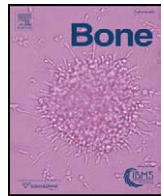




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Determinants of bone mineral density in obese premenopausal women[☆]

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ABSTRACT

Despite being a risk factor for cardiovascular disease and diabetes mellitus, obesity has been thought to protect against osteoporosis. However, recent studies have demonstrated a differential impact of specific fat compartments on bone mineral density (BMD) with visceral adipose tissue (VAT) having potential detrimental effects on BMD. Visceral obesity is also associated with dysregulation of the GH/IGF-1 axis, an important regulator of bone homeostasis. The purpose of our study was to evaluate the differential effects of abdominal fat depots and muscle, vitamin D, and hormonal determinants, including insulin-like growth factor-1 (IGF-1), testosterone, and estradiol, on trabecular BMD of the lumbar spine. We studied 68 healthy obese premenopausal women (mean BMI, 36.7 ± 4.2 kg/m²). Quantitative computed tomography (QCT) was used to assess body composition and lumbar trabecular BMD. There was an inverse association between BMD and VAT, independent of age and BMI ($p = 0.003$). IGF-1 correlated positively with BMD and negatively with VAT and, in stepwise multivariate regression modeling, was the strongest predictor of BMD and procollagen type 1 amino-terminal propeptide (P1NP). Thigh muscle cross sectional area (CSA) and thigh muscle density were also associated with BMD ($p < 0.05$), but 25-hydroxyvitamin D [25(OH)D], testosterone, free testosterone, and estradiol levels were not. 25(OH)D was associated inversely with BMI, total, and subcutaneous abdominal adipose tissue ($p < 0.05$). These findings support the hypothesis that VAT exerts detrimental effects, whereas muscle mass exerts positive effects on BMD in premenopausal obese women. Moreover, our findings suggest that IGF-1 may be a mediator of the deleterious effects of VAT on bone health through effects on bone formation.

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Introduction

Obesity is a risk factor for cardiovascular and metabolic disease. However, it has been thought that obesity protects against bone loss via mechanical loading and effects of hormones secreted or regulated by adipocytes [1–3]. Recent studies have suggested an inverse association between visceral adipose tissue (VAT) and bone mineral density (BMD) [4–6], whereas another study has demonstrated a potential protective effect of VAT on vertebral fractures in patients with diabetes mellitus [7]. Several studies have suggested that lean mass is the strongest predictor of BMD in premenopausal women [8–10], stronger than estrogen, testosterone, or progesterone [9]. Therefore, further studies are needed to determine the effects of body composition on

BMD in obese women and to investigate potential mechanisms of these effects.

The growth hormone (GH)/insulin-like growth factor-1 (IGF-1) axis is a major determinant of BMD [11–14] and is dysregulated in women in proportion to their degree of visceral adiposity [15,16]. In addition, obese women have been found to have lower rates of bone formation, as measured by type I collagen, suggesting that increased body fat suppresses new collagen formation [17]. We studied the association between BMD and IGF-1 and procollagen type 1 amino-terminal propeptide (P1NP) in obese premenopausal women to investigate the hypothesis that IGF-1 may be a mediator of effects of VAT on bone formation and bone density.

The purpose of our study was to investigate hormonal and body composition determinants of BMD in healthy obese premenopausal women. Our goal was to evaluate the effects of different abdominal fat depots, thigh muscle area and density, using quantitative computed tomography (QCT), and hormonal determinants, such as IGF-1, P1NP, 25-hydroxyvitamin D [25(OH)D], testosterone, and estradiol, on trabecular BMD of the lumbar spine using QCT. We specifically hypothesized that higher degrees of VAT would be associated with lower bone density in association with lower P1NP and IGF-1 levels in

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