ASSOCIATION BETWEEN BODY COMPOSITION AND BONE MINERAL DENSITY ASSESSED BY WHOLE BODY DUAL-ENERGY X-RAY ABSORPTIOMETRY

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Abstract. Despite the observation that higher body weight has protective effect against the development of osteoporosis, accumulating evidence suggests the presence of negative impact of obesity on bone function associated with the low-grade inflammation and production of proinflammatory cytokines from dysfunctional adipose tissue in obese individuals. These data stimulate the interest and suggest need for clarifying studies about the association between the body composition and bone mineral density. The aim of the current study was to evaluate the association between body mass index (BMI), body composition (fat mass and lean body mass) and the bone mineral density of the lumbar spine and femoral neck assessed by whole body scan using DXA (Dual-energy X-ray absorptiometry). A retrospective study was performed with analysis of patient data who have undergone whole body scan in Medical Center “Avis Medica” Pleven, Lunar Prodigy device. The values of T-score of the lumbar spine and femoral neck and their associations with body composition and BMI were analyzed. 111 women at a mean age of 59 ± 8 years were included in the study. In the patients with T-score values ≤ -2.5/ of the lumbar spine and femoral neck BMI was significantly lower. In the group of patients with T-score values of the lumbar spine ≤ -2.5/ (n = 27), significantly lower fat mass was found (2239.90 ± 607.63 grams) in comparison with the cases with T-score > -2.5/ (n = 84) (fat mass 2510.41 ± 570.68 grams; p = 0.037). The lean body mass in the patients with T-score ≤ -2.5/ of the lumbar spine (4025.30 ± 862.58 grams) was also significantly lower vs the group with T-score > -2.5/ (4760.09 ± 607.63 grams; p = 0.000). A significant difference of body lean mass was also found between the groups with different T-score of femoral neck (4110.60 ± 832.01 grams in patients with T-score of femoral neck ≤ 2.5, n = 15; 4802.01 ± 862.87 grams in those with T-score > 2.5, n = 96, p = 0.004). Regarding the fat mass and fat percentage in the groups with different T-score of the femoral neck, they were lower in the patients with osteoporosis with T-score < -2.5/, but the difference reached statistical significance only for the fat percentage (31 vs 38%, p = 0.006) but not for the fat mass (p = 0.081). The results of the current study confirm the protective effect of the higher lean and fat mass against the development of osteoporosis with possible leading role of the lean mass.

Key words: body composition, fat mass, lean mass, body mass index, bone mineral density

INTRODUCTION

The complex interaction between the fat and bone tissue has been confirmed. It is mediated by the action of adipokines, estrogens, bone-derived metabolic factors. This interplay influences bone remodeling, adipogenesis, glucose homeostasis and muscle function. Despite the observation that higher body weight has protective effect against the development of osteoporosis, accumulating evidence suggests the presence of negative impact of obesity on bone function associated with the low-grade inflammation and production of proinflammatory cytokines from dysfunctional adipose tissue in obese individuals. Other possible mechanism of negative effect is increased adipogenesis in the bone marrow that decreases bone mass in obesity [1].

In addition, important factors that determine the risk of development of osteoporosis are muscle function and body composition. It should be considered that disuse, nutritional deficiencies, chronic diseases, inflammation, insulin resistance, endocrine changes lead to accelerated age-related loss of muscle mass and strength i.e., sarcopenia. Moreover, it has been found that muscle and bone tissue share some common genetic, nutritional, lifestyle, and hormonal determinants [2] which underlines the necessity to evaluate changes in the body composition in patients with osteoporosis. There are different approaches to define the compartments of body composition, i.e., fat mass, fat-free mass, lean bone mass. Fat-free mass differs from lean body mass as the fat in cell membranes is excluded from fat-free
mass but is a part of the lean body mass due to the anatomical proximity of this small amount of fat to lean tissue [3]. Lean body mass measures skeletal muscle protein and contains body cell mass and the non-fatty intercellular connective tissue such as tendons, ligaments, basement membranes [3, 4]. Higher lean body mass and grip strength were positively associated with bone mineral density (BMD), while sarcopenia correlated with low BMD and osteoporosis [2].

Dual-energy X-ray absorptiometry (DXA) is a low-cost, rapid, widely used method for assessment of body composition. Whole-body DXA provides information about fat, bone, lean (bone-free) mass for each limb and the trunk [5]. DXA has been also validated for assessment of visceral adipose tissue (VAT). The accuracy of DXA for measurement of VAT was proved in comparison with the results of MRI in a large multiethnic cohort with 2689 participants [6]. It is currently the most commonly used technique for measurement of BMD [5].

Overweight and obesity as well as osteoporosis are diseases of social importance, whose prevalence is increasing worldwide. The fat and bone tissue have complex interaction. Muscle function is also of crucial importance for the bone metabolism. Despite the protective effect of high body mass index (BMI) on BMD, there are also observations about negative impact of obesity on bone metabolism. These data stimulate the interest and suggest need for clarifying studies about the association between body composition and BMD.

The aim of the current study was to evaluate the association between body composition (fat mass and lean body mass) and BMD of the lumbar spine and femoral neck assessed by whole body scan using DXA. The association between BMI and BMD of the lumbar spine and femoral neck was also analyzed.

Materials and methods
A retrospective study was performed with analysis of patient data who have undergone whole body scan in Medical Center “Avis Medica” Pleven, Lunar Prodigy device. Based on the scanning of the lumbar spine and both thighs, the content of the fat mass and lean body mass could be calculated. The values of T-score of the lumbar spine as well as the mean values of T-score of both femoral necks and their association with body composition (fat mass and lean body mass) and BMI were analyzed.

Results
111 women at a mean age of 59 ± 8 years were included in the study. The associations between BMI, body composition and BMD were evaluated.

Association between BMI and BMD
In the patients with T-score values ≤ -2.5/ of the lumbar spine (n = 27) BMI was significantly lower (25.14 ± 4.08 kg/m$^2$) as compared with those with T-score > -2.5/ (n = 84), (BMI 28.79 ± 5.93 kg/m$^2$; p = 0.004). Analogous results were obtained regarding osteodensitometry of the femoral neck. BMI in patients with mean T-score ≤ -2.5/ of both femoral necks (n = 15) was 24.93 ± 5.11 kg/m$^2$, and 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$^2$, the BMD of the lumbar spine (1.08 ± 0.21 g/cm$^2$) and femoral necks (0.90 ± 0.17 g/cm$^2$) was significantly higher as compared with the patients with BMI ≤ 25 kg/m$^2$ for both localizations (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).

Association between body composition and BMD
In the group of patients with T-score values of the lumbar spine ≤ -2.5/ (n = 27), significantly lower fat mass was found (2239.90 ± 607.63 grams) in comparison with the cases with T-score > -2.5/ (n = 84) (fat mass 2510.41 ± 570.68 grams; p = 0.037). The lean body mass in the patients with T-score ≤ -2.5/ of the lumbar spine (4025.30 ± 862.58 grams) was also significantly lower vs the group with T-score > -2.5/ (4760.09 ± 607.63 grams; p = 0.000). A significant difference of body lean mass was also found between the groups with different T-score of femoral neck (4110.60 ± 832.01 grams in patients with T-score of femoral neck ≤ 2.5, n = 15; 4802.01 ± 862.87 grams in those with T-score > 2.5, n = 96, p = 0.004). Regarding the fat mass and fat percentage in the groups with different T-score of the femoral neck, they were lower in the patients with osteoporosis with T-score < -2.5/, but the difference reached statistical significance only for the fat percentage (31 vs 38%, p = 006) but not for the fat mass (p = 0.081).

Discussion
Association between BMI and BMD
In the current study, significantly lower BMI was found in patients with T-score values ≤ -2.5/ of both
lumbar spine and femoral neck. BMD values of the two reference sites were statistically significantly higher in overweight patients (BMI > 25 kg/m²). Shen et al. (2015) evaluated bone structure in 672 men using quantitative computed tomography and have found that in non-obese men with BMI < 30 kg/m², the increasing in BMI was associated with higher volumetric BMD and percent cortical volume. However, in obese men, there was no further increase in these parameters [7].

It is well-known that adipose tissues in obese postmenopausal women could be a significant source of estrogen that may halt bone mineral loss [8, 9]. Androgen aromatization in adipocytes increases extragonadal production of estrogen and is suggested to be among major causes for higher BMD in overweight postmenopausal women together with mechanical strain on their bones [10]. The interaction between fat and bone tissue is complex and requires further research. Adipose tissue is a source of different adipokines (leptin, adiponectin, etc.), estrogen, proinflammatory cytokines (interleukin-6/IL-6, tumour necrosis factor-α/TNF-α), acute phase reactants such as C-reactive protein (CRP), which modulate bone function. Fat distribution, i.e., visceral and subcutaneous adipose tissue may also affect the bone metabolism [11]. It has been also hypothesized that obesity could have a negative impact on bone health. It is known that both adipocytes and osteoblasts are derived from a common multipotent mesenchymal stem cell. In this regard, increased adipocyte differentiation may be associated with decreased osteoblast differentiation and bone formation respectively. Another hypothesis that suggests presence of negative effect of obesity on bone health is associated with the low-grade inflammation in obese individuals that promotes increased osteoclast activity. Dysfunctional fat tissue acts as an active endocrine organ [12, 13]. IL-6 and TNF-α have a potential to stimulate osteoclasts activity through RANKL/RANK/osteoprotegerin pathway. Obesity is characterized with increased serum leptin level that might have diverse including negative impact on bone metabolism. Adiponectin inhibits osteoclastogenesis and its level is decreased in obese subjects. As an additional consideration, high-fat intake has been suggested to decrease intestinal calcium absorption and calcium availability. Moreover, it is suggested that obesity is associated with osteoarthritis that is mediated through different mechanisms apart from the mechanical overload, which supports the influence of systemic factors on musculoskeletal system [12].

Important factor that might be related to interindividual differences in bone function in obese subjects could be fat distribution. Abdominal obesity is associated with higher cardiovascular risk and development of insulin resistance in comparison with gluteofemoral obesity. Estrogen promote the accumulation of gluteofemoral fat, while loss of estrogen increases the abdominal fat deposition. Thus, presence of abdominal obesity should be considered also in patients with BMI < 30 kg/m² [14]. It has been demonstrated that many proinflammatory cytokines are predominantly secreted from the metabolic active VAT in abdominal obesity as compared with subcutaneous fat tissue [15]. Association between subcutaneous and visceral abdominal fat and bony characteristics, i.e., femoral cross-sectional area and cortical bone area assessed via computed tomography, has been analyzed in 100 healthy women at the age between 15 and 25 years. Positive associations were observed between subcutaneous fat tissue and bony parameters of appendicular skeleton, while for visceral adiposity, none of the relations were statistically significant which suggests the diverse impact of different fat tissue compartments on bone structure and function [16]. Analysis of fat tissue distribution (visceral vs subcutaneous fat) in the abdominal region and its correlation with trabecular BMD of the lumbar spine in 320 Chinese women at the age between 19 and 86 years has demonstrated negative correlation between VAT volume and trabecular BMD in women younger than 55 years, while subcutaneous fat tissue volume had no correlation. However, no significant association between both fat tissue compartments was present in the age group ≥ 55 years [17].

In addition, BMI does not differentiate weight variations based on the fat and lean mass, age-related body composition changes associated with decreased lean tissue, decreased height and increased fat tissue in elderly. The age-related decline in height is related to decrease in the height of intervertebral disks and vertebrae. Decline in the lean mass starts in the third decade of life. The association between the decreased lean body mass that starts and increase in fat deposition in elderly is termed “sarcopenic obesity”. Thus, elderly subjects with normal values of BMI may have excess of fat tissue and low muscle mass [18].

There are diverse data about osteoporotic fracture rate including increased rate at some skeletal sites such as upper arm [10]. Among 4642 postmenopausal non-Hispanic whites, those with highest BMI reported more falls in the last 12 months and
had lower measures of physical activity and function. Incidence of hip fractures and all central body fractures (pelvis, spine, ribs, and shoulder girdle) declined with BMI, while lower extremity fractures distal to the hip (femur shaft and distal) increased. This has been suggested to be associated with greater soft tissue padding at central sites in obesity. It has been observed that femur BMD increased parallel to BMI and its values correlate with lean, but not with the fat mass and whole body mass. However, femur BMD decreased relative to body weight in higher BMI categories possibly due to smaller fraction of the lean mass in obesity. The authors did not find variations of upper extremity fractures associated with BMI [19]. Increased body fat mass index has been associated with spinal fractures in women that has been suggested to be related to metabolically active abdominal adipose tissue [11]. Interestingly, the association between fat tissue distribution with BMD and vertebral fractures was also evaluated in severe obesity in 58 pre- and postmenopausal women with BMI higher than 40 kg/m². In postmenopausal women, total subcutaneous adipose tissue correlated negatively with BMD of total femur. It has been concluded that both visceral and subcutaneous fat may have negative impact on bone health in the pre- and postmenopausal women. High prevalence of vertebral fractures was registered in postmenopausal women (55%), but they were also observed in 32% of premenopausal women. Severe obesity has been suggested to increase the risk of vertebral fractures including in young women. Differences in lean or fat mass were not observed in cases with or without vertebral fractures [20]. In a study that included 342 men and women at a mean age of 62.5 years had higher rate of vertebral fractures vs cases with normal weight (Rudman et al., 2018). The authors have observed that BMI correlated negatively with BMD of femoral neck and lumbar spine, i.e., lumbar spine and femoral neck BMD were significantly lower in overweight and obese men and women compared with those of normal weight [21]. In a meta-analysis of Johansson et al. (2014) the link between BMI and future fracture risk at different skeletal sites was assessed based on the data from 25 prospective studies that included 398,610 women at the age between 20 and 105 years. Most of the osteoporotic (81%) and hip fractures (87%) were in non-obese women. It has been concluded that low BMI is a risk factor for osteoporotic fracture including hip fracture. However, it has been found that low BMI is a protective factor for fractures of tibia and fibula. Fractures of upper arm (humerus and elbow) were more common among women with high BMI, while obesity was protective for osteoporotic fracture as a whole and for hip and distal forearm fracture [22]. The complex pathogenesis of osteoporosis requires future research about the impact of the adipose tissue content and its distribution on the BMD, bone structure, the risk of development of osteoporotic bone transformation and osteoporotic fracture risk.

**Association between body composition and BMD**

In the current study, the lean body mass in the patients with T-score ≤ -2.5/ of the lumbar spine and femoral neck was significantly lower as compared with the group with T-score > -2.5/. Significantly lower fat mass was also found in patients with T-score ≤ -2.5/ of the lumbar spine, while in cases with T-score < -2.5/ of the femoral neck, the fat mass and fat percentage were also lower, but the difference reached statistical significance only for the fat percentage and not for the fat mass. Disadvantage of the current study is the lack of data about concomitant disease and drugs associated with secondary osteoporosis, presence of osteoporotic fractures that would expand the opportunities for precise conclusions.

There are reports that increasing predicted lean body mass index and appendicular skeletal muscle index (calculated using anthropometric equations) were significantly associated with a decreased risk of total osteoporotic fractures in men and women. It has been observed that muscle mass is more important factor than fat mass in preventing future osteoporotic fractures [11]. Mechanical signals of the muscular activity are suggested to control bone mass, architecture and strength. Inactivity is associated with bone loss, while exercises lead to improvement of bone density [23].

According to the official position of International Society for Clinical Densitometry (ISCD), among indications for whole DXA scan for assessment of body composition with regional analysis are obese patients undergoing bariatric surgery or other type of treatment, i.e., medical, diet, or weight loss regimens with anticipated large weight loss. In the cases, in whom weight loss exceeds approximately 10%, the fat and lean mass changes should be evaluated. Another major indication for total DXA body scan according to the ISCD recommendations is muscle weakness or poor physical functioning. DXA assessment of lean mass is suggested to be a highly reproducible method and should be used in the diagnostic work-up when sarcopenia is suspected together with functional testing (grip strength, quadriceps strength, gait speed mea-
measurement, get up and go test). Due to the lower specificity of functional tests, which may be pathologically changed also in other diseases, low muscle mass should be confirmed using DXA [24, 25].

A number of reports assess which compartment is more important as a determinant of BMD, i.e., lean mass or fat mass [26]. Ho-Pham et al. (2014) analyzed the correlation between lean mass, fat mass and BMD in 44 studies that included 20,226 patients (4,966 men and 15,260 women) at the age between 18 and 92 years. The correlation between lean mass and femoral neck BMD was significantly higher (0.39) as compared with the correlation with the fat mass (0.28) [26]. Moreover, it has been observed that lean mass and not the fat mass is the main predictor of peak BMD for both men and women at the age between 20 and 30 years. Thus, good physical activity may contribute to achievement of adequate peak bone mass in young population [27]. In 244 girls at the age between 9 and 12, lean mass was shown to be the main determinant of bone strength for appendicular skeletal sites, while fat mass was associated with bone strength in the weight-bearing skeleton but does not influence the bone strength in non-weight-bearing locations and even may potentially be detrimental. Fat mass was negatively associated with cortical thickness of the radius [28].

Analysis of the effect of body composition has led to the conclusion that lean mass is definitely beneficial on BMD, whereas the effect of fat mass is inconsistent. Bone strength is primarily improved due to the effect of muscle forces and not of the static loads of higher body weight [29]. A negative effect of increasing fat mass on BMD and bone quality has been also observed. Fracture risk in overweight/obese women and men might be increased after adjustment for higher BMD [21, 29].

Due to presence of common etiological factors for the development of osteoporosis and sarcopenia, some authors suggest the term “osteosarcopenia” for a new syndrome, in which these two pathological conditions occur together. Genetic factors play a role for the occurrence of both osteoporosis and sarcopenia. Moreover, excess alcohol intake and cigarette smoking have a negative impact, while balanced diet has a positive effect on both bone and muscle tissue. Physical exercises are of crucial importance for maintenance bone and muscle structure and function, while prolonged immobilization and reduced physical activity in elderly are associated with risk of simultaneous bone and muscle tissue loss. Good nutrition with adequate protein and vitamin D intake is another important preventing factor for both osteoporosis and sarcopenia. Inadequate protein intake has been documented in elderly and appropriate counseling is important in prophylaxis of both pathological conditions [30].

It should be considered that fracture risk is also related to other factors apart from BMI and body composition, i.e., early menopause, smoking, excessive alcohol consumption, vitamin D insufficiency, endocrine disorders (diabetes mellitus, thyroid pathology), glucocorticoid use, immobility, etc. [31, 32]. As an example, it has been observed that diabetes is a risk factor for osteoporotic, including hip fractures despite higher femoral neck T-scores in patients with diabetes vs nondiabetics. It has been hypothesized that increased fracture risk could be related to changes in bone structure in diabetic patients [33]. In this regard, determination of the individual fracture risk requires personalized approach with assessment of BMI, body composition, accompanying diseases and other potential determining factors.

**CONCLUSION**

In the current study, the lean body mass in patients with values of the T-score ≤ /-2.5/ of the lumbar spine and femoral neck were significantly lower as compared with the cases with T-score >/-2.5/. A significantly lower amount of fat tissue was found in patients with T-score ≤ /-2.5/ of the lumbar spine. However, the difference between the fat mass in the groups with T-score below or above /-2.5/ of the femoral neck did not reach statistical significance. The results suggest the protective effect of higher lean and fat mass against the development of osteoporosis with possible leading role of the lean mass. In this regard, maintenance of the adequate structure and function of the muscle tissue considering the importance of healthy lifestyle, protein intake and physical activity is also related to maintenance of bone structure and function. Regarding the role of the fat tissue, the prevailing opinion is that higher BMI has protective effects on BMD. However, in obese patients with higher BMI probably this protective effect is diminished and even there are observations for worsening of bone structure and function and increased fracture risk in severe obesity. Negative effect on bone metabolism of metabolically active VAT has been also suggested and these questions require assessment in future studies.
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