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Assessment of Bone Mineral Density in Individuals with Chronic Respiratory Diseases and Its Relationship with Thyroid Function

Kronik Solunum Sistemi Hastalığı Olan Bireylerde Kemik Mineral Yoğunluğunun Değerlendirilmesi ve Tiroid Fonksiyonları ile İlişkisi

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Abstract

Objective: Decreased bone mineral density (BMD) in patients with chronic respiratory diseases is a significant complication that increases the risk of osteoporosis and fractures. In this study, the effect of variability in thyroid function tests, including thyroid-stimulating hormone (TSH) and free thyroxine (FT4) levels, on BMD was evaluated, and the implications of the interaction between the endocrine and respiratory systems for bone health were examined.

Materials and Methods: Between July 2024 and July 2025, data (thyroid function tests and BMD results) from 124 patients with chronic respiratory diseases [chronic obstructive pulmonary disease, asthma, interstitial lung diseases (ILDs)] who were referred to pulmonary rehabilitation at Aydın Adnan Menderes University in Aydın were retrospectively evaluated. Patients were classified as normal, osteopenic, or osteoporotic according to the World Health Organization criteria. The relationship between thyroid function and BMD in the femur and lumbar regions was examined using Spearman correlation analysis.

Results: The study included 124 patients with a mean age of 65.07±9.70 years. 49.2% of patients were diagnosed with chronic obstructive pulmonary disease, 29.8% with asthma, and 21.0% with ILD. A negative correlation was observed between FT4 level and femoral neck BMD (r=-0.212, p=0.025), whereas TSH level was positively correlated with total femoral BMD (r=0.201, p=0.032).

Conclusion: This study found that the prevalences of osteopenia and osteoporosis are high among individuals with respiratory disease and that these prevalences are negatively correlated with T4 levels and positively correlated with TSH levels. These results emphasize the need to consider thyroid function when screening for osteoporosis in this disease group.

Keywords: Osteoporosis, bone mineral density, thyroid hormones, chronic obstructive pulmonary disease, asthma, interstitial lung disease

Öz

Amaç: Kronik solunum sistemi hastalıklarında kemik mineral yoğunluğunda (KMY) azalma, osteoporoz ve kırık riskini artıran önemli bir komplikasyondur. Bu çalışmada, tiroid uyarıcı hormon (TSH) ve serbest tiroksin (FT4) düzeylerini içeren tiroid fonksiyon testlerindeki değişkenliğin KMY üzerindeki etkisi değerlendirilerek endokrin ve solunum sistemleri arasındaki etkileşimin kemik sağlığına yansımaları incelenmiştir.

Gereç ve Yöntem: Temmuz 2024 ve Temmuz 2025 arasında Aydın Adnan Menderes Üniversitesi'nde kronik solunum sistemi hastalığı (kronik obstrüktif akciğer hastalığı, astım, interstisyel akciğer hastalıkları) olan, pulmoner rehabilitasyona yönlendirilen 124 hastanın verileri (tiroid fonksiyon testleri ve KMY sonuçları) retrospektif değerlendirildi. Hastalar, Dünya Sağlık Örgütü kriterlerine göre normal, osteopenik ve osteoporotik olarak sınıflandırıldı. Tiroid fonksiyonları ile femur ve lomber bölgelerdeki KMY ilişkisi Spearman korelasyon analizi ile incelendi.

Bulgular: Çalışmaya, yaş ortalaması 65,07±9,70 yıl olan 124 hasta dahil edildi. Hastaların %49,2'si kronik obstrüktif akciğer hastalığı, %29,8'i astım ve %21,0'i ınterstisyel akciğer hastalığı tanısı almıştı. FT4 düzeyi ile femur boyun KMY arasında negatif (r=-0,212; p=0,025), TSH düzeyi ile femur total KMY arasında pozitif ilişki (r=0,201; p=0,032) saptandı.

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Sonuç: Bu çalışmada solunum sistemi hastalığı bulunan kişilerde osteopeni ve osteoporoz prevalansının yüksek olduğu ve bu değerlerin FT4 düzeyleri ile negatif, TSH düzeyleri ile pozitif korelasyon gösterdiği saptandı. Bu sonuçlar, bu hastalık grubunda osteoporoz taramalarında tiroid fonksiyonlarının da dikkate alınmasının gerekliliğini vurgulamaktadır.

Anahtar kelimeler: Osteoporoz, kemik mineral yoğunluğu, tiroid hormonları, kronik obstrüktif akciğer hastalığı, astım, intertisyel akciğer hastalığı

Introduction

Osteoporosis is a skeletal disease characterized by deterioration in the microarchitecture of bone tissue and a decrease in bone mass (1). Approximately 200 million people worldwide are affected by osteoporosis, and this number is steadily increasing. A meta-analysis conducted in China reported a prevalence of osteoporosis of 25% among women and 15% among men (2). Estimates indicate that the number of osteoporotic fractures in Europe will reach 5.3 million by 2034, whereas approximately 2.1 million osteoporosis-related fractures occur each year in the United States (3). This makes osteoporosis a public health issue as significant as cardiovascular disease and diabetes. Therefore, early diagnosis and identification of risk factors are critical in reducing both mortality and healthcare costs.

Bone mineral density (BMD) is significantly lower in patients with chronic respiratory diseases than in the general population (4). It has been reported that the risk of osteoporosis is approximately fourfold higher in severe cases of chronic obstructive pulmonary disease (COPD), and it has been suggested that medications used to treat asthma may adversely affect bone mass (5,6). These findings indicate that the risk of osteopenia and osteoporotic fractures is increased among individuals with respiratory diseases and underscore the need for regular monitoring of bone health in this population. It has been reported that the mechanism of bone loss associated with COPD is multifactorial; chronic hypoxia, nutritional deficiencies, and glucocorticoid use play a role in this process (7). Although the global initiative for chronic obstructive lung disease guidelines recommend inhaled corticosteroids as a standard treatment to reduce exacerbations and inflammation, data on the effects of inhaled corticosteroids on fracture risk and osteoporosis remain conflicting (8,9).

Thyroid hormones play a critical role in regulating energy metabolism and bone health. They control the bone formation-resorption cycle by affecting the balance between osteoblast and osteoclast activity (10,11). Even small changes in these hormones can have clinically significant effects on BMD (11). Studies conducted in postmenopausal women have shown that an increase in free thyroxine (FT4) levels is associated with impairment in trabecular microarchitecture (12). Similarly, thyroid-stimulating hormone (TSH) levels have been reported to be positively correlated with trabecular bone score (13). Meta-analyses have demonstrated an increased risk of fractures in subclinical hyperthyroidism, particularly when TSH levels are below 0.10 mIU/L (14). However, it remains unclear whether treatment for this condition can prevent fractures. Large cohort studies of euthyroid individuals have reported that lower TSH and higher FT4 levels are associated with an increased risk of hip fracture (15,16). However, there is no clear consensus on the relationship between hypothyroidism and subclinical hypothyroidism, and BMD (13).

Current data suggest that the risk of osteoporosis in chronic respiratory diseases cannot be explained solely by classic factors such as pharmacological treatments and hypoxia; variability in thyroid hormone levels may also play an important role in osteoporosis risk. Therefore, investigating the association between thyroid function and BMD in individuals with respiratory dysfunction will increase awareness of the clinical management strategies for this group of patients.

Materials and Methods

Ethical Approval

Ethical approval for this research was obtained from the Aydın Adnan Menderes University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee protocol number: 2025/221, dated: 11.07.2025), and all procedures adhered to the ethical principles of the Declaration of Helsinki. Since the study involved a retrospective data review, the ethics committee approved the study and waived the requirement for participant consent.

Study Design and Patient Selection

This retrospective observational study was conducted between July 1, 2024, and July 1, 2025, at the Physical Medicine and Rehabilitation Outpatient Clinic of the Faculty of Medicine, Aydın Adnan Menderes University, Aydın, Türkiye. The study used electronic medical records of patients who were diagnosed with asthma, COPD, interstitial lung disease, or sarcoidosis and referred to the department of physical medicine and rehabilitation for pulmonary rehabilitation. Patients aged 40 years or older with respiratory dysfunction, no active infection, and no history of thyroid disease were included in the study. Patients diagnosed with thyroid disease, receiving thyroid hormone treatment, under the age of 40, or with missing data were excluded from the study. A total of 128 patients were evaluated; 124 with complete data were included in the final analysis.

Data Collection and Measurements

Patients' demographic data (age, gender, height, weight), thyroid function tests—TSH (0.35-4.94 uIU/mL) and (FT4; 0.70-1.48 ng/mL)—and BMD results were obtained from electronic patient records. Thyroid function tests were evaluated according to laboratory reference ranges, and those tests with values outside these ranges were classified into relevant categories.

Bone Mineral Density Assessment and Classification

BMD measurements were performed using dual-energy X-ray absorptiometry (DEXA). DEXA is the method accepted by the World Health Organization (WHO) as the standard for diagnosing

osteoporosis and is preferred because of its short screening time, low radiation exposure, and high accuracy. Measurements were taken in the femoral and lumbar vertebral regions. According to the WHO classification, patients were categorized as having normal bone mass (T-score ≥-1.0), osteopenia (T-score between -1.0 and -2.5), or osteoporosis (T-score ≤-2.5) (17).

Statistical Analysis

The statistical evaluation of the data was performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). To examine whether continuous variables followed a normal distribution, the Kolmogorov-Smirnov test was applied. Parameters exhibiting a normal distribution were reported as the arithmetic mean and standard deviation, whereas non-normally distributed variables were reported as the median and interquartile range (25^{th}-75^{th} percentiles). Categorical data were summarized as frequencies and percentages. For group comparisons, normally distributed data were analyzed using One-Way ANOVA, and the Kruskal-Wallis test was used for data not conforming to a normal distribution. Associations between categorical variables were assessed using the chi-square test. Spearman's rank-order correlation coefficient was used to evaluate associations between continuous variables. A significance level of $p<0.05$ was adopted as the threshold for statistical significance.

Results

A total of 124 participants were analyzed; 54.8% were men and 45.2% were women. The mean age of the study population was 65.07±9.70 years. 49.2% of patients were diagnosed with COPD, 29.8% with asthma, and 21.0% with interstitial lung disease (ILD). Among the 26 patients in the ILD group, 30.8% had idiopathic pulmonary fibrosis (IPF), 26.9% had sarcoidosis, 30.8% had ILD associated with connective tissue diseases, 7.7% had drug-related ILD, and 3.8% had other idiopathic ILD. The patients' demographic characteristics and distribution of diagnoses are presented in Table 1.

Table 1. Participants' demographic characteristics and diagnosis distribution

Characteristic	n	%
Total number of patients	124	100.0
Age (years)	65.07±9.70 (42-88)	-
Gender		
Male	68	54.8
Female	56	45.2
Diagnosis groups		
COPD	61	49.2
Asthma	37	29.8
ILD	26	21.0
Subgroups of ILD		
Idiopathic pulmonary fibrosis	8	30.8
Sarcoidosis	7	26.9
ILD associated with connective tissue diseases	8	30.8
Drug-induced ILD	2	7.7
Other idiopathic ILD	1	3.8

COPD: Chronic obstructive pulmonary disease, ILD: Interstitial lung disease

Among all patients included in the study, evaluation of BMD showed that 22.6% were classified as having normal BMD, 46.0% as having osteopenia, and 31.5% as having osteoporosis. The detailed distribution of BMD categories is presented in Table 2.

When the disease groups were compared, 18.0% of patients with COPD had normal bone density, 42.6% had osteopenia, and 39.4% had osteoporosis. In the asthma group, 21.6% had normal BMD, 56.8% had osteopenia, and 21.6% had osteoporosis. In the ILD group, 34.6% were normal, 38.5% had osteopenia, and 26.9% had osteoporosis. However, no statistically significant differences were found in BMD distributions among disease groups (p=0.188). The distribution of BMD across disease groups is presented in Table 3.

When comparing T-scores across respiratory diseases, significant differences were observed between patients with COPD and those with asthma for both femoral neck T-scores (p=0.026) and total femur T-scores (p=0.006). In contrast, no significant differences were found between COPD and ILD patients in femoral neck (p=0.174) and total femur T-scores (p=0.235), or between asthma and ILD patients in femoral neck (p=0.869) and total femur T-scores (p=0.224). No significant differences were detected in lumbar total T-scores among the three disease groups (p>0.05). The corresponding data are presented in Table 4.

According to the results of the Spearman correlation analysis, a statistically significant negative correlation was observed between FT4 levels and both femoral neck T-score (r=-0.212, p=0.025) and femoral neck BMD (r=-0.204, p=0.032). In addition, significant positive correlations were found between TSH levels and both total femur T-score (r=0.201, p=0.032) and total femur BMD (r=0.190, p=0.043). The correlations between thyroid function parameters and BMD are presented in Figure 1.

Discussion

This study investigated the relationship between thyroid function and BMD in individuals with chronic respiratory diseases and found that FT4 levels were negatively correlated with femoral neck BMD, whereas TSH levels were positively correlated with total femoral BMD. These findings suggest that the risk of

Table 2. Distribution of participants according to bone mineral density classification

BMD class	n	%
Normal (T-score ≥-1.0),	28	22.6
Osteopenia (-1.0> T-score >-2.5)	57	46.0
Osteoporosis (T-score ≤-2.5)	39	31.5
Total	124	100.0

Participants were classified according to WHO criteria
BMD: Bone mineral density, WHO: World Health Organization

Table 3. Bone mineral density classification by disease groups

		Normal n (%)	Osteopenia n (%)	Osteoporosis n (%)	Total
Disease	COPD	11 (18%)	26 (42.6%)	24 (39.4%)	61 (100%)
	Asthma	8 (21.6%)	21 (56.8%)	8 (21.6%)	37 (100%)
	ILD	9 (34.6%)	10 (38.5%)	7 (26.9%)	26 (100%)
Total		28 (22.6%)	57 (46%)	39 (31.4%)	124 (100%)

No significant difference was observed among disease groups, p=0.188
COPD: Chronic obstructive pulmonary disease, ILD: Interstitial lung disease

Table 4. Comparison of femur and lumbar vertebra bone mineral density and T-score values according to respiratory system diseases

	COPD	Asthma	ILD	p-value
Femur neck	-1.389±1.15	-0.809±0.88	-0.946±0.98	**0.026***
Femur neck BMD	0.732±0.15	0.769±0.11	0.753±0.11	0.394
Total femur	-1 (-2.1- -0.150)	-0.200 (-1.025-0.098)	-0.900 (-1.175-0.50)	**0.22****
Total femur BMD	0.868 (0.698-0.959)	0.92 (0.838-1)	0.867 (0.798-0.944)	0.143
L1-L4 total	-1.434±1.72	-1.435±1.41	-0.935±1.58	0.374
L1-L4 total BMD	0.926±0.19	0.894±0.16	0.919±0.23	0.738

*: A statistically significant difference was found between COPD and asthma patients in terms of femoral neck T-score (p=0.026). In contrast, no statistically significant difference was found in femoral neck T-scores between COPD and ILD patients (p=0.174) and between asthma and ILD patients (p=0.869).
**: A statistically significant difference was found between COPD and asthma patients in terms of femur total T-score (p=0.006). In contrast, there was no statistically significant difference in total T-scores of the femur between COPD and ILD patients (p=0.235) and between asthma and ILD patients (p=0.224).
COPD: Chronic obstructive pulmonary disease, ILD: Interstitial lung disease, BMD: Bone mineral density

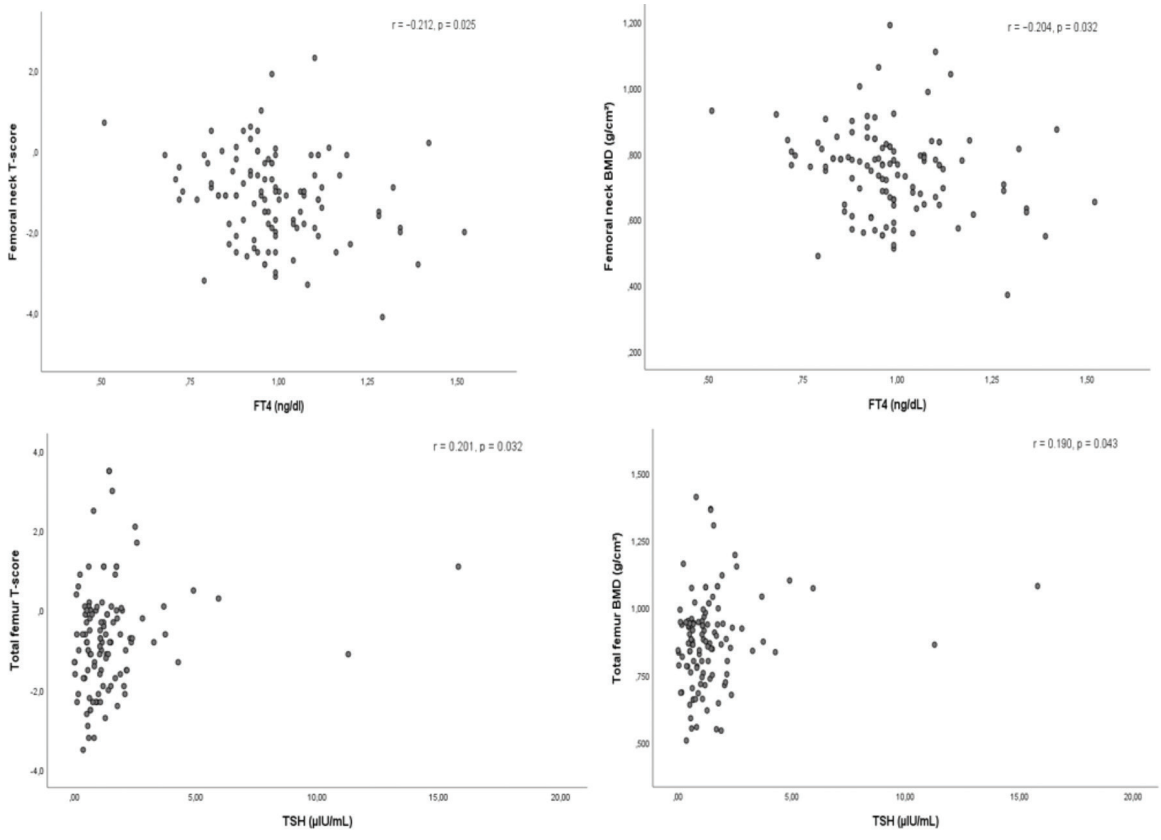

Figure 1. Correlation between thyroid function parameters and bone mineral density values
TSH: Thyroid-stimulating hormone, FT4: Free thyroxine

osteoporosis in individuals with chronic respiratory diseases may be related not only to the chronic disease itself or to the medications used for treatment, but also to alterations in the patients' endocrine systems.

Numerous studies published over many years have examined bone health in patients with chronic respiratory diseases (18-21). Osteoporosis is common in these patients due to hypoxia and the resulting increase in free oxygen radicals, caused by factors such as the medications used, particularly corticosteroids, nutritional deficiencies, and immobility associated with the disease (7,18).

In our study, 42.6% of COPD patients had osteopenia and 39.4% had osteoporosis; this distribution is consistent with previously published data. Indeed, a 2019 meta-analysis reported that the prevalence of osteoporosis ranged from 14% to 66%, with mean prevalences of 39% for osteopenia and 37% for osteoporosis (21). Pobeha et al. (22) reported that osteopenia or osteoporosis occurred in 50-70% of patients with COPD. In an epidemiological study conducted in Taiwan, this rate was found to be 21.21% (23).

Similar to findings in COPD, the susceptibility of individuals with asthma to osteoporosis is a noteworthy topic in the literature. In Jung et al.'s (24) retrospective study involving 7,034 patients, the prevalence of osteoporosis was significantly higher in individuals with a history of asthma than in those without asthma. In another study of respiratory diseases, the prevalence of osteoporosis was 53.6% among patients with asthma and 65.0% among patients with COPD, with an overall prevalence of 60.1% (19). In addition, Soen et al. (20) reported an increase in BMD measurements and in bisphosphonate prescription rates among asthma patients in clinical practice. In our study, only 21.6% of asthma patients had normal BMD, while 56.8% had osteopenia and 21.6% had osteoporosis. Although these rates are lower than those reported in some epidemiological studies, they appear to be consistent with the prevalence of osteoporosis reported in clinical practice. We believe that the decrease in BMD observed in patients with COPD and asthma may be attributed not only to the systemic effects of these diseases but also to their treatments and other risk factors.

BMD loss, observed in COPD and asthma patients, also represents a clinical problem in ILD patients. In a study of 196 newly diagnosed ILD patients, osteoporosis was detected in 44% and osteopenia in 36%. They reported these patients had a significantly increased risk of osteoporosis and required an aggressive approach involving early screening and various anti-resorptive treatments (25).

Similarly, Ikezoe et al. (26) compared 55 steroid-naive male IPF patients with equal numbers of patients in the COPD and smoker groups. Thoracic vertebral BMD was measured by computed tomography. In this study, 27.2% of patients had mean BMD values 2.5 standard deviations below the young-adult mean, suggesting that osteoporosis may develop not only as a result of pharmacological treatments but also via disease-specific mechanisms (26). In our study, the finding that 26.9% of the ILD group had osteoporosis, regardless of treatment status and year of illness, indicates that this patient group is at high risk. Consistent with the literature, this group should be screened early, and other factors that may affect osteoporosis should be examined to enable early treatment.

Our study found no statistically significant differences in the prevalence of osteoporosis among the asthma, COPD, and ILD groups. However, when BMD and T-scores were compared across regions, significant differences were found between patients with COPD and those with asthma in both femoral neck and total femur T-scores. This finding suggests that bone loss may be more pronounced in patients with COPD than in those with asthma. Conversely, the absence of a significant difference between diseases in lumbar measurements indicates that this difference is particularly pronounced in the femur.

In addition, the high prevalence of osteopenia and osteoporosis across all groups (77.5%) underscores the need for regular osteoporosis screening in this patient population. This high rate necessitates consideration of comorbid hormonal disorders that may affect skeletal health. Thyroid hormones are essential for maintaining bone metabolism in adults; however, thyroid dysfunction can have adverse effects on bone structure. Hyperthyroidism reduces bone mass by increasing bone turnover and thereby increases the risk of high-turnover osteoporosis (13). Evidence increasingly indicates that subclinical hyperthyroidism is associated with decreased BMD and increased fracture risk, particularly in postmenopausal women (27). Hypothyroidism is associated with low bone turnover and increased mineralization by reducing both osteoclastic resorption and osteoblastic activity; however, no consistent relationship between hypothyroidism and BMD has been demonstrated in adults (13). Despite these clinical findings, the cellular and molecular effects of thyroid hormones on bone have not yet been fully elucidated (27).

Several studies have indicated a higher prevalence of thyroid dysfunction among individuals with respiratory disorders than in the general population (15,28-31). In a study conducted by Chaudhary et al. (28), the prevalence of thyroid dysfunction in COPD patients was found to be 25%, and it was reported that thyroid dysfunction in COPD leads to a decrease in quality of life by increasing the frequency of exacerbations (28). In animal studies, it has been shown that osteogenesis decreases as the severity of COPD increases (32). In a review of thyroid function in COPD patients, the prevalence of thyroid dysfunction was reported to be 42.1%. It has been underlined that thyroid dysfunction can affect lung function and therefore patients should be screened regularly (29). They have reported that the risk of developing hyperthyroidism is high in patients with asthma, and that this is particularly true in patients over the age of 30 and in the first 3 years after the diagnosis of asthma (31). It has been reported that thyroid dysfunction has a higher prevalence in IPF patients compared to the general population and may predict mortality (30).

Thyroid function can have significant effects not only on the respiratory system but also on bone health. A large-scale study has shown that low TSH and high FT4 levels are associated with an increased risk of hip fracture (15). In the present study, the negative association observed between FT4 and femoral neck BMD is consistent with previous reports. In addition, TSH levels have been shown to be positively associated with bone microarchitecture and negatively associated with new fractures (13). The positive correlation between TSH and total femoral BMD observed in our study also supports these findings.

A clinically significant implication of our study is that osteoporosis screening in patients with chronic respiratory diseases should be based not only on age, gender, and steroid use but also on thyroid function. Especially in patients with high normal FT4 levels or low TSH levels, closer monitoring of BMD may be valuable in preventing osteoporotic fractures.

Study Limitations

This study has some limitations. Firstly, the results are limited in generalizability because data collection and analysis were performed at a single medical facility and involved a limited number of patients. Secondly, it has a retrospective design and examines only thyroid function among the factors affecting osteoporosis in this patient group. Therefore, to better understand the significance and specifics of this issue, multicenter prospective studies involving a substantially larger number of patients are needed to examine the many factors affecting osteoporosis.

Conclusion

In individuals with chronic respiratory diseases, osteoporosis should be considered related not only to hypoxia, corticosteroid use, or immobility, but also to alterations in the endocrine system. Our study showed that FT4 levels were negatively associated with femoral neck BMD, while TSH levels were positively associated with total femoral BMD. The clinically significant finding of our study is that osteoporosis screening in this group of patients should not be based solely on age, gender, and medication use; thyroid function tests should also be included in the evaluation. Patients with high-normal FT4 levels or low TSH levels should be monitored more closely, as this may help prevent osteoporotic fractures at an early stage.

Ethics

Ethics Committee Approval: Ethical approval for this research was obtained from the Aydın Adnan Menderes University Faculty of Medicine Non- Interventional Clinical Research Ethics Committee (protocol number: 2025/221, dated: 11.07.2025), and all procedures adhered to the ethical principles of the Declaration of Helsinki.

Informed Consent: The ethics committee waived the requirement for individual informed consent due to the retrospective design of the study.

Footnotes

Authorship Contributions

Concept: E.E., Ş.D.Y., Design: E.E., Ş.D.Y., Data Collection or Processing: Ş.D.Y., Analysis or Interpretation: E.E., Ş.D.Y., Literature Search: E.E., Ş.D.Y., Writing: E.E., Ş.D.Y.

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