MEDICAL UNIVERSITY - PLEVEN FACULTY OF MEDICINE

DEPARTMENT OF CARDIOLOGY, PULMONOLOGY AND ENDOCRINOLOGY

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EFFECT OF BODY COMPOSITION ON BONE MINERAL DENSITY MEASURED BY WHOLE-BODY DEXA

RESUMÉ

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The author is a part-time PhD student at the Department of Cardiology, Pulmonology and Endocrinology, Faculty of Medicine, Medical University - Pleven.

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The bibliography includes 158 literature sources - more than 50% of them are from the last 10 years, with 1 in Cyrillic and the rest in Latin.

The defense of the dissertation will take place on 11.07.2023 at 13.00 in Ambroise Pare Hall, MU - Pleven, "St. Kliment Ohridski" № 1 street. The defence materials are available on the website of MU - Pleven www.mu-pleven.bg

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Content:

ABBREVIATIONS USED:

BMI - body mass index

DEXA - Dual-energy x-ray absorptiometry

Kg - kilogram/s

kg/m^2 - kilogram/square meter

BMC - bone mineral content

BMD - bone mineral density

CT - computed tomography

I. INTRODUCTION

Overweight and obesity, as well as osteoporosis, are socially important diseases whose incidence is increasing worldwide. The complex interaction between adipose and bone tissue is well known, as is the key role of muscle mass and function in bone metabolism. Despite the protective effect of higher body mass index/body mass index (BMI) on bone mineral density (BMD), there is evidence of a negative impact of obesity on bone metabolism. Along with this, muscle mass and function have a key effect on BMD, determining the need to study the complex effects of body composition on bone health.

In clinical practice, low body weight is well established as a risk factor for osteoporosis, and the prevailing view on higher body weight and obesity is that they are associated with higher BMD. There is evidence that body weight and BMI are responsible for variation in BMD in the range 8.9-19.8%. According to the recommendations of the National Osteoporosis Foundation (1998), body weight less than 57.8 kg in postmenopausal women is a risk factor for the development of osteoporosis, therefore screening in this category of women is recommended.

Obesity and osteoporosis are chronic multifactorial diseases, and the prevalence of both has progressively increased in recent decades. The relationship between the two diseases has been studied in different aspects. A number of associations between the two diseases have been established on the basis of epidemiological, clinical and baseline studies. Both diseases are known to depend on genetic factors as well as environmental factors. The incidence of osteoporosis as well as of bone marrow fatty infiltration increases with ageing. A complex of adipocytokines and hormones influences both bone remodeling and the development of obesity. Both diseases are ameliorated by physical activity, and adipocytes and osteoblasts derive from common progenitor cells. Traditionally, obesity has been thought to be associated with greater bone strength, and women with low body weight of Caucasian or Asian race are at highest risk for developing osteoporosis. Current knowledge about obesity challenges

this notion. There is evidence that obese individuals may have an increased fracture risk, which raises the issue of the negative impact of adiposity on bone and calls into question the traditional view of the protective effect of higher body weight on the development of osteoporosis. It is well known that dysfunctional adipose tissue in obesity is not an inert structure, but is a dynamic tissue that is actively involved in metabolic processes and secretes a number of active substances, such as adipocytokines and inflammatory mediators, which can stimulate bone resorption. The positive effect of body weight on bone tissue raises the question of whether the effect is due to the action of adipose tissue, muscle tissue, or their joint action. The latter requires body composition testing, which is not currently widely applied in clinical practice. There are different models that define body composition. The ternary model introduces the concept of lean mass, which is body mass after subtraction of fat mass and bone mineral content. Since skeletal muscle mass is a major component of lean mass, the latter is often used as a parameter to estimate skeletal muscle mass.

Important factors that determine the risk of developing osteoporosis are muscle mass and function. It should be borne in mind that immobilization, nutritional deficiencies, chronic diseases, inflammation, insulin resistance and endocrine changes with age lead to accelerated loss of muscle mass and strength, respectively to sarcopenia. In addition, muscle and bone tissue have been found to have common determinants in terms of genetic factors, nutrition, lifestyle and hormonal balance, which underlies the need to assess changes in body composition in patients with osteoporosis. There are different approaches to define the components of body composition, which include fat mass, fat-free mass and lean mass. Fat-free mass differs from lean mass in that it excludes fat in cell membranes, which in turn is part of lean mass because of their anatomical localisation and negligible amount. Pure mass represents the proteins in skeletal muscle and contains the cellular composition of fat-free intercellular connective tissue (tendons, ligaments, basement membranes). Higher lean mass and grip strength show a positive correlation with BMD, whereas sarcopenia is associated with low BMD and osteoporosis.

Muscle tissue is key to metabolism, bone building and remodeling,

thermoregulation, and maintaining functional capacity. It can also serve as a depot for glycogen, fat and protein. Significant loss of muscle mass can lead to decreased basal metabolic intensity, impaired functional capacity, and poor quality of life. The aging process is associated with various anatomical changes that lead to impaired work capacity, impaired functional capacity, and a propensity for falls. To a large extent, impaired physical function in old age is associated with a gradual loss of bone tissue (osteopenia and osteoporosis) and a progressive reduction in lean mass and muscle mass, respectively. The loss of muscle mass is denoted by the term sarcopenia. Sarcopenia is associated with stable body weight due to parallel changes in body composition and an increase in adipose tissue with age. Sarcopenia, which occurs in the aging process, leads to gait disturbances, impaired work capacity and falls, whereby it can increase the risk of fractures in women with osteoporosis. In this regard, consideration of the processes of muscle and bone loss and their risk factors, associations and treatment options is essential.

II. AIM AND OBJECTIVES

Aim:

The aim of the present study was to assess the association of body weight and body composition (fat and lean mass) with BMD assessed by whole-body DEXA scanning.

Objectives:

1. To analyze DEXA (T-score), bone mineral content and BMD of lumbar spine and femoral neck in women with BMI > and <25 kg/m^2
2. To assess the influence of body composition on BMD by conducting the following analyses:
   2.1. To analyze the presence of differences in whole-body lean mass between women with lumbar spine and femoral neck BMD corresponding to a T-score ≤ and > /-2.5/
   2.2. To analyze the presence of differences in whole-body fat mass between women with lumbar spine and femoral neck BMD corresponding to T-scores ≤ and > /-2.5/
   2.3. To assess the presence of differences in bone mass between the lumbar spine and femoral neck BMD groups corresponding to a T-score ≤ and > /-2.5/.
3. To analyze the whole-body scan results and the distribution of visceral and subcutaneous adipose tissue by conducting the following analyses:
   3.1. Were there significant differences in fat mass and percent fat, lean mass and percent lean mass, and bone mass of the trunk, lower and upper extremities between groups with a total T-score < and ≥ /-1/
   3.2. Did android and gynoid fat and lean mass differ significantly, as did android to gynoid mass ratio between groups with T score < and ≥ /-1/.

II. MATERIAL AND METHODS:

1. Patients and methods

A retrospective study with data analysis of patients who underwent whole body DEXA scanning at Avis Medica Medical Center - Pleven, Lunar prodigy device was performed.

The study included 111 women with a mean age of 59±8 years. All patients included in the study were examined in the spine area and both hips, and the recorded parameters of osteodensitometry and body composition were analyzed. The results were from examinations performed in the spine area and femurs in anterior-posterior projection. Based on the data obtained from the spine and femur scans, the android and gynoid fat and lean mass can be estimated, based on which the fat and lean mass of the whole body is calculated. T-score values of lumbar spine, T-score of both femoral necks, BMD and BMC and their associations with BMI and body composition (fat and lean mass) were analyzed.

Whole-body examination data were analyzed in 16 women, with regional analysis of 14 anatomic regions (head, left and right upper extremity, left and right trunk, left and right lower extremity, ribs, pelvis, spine, android, and gynoid).

2. Statistical methods

Descriptive statistics, analysis of variance, Goset's t-criterion (Student-Fisher) were used for statistical analysis of the data. Values of $p<0.05$ were reported as statistically significant.

3. Ethical aspects

The study was retrospective and was approved by the Research Ethics Committee of the Medical University - Pleven.

III. RESULTS:

The study included 111 women with a mean age of 59±8 years. The mean height, weight and BMI values are presented in Table 1. 1. 45 of the study patients (40.54%) had a BMI≤25 kg/m^2 , and the remaining 59.46% (n=66) had a body mass index greater than 25 kg/m^2 (Fig. 1). The mean values of lean mass, fat mass and osteodensitometry parameters of lumbar spine, femoral neck and hips are presented in Table 2.

	Mean	Minimum	Maximum	Standard Deviation
Age	59	43	76	8
Weight	74	47	132	16
Height	163	150	179	6
BMI	27.9076	19.5312	42.6136	5.7400

Table. 1. Data on age, weight, height and BMI of the studied group of women.

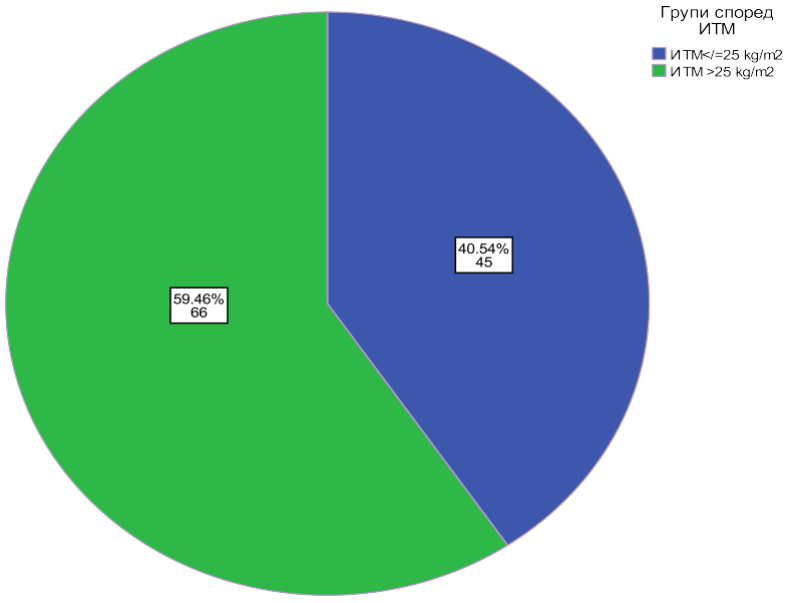

Fig. 1. Distribution of patients according to BMI values.

	Mean	Minimum	Maximum	Standard Deviation
Fat mass (g)	2444.6133	919.7501	3423.0954	588.7277
Lean mass (g)	4204.0353	2096.9119	6080.2499	865.4411
Percentage of fat	.3711	.1314	.4965	.0878
L1-L4_BMD	1.02595495	.52697552	1.77586229	.20809400
L1-L4 BMC	53.204193	7.183261	105.969767	19.870274
L1-L4_T-score	-1.324249	-5.441871	4.965519	1.749111
L1-L4_Z-score	-.3725649	-3.8214244	5.3790892	1.6450870
Average BMD of both femoral necks	.8456	.5962	1.2329	.1631
Average BMC of both femoral necks	4.2641	2.9659	9.2259	1.0835
Mean T-score of both femoral necks	-1.3905	-3.1780	1.4026	1.2112
Mean Z-score of both femoral necks	-.2476	-2.1183	2.2775	1.0974
Average BMD of both hips	.8906	.5947	1.2434	.1740
Average BMC on both hips	29.2039	17.2163	48.8842	6.4405
Average T-score of both hips	-.9628	-3.2779	1.8705	1.4048
Average Z-score of both hips	-.1194	-1.9723	2.5890	1.2987

Table 2. Mean values of lean mass, fat mass and osteodensitometry parameters of lumbar spine, femoral neck and hips.

1. **Association between BMI and BMD of the lumbar spine and femoral neck. Bone mineral content and BMD of lumbar spine and femoral neck in women with BMI > and <25 kg/m^2**

Patients with lumbar spine T-scores ≤ /-2.5/ (n=27) had a significantly lower BMI (25.14±4.08 kg/m^2) compared to cases with T-scores > /-2.5/ (n=84), (BMI 28.79±5.93 kg/m^2 ; p=0.004). Similar results were found regarding femoral neck osteodensitometry results. BMI in patients with a mean T-score ≤ /-2.5/ on both femoral necks (n=15) was 24.93±5.11 kg/m^2 . In the group with T-score > /-2.5/ (n=96), BMI (28.37±5.71 kg/m^2) was statistically significantly higher (p=0.031). In patients with BMI>25 kg/m^2 lumbar spine BMD (1.08±0.21 g/cm^2) and femoral neck BMD (0.90±0.17 g/cm^2) were significantly higher compared to patients with BMI≤25 kg/m^2 for both locations (lumbar spine BMD 0.93±0.16 g/cm^2 ; p=0.000; femoral neck BMD 0.76±0.09 g/cm^2 ; p=0.000).

Patients with BMI >25 kg/m^2 (N=66) had significantly higher BMC (57.26±18.96 g) compared to cases with BMI≤25 kg/m^2 (n=45, BMD 47.25±19.87 g), (p=0.009) (Table 3, Fig. 2).

	Groups according to BMI	N	Mean	Std. Deviation	p-value
BMC of lumbar spine (L1-L4)	≤25 kg/m^2	45	47.25309572	19.870936306	0.009
	>25 kg/m^2	66	57.26175973	18.964404298	
BMC of both femoral necks	≤25 kg/m^2	45	3.861025	.6119811	0.001
	>25 kg/m^2	66	4.538851	1.2425883	

Table. 3. Difference in BMC at the lumbar spine (L1-L4) and both femoral necks in patients with BMI ≤ and >25 kg/m^2 .

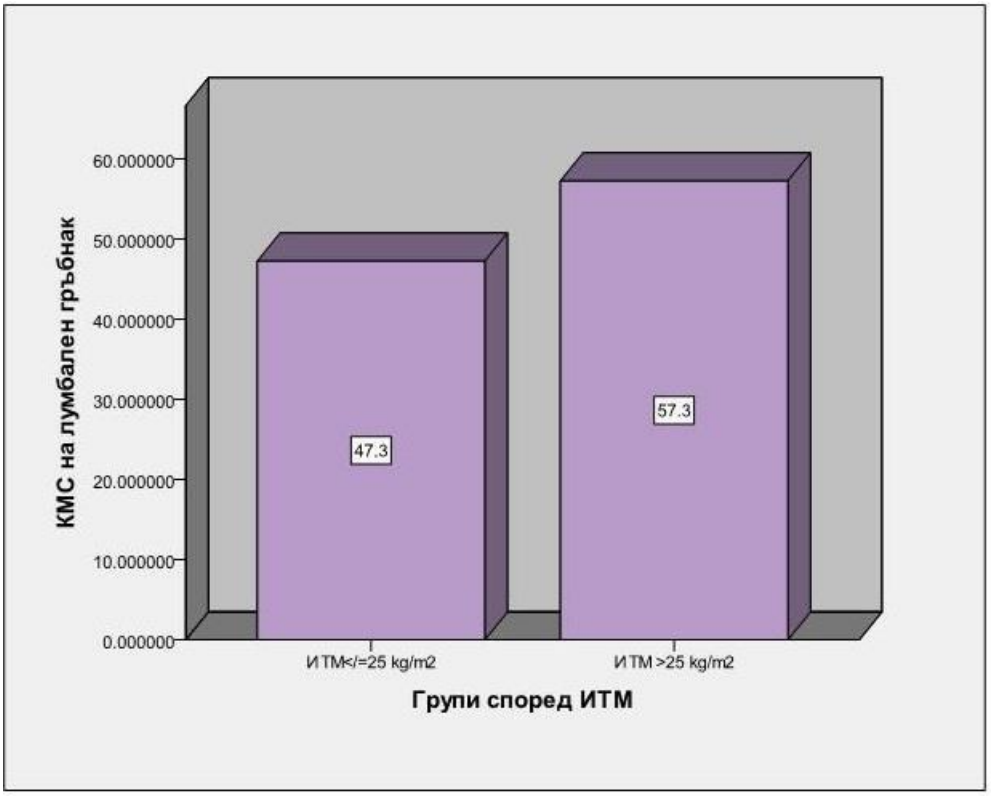

Fig. 2. BMC in the lumbar spine region (L1-L4) in patients with BMI ≤ and >25 kg/m^2 .

Similar results were found when comparing the BMD of both femoral necks, which was also significantly higher in patients with BMI > 25 kg/m^2 (4.53±1.24) compared to those with BMI ≤ 25 kg/m^2 (3.86±0.61), (p=0.001) (Table 3, Fig. 3).

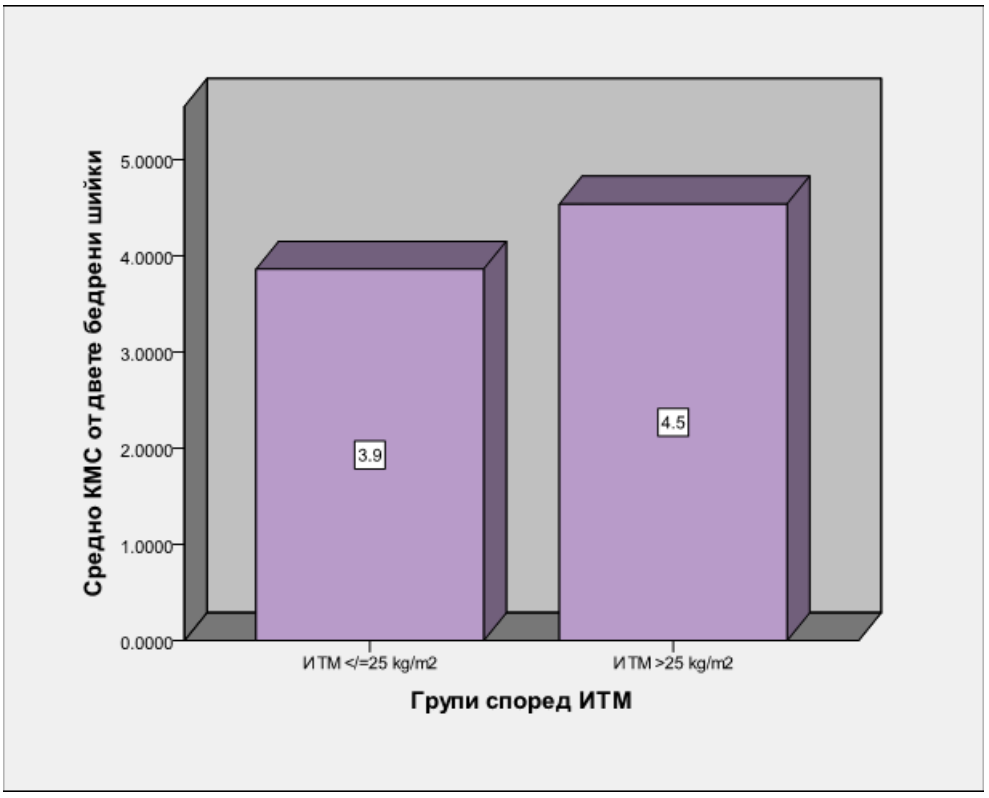

Fig. 3. BMC of both femoral necks in patients with BMI ≤ and >25 kg/m^2 .

The BMD in the lumbar spine region (L1-L4) in subjects with BMI ≤ 25 kg/m^2 was 0.93±0.16, which was significantly lower compared to subjects with BMI > 25 kg/m^2 (1.08±0.21; p=0.000). A statistically significant difference was also found between T-score values in the lumbar spine region (L1-L4) in subjects with different BMI (-2.10±1.39 in patients with BMI ≤ 25 kg/m^2 ; -0.79±1.77 in BMI > 25 kg/m^2 ; p=0.000). In cases with BMI > 25 kg/m^2 , significantly higher BMD and T-score values were also found in the area of both femoral necks and both thighs compared to patients with BMI ≤ 25 kg/m^2 (p=0.000) (Table 4).

	Groups according to BMI	N	Mean	Std. Deviation	p-value
BMD of lumbar spine (L1-L4)	≤25 kg/m^2	45	.9382236761	.16655411580	0.000
	>25 kg/m^2	66	1.0857717326	.21340695673	
T-score of lumbar spine (L1-L4)	≤25 kg/m^2	45	-2.10369158	1.395597714	0.000
	>25 kg/m^2	66	-.79281132	1.775280544	
BMD of both femoral necks	≤25 kg/m^2	45	.761510	.0900015	0.000
	>25 kg/m^2	66	.902873	.1770096	
T-score of both femoral necks	≤25 kg/m^2	45	-2.060943	.6358461	0.000
	>25 kg/m^2	66	-.933416	1.2983035	
BMD of both hips	≤25 kg/m^2	45	.791838	.0994083	0.000
	>25 kg/m^2	66	.957939	.1821351	
T-score of both hips	≤25 kg/m^2	45	-1.806813	.7742566	0.000
	>25 kg/m^2	66	-.387256	1.4506183	

Table 4. Comparison of BMD and T-score with different localization (lumbar spine, both femoral necks and both hips) in patients with BMI ≤ and >25 kg/m^2 .

2. Association between body composition and BMD. Lean and fat mass in women with lumbar spine and femoral neck BMD corresponding to T score ≤ and > /- 2.5/

The mean age of patients with a lumbar spine T-score ≤ /-2.5/ (n=27) was 63±6.5 years and was significantly higher compared to cases with a T-score > /-2.5/ (n=84) (57±8 years; p=0.001). Body weight (65.89±10.70 kg) and BMI (25.14±4.08 kg/m^2) in cases with osteoporosis defined on the basis of lumbar spine T-score values ≤ /-2.5/, were significantly lower compared to patients with a T-score > /- 2.5/ - body weight (76.25±16.98 kg. ; p=0.004) and BMI (28.79±5.93 kg/m^2 ; p=0.004), respectively. There was no statistically significant difference in height between the two groups of patients (Table 5).

Patients with lumbar spine T-score ≤ /-2.5/ (n=27) were found to have significantly lower fat mass (2239.90±607.63 grams) compared to cases with T-score > /-2.5/ (n=84) (fat mass 2510.41±570.68 grams; p=0.037). The amount of lean mass in subjects with T-score ≤ /-2.5/ on lumbar spine (4025.30±862.58 grams) was also significantly lower compared to the group with T-score > /-2.5/ (4760.09±607.63 grams; p=0.000) (Table 5).

The mean age of patients with a T-score of both hips ≤ /-2.5/ (n=15) was higher (62±6.5 years) compared to cases with a T-score > /-2.5/ (n=96) (58.19±8.18 years), but the difference did not reach statistical significance (p=0.089). Body weight (65.20±12.61 kg) and BMI (24.93±5.11 kg/m^2) in cases with osteoporosis, defined on the basis of T-score values of both hips ≤ /-2.5/, were significantly lower compared to patients with T-scores >/-2.5/ - body weight (75.06±16.42 kg. ; p=0.028) and BMI (28.37±5.71 kg/m^2 ; p=0.031), respectively. There was no statistically significant difference in height between the two groups of patients (p=0.732) (Table 6).

A statistically significant difference was also found in terms of lean mass between the groups with different femoral neck T-scores (4110.60±832.01 grams for femoral neck T-score ≤2.5, n=15 and 4802.01±862.87 grams for T-score>2.5, n=96, p=0.004). When comparing the groups by femoral neck T-score, the percentage of fat was significantly lower in osteoporosis patients with T-score < /-2.5/ (31 vs. 38%, p=006), but the difference in fat mass did not reach statistical significance (p=0.081) (Table 6).

	Groups according to lumbar spine T-score value	N	Mean	Std. Deviation	p-value
Age	>-2.5 SD	84	57.32	8.048	0.001
	≤-2.5 SD	27	63.00	6.569	
Weight	>-2.5 SD	84	76.25	16.989	0.004
	≤-2.5 SD	27	65.89	10.703	
Height	>-2.5 SD	84	162.71	6.350	0.551
	≤-2.5 SD	27	161.89	5.833	
BMI	>-2.5 SD	84	28.794782	5.9303587	0.004
	≤-2.5 SD	27	25.147643	4.0829552	
Fat mass	>-2.5 SD	84	2510.411678	570.6802046	0.037
	≤-2.5 SD	27	2239.907253	607.6384922	
Lean mass	>-2.5 SD	84	4760.092747	607.6384922	0.000
	≤-2.5 SD	27	4025.302607	862.5897706	
Fat percentage (%)	>-2.5 SD	84	.387577	.0821022	0.000
	≤-2.5 SD	27	.319987	.0868055	
Percentage of lean mass (%)	>-2.5 SD	84	.680013	.0868055	0.000
	≤-2.5 SD	27	.612423	.0821022	

Table 5. Body composition in patients with lumbar spine T-score > and ≤-2.5.

	Groups according to the value of the average T-score of both hips	N	Mean	Std. Deviation	p-value
Age	>-2.5 SD	96	58.19	8.184	0.089
	≤-2.5 SD	15	62.00	6.579	
Weight	>-2.5 SD	96	75.06	16.428	0.028
	≤-2.5 SD	15	65.20	12.616	
Height	>-2.5 SD	96	162.59	5.647	0.732
	≤-2.5 SD	15	162.00	9.304	
BMI	>-2.5 SD	96	28.371637	5.7167183	0.031
	≤-2.5 SD	15	24.938058	5.1174143	
Fat mass	>-2.5 SD	96	2483.148782	529.6201680	0.081
	≤-2.5 SD	15	2197.986250	862.8787315	
Lean mass	>-2.5 SD	96	4802.013750	862.8787315	0.004
	≤-2.5 SD	15	4110.601218	832.0117431	
Fat percentage (%)	>-2.5 SD	96	38.0064	.0780950	0.006
	≤-2.5 SD	15	31.3998	.1232684	
Percentage of lean mass (%)	>-2.5 SD	96	68.6002	.1232684	0.006
	≤-2.5 SD	15	61.9936	.0780950	

Table 6. Body composition in patients with T-score of both hips > and ≤-2.5.

3. Bone mass in individuals with lumbar spine and femoral neck BMD corresponding to a T-score ≤ and > /-2.5/

BMD of the lumbar spine, femoral neck, and both hips was significantly lower in individuals with a lumbar spine T-score ≤ /-2.5/ compared with those with a T-score > /-2.5/ (Table 7). On the other hand, BMD was significantly lower in individuals with a femoral neck T-score ≤ /-2.5/ at the femoral neck and both hips, but not at the lumbar spine (Table 8).

	Groups according to lumbar spine T-score value	N	Mean	Std. Deviation	Std. Error Mean	p-value
Lumbar spine BMC L1-L4	>-2.5 SD	84	58.9305748	17.1618966	1.87251644	0.000
	≤-2.5 SD	27	35.3887836	17.1655160	3.30350509	
Average BMC value of femoral neck	>-2.5 SD	84	4.445178	1.1681381	.1274543	0.002
	≤-2.5 SD	27	3.700568	.4182344	.0804892	
Average BMC of both hips	>-2.5 SD	84	30.722815	6.3014474	.6875443	0.000
	≤-2.5 SD	27	24.478517	4.2532168	.8185320	

Table. 7. BMC in different zones in subjects with lumbar spine BMD corresponding to T-score ≤ and > /-2.5/.

	Groups according to femoral neck T-score value	N	Mean	Std. Deviation	Std. Error Mean	p-value
Lumbar spine BMC L1-L4	>-2.5 SD	96	53.6396157	20.1216005	2.05365225	0.562
	≤-2.5 SD	15	50.4174889	18.5797173	4.79726238	
Average BMC value of femoral neck	>-2.5 SD	96	4.405067	1.0859366	.1108329	0.000
	≤-2.5 SD	15	3.361589	.4612740	.1191004	
Average BMC of both hips	>-2.5 SD	96	30.098650	6.2680613	.6397313	0.000
	≤-2.5 SD	15	23.477737	4.3235275	1.1163300	

Table 8. BMC in different zones in subjects with femoral neck BMD corresponding to T-score ≤ and > /-2.5/.

4. Fat, lean mass, and BMD of different anatomic sites in individuals with total T-score < and ≥ /-1/. Android and gynoid fat and lean mass in individuals with T-score < and ≥ /-1/

In 16 women with a mean age of 49±6 years, whole-body examination data were analyzed with regional analysis of 14 anatomic regions (head, left and right upper extremity, left and right trunk, left and right lower extremity, ribs, pelvis, spine, android, and gynoid). The mean body weight of the patients in the study group was 78 kg (range 47-114 kg). The results are presented in Tab. 9.

There were no significant differences between the amount of fat, lean mass and lower limb BMD in individuals with T-scores < and ≥ /-1/. Total, lean mass, and trunk BMD also did not differ between the two subgroups. Lean torso mass in individuals with T-score < /-1/ was 16428.50 grams, which was significantly lower compared to cases with T-score > /-1.0/ (21519.00 grams, p=0.031) (Table 10).

	Mean	Minimum	Maximum	Standard Deviation
Height	164	150	170	7
Weight	78	47	114	23
Age	49	43	61	6
Lower limb fat percentage (%)	41.6	22.3	51.7	10.4
Total lower limb mass (kg)	27.8125	13.9000	42.3000	8.7011
Lower limb fat mass (grams)	11712	4017	19409	5450
Lean mass of lower limbs (grams)	15218	8774	21855	3937
Lower limb BMC	870	589	1198	190

Percentage of fat of the torso (%)	41.7725	19.5000	55.5000	13.9470
Total torso mass (kg)	37.3125	19.6000	51.5000	10.2467
Torso fat mass (grams)	16399	3741	26552	8214
Lean torso mass (g)	20246	15409	25556	3132
BMC of the torso	662	433	935	180
Android adipose tissue (%)	43.1	15.4	58.3	15.9
Total mass in android zone (kg)	5.9	2.7	8.0	1.8
Android fat mass (grams)	2723	418	4662	1465
Android lean mass (grams)	3089	2291	3822	501
BMC Android Zone	47	35	65	11
Gynoid adipose tissue_%	44.4000	22.9000	56.3000	11.5857
Total mass in gynoid zone (kg)	13.0625	7.0000	19.2000	3.7275
Gynoid adipose tissue (grams)	5934	2176	9958	2766
Lean mass in gynoid zone (grams)	6876	4383	8931	1491
BMC gynoid area	255	174	375	66
Total amount of adipose tissue (%)	40.9	23.1	52.4	11.5
Total weight (kg)	78.6	41.2	110.8	21.9
Total amount of adipose tissue (grams)	32916	10091	51080	15376
Total amount of lean mass (grams)	43331	29464	56752	8509
Total BMC	2322	1668	3101	506
Torso/total mass ratio	.48	.37	.53	.05
Lower limb/total mass ratio	.36	.32	.45	.04
Ratio of sum of upper and lower limbs to total mass	1.0150	.8300	1.5200	.2234
Visceral adipose tissue	1060	74	1915	665
Head BMD	506.9514	1.6740	2160.0000	937.4401
BMD upper limbs	.7815	.6240	.9420	.1212

Lower limbs BMD	145.2840	.9660	1154.0000	407.5828
BMD torso	.9220	.7560	1.1980	.1523
BMD ribs	.7902	.6330	.9720	.1257
Pelvic BMD	.9384	.7250	1.3360	.1980
BMD spine	1.0778	.8790	1.2710	.1571
Total BMD	1.1099	.9380	1.3640	.1392
Android Mass %	43.1	15.4	58.3	15.9
Gynoid mass %	44.4000	22.9000	56.3000	11.5857
Total %	40.9	23.1	52.4	11.5
Ratio of android to gynoid mass	.9613	.4300	1.1700	.2273

Table. 9. Data from regional analysis of 14 anatomical regions in 16 patients of the study population.

Comparison of the studied parameters in women with normal BMD values corresponding to T-score ≥ /-1/ (n=10) with cases with T-score < /-1.0/ (n=6) revealed significantly higher values of total lean mass as well as regional lean mass in the android, gynoid and trunk area in subjects with normal T-score values ≥ /-1/. Regarding fat mass, including with analysis of its distribution in the android and gynoid zones, the difference did not reach statistical significance between subgroups with T-scores below and above /-1/. Comparison of the total amount of soft tissue (fat and lean mass) in the android and gynoid zones showed no significant differences between individuals with T-scores below and above /-1/ (Table 10).

	Groups according to T-score values	N	Mean	Std. Deviation	p-value
Lower limb fat percentage (%)	≥ -1 SD	10	41.283	10.9218	0.882
	< -1 SD	6	42.700	12.3037	
Total mass of lower limbs	≥ -1 SD	10	30.266667	7.7409732	0.184
	< -1 SD	6	20.450000	9.2630988	
Fat mass of lower limbs	≥ -1 SD	10	12614.00	5441.008	0.461
	< -1 SD	6	9007.00	6356.890	
Lean mass of lower limbs	≥ -1 SD	10	16700.17	3092.108	0.055
	< -1 SD	6	10770.50	2823.477	
Lower limb BMC	≥ -1 SD	10	933.17	166.797	0.103
	< -1 SD	6	680.00	128.693	

Percent torso fat mass (%)	≥ -1 SD	10	43.513333	11.8953548	0.582
	< -1 SD	6	36.550000	24.1123412	
Total torso mass	≥ -1 SD	10	40.116667	8.6402353	0.200
	< -1 SD	6	28.900000	13.1521861	
Fat mass of the torso	≥ -1 SD	10	17878.33	7545.793	0.419
	< -1 SD	6	11960.00	11623.421	
Lean mass of the torso	≥ -1 SD	10	21519.00	2353.953	0.031
	< -1 SD	6	16428.50	1441.791	
BMC of the torso	≥ -1 SD	10	717.50	170.304	0.137
	< -1 SD	6	494.00	86.267	
Percent android fat tissue (%)	≥ -1 SD	10	45.283	12.3707	0.536
	< -1 SD	6	36.400	29.6985	
Android Total Mass	≥ -1 SD	10	6.317	1.4511	0.219
	< -1 SD	6	4.450	2.4749	
Android fat mass	≥ -1 SD	10	2975.83	1319.233	0.440
	< -1 SD	6	1964.00	2186.374	
Android lean mass	≥ -1 SD	10	3302.17	351.149	0.020
	< -1 SD	6	2450.00	224.860	
BMC in android zone	≥ -1 SD	10	49.83	10.226	0.144
	< -1 SD	6	37.00	1.414	
Percent gynoid fat tissue (%)	≥ -1 SD	10	44.450000	12.7274114	0.985
	< -1 SD	6	44.250000	11.3844192	
Total gynoid mass	≥ -1 SD	10	14.150000	3.2617480	0.167
	< -1 SD	6	9.800000	3.9597980	
Gynoid fat mass	≥ -1 SD	10	6419.33	2826.954	0.432
	< -1 SD	6	4478.00	2815.699	
Ginoid lean mass	≥ -1 SD	10	7453.33	1132.008	0.045
	< -1 SD	6	5145.00	1077.631	
BMC in gynoid zone	≥ -1 SD	10	275.83	61.558	0.116
	< -1 SD	6	190.50	23.335	
Percentage of total fat mass (%)	≥ -1 SD	10	41.717	10.7091	0.764
	< -1 SD	6	38.550	18.4555	
Total amount of fat mass	≥ -1 SD	10	35662.17	14480.426	0.424
	< -1 SD	6	24678.00	20629.133	
Total amount of lean mass	≥ -1 SD	10	46731.17	6362.934	0.036
	< -1 SD	6	33130.50	5185.214	
Total BMC	≥ -1 SD	10	2496.50	453.371	0.089
	< -1 SD	6	1799.00	185.262	
Torso mass/total mass ratio	≥ -1 SD	10	.4983	.02483	0.174
	< -1 SD	6	.4400	.09899	
Lower limb mass/total mass ratio	≥ -1 SD	10	.3500	.02828	0.227
	< -1 SD	6	.3950	.07778	
	≥ -1 SD	10	.948333	.1064738	0.156

Ratio of the sum of the mass of the upper and lower limbs to the total mass	< -1 SD	6	1.215000	.4313351	
Est_visceral_adipose	≥ -1 SD	10	1158.83	641.861	0.511
	< -1 SD	6	765.00	896.611	
BMD of the head	≥ -1 SD	10	361.989500	880.8417105	0.492
	< -1 SD	6	941.837000	1329.5912654	
BMD of upper limbs	≥ -1 SD	10	.812667	.1194750	0.233
	< -1 SD	6	.688000	.0905097	
BMD of lower limbs	≥ -1 SD	10	193.380667	470.6054631	0.603
	< -1 SD	6	.994000	.0395980	
BMD of the torso	≥ -1 SD	10	.977167	.1336165	0.069
	< -1 SD	6	.756500	.0007071	
BMD of the ribs	≥ -1 SD	10	.828833	.1195699	0.142
	< -1 SD	6	.674500	.0586899	
BMD of the pelvis	≥ -1 SD	10	1.001667	.1883005	0.122
	< -1 SD	6	.748500	.0332340	
BMD of the spine	≥ -1 SD	10	1.143833	.1165031	0.023
	< -1 SD	6	.879500	.0007071	
Total BMD	≥ -1 SD	10	1.161167	.1199524	0.062
	< -1 SD	6	.956000	.0254558	
Percent android mass (%)	≥ -1 SD	10	45.283	12.3707	0.536
	< -1 SD	6	36.400	29.6985	
Percent gynoid mass (%)	≥ -1 SD	10	44.450000	12.7274114	0.985
	< -1 SD	6	44.250000	11.3844192	
Ratio of android to gynoid mass	≥ -1 SD	10	1.026667	.0831064	0.174
	< -1 SD	6	.765000	.4737615	

Table. 10. Comparison of fat content, lean mass, BMD in different anatomical regions in subjects with T-score ≥ and < /-1.0/.

V. DISCUSSION

1. Association between BMI and BMD

In the present study, a significantly lower BMI was found in patients with T-score values ≤ /-2.5/ in both the lumbar spine and femoral neck regions. BMD values in both reference locations were statistically significantly higher in overweight patients (BMI>25kg/m). ^{2}

It is well known that adipose tissue in postmenopausal obese women is a source of significant estrogen production, which may protect against reduction in BMD (Gillette-Guyonnet et al., 2000, Siiteri 1987). Androgen aromatization in adipocytes increases extragonadal production of estrogens and is thought to be the main cause of higher BMD values in postmenopausal overweight women, along with the mechanical strain on bone at higher body weight (Almeida et al., 2017). The interaction between fat and bone is complex and needs further studies. Adipose tissue is a source of various adipokines (leptin, adiponectin, etc.), estrogens, proinflammatory cytokines (IL-6, TNF-α), acute phase proteins such as C-reactive protein/CRP that modulate bone function. The distribution of adipose tissue into visceral and subcutaneous may also influence bone metabolism (Hong et al., 2021). There is a hypothesis regarding the negative impact of obesity on bone health. Adipocytes and osteoblasts are known to originate from common multipotent mesenchymal stem cells. In this regard, an increased degree of differentiation towards adipocytes may lead to a decrease in differentiation to osteoblasts and consequently to reduced bone formation. Another hypothesis links the negative effect of obesity and bone function to the presence of low-grade inflammation in obese patients, which leads to increased osteoclast activity. Dysfunctional adipose tissue acts as an active endocrine organ (Cao, 2011),(Das 2001). IL-6 and TNF-α have the potential to stimulate osteoclast activity via the RANKL/RANK/osteoprotegerin system. Obesity is characterized by elevated serum leptin levels, which can have mixed, including negative effects on bone metabolism (Cao, 2011).

Similar results were reported by Agarwal et al. (2016, India), who studied 500

patients aged 25 years and older and analyzed DEXA results and associations of BMD with body weight in different age groups (25-39 years, 40-59 years, and over 60 years). Overweight and obese patients were found to have higher BMP. In a study population of 5,892 patients in Iran (aged 20 to 91 years, divided into three subgroups - normal weight, overweight and obese) in whom DEXA was performed on central areas (lumbar spine L1-L4 and proximal femur - femoral neck and total hip), higher BMD values were found in obese and overweight individuals in all subgroups, viz.Pre-, postmenopausal women and men (Salamat et al., 2016). Shen et al. (2015) evaluated bone structure in 672 men using quantitative computed tomography and found that in non-obese cases with a BMI < 30 kg/m^2 increasing body weight was associated with higher volumetric BMD, a percentage of cortical bone volume. On the other hand, obese men did not show a subsequent increase in these parameters with increasing BMI.

In analyzing DEXA scan results in 1406 South Korean men and women between the ages of 19 and 80 years, Cui et al. (2007) found a positive correlation between fat mass and BMD of all areas in postmenopausal women only, and found that fat mass was the sole determinant of BMD of the lumbar spine, distal forearm, and calcaneus, whereas in the hip area, both fat mass and lean mass were determinants, with a slightly greater involvement of lean mass. A significant positive association between fat mass and BMD was also found in adult males for the forearm and calcaneus zones, whereas lean mass had a positive correlation for all zones (distal forearm, calcaneus, lumbar spine L1-L4, femoral neck, trochanter, Ward's triangle). In young males, on the other hand, only lean mass showed a positive correlation with BMD for all zones examined, whereas fat mass was found to have a negative association again for all zones.

In this regard, studies on differences in BMD, BMD and fracture risk in larger populations with different BMIs - respectively overweight groups and different degrees of obesity, including high-grade forms, will clarify the impact of body weight variation on bone health. The issue of age and sex variations between body weight and BMD also requires further study.

Also of interest is the question of the accuracy of BMD measurement in obese patients. Binkley et al. (2004) conducted a study of BMD with DEXA in 127 patients (52 women/75 men) who had a fat panniculus anterior to the proximal femur. Two scans of the proximal femur were performed before and after repositioning of the fat panniculus. In 49% of the men and 56% of the women, there was a difference in BMD on the two measurements in any of the areas (femoral neck, trochanter, or total hip) that was above the minimum significant difference. There was no definite pattern of change in BMP - with both increases and decreases in BMP observed in the different zones examined. Therefore, it was concluded that the fat panniculus may alter the precision of the BMP measurement in the proximal femoral area, which may compromise the diagnosis of osteoporosis and the monitoring of the effect of the administered therapy. In this regard, repositioning of the fat panniculus anterior to the proximal femur should be a routine part of the densitometric examination. Yu et al. (2012) conducted a study on the effects of adiposity on the accuracy of DEXA and quantitative CT in measuring BMD in the lumbar spine using a phantom before and after simulating adiposity up to 12 kg. In addition, they evaluated the accuracy of the methodologies in 13 healthy adult volunteers simulating an additional amount of adipose tissue up to 7.5 kg. The addition of layers of adipose tissue around the lumbar spine in the phantom resulted in a linear increase in BMD when measured by DEXA, but minimally altered BMD values of the trabecular bone of the spine as measured by quantitative CT. Interestingly, in healthy volunteers, the addition of fat layers resulted in a decrease in BMD at the lumbar spine and did not change BMD of the femoral spine measured by DEXA, but increased BMD of the lumbar spine using quantitative CT.

2. Association between body composition and BMD

In the present study, a significantly lower lean mass was found in patients with T-scores ≤ /-2.5/ at the lumbar spine and femoral neck compared with cases with T-scores >/-2.5/. Patients with T-score ≤ /-2.5/ on lumbar spine also had significantly

lower fat mass, whereas when comparing cases with T-score below and above /-2.5/ on femoral neck, fat mass and fat percentage were also lower in patients with osteoporosis, but the difference reached statistical significance only for fat percentage but not for fat mass. The results of the present study support the leading role of lean mass, (resp. muscle mass as a major component of lean mass) in maintaining BMD. A drawback of the present study is the lack of data regarding comorbidities, medication intake that is associated with the development of secondary osteoporosis, and information regarding the presence of osteoporotic fractures, which would improve the possibilities for precise conclusions.

Zhao et al. (2007) investigated body composition (fat mass, lean mass, fat percentage, BMI, bone mass) in two large ethnic groups, 1,988 non-native Chinese and 4,489 Caucasians descended from 512 ancestors. In both study populations, after adjusting for the mechanical effect of body weight on bone mass, a negative correlation was found between fat mass and percent fat and bone mass. A positive correlation between lean mass and bone mass was also found, again after adjustment for the effect of body weight, suggesting that the positive effect of lean mass on bone mass was not entirely related to mechanical loading in the context of higher body weight.

In assessing the effect of body composition on BMD, lean mass was found to have a definite positive effect on BMD, whereas the data on fat mass were mixed. Bone strength is thought to improve due to the effects of muscle forces rather than static loading from higher body weight (Leslie et al., 2014). In some studies, there is a negative association of increasing BMI with BMD and bone quality. There is evidence that fracture risk in overweight and obese patients of both sexes may be increased after adjustment for higher BMD values (Rudman et al., 2018; Leslie et al., 2014).

Liu et al. (2004) analyzed body composition and associations with BMD measured by DEXA in 282 young women of childbearing age in China. Fat mass was the main factor that determined BMI. BMI and lean mass correlated positively with BMD at the lumbar spine (L2-L4), femoral neck, and total BMD. Lean mass was found to be the only independent factor that determined lumbar spine BMD, femoral neck

BMD, and total BMD. The correlation between BMI and BMD was improved after adjustment for the effect of fat mass, but was reduced to absent after adjustment for the effect of lean mass. These data lead to the conclusion that in young women of childbearing age in China, lean mass is a major determinant of BMD.

In studies of a population of healthy middle-aged premenopausal women from South Asia (Sri Lanka), a positive correlation was found between lean mass, fat mass and bone mass. The leading factor determining bone mineral content and BMD was lean mass, and this association was independent of age and BMI. The role of physical activity and vitamin D levels, which are associated with maintenance of lean mass - and muscle mass and function, respectively - is considered to explain these results (Lekamwasam et al., 2009).

The relationship between body composition and BMD was evaluated in the perimenopausal period by Li et al. (2004, USA) in 43 women. Perimenopause is a period of transition to menopause that is characterized by accelerated bone loss, which determines the subsequent development of osteoporosis. A decrease in lean mass, an increase in body weight and fat mass also develops during this period. In 14% of perimenopausal women, osteopenia was found in the lumbar spine and femoral neck area. Total fat mass and lean mass showed a positive correlation with BMD at the lumbar spine and femoral neck, but after applying regression analysis, only lean mass and ethnicity were found to be reliable predictors of BMD with these reference locations. In perimenopausal women, fat mass was not found to be a significant predictor of BMD in different skeletal sites.

The existence of a difference in the effect of body composition on BMD in pre- and postmenopausal women was assessed in a study by Douchi et al. (1997, Japan) in 196 premenopausal and 128 postmenopausal women. Total fat, lean mass and BMD of the lumbar spine (L2-L4) and of the whole body were measured by DEXA. Total lean mass was significantly higher in premenopausal compared with postmenopausal women, whereas body weight, BMI, and fat mass were similar in both groups. Lean mass was found to be the leading factor determining lumbar spine and whole body

BMD in premenopausal women. In postmenopausal women, the most significant factor determining lumbar spine BMD was total fat mass, and total lean mass was the main factor determining whole-body BMD. These results lead to the conclusion that there are differences between the effects of body composition on BMD in pre- and postmenopausal women, and it was found that total lean mass was the most significant factor determining BMD in young women of childbearing age, whereas having a greater amount of fat mass may have some advantages in maintaining BMD in postmenopausal women.

Similar results were found in the study by Ijuin et al. again in a Japanese patient population (2002, Japan). 360 pre- and 193 postmenopausal women were studied. Fat mass, lean mass and BMD (of lumbar spine L2-4, pelvis, limbs and whole body) were measured by DEXA. In young women of childbearing age, lean mass correlated independently with BMD of upper and lower limbs bilaterally, pelvis and whole body, whereas fat mass showed no positive correlation for these areas except for the pelvis. On the other hand, in postmenopausal women, fat mass was found to correlate independently with BMD of the left upper limb, both lower limbs, pelvis and whole body, whereas lean mass correlated with BMD in only three areas, left and right upper limbs and left leg. These differences lead to the conclusion that lean mass is a determinant of BMD in premenopausal women, whereas fat mass has a significant impact on BMD in the postmenopausal period.

In 1579 healthy women aged 40-90 years (1448 postmenopausal, 131 perimenopausal), Namwongprom et al. (2013, Thailand) found different effects of lean and fat mass on different parts of the skeleton, as well as depending on the onset of menopause. In postmenopausal women, the effect of lean mass was significantly greater relative to that of fat mass for BMD of all skeletal sites except for the whole body. In perimenopausal women, only lean mass had a positive effect on BMD for all sites except the lumbar spine. The most pronounced effect of both lean mass and fat mass was found for BMD of lumbar spine, which is mainly composed of trabecular bone, followed by femur and femoral neck, which are a combination of trabecular and

cortical bone. Concerning the whole body (cortical bone dominated), lean mass had a positive effect, whereas a significant negative association was found for fat mass. The data from this study support the hypothesis that lean and fat mass have different effects on different parts of the skeleton due to differences in the effects on trabecular and cortical bone. In perimenopausal women, lean mass showed a positive effect on BMD of femur, femoral neck and whole body, but not on lumbar spine, respectively in this category of cases lean mass affected mainly cortical bone and had little effect on trabecular bone.

The role of adipose and muscle tissue on BMD and the development of osteoporosis probably depends on the age of adipose tissue accumulation, respectively the age of development of obesity, the rate of muscle mass loss, the level of circulating adipocytokines and myokines, along with the influence of concomitant factors such as age, sex, race, comorbidities and medication intake. For a comprehensive assessment, along with consideration of these factors, bone quality analysis by trabecular bone score/TBS should also be considered, as well as mandatory morphometric analysis of spinal vertebrae. A shortcoming of the present study is the lack of information regarding these additional factors and findings. In relation to the established key role of lean mass and muscle mass, respectively, for BMD, as well as the high rate of combined osteoporosis and sarcopenia, the impossibility of determining muscle mass based on anthropometric measurements should also be considered. In this regard, the results of this thesis provide a rationale for the promotion of whole-body scanning and body composition determination in our country, which is currently of limited application. Maintaining good muscle tissue structure and function as well as optimal body composition is key to bone health. This is associated with a healthy lifestyle, protein intake, vitamin D and adequate physical activity. The high degree of association of body composition and BMD, the need to maintain muscle mass and function, and the optimal ratio of body composition components are the basis for developing recommendations for screening, prevention and treatment in the presence of complex abnormalities, which will also improve the effect of osteoporosis

treatment.

3. Role of muscle mass and function on bone mineral density and osteoporosis risk

The amount of lean mass in the present study was significantly higher in patients with a T-score >/-2.5/ at both the lumbar spine and femoral neck. On the other hand, fat mass was statistically significantly higher in cases with T-score >/-2.5/ only for lumbar spine but not for femoral neck location.

The question of which part of body composition is a more important determinant of BMD, lean or fat mass, has been the subject of investigation in a number of studies. The results of the present study support data from a meta-analysis by Ho-Pham et al. (2014), who analyzed results from 44 studies of 20 226 patients (4966 men and 15 260 women) aged 18 to 92 years and found a higher degree of correlation of lean mass compared with fat mass with femoral neck BMD. The association between lean mass and femoral neck BMD was more pronounced in men compared with women. In women of childbearing age, lean mass also correlated more strongly than fat mass with femoral neck BMD and whole body BMD. On the other hand, in postmenopausal women, the effects of lean and fat mass on bone mineral density were similar.

Hong et al. (2021) observed that higher lean mass index and limb muscularity index (calculated based on anthropometric data) were associated with reduced risk of osteoporotic fractures in both sexes. Muscle mass, as assessed by anthropometric measurements, was found to be a more significant protective factor relative to fat mass with respect to the risk of developing future osteoporotic fractures.

In 202 postmenopausal women aged 48 to 84 years (mean age 64 years), Nakaoka et al. (2001) found that lean mass correlated positively with BMD in all zones. BMD was measured at the lumbar spine, hip, radius, and whole body. A high degree of correlation was found for hip BMD with both fat mass and lean mass, whereas fat mass did not correlate independently with whole body and radius BMD. Based on the results, the authors concluded that lean mass is a leading determinant of

BMD to a greater extent than fat mass in all areas of the bony skeleton except the femoral neck.

Benetos et al. (2009, France) studied 169 men over 60 years of age and found that lean mass correlated with BMD and T-score values of the lumbar spine, femoral neck and whole body, respectively. No effect of fat mass on BMD was observed. In addition, no association was found between the presence of arterial hypertension, diabetes mellitus and dyslipidemia and BMD. A positive association was found between fat mass, presence of arterial hypertension, diabetes mellitus and dyslipidemia with aortic pulse wave velocity/pulse wave velocity, whereas lean mass had no effect on this parameter. On the basis of these results, it was concluded that men with high lean mass and low fat mass had the best BMD and arterial vascular performance in aging.

Ho-Pham et al. (2010, Vietnam) studied the association of lean and fat mass with BMD in 210 postmenopausal women aged between 50 and 85 y. They found that greater amounts of both lean and fat mass correlated with higher BMD values at the lumbar spine, femoral neck, and whole body. Using multiple linear regression analysis, lean mass was found to be the leading predictor of BMD in all locations. It was calculated that regardless of age, each 5 kg increase in lean mass was associated with a 0.034, 0.031, and 0.036 g/cm2 increase in BMD at the lumbar spine, femoral neck, and whole body, respectively. While a 5 kg increase in fat mass was associated with a 0.022, 0.017, and 0.001 g/cm2 increase in BMD of lumbar spine, femoral neck, and whole body, respectively. After accounting for the effect of lean mass, the association of fat mass with whole-body BMD was not statistically significant ($p = 0.90$).

Namwongprom et al. (2013, Thailand) examined the association between body composition and BMD of the lumbar spine, hip, and femoral neck measured by DEXA in 1579 healthy women aged 40-90 y. Of the subjects, 1448 (91.7%) were postmenopausal and 131 (8.3%) were perimenopausal. In postmenopausal women, after adjusting for the influence of age, height and duration of menopause, both fat mass and lean mass were found to correlate positively with BMD and were analyzed

as independent factors. For BMD all skeletal sites, except for whole body, the effect of lean mass was significantly greater relative to that of fat mass. Regarding perimenopausal women, only lean mass had a positive effect on BMD for all sites except the lumbar spine. The positive correlations found between body composition and BMD in the study population showed differences depending on the study area and onset of menopause. The correlation between lean mass and BMD in different skeletal zones in postmenopausal women ranged between 0.40 and 0.55 and was higher compared to the correlation of fat mass (0.18 - 0.42). The most pronounced effect of both lean and fat mass was found for the BMP of the lumbar vertebrae, which are composed mainly of trabecular bone, followed by the femur and femoral neck, which are a combination of trabecular and cortical bone. Concerning the whole body (cortical bone dominated), lean mass had a positive effect, whereas a significant negative association was found for fat mass. The results obtained regarding the different effects of lean and fat mass on different parts of the skeleton can be related to different effects on trabecular and cortical bone. In perimenopausal women, lean mass showed a positive effect on femoral, femoral neck and whole body BMD, but not on lumbar spine. These results indicate an effect of lean mass predominantly on cortical bone and little effect on trabecular bone in perimenopausal women. While lean mass showed a positive effect on BMD in postmenopausal and perimenopausal women, fat mass had a positive effect only in postmenopausal women, probably due to production of estrogens in adipose tissue in this category of cases, whereas before menopause the main source of estrogens was the ovaries. The results in the present study support the observations of Namwongprom et al. regarding the leading effect of lean mass on femoral and cortical BMD, respectively.

There are observations that lean mass, not fat mass, is the main predictor of peak BMD in both sexes and in individuals aged 20 to 30 years. Significantly, good physical activity may contribute to higher peak bone mass values in young individuals (Nguyen et al., 2020). Muscle mass and function play a significant role in the development of osteoporosis. The decrease in muscle mass with advancing age and the presence of

common aetiological factors between osteoporosis and sarcopenia also define the hypothesis of a common syndrome called "osteosarcopenia" (Fagundes Belchior et al., 2020).

Mechanical signals given during muscle activity are thought to control bone mass, structure and strength. Immobilization is associated with bone loss, whereas physical activity leads to an improvement in bone density (Schultheis, 1991). The main approaches to maintaining muscle mass and function are physical activity and nutrition. Physical exercise improves muscle function and in some cases increases muscle mass. Improved function may be related not only to the contractile abilities of the muscles but also to the metabolism of muscle tissue, including improved insulin sensitivity. Physical exercise has been found to be more effective in preventing muscle loss than in restoring it. In this regard, in patients with sarcopenia, physical exercise can successfully improve function, but with advancing age, regaining lost muscle mass is a difficult task. Recovery of muscle strength and function is less effective in the elderly compared to the young population when the same regimen is followed. In this regard, measures to prevent the development of sarcopenia are essential and are more effective than treating sarcopenia that has already occurred. Progressive loss of muscle mass begins in middle age and the rate of loss increases with advancing age. Therefore, targeted interventions are needed to slow and stop the negative effects of sarcopenia with advancing age (Wolfe, 2006).

Considering the leading role of muscle mass in bone health, as well as the frequent association of osteoporosis with sarcopenia, an analysis of the *role of environmental factors on body composition, the adverse changes in body composition with age, and the possibilities for prevention of these pathological abnormalities is essential*.

To maintain and optimize the condition of bones and muscles in the elderly, it is necessary to build an individualized optimal diet and exercise regimen, as well as adequate nutrition with intake of vitamin D, calcium and protein. In terms of choice of type of physical activity, regular walking has little or no effect on muscle and bone

tissue. Good results regarding improvement of muscle mass and strength are given by the application of exercises against progressively increasing resistance, but these workouts give mixed results in terms of muscle function and tendency to falls (Daly, 2017).

4. Bone mass in individuals with bone mineral density of the lumbar spine and femoral neck corresponding to a T-score ≤ and > /-2.5/

BMD of the lumbar spine, femoral neck, and both hips was significantly lower in individuals with a lumbar spine T-score ≤ /-2.5/ compared with cases with a T-score > /-2.5/. On the other hand, in individuals with a femoral neck T-score ≤ /-2.5/, BMD was significantly lower at the femoral neck and both hips, but not at the lumbar spine. Considering the early reduction of BMD in the vertebral column (Boyanov M., 2005), the results suggest possible measurement errors.

In a Bulgarian population of 1070 women, Boyanov M. (2005) performed DEXA of the lumbar spine and femoral neck with the Hologic device. As a control group, 130 healthy premenopausal women aged 25 - 39 years were also examined to assess peak bone mass. There was a decline in BMD with age, which was more pronounced in the first 5 years after the onset of menopause. Significantly slower bone loss was observed in the proximal femur compared with the vertebral bodies. A BMD value of 0.075g/cm^2 was found to be reached around the age of 75 years.

Moayyeri et al. (2005, Iran) conducted a study in 4229 patients (3848 females, mean age 53.4 ± 11.8 years, and 340 males, mean age 49.7 ± 16.3 years) on the concordance or discrepancy in the diagnosis of osteoporosis based on the DEXA results of the two reference areas, lumbar spine and hip. T-score concordance in both locations was found in 58.3% of cases. Minimal diagnostic mismatch was defined as cases in which the T-score values of lumbar spine and femur were from adjacent WHO diagnostic categories (osteoporosis and osteopenia or osteopenia and normal findings). When T-score values in one area indicated the presence of osteoporosis and in the other area normal findings, cases were defined as a significant discrepancy. Minimal

discrepancy in T-score values was found in 38.9% (n=1631) of cases and significant discrepancy in 2.7% (n=115). Of the patients with a significant diagnostic discrepancy, 94 patients were found to have normal femoral findings and osteoporosis of the lumbar spine, and the opposite was true in 21 patients with osteoporosis of the femur and normal lumbar spine findings. The combinations of findings in the group with minimal diagnostic discrepancy in descending order were: presence of lumbar spine osteopenia and normal femoral finding (n=713), lumbar spine osteoporosis and femoral osteopenia (n=554), normal lumbar spine finding and femoral osteopenia (n-255), and lumbar spine osteopenia combined with femoral osteoporosis (n=109). A greater discrepancy was observed in women, 42.2% versus 36.5% in men, $p = 0.042$. The mean age of patients with a discrepancy (54.8 years) was significantly higher compared to cases with a match (52.5 years, $p < 0.001$). Of the 3848 women studied, the number of cases with a T-score mismatch in both locations was significantly higher in postmenopausal women (951 of 2027) compared with premenopausal women (671 of 1821; $p < 0.001$). Late menopausal women (>50 years) had a higher incidence of diagnostic discrepancy, and those undergoing hormone replacement therapy had a lower incidence. Presence of obesity with a BMI > 30 kg/m^2 was found to be a risk factor for significant discrepancy in T-score values (Moayyeri et al., 2005).

The results of the present study and data from the literature suggest a possible discrepancy in the results of DEXA examination of the lumbar spine and femur. This could be due to inhomogeneous loss of BMD in different parts of the skeleton or to measurement errors related to the presence of degenerative changes in the spine (osteophytes, osteosclerosis, osteochondrosis), aortic calcifications. Differences in T-scores are also found when scanning the lumbar spine in anterior-posterior and lateral projection in the same patient. Metallic clothing items, coins not removed during the examination may also lead to variations in the results obtained (Moayyeri et al., 2005)).

In addition, osteoporotic fractures occur with significant frequency in patients with osteopenia or even normal BMD. The possible presence of changes in bone microarchitectonics and bone quality, respectively, that cannot be assessed by DEXA

requires caution in interpreting the results and assessing the risk of osteoporosis and osteoporotic fractures.

5. Android and gynoid fat and lean mass in individuals with T score < and ≥ /-1/

Comparison of data from regional body composition analysis in 14 anatomic regions (head, left and right upper extremity, left and right trunk, left and right lower extremity, ribs, pelvis, spine, android, and gynoid) in 16 women between subgroups with normal BMD values corresponding to T-scores ≥ /-1/ (n=10) and cases with T-scores < /-1.0/ (n=6), significantly higher values of total lean mass and regional lean mass were found in the android, gynoid, and trunk areas in those with a T-score ≥ /-1/, whereas the difference did not reach statistical significance for fat mass including the android area. These data support the leading role of lean mass and muscle mass, respectively, in maintaining normal BMD values. Comparison of the total amount of soft tissue (fat and lean mass) in the android and gynoid zones also showed no significant differences between individuals with different T-score values. It should be noted that the study sample was small and the mean body weight of the patients in the study group was 78 kg (range 47-114 kg).

Ma et al. (2022) examined the effect of android and gynoid adipose tissue in 2881 individuals (1245 men and 1636 women, mean age 49 years). They found a positive association of both android and gynoid adipose mass with BMD of the hip, femoral neck and lumbar spine in both sexes. The results were similar for adipose tissue with both localizations.

Fan et al. (2022, China) conducted a study on the association of fat distribution with BMD in 357 healthy postmenopausal women without obesity, aged between 60.2 and 86.7 y. They found a positive correlation between fat mass and BMD, which persisted after adjustment for the effect of lean mass. Concerning the ratio of android to gynoid adipose tissue, a negative effect on BMD was found for most of the analysed areas, including whole body, thigh, femoral neck, upper, lower limb and head. Given

these observations, it was concluded that controlling for the accumulation of abdominal adipose tissue would have a beneficial effect on postmenopausal BMD.

In this regard, an analysis in larger populations of obese patients is needed to assess the influence of android and gynoid adipose tissue on BMD, respectively the presence of differences in the influence of visceral and subcutaneous adipose tissue on bone function.

VI. CONCLUSIONS

1. Higher BMD values were observed in individuals with BMI>25 kg/m^2 , with mean body weight values in the study group of 74±16 kg and mean BMI values of 27.90±5.74 kg/m^2 . These data suggest that a higher BMI in non-obese patients is a protective factor against the development of osteoporosis, but it should be borne in mind that anthropometric measurements do not provide information on body composition, respectively on the amount of fat and lean mass.

2. In the present study, a significantly lower lean mass was found in patients with T-scores ≤ /-2.5/ at the lumbar spine and femoral neck compared to cases with T-scores > /-2.5/.

3. In patients with T-score ≤ /-2.5/ on lumbar spine, significantly lower fat mass was also found, while when comparing cases with T-score below and above /-2.5/ on femoral neck, the difference did not reach statistical significance. These results confirm the protective effect of higher lean and fat mass in relation to the development of osteoporosis, with a likely leading role of lean mass and muscle mass, respectively.

4. There were differences in the effect of lean mass and fat mass on lumbar spine and hip, with a leading effect of lean mass on hip BMD. This result indicates possibly different effects of fat and lean mass on bones with different structures, respectively a predominant effect of lean mass on cortical bone.

5.The BMC of the lumbar spine, femoral neck and both hips was significantly lower in individuals with a lumbar spine T-score ≤ /-2.5/ compared to cases with a T-score > /-2.5/. In patients with a femoral neck T-score ≤ /-2.5/, BMC was significantly lower at the femoral neck and both hips but not at the lumbar spine. Given the early reduction of BMC in the vertebral column in practice, false-negative results should be considered when measuring BMD at the lumbar spine.

6. Regional analysis of body composition revealed no difference between the amount of soft tissue (fat and lean mass) in the android and gynoid zones in individuals

with different T-score values below and above /-1/.

7.The regional amount of lean mass in the android, gynoid, and trunk areas was higher in subjects with T-score ≥ /-1/, whereas for fat mass the difference did not reach statistical significance. These data support the leading role of lean mass and muscle mass, respectively, in maintaining normal BMD values.

VII. CONTRIBUTIONS

1. Higher BMD values were found in individuals with BMI > 25 kg/m^2, which is a confirmatory observation. Patients with high-grade obesity were not included in the present study, which should be considered in relation to the data on the negative impact of low-grade inflammation on bone structure and function in obesity.

2. This thesis is the first study in the country on the influence of body composition on BMD of lumbar spine and femoral neck in a Bulgarian patient population.

2.1. We found statistically significant higher values of fat mass and lean mass in individuals with T-score > /-2.5/ of lumbar spine compared to cases with T-score < /-2.5/.

2.2. Similarly, femoral neck T-scores > /-2.5/ were found to have higher values of fat mass and lean mass compared with individuals with T-scores < /-2.5/, but the difference reached statistical significance only for lean mass but not for fat mass. This result supports the likely leading role of lean mass with respect to BMD.

2.3. The established protective effect of higher lean and fat mass on the presence of osteoporosis, with a likely leading role for lean mass, is of key practical importance given the high incidence of the combination of osteoporosis and sarcopenia with advancing age and the trend towards an ageing population.

3. The results of this dissertation are the basis for the popularization of whole-body scanning and body composition determination in our country, which is currently of limited use despite its high value in the diagnostic aspect, as well as for the definition of a personalized therapeutic approach.

VIII. SCIENTIFIC PUBLICATIONS AND REPORTS RELATED TO THE THESIS

1. **Publications in refereed journals:**

   1. Nikolov M., Lambova S., Nikolov N. Association between body composition and bone mineral density assessed by whole body Dual-Energy X-ray absorptiometry. Rheumatology (Bulgaria), 2022, 30(3):9-14; ISSN: 1310-0505; Scopus

2. **Publications in non-refereed journals:**

   2.1. Kirilov N., Todorov S., Nikolov N., Nikolov M. Evaluation of care for secondary prevention of osteoporosis in patients with previous fractures. Trends in Health Care in the 21st Century. 26-27 March 2020. 27-27-27, 2012. Seventh national student conference with international participation. MU Pleven 2020, pp. 128-132; ISBN: 978-954-756-250-9

   2.2. Nikolov, M., Lambova, S. Osteoporosis and sarcopenia in rheumatological practice. Medical Magazine, 2023, April, pp. 68-72; ISSN: 1314-9709

3. **Participation in scientific forums abroad and in Bulgaria:**

   3.1. Nikolov M, Nikolov N. Assessment of the influence of lean mass with body composition by dual-energy X-ray absorptiometry on the bone mineral density. Ann Rheum Dis 2020;79:1756; EULAR 2020.

   3.2. Nikolov M, Nikolov N, Kirilova E, Kirilov N. Assessment of bone mass in postmenopausal women. Osteoporos Int 2020; 31 (Suppl 1):S436-7; WCO-IOF-ESCEO 2020.

   3.3. Nikolov M, Nikolov N. Assessment of muscle mass in postmenopausal women. Osteoporos Int 2020; 31 (Suppl 1):S440-1; WCO-IOF-ESCEO 2020.

3.4. Nikolov M., Lambova S., Nikolov N. Bone mineral density in subjects with normal body mass index and overweight. National Conference on Rheumatology 29.09. - 02.10.2022, Golden Sands.

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