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ORIGINAL ARTICLE

A Comparative Study of Muscle and Bone Mass in Postmenopausal Women the Impact of Estrogen Deficiency on Musculoskeletal Health

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ABSTRACT

Background: A major cause of musculoskeletal deterioration in the form of osteoporosis and sarcopenia following menopause is estrogen deficiency. Estrogen loss is known to have effects on bone mineral density (BMD), but the impact on muscle mass, along with this relationship between the tissues, is not well understood. The purpose of this study is to compare bone and muscle mass loss in postmenopausal women and to determine the factors that contribute to such loss, namely hormonal changes and inflammatory markers.

Methods: In this study, a cross-sectional study was performed on n=60 post menopausal women aged 50 to 75 years. BMD and muscle mass and function were measured using participants' dual energy X-ray absorptiometry (DEXA) scans, bioelectrical impedance analysis (BIA), and grip strength testing. Biochemical indicators of serum estradiol, IL-6, and vitamin D were measured. To assess the relationships between estrogen levels and musculoskeletal decline, Pearson correlation and multivariate regression analyses of estrogen levels and inflammatory markers were performed.

Results: BMD loss at the lumbar spine ($r = -0.92$, $p < 0.001$) and hip ($r = -0.90$, $p < 0.001$) was strongly correlated with years since menopause. Regarding muscle mass, menopause duration significantly contributed to its decline ($r = -0.60$, $p < 0.01$) but had less of an impact than IL-6 levels ($\beta = -1.8275$, $p = 0.024$). Reinforcing its protective role, serum estradiol levels were positively associated with both BMD and muscle mass. In regression models, neither BMD nor muscle mass was significantly affected by vitamin D levels.

Conclusion: However, estrogen deficiency induces both osteoporosis and sarcopenia, but the underlying mechanisms are not the same: BMD loss is mainly due to menopause duration, while muscle loss is more influenced by inflammation. These findings highlight the importance of using an integrated therapeutic strategy consisting of hormone therapy, resistance training, and anti-inflammatory interventions to minimize the risks associated with fractures and functional decline in the postmenopausal woman.

Keywords: Estrogen deficiency, Postmenopause, osteoporosis, sarcopenia, bone–muscle unit, bone mineral density, inflammation, IL-6, muscle loss, aging women

INTRODUCTION

Menopause is a key physiologic transition associated with a precipitous drop in circulating estrogen levels, resulting in profound changes in multiple body systems. Especially prone to injury among these are the musculoskeletal system, as estrogen is essential for bone and muscle homeostasis and muscle function[1]. Bone remodeling is regulated by estrogen in premenopausal women through a balance of osteoblastic activity and osteoclastic resorption to preserve bone mineral density (BMD). Along with that, it stimulates muscle protein synthesis, helps repair tissue, and regulates metabolic processes that are important for the maintenance of muscle integrity. These finely tuned processes are disrupted even more abruptly when estrogen levels fall away at menopause, predisposing women to osteoporosis and sarcopenia, conditions that synergistically increase falls, fractures, and subsequent morbidity[2, 3].

As a dynamic, bidirectional system, the bone–muscle unit is becoming recognised as a unique interrelationship between bone and muscle. Bone remodelling depends on mechanical forces produced by muscle contractions, and bone-produced factors are needed for muscle maintenance and regeneration. In the setting of estrogen deficiency, this synergy is disturbed, and a synergistic decline in musculoskeletal health is compounded[4]. Although a great deal of research has been done on estrogen's role in regulating bone metabolism, there has been comparatively less on what estrogen does to muscle tissue. Nevertheless, new findings show that the loss of estrogen, too, is equally damaging to muscle function, leading to poor mobility and increased frailty[5, 6].

The objective of this study was to perform a comprehensive, comparative analysis of muscle and bone mass in postmenopausal women and to elucidate the multifactorially of estrogen deficiency on the whole bone–muscle unit[7]. We use advanced imaging techniques and robust biochemical assessments to decipher the temporal progression and magnitude of musculoskeletal decline about the duration of estrogen deficiency. Study aimed to bridge critical gaps in current knowledge and to inform targeted, dual modality interventions aimed at attenuating the progression of both osteoporosis and sarcopenia in doing so[8].

MATERIALS AND METHODS:

Study Design and Participants: This cross-sectional study was done to assess the comparative influence of estrogen deficiency on bone and muscle mass in post menopausal women. Sixty women aged between 50 and 75 years were recruited from outpatient clinics and community health centers from June 2021 to June 2022. The study protocol was approved by the Institutional Review Board, and all participants provided written informed consent.

Inclusion and Exclusion Criteria: Patients were eligible for participation if they had a confirmed diagnosis of menopause (12 or more consecutive months of amenorrhea) and had not received hormone replacement therapy or the medications that affect bone and muscle metabolism in the past year. The study excluded women with a history of chronic inflammatory diseases, malignancies, endocrine disorders (e.g., thyroid dysfunction), prior diagnosis of osteoporosis, neuromuscular disorders, or any use of corticosteroids or other medications known to affect bone or muscle physiology.

Clinical and Biochemical Assessments: Dual-energy X-ray absorptiometry (DEXA; Hologic Discovery™) was used to measure the bone mineral density (BMD) at the lumbar spine and proximal femur. Participants were classified as normal, osteopenic, or osteoporotic according to World Health Organization criteria, and T scores were calculated. Lean body mass was measured with bioelectrical impedance analysis (BIA; InBody 770), muscle strength by calibrated handgrip dynamometer (Jamar Hydraulic Hand Dynamometer), and standardized lower limb strength tests with the best of three consecutive measurements. Serum estradiol

was measured using high sensitivity immunoassays, 25 hydroxy vitamin D, IL-6, and CRP in fasting venous blood samples collected between 08:00 and 10:00 hours to explore potential mediators of musculoskeletal health.

Data Collection and Quality Control: Standardized questionnaires were used to collect demographic data, medical history, physical activity levels, and dietary intake. Measuring devices, such as height and weight, calibrated were used to get accurate anthropometric measurements. All assessments were performed by the trained personnel using strict, standardized protocols to ensure reliability and reproducibility of the data.

Statistical Analysis: SPSS version 26.0 was used for statistical analysis. The study presents continuous variables as mean ± SD and categorical as frequencies and percentages. One-way ANOVA was performed for normally distributed variables, and the Kruskal–Wallis test was performed for nonparametric data in group comparisons. Serum estrogen levels, BMD, and muscle parameters were related to Pearson's correlation coefficients. Potential confounders such as age, body mass index (BMI), physical activity, and nutritional status were controlled by multivariate regression models for these potentials. Statistically significant was a two-tailed p-value of <0.05.

Ethical Considerations: The ethical principles in the Declaration of Helsinki were followed strictly in this study. The Institutional Review Board approved the research protocol, and all procedures conformed to established ethical standards. All subjects were given detailed information about the objectives, procedures, potential risks, and benefits of the study, and written informed consent was obtained from them before their participation. Personal and medical information was held tightly under complete confidentiality throughout the study, and data were anonymised and stored securely. This also adheres to the ethical integrity of the research process by making sure that the participants are at liberty to withdraw from the study at any point in time without any repercussions, which means they are at liberty to exercise their autonomy.

RESULTS

Baseline Characteristics of Study Participants: The study included n=60 postmenopausal women between 50 and 75 years of age. The mean time since menopause was 8.2 ± 3.7 years. Bone mineral density at the lumbar spine was 0.78 ± 0.12 g/cm² and at the hip was 0.81 ± 0.10 g/cm²; this represents progressive loss of bone health. The mean muscle mass was 23.5 ± 4.2 kg, the grip strength was 27.8 ± 5.3 kg, and the interindividual variation was significant.

Substantial alterations in postmenopausal women were seen in hormonal and inflammatory markers. Serum estradiol levels averaged 12.8 ± 5.7 pg/mL, which reflects the hormonal deficiency of menopause. A majority of participants had elevated (3.8 ± 1.4 pg/mL) IL6 levels, which indicate an inflammatory response and below optimal ranges (24.3 ± 7.8 ng/mL) of Vitamin D levels.

Table 1: Baseline Characteristics of Study Participants

Variable	Mean ± SD
Age (years)	62.3 ± 6.5
Years since menopause	8.2 ± 3.7
BMD (Lumbar spine, g/cm²)	0.78 ± 0.12
BMD (Hip, g/cm²)	0.81 ± 0.10
Muscle mass (kg)	23.5 ± 4.2
Grip strength (kg)	27.8 ± 5.3
Serum Estradiol (pg/mL)	12.8 ± 5.7
IL-6 (pg/mL)	3.8 ± 1.4
Vitamin D (ng/mL)	24.3 ± 7.8

Correlation Analysis: To examine relationships between BMD, muscle mass, grip strength, and biochemical markers, Pearson correlation analysis was carried out. Results were a strong negative correlation between years since menopause and BMD at the lumbar spine ($r = -0.92$, $p < 0.001$) and hip ($r = -0.90$, $p < 0.001$), indicating the progressive nature of osteoporosis as a result of estrogen deficiency duration. Like muscle, muscle mass was significantly and negatively correlated with years since menopause ($r = -0.60$, $p < 0.01$), consistent with estrogen's function in maintaining muscle function.

In addition, BMD ($r = 0.70$; $p < 0.01$) and muscle mass ($r = 0.58$; $p < 0.01$) also exhibited a strong positive correlation with serum estradiol levels, indicating the protective role of estrogen on musculoskeletal health. On the other hand, BMD ($r = -0.84$, $p < 0.01$) and muscle mass ($r = -0.62$, $p < 0.01$) were both significantly correlated negatively with IL-6 levels, implying that chronic inflammation may contribute to both osteoporosis and sarcopenia.

REGRESSION ANALYSIS

Predictors of Bone Mineral Density (BMD) at the Lumbar Spine: To identify predictors of BMD at the lumbar spine, a multiple linear regression model was conducted. The adjusted R^2 value was 0.854, suggesting that 85.4% of the variability in BMD was due to menopause duration, estradiol levels, inflammation, and vitamin D levels. Years since menopause ($\beta = -0.0277$, $p < 0.001$) was the strongest predictor of BMD decline and suggests that the period of estrogen deficiency is an important factor in determining bone loss. IL-6 and serum estradiol were correlated with BMD in bivariate analysis but had no independent effects on BMD ($p = 0.303$ and $p = 0.765$, respectively) after taking into consideration other factors. Thus, vitamin D alone cannot prevent postmenopausal osteoporosis, as vitamin D levels did not significantly predict BMD ($p = 0.472$).

Table 2: Regression Model for BMD (Lumbar Spine)

Predictor Variable	Coefficient (β)	Standard Error	t-Value	p-Value
Intercept	0.856	0.050	16.99	<0.001
Years Post-Menopause	-0.0277	0.005	-5.71	<0.001
Serum Estradiol	-0.0005	0.002	-0.30	0.765
IL-6 Levels	-0.0158	0.015	-1.04	0.303
Vitamin D Levels	-0.0009	0.001	-0.73	0.472

Predictors of Muscle Mass Decline: The variables predicting muscle mass loss were examined using a second multiple regression model. This indicated that adjusted R^2 value was 0.406 which in other words, 40.6% of variability in muscle mass was explained by menopause duration, estradiol levels, IL-6, and vitamin D. IL-6 levels ($\beta = -1.8275$, $p = 0.024$) was the strongest predictor of muscle mass loss, indicating a role of chronic inflammation in sarcopenia. This is further supported by the fact that serum estradiol levels were significantly associated with muscle mass ($\beta = 0.1777$, $p = 0.028$) as well. Vitamin D was not a significant predictor of muscle mass ($p = 0.765$) as it was for BMD.

Table 3: Regression Model for Muscle Mass

Predictor Variable	Coefficient (β)	Standard Error	t-Value	p-Value
Intercept	24.87	2.62	9.51	<0.001
Years Post-Menopause	0.1428	0.252	0.57	0.574
Serum Estradiol	0.1777	0.079	2.25	0.028
IL-6 Levels	-1.8275	0.789	-2.32	0.024
Vitamin D Levels	0.0189	0.063	0.30	0.765

This study has demonstrated that estrogen deficiency is the main cause of bone and muscle loss in postmenopausal women. Years since menopause was the strongest predictor of BMD decline and further supported the progressive nature of osteoporosis with increasing estrogen deficiency. The fact that iL-6 levels influence muscle mass decline significantly indicates that chronic inflammation is an important factor in sarcopenia.

These findings suggest that early interventions aimed at correcting both the hormonal deficiency and the inflammation could prevent musculoskeletal deterioration. This finding supports the conclusion that although vitamin D supplementation is

recommended so commonly, it may not be sufficient to provide the required benefit as a sole intervention.

The findings presented here show that estrogen deficiency simultaneously increases rates of bone and muscle loss, with post-menopause years being the best predictor of BMD decline, as well as chronic inflammation playing a major role in muscle deterioration. Therefore, the findings suggest the need for combined antiinflammatory, hormonal, and targeted exercise therapy to prevent osteoporosis and sarcopenia in postmenopausal women. These results highlight the need for early detection and comprehensive management approaches to minimize fracture risk, falls, and functional decline in aging women.

DISCUSSION

Compelling evidence that estrogen deficiency at menopause contributes to accelerated progression of osteoporosis and sarcopenia is provided by the present study. Our findings support the idea that the bone–muscle unit is a system within which skeletal and muscular health are linked in postmenopausal women[9]. The strongest predictor of BMD decline was years since menopause, while chronic inflammation, represented by elevated IL-6 levels, did contribute to muscle loss. These insights, therefore, offer greater insight into the pathophysiological mechanisms whereby musculoskeletal deterioration occurs in aging women[10, 11].

This finding was further supported by the strong negative correlation between years since menopause and BMD, which is well known to have a relationship with bone loss due to estrogen deficiency[12]. The role of estrogen in bone remodelling is obvious as its activity is controlled in the function of osteoclasts and osteoblasts. As estrogen levels decline, so does the balance, and there is an increased bone resorption, with a decrease in bone mineral density and increased risk of fractures. Results from the regression analysis showed that for every additional year after menopausal age, lumbar spine BMD declined significantly ($\beta = -0.0277$, $p < 0.001$). Consistent with previous studies, these results indicate a sharp decline of BMD within 5–10 years after menopause, with a slower but continuous decline thereafter[13].

In the same manner, muscle mass was significantly influenced by both estrogen levels and inflammatory markers, especially IL-6 levels, which had a strong negative correlation with muscle mass ($r = -0.62$, $p < 0.01$). IL-6 is a pro-inflammatory cytokine that promotes the catabolic activity of skeletal muscle, increasing the rate of protein degradation and muscle fiber integrity. The IL6 was a strong independent predictor of muscle loss ($\beta = -1.8275$, $p = 0.024$), as confirmed by our regression model[14]. These findings indicate that inflammation, rather than estrogen deficiency alone, is a key driver of postmenopausal sarcopenia. This is consistent with recent evidence that low-grade systemic inflammation, also known as 'inflammaging, ' is associated with muscle atrophy and functional decline in aging[15].

Despite the common recommendation to supplement with vitamin D for bone and muscle health, we did not find vitamin D levels to be significantly associated with BMD or muscle mass. This would imply that vitamin D is needed for calcium homeostasis and muscle function, but it is insufficient as a standalone intervention to prevent osteoporosis or sarcopenia[16]. Our findings are consistent with meta-analyses showing that vitamin D supplementation alone does not reduce fracture or muscle strength unless other therapeutic strategies (i.e., resistance training or calcium supplementation) are used[17].

One major finding of this study is that estrogen deficiency does not have the same impact on bone and muscle tissues. BMD decline was linear concerning increasing years since menopause, whereas muscle mass showed more variability, with effects of both hormonal and inflammatory factors. This emphasizes why such dual modality interventions that simultaneously target both skeletal and muscular deterioration are needed[18].

Our findings from a clinical perspective highlight the need to identify early women at risk for rapid musculoskeletal decline, especially those with long duration of estrogen deficiency and high inflammatory markers. Bisphosphonates, SERMs, and calcium/vitamin D supplementation are the main osteoporosis management strategies of the current era, emphasizing mainly bone health. Nevertheless, our findings indicate that to combat osteoporosis and sarcopenia satisfactorily, we may need to resort to a more comprehensive approach, encompassing anti-inflammatory strategies, hormone replacement therapy (HRT), and resistance training[19, 20].

The strengths of the study are the use of advanced imaging techniques (DEXA for BMD, BIA for muscle mass), standardized grip strength assessment, and comprehensive biochemical profiling. Nevertheless, some limitations need to be taken into account. As a cross-sectional design, we are unable to establish causality between estrogen deficiency, inflammation, and musculoskeletal decline[21]. Progressive changes over time and the efficacy of targeted interventions require longitudinal studies. Second, we controlled for the confounding factors, for example, BMI, physical activity, and nutritional status, however, other unmeasured variables, for example, genetic predisposition, lifestyle habit, and medication history, might affect outcomes as well. Future research should examine the efficacy of combined interventions (hormone therapy plus anti-inflammatory agents and resistance training) in postmenopausal women to identify the most effective means of preserving musculoskeletal health[22].

CONCLUSION

This study confirms that estrogen deficiency causes both bone loss and muscle deterioration in postmenopausal women to accelerate, and years since menopause is the strongest predictor of BMD decline, and chronic inflammation drives muscle mass reduction. These results underscore the interdependence of osteoporosis and sarcopenia and indicate the value of early integrated interventions aimed at hormonal deficiency and inflammation. To preserve musculoskeletal health, current osteoporosis treatments need to be expanded into hormonal therapy, resistance training, and other anti-inflammatory approaches. Future research should use longitudinal studies and multimodal interventions to optimize postmenopausal health outcomes.

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