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The relationship between insulin resistance, bone mineral density, and fracture risk in postmenopausal women

Odnos između insulinske rezistencije, mineralne gustine kostiju i rizika od frakture kod žena u postmenopauzi

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Abstract

Background/Aim. Skeletal muscles and bones are essential tissues that, in addition to supporting the body, are the primary site of postprandial glucose intake, which is significantly associated with insulin resistance. The aim of this study was to determine the effect of insulin resistance on bone mineral density (BMD) and fracture risk and re-evaluate the relationship between muscle properties and BMD and insulin resistance in postmenopausal women in Serbia. **Methods.** Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) was calculated in postmenopausal women who were divided into two groups. The "cut-off" value of insulin resistance for the group with "Low HOMA-IR" was < 2, and for "High HOMA-IR" > 2. Fat mass (FM), lean mass (LM), and BMD were measured on the hip and spine using a densitometer with dual-energy X-ray absorptiometry. **Results.** FM and LM had an evident impact on BMD. The decrease in LM and fat buildup was associated with a higher incidence of insulin resistance. A positive correlation was confirmed between HOMA-IR and BMD on the spine and hip, but there was no correlation between insulin resistance and fracture risk. **Conclusion.** LM and FM have significant effects on BMD. The association between LM, FM, BMD and the onset of insulin resistance in postmenopausal women is confirmed. However, women with higher insulin resistance levels and higher BMD do not have a lower fracture risk.

Key words:
bone density; fractures, bone; insulin resistance; postmenopause; risk assessment; serbia.

Apstrakt

Uvod/Cilj. Skeletni mišići i kosti su važna tkiva koja, osim uloge u držanju tela, predstavljaju i primarno mesto preuzimanja glukoze nakon obroka, što je značajno povezano sa rezistencijom na insulin. Cilj rada bio je da se utvrdi uticaj insulinske rezistencije na mineralnu gustinu kosti (MGK) i rizik od nastanka preloma, kao i da se ispita veza između karakteristika mišića i MGK i insulinske rezistencije kod žena u postmenopauzi u Srbiji. **Metode.** Homeostatski model – rezistencija na insulin (HOMA-IR), izračunat je kod žena u postmenopauzi koje su bile podeljene u dve grupe. Granične vrednosti (*cut-off*) insulinske rezistencije za grupu sa „niskim HOMA-IR" bila je < 2, a za grupu sa „visokim HOMA-IR" > 2. Masno tkivo (MT), bezmasno tkivo (BT) i MGK mereni su na kuku i kičmenom stubu pomoću denzitometra sa dvoenergetskom X-zračnom apsorpciometrijom. **Rezultati.** MT i BT su imali očigledan uticaj na MGK. Smanjenje BT i nakupljanje masti bilo je povezano sa višom učestalošću nastanka rezistencije na insulin. Primećena je pozitivna korelacija između HOMA-IR i MGK na kičmi i kuku, ali nije postojala korelacija između insulinske rezistencije i rizika od nastanka preloma. **Zaključak.** MT i BT imaju značajan uticaj na MGK. Potvrđena je povezanost između MT, BT, MGK i nastanka insulinske rezistencije kod žena u postmenopauzi. Međutim, žene sa višim nivoom insulinske rezistencije i većim MGK nemaju niži rizik od nastanka preloma.

Ključne reči:
kost, gustina; kost; prelomi; insulin, rezistencija; postmenopauza; rizik, procena; srbija.

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Introduction

Skeletal muscle is a vital tissue that supports body posture and is also the primary glucose uptake site after a meal. Skeletal muscle is significantly related to insulin resistance [1]. The connection between bone strength or mineral bone density (BMD) and insulin resistance is very complex [2]. According to the study, when the inflammatory response is inadequate, as in the case of aging muscles, acellular fat droplets and adipocytes tend to accumulate, so the development of insulin resistance may be the inflammatory response of the muscles [3]. This results in the secretion of different cytokines, chemokines, and adipocytes, which affects insulin resistance [1, 3].

The World Health Organization (WHO) has defined natural menopause as the least twelve consecutive months of amenorrhea, not physiological and pathological causes. According to statistics, the mean age of natural menopause is 51 years in industrialized nations, compared to 48 years in low and non-industrialized nations [1]. With the average life span extended to 70 years, most women will spend more than one-third of their life beyond the menopausal transition. Besides, the proportion of menopausal women is rising since the aging population is expanding rapidly.

A significant number of studies, on the other hand, discuss the impact of reduced muscle mass on BMD and the consequences that result from them, in the first place, a higher incidence of osteoporotic fractures [4]. It is known that muscle mass and osteoporosis, and metabolic disorders are closely related. However, data on the association of muscle properties, bone mass, and insulin resistance are lacking [5].

The aim of this study was to determine the effects of insulin resistance on bone mineral density and fracture risk and evaluate the relationship between muscle properties (muscle mass, muscle strength, and physical performance) and bone mineral density and insulin resistance in postmenopausal women in Serbia.

Methods

Ethical concerns

The protocol, as well as the study procedures, were approved by the Ethics Committee, the Clinical Center in Kragujevac (Nº 01/17-3765), and the Faculty of Medical Science, University of Kragujevac (Nº 01-15581/3-6) from November 2017 to June 2018.

Study design

The study was conducted at the Clinical Center Kragujevac, the reference healthcare institution for osteodensitometry in the region of central Serbia. The study was designed as a clinical, non-interventional, observational, cross-sectional study and included 66 women over 65 years of age who were selected through random sampling. Participants were divided into two groups and based on the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) limit values as used in the study by Nikolić et al. [6]. The cut-off value for participants from the group "Low HOMA-IR" was < 2, and for those from the group "High HOMA-IR", the values of insulin resistance were > 2. Among the study participants were 44 women with osteoporosis (T score < 2.5) and 22 women with normal bone mineral density or osteopenia (T score ≥ -2.5, without fracture data).

Inclusion and exclusion criteria

The inclusion criteria were confirmed as a menopause of at least five years based on no menstruation. None of the participants had the diseases that affect BMD, such as hyperthyroidism, hyperparathyroidism, renal failure, malabsorption syndrome, chronic colitis, multiple myeloma, leukemia, chronic arthritis, diabetes mellitus (DM), or previous use of therapy that interfere with bone metabolism (e.g., glucocorticoids, heparin, warfarin, thyroxin, and estrogen). Moreover, the exclusion criteria were cigarette smoking, alcohol intake, body mass index (BMI) > 30 kg/m^2, and < 19 kg/m^2, respectively. Before joining the study, all participants confirmed their participation with their signatures.

The insulin resistance

Index expressed as HOMA-IR was calculated using the following equation, as described by Matthews et al. [7]: HOMA-IR = [glucose (mg/dL) × insulin (μU/mL)]/405 for each participant. Due to its simplicity and calculation, the most commonly used technique in clinical practice but also in epidemiological studies for the assessment of insulin resistance was the homeostatic test (HOMA-IR) [7].

Osteodensitometric, anthropometric, and body composition measurements

BMD (g/cm^2) was measured on the lumbar spine (LS) in the region L1-L4 and total hip in all participants. The measurement was done with a densitometer with X-ray energy absorption (DXA) (QDR 4,500, Hologic Model Discovery Inc., Waltham, MA) [8]. Participants did not wear metal items (e.g., clips, belts, brassieres, jewelry) or shoes. They were instructed to be motionless during the scan. Daily standardized quality control of DXA instruments was performed using the manufacturer's phantom spine before the start of the study. The definition of osteopenia and osteoporosis was made using WHO: -2.5 < T-score < -1 and T-score -2.5, respectively. Body weight and height were obtained from the mean of three measurements. The accurate and precise values of these body composition parameters were also estimated from the DXA scan of the total body, which included bone mineral content (BMC), lean mass (LM), and fat mass (FM).

Following the manufacturer's guidelines, all scans were obtained and analyzed by the same experienced operator [9]. Muscle strength was measured using the handgrip (HG) test

– (HGT) dynamometer and is closely related to the muscle strength of the lower extremities [10]. In our study, the Jamar dynamometer was used, which is small, portable, and easy to handle. It was considered a reduced muscle strength HGT < 16 kg [11]. To measure physical performance, we used the walk's speed test at a distance of 4 m (gait speed-GS). Physical ability was considered reduced when the gait speed was < 0.8 m/s for 4 m [12].

Fracture risk

Fracture Risk Assessment Tool (FRAX) algorithm was used to calculate the probability of major osteoporotic fractures and hip fracture (www.sheffield.ac.Uk/FRAX/) [13, 14], using data specific to our country. FRAX Index 1 represented the probability of a major osteoporotic fracture (clinical fracture of the spine, forearm, hip, or shoulder), while FRAX Index 2 represented the probability of hip fracture.

Statistical analyses

IBM SPSS version 20 (IBM Company, Armonk, NY) was used for all statistical analyses. The outcome variables used were BMDs of the whole body and at skeletal sites. The sample size was calculated using G*Power software version 3.1, and 66 subjects were required for a 90% power and 5% for the *t*-test. The cases and controls were distributed between

Table 1

Basic anthropometric characteristics of study population divided into the low-HOMA-IR (n = 44) and high-HOMA-IR (n = 18) groups

Parameters	Mean ± SD	SE	*p*-values
Age (years)			
low	70.89 ± 4.84	0.73	0.812
high	71.83 ± 4.81	1.13	
Body height (cm)			
low	160.36 ± 6.62	1.00	0.199
high	159.33 ± 7.50	1.77	
Bodyweight (kg)			
low	64.45 ± 9.77	1.47	0.071
high	72.56 ± 14.80	3.49	
Body mass index (kg/m^2)			
low	25.061 ± 3.52	0.53	0.046
high	28.133 ± 4.91	1.16	
Waist size (cm)			
low	77.64 ± 11.41	1.72	0.008
high	92.28 ± 19.57	4.61	
Lean mass (kg)			
low	3,395.06 ± 372.98	156.85	0.005
high	3,573.09 ± 583.04	137.43	
Fat mass (kg)			
low	2,411.89 ± 636.12	196.65	0.035
high	2,981.78 ± 994.23	234.87	
Total mass (g)			
low	62,335.07 ± 894.45	135.87	0.011
high	69,759.96 ± 1495.45	352.33	
Body fat (%)			
low	38,132.66 ± 587.67	189.56	0.483
high	41,600.56 ± 781.45	184.45	
Handgrip test (kg)			
low	12.40 ± 9.14	1.39	0.954
high	14.29 ± 8.31	2.01	
Gait speed (m/s)			
low	0.378 ± 0.17	0.03	0.736
high	0.360 ± 0.16	0.04	
Hip BMD (g/cm^2)			
low	0.693 ± 0.09	0.01	0.557
high	0.728 ± 0.10	0.02	
Lumbar spine BMD (g/cm^2)			
low	0.756 ± 0.10	0.01	0.179
high	0.825 ± 0.13	0.03	
BMC (g)			
low	1,592.38 ± 275.11	41.47	0.674
high	1,594.74 ± 328.94	77.53	
Lean + BMC (g)			
low	38,222.76 ± 3.99	2.02	0.004
high	39,942.17 ± 6.20	1.46	

HOMA-IR – Homeostatic model assessment – insulin resistance (the cut-off value for HOMA-IR was 2); BMD – bone mineral density; BMC – bone mineral content; SD – standard deviation; SE – standard error.
Independent *t*-test confirmed statistical differences for normally distributed data with the level of significance of 0.05.

two groups [15]. The values of all variables for the whole body and regional sites were presented as mean (M) ± standard deviation (SD). Comparison of mean values between two groups of subjects, those with osteoporosis and those with normal BMD/osteopenia, were classified according to their spine, bones, and BMD of the entire body, as well as weight, height, BMI, LM, FM, total weight and body fat. Correlation analyses of the whole body, regional sites BMD, and T-scores with the independent variables such as weight, LM, FM, and BMD were performed to obtain Pearson's correlations. We used stepwise multiple linear regression analysis to obtain determinants/predictors for the outcome variables. All *p*-values were reported significant at 0.05 or less [16].

Results

The average values and SD /standard errors (SE) of means of the examined parameters according to the level of HOMA-IR are shown in Table 1. BMI, waist size, LM, FM, total mass, and lean + BMC were significantly different in Low-HOMA-IR and High-HOMA-IR groups ($p < 0.05$). Other tested parameters were not significantly different in those groups (Table 1).

The average age of participants was 71.20 ± 4.72 years, with the range being 65 to 83. For women with normal bone mass/osteopenia, the mean (± SD) age was 70.91 ± 4.97 years, while the mean (± SD) age for women with osteoporosis was 71.34 ± 5.09 (Table 2).

In the study population, regarding their BMD values, LM was shown to have a higher degree of positive correlation with BMD on the lumbar spine ($\beta = 0.418$, $p < 0.001$) but also had a significant effect on the hip ($\beta = 0.416$, $p < 0.01$). In contrast, FM showed a high degree of positive correlation with both BMD on at the hip ($\beta = 0.473$, $p < 0.001$) and the lumbar spine ($\beta = 0.480$, $p < 0.001$).

In this study, the results showed a significant degree of a positive correlation between HGT and BMD on the hip ($\beta = 0.331$, $p < 0.01$) and spine ($\beta = 0.243$, $p < 0.05$), whereas GS was only correlated with BMD on the hip ($\beta = 0.268$, $p < 0.05$) (Table 3).

A positive correlation was confirmed between HOMA-IR and FM ($\beta = 0.322$, $p < 0.05$) and total mass ($\beta = 0.287$, $p < 0.05$). However, there was no correlation between HOMA-IR and LM ($\beta = 0.163$, $p > 0.05$) (Table 4). A significant degree of positive correlation was obtained between HOMA-IR and body mass index ($\beta = 0.381$, $p < 0.01$) and waist circumference ($\beta = 0.405$, $p = 0.001$). A high degree of positive correlation was also observed between HOMA-IR and BMD on the spine ($\beta = 0.362$, $p = 0.01$) and the T score of the spine ($\beta = 0.359$, $p = 0.01$). Besides, a correlation was also shown between HOMA-IR and hip BMD ($\beta = 0.264$, $p < 0.05$) and hip T score ($\beta = 0.305$, $p < 0.05$). In the study, no correlation was confirmed between insulin resistance and muscle strength measured by HG and physical performance measured by GS (Table 4).

Table 2

Comparison of anthropometric parameters and Dual-Energy X-Ray Absorptiometry (DXA) in women with normal BMD/osteopenia and women with osteoporosis

Parameters	Women with normal BMD/osteopenia (n = 22)	Women with osteoporosis (n = 44)	*p*-value
Age (years)	70.91 ± 4.97	71.34 ± 5.09	0.935
Weight (kg)	74.77 ± 9.47	63.41 ± 11.25	0.000
Height (cm)	161.77 ± 4.68	159.20 ± 7.61	0.096
Body mass index (kg/m^2)	28.57 ± 3.47	24.88 ± 3.99	0.000
HOMA-IR	2.684 ± 1.98	1.566 ± 1.13	0.005
Lean mass (g)	37,513.73 ± 4,128	33,168.40 ± 3979	0.000
Fat mass (g)	30,973.18 ± 6,613	23,859.95 ± 7,593	0.000
Total mass (g)	72,986.69 ± 9,162	61,197.15 ± 10,600	0.000
Body fat (%)	42.10 ± 4.98	38.14 ± 6.91	0.020
BMD LH (g/cm^2)	0.78 ± 0.06	0.66 ± 0.07	0.000
BMD spine (g/cm^2)	0.89 ± 0.08	0.72 ± 0.07	0.000
Bone mineral content (g)	1,790.69 ± 227	1,510.26 ± 272	0.000
Lean + BMC (g)	42,013.52 ± 4,282	37,337.20 ± 4,269	0.000

All values are given as mean ± standard deviation.
LH – left hip; for other abbreviations see under Table 1.

Table 3

Correlation between bone mineral density (BMD) and muscle parameters

Parameters	Hip BMD		Spine BMD	
	r	*p*-value	*r*	*p*-value
Lean mass	0.416	0.01	0.418	0.001
Fat mass	0.473	0.000	0.480	0.000
Handgrip test	0.331	0.007	0.243	0.049
Gait speed	0.268	0.031	0.232	0.061

r − **Pearson correlation coefficient.**

Table 4

Correlation between body composition parameters, bone mineral density (BMD), and Homeostasis Model Assessment of Insulin Resistance (HOMA-IR)

Parameters	*r*	*p*-value
Lean mass	0.163	0.213
Fat mass	0.322	0.012
Total mass	0.287	0.026
Body mass index	0.381	0.003
Waist circumference	0.405	0.001
Hip BMD	0.264	0.043
Spine (L1-L4) BMD	0.362	0.005
T score Hip	0.306	0.019
T score Spine	0.359	0.005
Handgrip test (kg)	0.031	0.815
Gait speed (m/s)	0.121	0.356
FRAX Index 1	-0.070	0.588
FRAX Index 2	-0.111	0.389

r − **Pearson correlation coefficient; Fracture Risk Assessment tool (FRAX) Index 1 – the probability of a major osteoporotic fracture (clinical fracture of the spine, forearm, hip, or shoulder); FRAX Index 2 – the probability of hip fracture.**

Univariate regression analysis with HOMA-IR as the dependent variable showed marginally significant associations between HOMA-IR and lumbar spine BMD ($p = 0.055$, stand. beta coefficient = 0.311), which means that an increase of HOMA-IR will lead to an increase of values of BMD of the spine (Table 5). Furthermore, univariate regression analysis confirmed the association between HOMA-IR and changes in the T-score of the spine ($p = 0.009$, stand. beta coefficient = 0.387) (Table 6). Regarding the significance of blood markers as predictors, we statistically confirmed the significance of Insulin level ($p = 0.000$, stand. beta coefficient = 0.241), glucose level ($p = 0.000$, stand. beta coefficient = 0.350) and inversed association and marginally significance of free thyroxine (fT4) levels ($p = 0.071$, stand. beta coefficient = -0.027) (Table 7).

Considering that the association between other tested parameters and HOMA-IR appears to be statistically insignificant in univariate linear regression analysis, other variables are not recognized as predictors of changing HOMA-IR values in postmenopausal women (Tables 5–7).

Table 5

Univariate linear regression analysis between HOMA-IR and hip BMD, femoral neck BMD and lumbar spine BMD

Variables	Unstandardized coefficient	SE	Standardized coefficient	*t*	Sig.	95.0% CI for B	
	(B)		β			lower bound	upper bound
Hip BMD	0.602	3.315	0.036	0.181	0.857	-6.036	7.239
Femoral neck BMD	0.544	3.128	0.032	0.174	0.863	-5.719	6.807
Lumbar spine BMD	4.334	2.211	0.311	1.960	0.055	-.093	8.762

Dependent variable: HOMA-IR; Predictors (constant): lumbar spine BMD, femoral neck BMD, hip BMD.
B – coefficient of the model; Sig. – significance level; CI – confidence interval; for other abbreviations, see under Table 1.

Table 6

Univariate linear regression analysis between HOMA-IR and T and Z score (hip and spine) and Fracture risk Assessment Tool (FRAX 1 and 2)

Variables	Unstandardized coefficients	SE	Standardized coefficients	*t*	Sig.	95.0% CI for B	
	(B)		(β)			lower bound	upper bound
T score (hip)	0.136	1.431	0.066	0.095	0.924	-2.732	3.005
Z score (hip)	0.578	1.394	0.274	0.414	0.680	-2.218	3.373
T score (spine)	0.588	1.369	0.387	0.429	0.009	-2.156	3.332
Z score (spine)	-0.234	1.385	-0.154	-0.169	0.867	-3.011	2.544
FRAX-1	0.073	0.122	0.287	0.594	0.555	-0.172	0.317
FRAX-2	-0.027	0.240	-0.062	-0.114	0.910	-0.509	0.454

Dependent variable: HOMA-IR; Predictors (Constant): T and Z score (hip and spine), Fracture risk Assessment Tool FRAX Index 1 and 2 (FRAX Index 1 – the probability of a major osteoporotic fracture (clinical fracture of the spine, forearm, hip, or shoulder); FRAX Index 2 – the probability of hip fracture).
B – coefficient of the model; SE – standard error; Sig. – significance level; CI – confidence interval; for other abbreviations, see under Table 1.

Table 7

Univariate linear regression analysis between Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and blood markers

Variables	Unstandardized coefficient (B)	SE	Standardized coefficient (β)	*t*	Sig.	95% CI for B	
						lower bound	upper bound
Vitamin D	-0.002	0.002	-0.015	-1.021	0.313	-0.006	0.002
Somatotropin	-0.011	0.010	-0.015	-1.143	0.259	-0.031	0.009
IGF	0.000	0.001	-0.005	-0.367	0.715	-0.002	0.001
TSH	0.029	0.021	0.019	1.407	0.166	-0.013	0.071
fT4	-0.013	0.007	-0.027	-1.852	0.071	-0.028	0.001
TgAt	0.095	0.000	0.010	0.717	0.477	0.000	0.000
TPOAt	0.078	0.000	-0.007	-0.486	0.630	0.000	0.000
PTH	-0.001	0.001	-0.011	-0.767	0.447	-0.003	0.001
Insulin	0.248	0.004	0.925	65.560	0.000	0.241	0.256
Glucose	0.414	0.032	0.186	13.112	0.000	0.350	0.477

Dependent Variable: HOMA-IR; Predictors: (Constant), Glucose, Vitamin D, somatropin; TPOAt – anti-thyroid peroxidase antibodies; TSH – thyroid-stimulating hormone, fT4 – free thyroxine; TgAt – antithyroglobulin antibody; IGF – insulin growth factor; PTH – parathyroid hormone.

B – coefficient of the model; Sig. – significance level; SE – standard error; CI – confidence interval.

No significant difference was observed ($p = 0.935$) in age between women with osteoporosis (M = 69.5 years) and women in group with normal bone mass/osteopenic (M = 70 years). All participants were postmenopausal. The subjects' mean BMI was 26.11 kg/m^2 and ranged from 15.6 to 35.6 kg/m^2. The mean BMI for women with normal BMD/osteopenia was 15% higher (28.57 kg/m^2) than in women with osteoporosis (24.88 kg/m^2) ($p < 0.001$). The group of women with normal BMD/osteopenia had an 18% higher body mass ($p < 0.001$), 13% more LM ($p < 0.001$), and even 30% more FM ($p < 0.001$). This group of women had about 9% more LMI ($p = 0.003$) and about 25% more FMI ($p = 0.001$). HOMA-IR had a mean of 1.92 in the subjects and ranged from 0.2 to 6.7. HOMA-IR values were 1.56 in the subjects with osteoporosis and 2.68 in the group with normal BMD/osteopenia (Table 3).

Discussion

The association between muscle properties, BMD, and insulin resistance in this study was evaluated based on body composition parameters, muscle strength, and physical performance [17]. Based on these parameters, we provide clinical evidence that body composition changes, muscle strength, and physical performance are associated with decreased BMD. In addition, adipose tissue accumulation and an increase in total mass are closely related to insulin resistance. Finally, we confirmed the association between BMD and insulin resistance in postmenopausal women in Serbia.

FM is a significant source of proinflammatory cytokines that mediate bone metabolism, and postmenopausal women tend to accumulate visceral fat. Some authors [16, 18] reported in their studies the independent effect of FM on BMD over estrogens, insulin, and leptin. It was also observed that the relative contribution of body composition parameters to BMD depends on gender, ethnicity, and age [19].

Ho-Pam et al. [8], in their study, state that LM and FM are significant precursors to BMD. Our study results are consistent with the fact that a positive correlation was obtained between LM and FM and BMD on the hip and spine. Several studies have suggested a positive correlation between HGT and BMD in elderly people [18], whereas some studies have suggested the opposite [19]. Our study is consistent with the study that revealed a significant positive correlation between muscle strength and BMD. The results showed that HGT had a high degree of positive correlation with the BMD of the hip and a significant positive correlation with the BMD of the lumbar spine. Although multiple physiological and psychological factors influence GS, this is the most useful clinical practice test. It appeared to be a significant predictor of health events in the elderly [20]. GS had the highest degree of positive correlation with hip BMD, which confirms that maximum GS can be a useful and specific test for predicting bone status in older postmenopausal women [21].

In the present study, LM, muscle strength, and physical performance were not associated with insulin resistance. In contrast, adipose tissue and BMD on the hip, and especially on the spine, were significantly associated with insulin resistance: women with higher adipose tissue showed higher insulin resistance levels. Therefore, our study implies that the reduction of LM accompanied by its damage and the accumulation of adipose tissue contributes to insulin resistance development. Study results are in line with results reported by Park et al. [22]. These authors state in their research that LM reduction with muscle damage and fat accumulation has a close positive relationship with developed insulin resistance. The relationship between BMD and insulin resistance has been studied in different populations, and mixed results have been obtained. In a study by Kalamari M. et al. [2] involving Caucasian postmenopausal women, a statistically significant positive association between hip BMD and insulin resistance was demonstrated [2], which is consistent with our study results. The main predictors in changing the metabolic profile in postmenopausal women are lumbar spine BMD, T score of the spine, fT4, insulin, and glucose levels. Study results are in accordance with the

results of the study by Srikanthan et al. [23]. They confirmed the association between insulin resistance and strength femoral neck and suggested that obesity and hyperinsulinemia may not be bone-protective. They add just that to the growing body of evidence that points to the importance of measuring bone strength relative to load in assessing and understanding fracture risk [23]. This is consistent with our results, which indicate that although it has been found that there is a positive correlation between insulin resistance and BMD, there is no correlation between insulin resistance and fracture risk. This means that women with higher insulin resistance levels and higher BMD do not have a lower fracture risk.

Several studies have investigated the correlation between muscle parameters, fat accumulation, and insulin resistance [23]. With aging, muscle mass is lost, and muscle damage and fat accumulation occur. Specifically, the infiltration of muscle tissue by fat leads to the activation of apoptotic cells and the release of inflammatory cytokines and adipokines, leading to the development of insulin resistance [24]. On this basis, the idea that local inflammation in the muscle followed by the accumulation of fat by secretion of cytokines and adipokines instead of a decrease in muscle strength and physical performance may have a more important role in the production of insulin resistance [25]. In this regard, our results may provide clinical evidence to support the results of other studies.

Conclusion

The results suggest that LM and FM significantly affect BMD and muscle strength, and physical performance in postmenopausal women. Besides, a decrease in LM, muscle damage, and fat buildup is associated with a higher incidence of insulin resistance in these women. Finally, BMD on the hip, and especially on the spine, is associated with the onset of insulin resistance. However, there is no correlation between insulin resistance and fracture risk. These results significantly contribute to understanding the changes that occur in the body with aging in postmenopausal women.

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