Thyroid Dysfunction Does Not Affect the Bone Mineral Density in Postmenopausal Women

Postmenapozal Kadınlarda Tiroid Disfonksiyonu Kemik Mineral Yoğunluğunu Etkilememektedir

Tiroid Disfonksiyonunun Kemik Mineral Yoğunluğuna Etkisi / The Effect of Thyroid Disfunction on the Bone Mineral Density

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Özet

Giriş: Postmenapozal kadınlarda tiroid fonksiyon bozukluğu durumunda kemik mineral yoğunluğunun (KMY) etkilenip etkilenmediğini araştırmaktır. Gereç ve Yöntem: Çalışmaya randomize seçilmiş, en az 1 yıldır postmenapozal dönemde olan 2006 - 2008 tarihleri arasında başvurmuş 261 olgu dahil edildi. Olguların tiroid stimülan hormon (TSH), triiyodotironin (serbest T3), tiroksin (serbest T4) ve tiroid otoantikorları ölçümleri yapıldı. Tiroid fonksiyon bozukluğu olanlar; hipertiroidi, hipotiroidi ve otoimmün tiroidit olarak gruplandırılırken, tiroid fonksiyon bozukluğu olmayanlar kontrol grubu olarak kabul edildi. Kemik Mineral Yoğunluğu (KMY) ; DEXA yöntemi kullanılarak Lomber 1-4 vertebra ve femur boynu bölgelerinde ölçüldü. Bulgular: Tiroid disfonksiyonu olan grup ve kontrol grupları karşılaştırıldığında; L1-L4 T-skoru hipotiroidi olan 56 (21.5%) olguda -1.26 ±1.25, hipertiroidi olan 42 (16.1%) olguda -1.46 ±1.36, otoimmun tiroidit saptanan 37 (14.2%) olguda ise -1.51 ±1.22 olarak saptandı. Kontrol grubunda olan 126 (olguda 48.3%) L 1-4 T- skoru -1.28 ±1.20 idi. Femur boynu T-skoru hipotiroidi olan 56 olguda -0.31 ±1.15, hipertiroidi olan 42 olguda -0.80 ±1.41, otoimmun tiroidit saptanan 37 olguda ise -0.60 ±1.19 olarak saptandı. Kontrol grubunda olan 126 olguda ise femur boynu T skoru-0.55 ±1.08 olarak saptandı. Kontrol grubu ile hipotroidi, hipertroidi ve otoimmün troidit grupları karşılaştırıldığında ayrıca kontrol gurubu ile çalışma grupları kendi aralarında karşılaştırıldığında hem L 1-4 T-skoru hem de femur boynu T-skoru arasında anlamlı bir fark izlenmedi. Tartışma: Bu çalışmada postmenopozal kadınlarda tiroid fonksiyon bozukluklarının tipine de bağlı olmaksızın KMY üzerinde etkisi olmadığı saptandı.Sonuçlar tiroid disfonksiyonun postmenopozal kadınlarda osteoporoz gelişimine etkisinin olmadığını bunun muhtemel nedeninin de tiroid hormonlarının etkisini maskeleyen başka bir takım mekanizmalar olduğunu düşündürmektedir.

Anahtar Kelimeler

Tiroid Disfonksiyonu; Kemik Mineral Yoğunluğu; Postmenopozal

Abstract

Aim: To investigate the relationship between bone mineral density (BMD) and thyroid dysfunction in postmenopausal women. Material and Method: A total of 261 postmenopausal women, who were examined between 2006 and 2008, were included in this prospective cohort study. Levels of thyroid stimulating hormone (TSH), free T3 (triiodothyronine), free T4 (tiroxin), and thyroid antibodies (anti-thyroglobulin antibody -antiTG Ab; anti-thyroid peroxidase antibody - antiTPO Ab) were measured in all subjects. The subjects were classified into four groups: hyperthyroidism, hypothyroidism, autoimmune thyroiditis, and euthyroid(control). Bone mineral densities (BMDs) from the lumbar 1–4 (L 1–4) vertebrae and the femoral neck regions of interest were measured using the dual energy x-ray absorptiometry (DEXA) method and used to yield T-score values which were compared between groups. Results: The mean L1 – 4 T-score was 1.26 ± 1.25 in 56 cases (21.5%) with hypothyroidism ; -1.46 ± 1.36 in 42 (16.1%) cases with hyperthyroidism and -1.51 ± 1.22 in 37 cases (14.2%) with autoimmune thyroiditis . The mean L1 – 4 T-score of the control group that consisted of 126 (48.3%) cases was -1.28 ± 1.20. The mean femoral neck T-score was -0.31 ±1.15 in hypothyroid group; -0.80 ±1.41 in hyperthyroid group and -0.60 ±1.19 in cases with autoimmune thyroiditis . The mean femoral neck T-score of the control group was -0.55 ±1.08. When the T-scores of the entire L1 – 4 region and those of the femoral neck were compared, the values were not significantly different between the four patient groups (p = 0.680 and p = 0.258, respectively). Discussion: The present study indicated that thyroid dysfunction does not significantly affect BMD in postmenopausal women with hyperthyroidism, hypothyroidism, or autoimmune thyroiditis. This result suggests that thyroid dysfunctions do not have a significant role in the development of osteoporosis during the postmenopausal period, perhaps because there may be other mechanisms at work that blunt or mask the effects of thyroid hormones.

Keywords

Thyroid Dysfunction; Bone Mineral Density; Postmenopausal

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Introduction

Osteoporosis a condition characterized by reduction in bone mass with deformation in the bone microarchitecture ,is one of the most common disease in the general population and one of the most common diseases of any kind observed in the geriatric population. It is frequently encountered in clinics along with other chronic disorders, such as cardiac disease, diabetes, and cancer [1]. It is clear that osteoporosis and related bone fractures will be a serious community health care problem in the coming years with the expected extended average lifespan. It is known that thyroid hormone is necessary for normal bone growth and maturation, but the relevant mechanism for thyroid hormone regulation of bone metabolism is not well understood [2]. The hypothalamic-pituitary-thyroid axis, which maintains normal euthyroid status, is a key homeostatic regulator of skeletal development that may determine fracture risk [3,4].

However, studies examining whether there is a relationship between thyroid function and osteoporosis and fracture risk have had conflicting results .

In this study, our aim was to investigate the relationship between thyroid hormone dysfunction and bone mineral density (BMD) in postmenopausal patients. Because the preclinical period of osteoporosis is without bone fracture or any other clinical symptoms, the gold standard method for osteoporosis detection is measuring BMD. Thus, we used this method to demonstrate osteoporosis in our study.

Material and Method

This prospective cohort study was conducted at an education and research hospital between the years 2008 – 2011. The study was approved by the Local Ethics Committee. A total of 261 women were enrolled consecutively in this study. The women were postmenopausal for ≥ 1 year , had not received hormone replacement therapy, had not received any treatments for osteoporosis/osteopenia (e.g. antiresorptive agents, calcium or vitamin D). They also had not received any drugs that affect bone metabolism, such as corticosteroids, or had any chronic disorders or history of illegal drug use. The patient's age, age of menopause onset, duration of menopause, menopause type, weight, and height were recorded. Each patient's body mass index (BMI) was calculated using the kg/m2 formula. The BMD in lumbar 1–4 (L1–4) vertebrae and the femoral neck regions were measured with the Hologic QDRV4500W device using dual energy x-ray absorptiometry (DEXA) method and the T-scores values from L1 – 4 and total femur were recorded.

The levels of thyroid stimulating hormone (TSH), free triiodothyronine (f-T3), free thyroxine (f-T4), and thyroid antibodies (anti-tiroglobulin antibody, antiTG Ab; anti-troidperoksidaz antibody, antiTPO Ab) of all subjects were measured. TSH, f-T3, and f-T4 were evaluated using chemiluminescence method. AntiTG Ab and antiTPO Ab levels were determined with a commercially available radioimmunoassay kit (Roche cobas e601 hormon analyzer). The subjects were diagnosed with newly developed thyroid dysfunction in accordance with reference values (TSH :0.27-4.2 , f-T3 :1.8-4.6 , f-T4 : 0.9-1.7 , antiTPO : 0-34 , antiTG : 0-115). The thyroid dysfunctions were classified as hyperthyroidism, hypothyroidism, or autoimmune thyroiditis. None of the patients had a previous thyroid dysfunction diagnosis or received prior therapy for thyroid dysfunction. Those without thyroid dysfunction were placed in the control group.

For statistical analysis, SPSS statistics package program (version 11.5) was used. The distribution of variables was tested using the Shapiro-Wilk normality test. The normally distributed variables were analyzed using one-way analyses of variance (ANOVAs). The statistical values for continuous variables are reported as means ± standard deviations (SDs). Statistical significance was set at $p \leq 0.05$.

Results

The mean age of the all subjects was 56.0 ± 8.1 years (range, 44–71). The mean menopause onset age was 46.9 ± 5.8 years, and menopause duration was calculated as 9.2 ± 7.9 years. The mean L1–4 T-score was -1.34 ± 1.23 and the mean femoral neck T-score was -0.55 ± 1.17.

According to the subjects' thyroid hormone values and antibody levels, 56 women (21.5%) were diagnosed with hypothyroidism, 42 (16.1%) were determined to have hyperthyroidism, and 37 (14.2%) were diagnosed with autoimmune thyroiditis. The remaining 126 women (48.3%) were allocated to the control group (Table 1). The patients' mean age, age of menopause onset, duration of menopause, and BMI were similar between the four groups ($p > 0.05$) (Table 1). The BMD T-scores for the L1–4 region and the femoral neck did not differ significantly between the groups ($p = 0.680$ and $p = 0.258$, respectively) (Table 1).

Table 1. Mean (±SD) demographic and BMD values were similar between the groups ($p > 0.05$).

Parameter		Group				P value
		Euthyroid control	Hypo-thyroidism	Hyper-thyroidism	Autoimmune thyroiditis	
Age, y		54.9 ± 7.5	56.4 ± 8.8	58.5 ± 8.9	56.6 ± 7.9	0.074
Age of menopause, y		46.8 ± 6.4	47.2 ± 4.7	46.9 ± 5.4	46.7 ± 5.6	0.968
Menopause duration, y		8.3 ± 7.1	9.2 ± 7.9	11.6 ± 8.5	9.9 ± 9.6	0.121
BMI, kg/m2		29.7 ± 5.5	29.2 ± 4.9	28.6 ± 5.8	29.1 ± 5.2	0.663
BMD T-score	L1-L4	-1.28 ± 1.20	-1.26 ± 1.25	-1.46 ± 1.36	-1.51 ± 1.22	0.680
	Femoral neck	-0.55 ± 1.08	-0.31 ± 1.15	-0.80 ± 1.41	-0.60 ± 1.19	0.258

Discussion

In the present study, postmenopausal subjects with hypothyroidism, hyperthyroidism, and autoimmune thyroiditis had BMDs in the L1-L4 and femoral neck regions that were similar to BMD values in euthyroid controls of similar age and menopause history. These findings provide evidence indicating that these thyroid dysfunction conditions do not disrupt bone metabolism in postmenopausal women.

Thyroid hormones increase bone resorption and bone formation, resulting in an approximately 10% loss in bone mass per remodeling cycle as demonstrated by patients with thyrotoxicosis [5]. Therefore, hyperthyroidism a major cause of secondary osteoporosis [6]. Hypothyroidism reduces bone turnover that affects both bone resorption and formation in a manner

that is similar to hyperthyroidism. The bone formation phase in hypothyroidism is prolonged by the lengthened mineralization phase [7].

Subclinical hyperthyroidism (suppressed TSH in the presence of normal T3 and T4 levels) and TSH suppression by an overdose of T4 replacement are associated with reduced BMD and fracture [8–11]. Recent studies have reported that subclinical hyperthyroidism can increase the risk of fracture, especially in the hip and the lumbar spine of postmenopausal women [8–12]. Metabolic changes related to thyroid hormones can affect BMD and mass [13]. It was reported that hypothyroidism and hyperthyroidism reduced BMD and increased bone fractures [13]. Thyrotoxicosis causes expedited growth, increased bone age, and reduced bone mass. On the other hand, hypothyroidism causes insufficient osteogenesis and growth failure [14].

Thyroid dysfunction is a common problem in perimenopausal and postmenopausal women [8,9,13]. Therefore, it may be important to emphasize TSH measurement for postmenopausal women with low BMD, even if thyroid disease is not present [15]. Risk of osteoporosis has been reported to be increased in postmenopausal patients, and further increased in those with thyroid diseases [14] Yet the occurrence of vertebra fractures appears to be independent of age and BMD in postmenopausal women with low TSH values [14–16]. It was reported that the risk of new hip and vertebral fractures is increased in with low TSH levels, and that normalization of TSH levels as a result of thyroid hormone therapy can prevent that increase in risk [8].

A previous study investigating associations between bone status and levels of TSH and f-T4 in postmenopausal women after long-term treatment for thyroid disorders suggested that TSH levels might support regulation of BMD [18]. Murphy et al. [15] analyzed the relationship between physiological variation in normal thyroid status and BMD, as well as the relationship between thyroid status and non-vertebral fracture, in healthy postmenopausal women. They determined that higher levels of f-T3 and f-T4 were associated with increased bone loss and lower BMD in the hip. Indeed, BMD correlates positively with TSH in healthy postmenopausal women receiving T4 or drugs that affect bone metabolism and osteoporosis is more frequently observed in women with low to normal levels of TSH . However, BMD has been reported to be independent of T4 levels [17].

In a large population-based, cross-sectional study of women over 40 years of age, the prevalence of osteoporosis as determined by ultra-distal forearm BMD measurements was found to be higher in women who self-reported hyperthyroidism (N = 944) than in women without self-reported thyroid disease (N = 5778) confirmed by serum TSH levels. Moreover, the women with the lowest TSH levels (<0.5 mIU/L) had lower forearm BMD measurements [20]. Yet the putative relationship between thyroid hormone levels and bone loss or BMD remains controversial as other researchers could not find any significant associations when they investigated these associations [23]. Interestingly, Grimnes et al. [21] found that abnormally high TSH levels (>4.6 mIU/L) were associated with femoral neck BMD above that observed in euthyroid women, while an association between TSH levels and BMD did not hold in women with normal TSH levels and BMD values.

Van der Deure et al. [22] performed a longitudinal investigation of 151 men and women who were ≥55 years of age for a period 8.7 years. No associations were identified between f-T4 or TSH levels with fracture risks in subjects with nonthyroidal illness. There were also no associations between patients who received drugs that affected bone metabolism. BMD correlated inversely with f-T4 levels and positively with TSH levels, although the correlation with f-T4 was stronger. Bauer et al. [8] determined that low thyrotropin levels were not associated with bone loss in postmenopausal women. This study group performed another prospective cohort study in 2001 that determined exogenous thyroid hormone therapy was not a risk factor for fracture in women with normal serum TSH concentrations. However, women with low serum TSH levels were at an increased risk for new hip and vertebral fractures [24]. A study conducted by Pala et al. [23] showed there was no significant correlation between BMD and TSH values in healthy, postmenopausal women. This observation indicated that TSH value was not a good marker for evaluating BMD.

In conclusion, the present study indicated that thyroid dysfunction does not significantly affect BMD in postmenopausal women with hyperthyroidism, hypothyroidism, or autoimmune thyroiditis. This result suggests that thyroid dysfunctions do not have a significant role in the development of osteoporosis during the postmenopausal period, perhaps because there may be other mechanisms at work that blunt or mask the effects of thyroid hormones.

Competing interests

The authors declare that they have no competing interests.

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