and 2–3 s for the eccentric (lowering) phases. Training sessions were conducted for 52 weeks with a frequency of 2 times per week for approximately 50 min under close supervision of a personal trainer (1–2 trainers per subject). This approach ensured proper technique, provided motivation and encouragement, and decreased risk of injury. All training sessions were conducted at Oregon State University, Corvallis, OR. For every participant, trainers recorded all sets, repetitions, intensity (% of 1RM); weight lifted and calculated volume of work at each training session. Participants performed two warm-up sets of 10–12 repetitions at 50% of 1RM for each exercise. For each exercise, participants performed three working sets at 60–75% of 1RM (set 1= 8 reps; set 2= 10 reps and set 3= 12 reps). Each set was followed by approximately 60 s of rest. Prior to and after each exercise session participants completed a 15–20 min warm-up and 10 min cool down program consisting of exercises focusing on proper alignment, posture, muscle engagement, abdominal strength and flexibility designed to decrease the possibility of injury [9].

The training programs were well tolerated by all participants. None of the participants developed any overuse or other types of injury sufficient to warrant any program modifications, withdrawal, or interruption in their training schedules.

Back squat exercise

The squat is a lower body exercise used in weight training where a barbell is held across the upper back. The squat is performed by (squatting down) bending the legs at the knees and hips, lowering the torso between the legs, and then reversing direction to stand up straight again while maintaining spine alignment. The torso remains relatively upright and completely uninvolved in the lift in any capacity but as a supporting structure.
Deadlift exercise

The deadlift is an exercise where one lifts a loaded barbell off the ground from a stabilized bent-over position with emphasis on the muscles of the lower and upper back and legs. For a more detailed description of the squat and deadlift exercises please refer to Baechle and Earle [3].

Dietary analysis: block food frequency questionnaire

At the conclusion of the study participants completed a computer-scored 100-item Block Food Frequency Questionnaire [5] designed by the National Cancer Institute. Information regarding average daily calcium, protein and grams of protein per kilogram of body weight were obtained using this tool at baseline and month 12 of the study.

Physical activity

Habitual physical activity levels were assessed using a questionnaire administered during a laboratory visit [1,4]. The questionnaire asked subjects to recall the duration and intensity of their typical weekly recreational, leisure, and household activities at baseline and at the conclusion of the study.

Statistical analysis

Data were entered and analyzed using SPSS statistical software (SPSS Inc., Version 11.0, Chicago, IL). A 4 (experimental condition)×3 (time) repeated measures multivariate analysis of variance (RM MANOVA) was used to analyze the effects of training on lower body strength (quadriceps, hamstrings, hip abduction) and upper body strength (pectoralis and latissimus dorsi), and diet. Where significant multivariate effects were detected, univariate F-tests were used to isolate the specific dependent variables that were significant. Analysis of covariance was conducted to determine the effect of group and training on lumbar spine BMD while controlling for initial values of lumbar spine BMD. A 4 (experimental condition)×2 (time) RM MANOVA was conducted to determine the main effect of HRT and resistance training on femoral neck BMD, trochanter BMD, total hip BMD, and body composition. Again, when a significant multivariate effect was detected, univariate analyses were performed to evaluate group-wise differences and Tukey post-hoc tests were used to evaluate pair-wise differences. For all statistical tests, alpha was set at the \( P<0.05 \).

Results

Retention and compliance

At baseline, sample sizes were: NHRT plus exercise (\( n=35 \)); HRT plus exercise (\( n=37 \)); HRT no exercise (\( n=35 \)); and 4) control (\( n=34 \)). Overall, 122 of 141 (86.5%) of enrolled participants completed the one-year study. Retention rates were: 83% NHRT plus exercise, 89% HRT plus exercise; 91% HRT no exercise; and 82% control group. Women did not complete the study for the following reasons: 1) stopped taking HRT (\( n=3 \)) or started taking HRT (\( n=2 \), 2) moved out of the area (\( n=5 \), 3) personal reasons, not related to the study (\( n=4 \), and 4) did not enjoy the exercise program (\( n=5 \)). Attendance for the exercise sessions for the non-HRT plus exercise (84.7 ± 12.8%) and HRT plus exercise group (86.2 ± 11.4%) were similar. Log books that were collected quarterly suggest that compliance for all women taking daily HRT medication was reasonable with participants only forgetting to take their daily medication on average 2.47 ± 1.2 times per month.

Bone mineral density

At baseline independent \( t \)-test revealed no significant differences between groups prior to randomization (HRT or no HRT) for total hip BMD, femoral neck BMD or greater trochanter BMD (all \( P>0.05 \). Absolute values for BMD (Mean±S.D.) are presented in Table 2. However, to elucidate interpretation, data are presented in terms of percent change in the following Discussion section.

Lumbar spine BMD

The control group was significantly lower than the other three groups, \( P\leq0.001 \). Over the course of our one-year observation, the control group had a BMD loss of \( 3.60\pm3.70\% \) at the lumbar spine whereas the HRT no exercise group lost \( -0.66\pm3.2\% \). In contrast, HRT plus exercise group resulted in an increase of \( 0.70\pm2.2\% \) in lumbar spine BMD, while the NHRT plus exercise group had a \( 0.43\pm4.3\% \) increase (Fig. 1).

Greater trochanter BMD

Over the course of 1 year of resistance training, the NHRT plus exercise and HRT plus exercise groups increased BMD \( 0.43\pm3.5\% \) and \( 0.44\pm2.6\% \), respectively \( P>0.05 \). The HRT no exercise group declined \( -0.60\pm4.6\% \), whereas the control group lost \( -1.5\pm3.2\% \) (Fig. 2).

Femoral neck BMD

The NHRT plus exercise and HRT plus exercise groups lost \( -1.2\pm4.3\% \) and \( -0.61\pm2.9\% \), respectively. The control group lost the most bone over 1 year at a rate of \( -3.9\pm3.8\% \), \( P>0.05 \) whereas the HRT no exercise group had a similar loss as the NHRT plus exercise group of \( -1.2\pm3.3\% \) (Fig. 3).

Total hip BMD

The NHRT plus exercise and HRT plus exercise groups declined at the total hip BMD by \( -0.30\pm3.1\% \) and \( -0.52\pm3.6\% \), respectively. The control group declined the most at an average rate of \( -1.2\pm3.3\% \). Even though the NHRT plus exercise group experienced a statistically significant decrease in total hip BMD, it was not a clinically meaningful loss. However, the HRT plus exercise group experienced a non-significant decrease in total hip BMD, which may be a clinically meaningful loss. This is due to the wide confidence intervals of the decrease in total hip BMD in the HRT plus exercise group.

Fig. 1. Percent change (±S.E.) for lumbar spine (L1–L4) BMD at the completion of the one-year exercise (Ex) interventions. * \( P<0.005 \). At the conclusion of the study, the NHRT and HRT exercise groups had greater BMD than the HRT and control groups. The control group had lower BMD than the NHRT and HRT exercise groups and HRT group \( P<0.05 \).
−2.4±2.3%, *P >0.05 whereas the HRT no exercise group lost −0.79± 2.9% at the hip (Fig. 4).

**Strength analyses**

At baseline, no between group differences on any of the individual strength measures (quadriceps, hamstring, hip abduction, pectoral (chest) and latissimus dorsi (upper back) strength were observed. Six and 12 month results reflect percent change from baseline.

**Upper body strength**

At 6-month follow-up the HRT plus exercise and NHRT plus exercise groups increased upper body strength by 28±16% and 30±13% respectively (both *P ≤0.01). At 12 months the overall increase in upper body strength was 41±18% and 37±22% respectively, (both *P ≤0.01). After 6 months, the gain in upper body strength in the HRT no exercise and control groups was not significant (9±23% and 6±20%, respectively) and did not change over the final 6 months of the study (*P >0.05). Improvements in strength for the exercise groups were significant when compared to the non-exercising groups at months 6 and 12 regardless of HRT status. However, no significant differences were observed between the HRT plus exercise and NHRT plus exercise group responses (*P >0.05) (Table 3).

**Lower body strength**

At 6-month follow-up both the HRT plus exercise and NHRT plus exercise groups increased their lower body strength 19±16% and 26±10% respectively (both *P ≤0.01). At 12 months the overall increase in lower body strength was 25±22% and 35±13%, respectively (both *P ≤0.01). At 6 months, lower body strength in the HRT no exercise and control groups decreased −1.7±13% and −5±9%, respectively (both *P >0.05). Overall the non-exercisers experienced a non-significant decrease in lower body strength from baseline of −2.2±17% and −7.0±13%, respectively (both *P >0.05). In the exercising groups, improvements in strength were significant when compared to the non-exercising groups at months 6 and 12 regardless of HRT status. However, no significant differences were observed between the HRT plus exercise and NHRT plus exercise groups (both *P >0.05) (Table 3).

**Mean training volumes of work**

A 2 (group: NHRT +exercise and HRT +exercise) × 12 (time) repeated measures analysis of variance was employed to compare mean training volume of work completed by the two exercise groups over time. During the study mean training volume of work significantly increased for both exercise groups (P ≤0.001) however, no differences existed between the HRT
plus exercise and NHRT plus exercise groups over the 12 month intervention \( (P=0.84) \) (Fig. 5).

**Body composition**

At baseline no significant between group differences (Table 2) were detected for either total body lean mass or total body fat mass \( (P \leq 0.05) \). There was an overall increase in lean mass of 4.6±2.7% and 3.9±2.7%, respectively for the HRT plus exercise and NHRT plus exercise groups after 12 months of training \( (P \leq 0.05) \). Improvements in lean mass in exercisers were significant when compared to the non-exercising groups at month 12 regardless of HRT status. However, no significant differences were observed for lean mass and fat mass between the HRT plus exercise and NHRT plus exercise groups \( (P>0.05) \) (Table 2) at the conclusion of the study. The non-exercising HRT and control groups experienced no changes in lean mass non-significant increases in lean mass over the course of the intervention. Improvements in lean mass in the HRT plus exercise and NHRT plus exercise groups were significant when compared to the non-exercising groups at month 12 regardless of HRT status.

**Dietary protein, calcium and energy expenditure analyses**

No significant between group differences were observed on any of the dietary variables (calcium and protein) assessed or energy expenditure \( (P>0.05) \) (Table 1).

**Discussion**

Our results demonstrate that regardless of hormone replacement therapy status, free weight squat and deadlift exercises performed 2 days per week prevented bone loss at the spine. Additionally, resistance training attenuated declines in bone at the femoral neck, greater trochanter, and total hip in comparison to the control group, and resistance training was as effective as HRT alone in attenuating loss of bone at all sites reported. In this group of women, resistance training may be as effective as HRT in attenuating or preventing bone loss without the potential side effects often associated with a pharmacological approach. Furthermore, resistance training also increased lean mass and muscle strength, both of which are important determinants of functional independence and lower fall risk in older women.

Though the suppression of bone remodeling in response to hormone replacement therapy is well documented \([11,33]\) the response to exercise and exercise plus HRT in postmenopausal women is unclear. To date, several studies have reported that the combination of weight-bearing exercise and estrogen replacement therapy was more effective than either exercise alone or estrogen replacement therapy alone in increasing total body and spine BMD in older postmenopausal women \([13,19]\). Our findings with early postmenopausal women do not support this hypothesis since resistance training plus HRT did not produce greater gains in bone mass, muscle strength and lean mass than resistance training alone. However, we must point out that the women in the Kohrt et al. \([19]\) study were 60 to 72 years of age and HRT may have an additive effect when combined with weight-bearing exercise in women beyond early stages of menopause.

Even though we report small increases of +0.43% and +0.70%, at the lumbar spine for the non-HRT plus resistance training and HRT plus resistance training groups, these increases were significant when compared to the declines reported by the control and HRT no resistance training groups. Additionally, the non-HRT plus resistance training and HRT plus resistance training groups significantly increased trochanter BMD by +0.44% and +1.0%, respectively, compared to decreases of −0.60% and −1.64% for HRT no resistance training and control groups, respectively.

While the increases in BMD at these two sites (i.e., spine and trochanter) were small, they are similar to changes reported in previous studies involving postmenopausal women \([13,18,22,26,31,32,34]\) and the effect sizes reported in a meta-analysis \([17]\). These small increases, if maintained over time, can translate into long-term preservation of bone mass compared to the expected age-related losses. It is also important to point out that resistance training significantly attenuated bone loss at the trochanter when compared to the control group as well as the hormone replaced no resistance-training group. Importantly, the mean age of participants in many of these previous studies ranged from 60 to 70 years of age \([13,19,26,27,29–31]\), whereas the average age of our participants at baseline was 52 years. Our results indicate that substantially younger women can derive benefits from resistance training. If resistance training is continued, it may be possible for women to attain greater BMD into their 60s and 70s.

The onset of menopause is associated with the most rapid period of postmenopausal bone loss due to the initial and rapid withdrawal of estrogen \([7,10,29]\). Few studies have included
early postmenopausal women as the study population and it is possible that the competing affects of hypoestrogenism diminish the efficacy of exercise to arrest bone loss. Our population represents a critical point in time for intervention, especially since this group of women is at the peak of postmenopausal bone loss. Thus, halting this loss has the potential to result in greater bone savings.

Our study was unique and designed to maximize changes in bone and exercise compliance. The majority of resistance training interventions that have focused on attenuating or increasing bone mineral density in postmenopausal women have employed traditional resistance training programs involving 8–12 total body exercises 3 days per week [13,22,26,32] and typically lasting 60–70 min per session. If we eliminated the warm-up and cool down portions of our resistance training program, the two site specific exercises, free weight squats and deadlift, took approximately 10 min per day, 2 days per week. The exercises required minimal equipment (squat rack and weights) and is an exercise program one could potentially do at home once the participants are correctly instructed by an expert trainer on how to perform each exercise correctly. Inclusive of all program elements, 2 days per week, 45 min per session (10 min of resistance exercises and 35 min of warm-up and cool down exercises) is a reasonable amount of time to ask of any individual to exercise especially given the potential benefits one could derive from such an exercise program. Findings from our study suggest that these two site specific exercises (squat and deadlift) attenuated bone loss at the spine and greater trochanter regardless of HRT status.

In addition to BMD improvements, resistance training can impact other variables associated with decreased risk of fractures and disability. Beginning at ~40 years of age, humans experience a gradual, but progressive, decline in the peak voluntary isometric torque, dynamic torque, and maximal contraction velocity of the lower limb skeletal muscles [20]. This age-related decline in muscle function appears to be due to reductions in muscle quantity and to changes in muscle quality [6]. Skelton and colleagues [35] have proposed that estrogen confers a beneficial effect by altering muscle function at the level of the cross-bridge, thus suggesting that the menopause may also be associated with an increased decline in strength as well as bone loss. However, our group observed no differences in the cross sectional area (CSA), fiber type distribution, and Ca$^{2+}$-activated contractile properties of slow vs. fast vastus lateralis muscle fibers obtained from early HRT and non-HRT replaced post-menopausal women at baseline. These findings provide additional evidence that HRT does not appear to attenuate or preserve muscle strength or lean mass in HRT replace postmenopausal women [39].

Our exercise program produced significant increases in both lower and upper body strength regardless of HRT status. Moreover, our participants did not experience a plateau of strength increase after 6 months of training. We were also surprised to see the large increases in upper body strength for both resistance training groups. The isometric contraction of upper body muscle groups required in stabilizing the body when executing a free weight squat and deadlift could have indirectly produced the upper body strength increases we observed. Since women have relatively weak upper body strength when compared to men [16,24,34,36] an isometric stimulus from these two exercises may have been sufficient to induce the gains in upper body strength observed. Additionally, both exercise groups experienced an increase in lean mass of approximately 4% regardless of HRT status.

To our knowledge, this is the first exercise intervention study to examine the effects of a site specific resistance training program using two very unique free weight exercises, squats and deadlift, in this population of early postmenopausal women as a strategy to reverse or attenuate bone loss at the spine. All participants were considered postmenopausal for no more than 36 months by their physician (HRT: 27.16±10.07 months and no HRT: 24.6±10.07 months post-menopause). Additionally, participants in the HRT groups consumed 0.625 mg conjugated equine estrogen (brand name Premarin®) as prescribed by their physicians.

Several limitations of this study design must be noted. First, this was not a randomized clinical trial design. Rather participants were self selected as either HRT or non-HRT replaced. Thus, in this group of women, those who chose HRT may have had different socioeconomic status and education that influenced their awareness of the importance of physical activity and nutrition than those who did not chose HRT. Although we attempted to control for some of these potential confounding factors we may not have been able to account for all of them. Self-selection may influence the baseline values or the pre- and post-values of the non-trained groups. For instance women not taking HRT may be more health conscience and more likely to perform exercise that might increase or maintain their bone mass than women not on HRT, or vice versa. However, there is little reason to expect that women who chose to take HRT would have different physiological responses to strength training compared to women who chose not to take HRT. Thus, self-selection would not be expected to confound the interpretation of adaptations noted for the HRT-trained and non HRT-trained groups in this study. This strengthens our conclusion that strength training provides similar benefits as HRT in this population of participants.

Within the limitations of this study, we have shown that two site specific resistance training exercises, squat and deadlift can be an effective substitute for HRT in preserving lumbar spine BMD during the early stages of menopause. Regular participation in a resistance training program could potentially decrease the dosage of drugs required to induce bone formation in ways that enhance efficacy and reduce the risk of side effects associated with drug therapies.

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