



## Prevalence of Osteoporosis and Osteoporotic Vertebral Fractures in Turkish Patients with Ankylosing Spondylitis: A Retrospective Cross-sectional Study

*Türk Ankilozan Spondilit Hastalarında Osteoporoz ve Osteoporotik Vertebral Fraktür Prevalansı: Retrospektif Kesitsel Çalışma*

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### Abstract

**Objective:** Ankylosing spondylitis (AS) is a chronic inflammatory disease mainly affecting the vertebral column that is the prototype of the spondyloarthritides and is characterized by bone marrow edema, osteitis, erosions, enthesopathy, new bone formations and sclerosis. A decrease in bone mineral density (BMD), in addition to later restrictions in movement and muscle weakness, predisposes the patient to osteoporotic fractures. In this retrospective study, we aimed to assess the prevalence of osteoporosis (OP) and osteoporotic vertebral fractures.

**Materials and Methods:** This study was conducted in Ege University Faculty of Medicine, Departments of Physical Medicine and Rehabilitation and Rheumatology on patients who were diagnosed with AS and who had in the previous year received a BMD examination. Demographic and disease information, Bath Ankylosing Spondylitis Disease Activity index scores and if present, findings of vertebral radiographs and vitamin D levels were recorded from patient files. These parameters were used to compare patients with or without OP.

**Results:** One hundred consecutive patients that were seen in our outpatient clinic and who met the inclusion criteria were enrolled in this study. In BMD examinations, 48% of subjects were found to have OP or osteopenia. Sixty radiographs were reached and 16% of subjects were found to have at least one vertebral fracture. We detected a significant difference between these groups regarding age, sex, disease duration and BMD and T-scores at the levels of femur neck and total hip ( $p<0.05$ ). We did not detect a significant correlation between clinical parameters and parameters related to OP ( $p>0.05$ ).

**Conclusion:** The presence of concomitant OP in patients with AS is significant for increased fracture risk, also recurrent vertebral fractures may exacerbate the spinal deformities caused by the disease itself. It bears importance that clinicians be aware of increased risk of OP to be able to better manage pain and function loss in this patient population.

**Keywords:** Ankylosing spondylitis, fracture, osteoporosis

### Öz

**Amaç:** Ankilozan spondilit (AS), spondilozartropati ailesinin prototipi olup kemik iliği ödemi, osteit, erozyonlar ile entezopati, yeni kemik oluşumu ve sklerozun bir arada seyrettiği, omurgayı etkileyen bir enflamatuvar hastalıktır. Özellikle erken dönemlerde omurgada kemik mineral yoğunluğu (KMY) azalması, ileri dönemde hareket kısıtlılığı, kas güçsüzlüğü ile birlikte osteoporotik kırıklara zemin hazırlar. Bu retrospektif çalışmada, AS'li hastalarda retrospektif olarak osteoporoz (OP) varlığı ve osteoporotik vertebral kırık prevalansını değerlendirmeyi amaçladık.

**Gereç ve Yöntem:** Araştırmaya Ege Üniversitesi Tıp Fakültesi, Fiziksel Tıp ve Rehabilitasyon ve Romatoloji Polikliniklerinden AS tanısı ile takipli ve son 1 yıl içerisinde KMY ölçümü yapılmış hastalar dahil edilmiştir. Gönüllülerin demografik ve hastalık özellikleri, KMY, varsa vertebra radyografik incelemeleri, D vitamini, Bath Ankilozan Spondilit Hastalık Aktivite indeksi (BASDAI) skorları ve kullandıkları ilaçlar hasta dosyalarından kayıt edilmiştir. Daha sonra KMY ölçümüne göre OP saptanan ve saptanmayan hastalar, incelenen klinik parametreler açısından karşılaştırılmıştır.

**Bulgular:** Polikliniklere ardışık olarak başvuran ve dahil edilme kriterlerini karşılayan 100 hasta çalışmaya dahil edilmiştir. Hastaların %48'inde OP ve osteopeni saptanmıştır. Hastaların 60'ının son 1 yıl içerisinde çekilmiş iki yönlü vertebral direkt grafileri mevcut olup, hastaların %16'sında vertebral çökme kırıkları saptanmıştır. OP mevcut olan ve olmayan hastalar arasında yaş, cinsiyet, hastalık süresi ve femur boyun ve total kalça T-skorları açısından anlamlı fark saptanmıştır ( $p<0,05$ ). İncelenen klinik parametreler ile OP ile ilişkili değişkenler arasında anlamlı ilişki izlenmemiştir ( $p>0,05$ ).

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**Sonuç:** AS hastalarında OP varlığı, kırık riski açısından anlamlı olup, tekrarlayan vertebral kırıklar hastalığa bağlı omurga deformitesini daha da şiddetlendirebilir. Ağrı ve fonksiyon kaybının önlenmesi açısından hekimlerin bu hasta grubunda OP riskinin farkında olması önemlidir.

**Anahtar kelimeler:** Ankilozan spondilit, fraktür, osteoporoz

## Introduction

All rheumatological diseases have been associated with lower bone mineral density (BMD) and fragility fractures. It is well known that untreated inflammation as well as immobility, reduced physical activity and some medications used in the treatment of these disease all contribute to higher risk for osteoporosis (OP) (1). Ankylosing spondylitis (AS) is the prototype of a group of diseases called spondyloarthritides (SpA). The difference of AS from other rheumatological conditions is its affinity for new bone formations in addition to erosions and generalized demineralization (2). This increased risk for OP and osteoporotic fractures also poses a risk for vertebral and other fractures to go unnoticed in this patient group who are used to chronic pain. The relationship between AS and OP has been well established, in fact OP has been reported to be the most common comorbidity in patients with AS (3). Although there has been speculation that AS and low BMD may have a common genetic background, no objective evidence of said relationship has been discovered to date (4). Inversely and interestingly, it has been reported that OP may increase the risk for development of AS in same patients (4). It has been long accepted that immobilization and chronic inflammation predispose patients with AS to OP. Corticosteroid use is less common in AS than other rheumatological diseases and treatment with anti-inflammatory medications has been associated with better bone mineral scores (5). Briot et al. (6) reported increases in lumbar BMD values in patients receiving anti TNF- $\alpha$  therapies.

OP risk factors as well as incidence of fractures vary across countries and age groups. In this context it would be expected that ratios of AS patients with OP could show differences in different populations. In a prospective study from Taiwan, patients with AS were reported to be at a 2.17 times higher risk for OP than healthy subjects (5). On the other end of the spectrum, a study from Germany found OP incidence to be 40.7% among patients with AS (7). As inferred from these data, AS poses a higher risk for OP, the incidence of OP and fragility fractures in Turkish AS patients remain unknown.

Therefore, the aim of our study was to assess the frequency and severity of OP in Turkish patients with AS.

## Materials and Methods

### Setting and Participants

This retrospective cross-sectional study was conducted in Ege University Faculty of Medicine, Departments of Rheumatology and Physical Medicine and Rehabilitation. Ethics approval was obtained from the Ethics Committee of Ege University Medical Research on 18.05.2022 with the approval number 22-5T/62.

Sample size calculation was carried out using G-Power software (Düsseldorf, Germany) and with an effect size of 0.3 and alpha value of 0.05, the minimum (min) required number of volunteers was found to be 28. Consecutive 100 patients with AS/axial SpA that visited the rheumatology and physical medicine and rehabilitation outpatient clinics who had in the previous year received a Dual X-ray absorptiometry (DXA) measurement were included in the study. Patients having another disease that may cause OP or patients without DXA examinations in the previous year were excluded.

### Study Parameters

Demographic data, and if present, levels of vitamin D, calcium phosphorus, body mass index and Bath Ankylosing Spondylitis Disease Activity index (BASDAI) scores were recorded. Total hip, femoral neck and total lumbar (L1-L4) T-score values were recorded from the DXA results. DXA measurements were obtained with the patient in the supine position. Osteopenia and OP were defined as T-scores below -1 and below or equal to -2.5, respectively. The lateral radiographic images of patients that were taken in the last year were examined for osteoporotic fractures. Patient files were examined and any symptom that may be related to osteoporotic fractures were noted. Patients' medications were also recorded. Disease duration was defined as the time from the first diagnosis.

### Statistical Analysis

Statistical analysis was conducted using Statistical Package for the Social Sciences version 20.0 (SPSS, IBM, New York). Descriptive statistics were used for demographic data (frequency, number, percentage, mean and standard deviation). Shapiro-Wilk test was used to evaluate for normalcy of data. Parameters from patients with or without osteopenia, OP and vertebral fractures were compared using chi-square for nominal and ordinal data. Continuous data were compared using independent samples t-test or Kruskal-Wallis analysis, depending on the normalcy of the data. BASDAI was compared using Kruskal-Wallis since it is an ordinal measure. Correlation analyses were used for assessing the association between clinical and laboratory parameters.

## Results

One hundred consecutive patients with AS that had received a DXA examination in the previous year were included in the study. Patient demographic and disease characteristics are presented in Table 1. Mean age was found to be 51.1 $\pm$ 10.2 years and mean duration of diagnosis was 15.0 $\pm$ 8.3 years. Median BASDAI score was 3 (min: 0, maximum: 8). Eighty one subjects used NSAIDs and 14 used anti TNF- $\alpha$  medications.

DXA, vertebral radiographs and vitamin D values are presented in Table 2. Based on the findings from DXA examinations, 12

subjects were osteoporotic and 36 were osteopenic. Vertebral radiographs were present in 60 subjects. Of those, 16 (26.6%) showed at least one vertebral fracture. This percentage translated to 16% of all our subjects. Sixteen subjects were taking oral or intravenous bisphosphonates while 2 were on denosumab. Twenty subjects were found to take only vitamin D and calcium supplementation. Of the 16 subjects with proven vertebral fractures, 13 (81.25%) were on anti-osteoporotic medications. When patients with and without osteopenia and OP were compared regarding disease and demographic characteristics, it was revealed that patients with OP/penia were significantly older and had longer disease duration than those patients without OP/penia ( $p < 0.05$ ). More patients with OP/penia were females ( $p < 0.05$ ). No significant difference was detected regarding BASDAI score, vitamin D levels, NSAID or anti TNF- $\alpha$  use ( $p > 0.05$ ). Data from patients with and without OP/penia are presented in Table 3.

Correlation analyses did not reveal a significant correlation between the studied parameters, apart from a positive correlation between age and disease duration ( $p = 0.01$ ,  $r = 0.92$ ) which is to be expected.

**Table 1. Demographic and clinical data for all patients (n=100, %)**

Sex, male, n	54
Age, years, mean $\pm$ SD	51.1 $\pm$ 10.2
Disease duration, years, mean $\pm$ SD	15 $\pm$ 8.3
BASDAI score, median (min-max)	3 (0-8)
NSAID use, n	81
Anti TNF- $\alpha$ use, n	14
OP treatment, n	
Bisphosphonate	16
Denosumab	2
Only calcium and vitamin D	20

SD: Standard deviation, n: Number, BASDAI: Bath Ankylosing Spondylitis Disease Activity index, NSAID: Non-steroidal anti-inflammatory drug, anti TNF- $\alpha$ : Anti tumor necrosis alpha, OP: Osteoporosis, min-max: Minimum-maximum

**Table 2. Parameters related to osteoporosis in all subjects (n=100, %)**

<b>DXA result, n</b>	
Osteopenia	36
Osteoporosis	12
<b>X-ray present, n</b>	
Fracture present, n	16
<b>Number of fractures, n</b>	
1	10
2	4
3	2
Vitamin D, ng/mL, mean $\pm$ SD	19.1 $\pm$ 12.5

n: Number, DXA: Dual X-ray absorptiometry, SD: Standard deviation

## Discussion

In this retrospective cross-sectional study we have detected that 16% of our subjects had at least one vertebral fragility fracture. Prevalence of osteoporotic fractures in SpA patients varies in the literature. Ralston et al. (8) reported vertebral fractures in up to 18% of patients with AS while a study that examined 157 patients found osteoporotic fractures in 9.5% of patients (9). These numbers may be similar to the literature but are higher than the general population and show us that patients with AS have increased fracture risk, regardless of disease activity status. We have observed that not all patients with DXA results had a radiographic examination in our hospital database. OP is a diffuse disease and inflammation causes diffuse bone mineral loss (10). In patients with SpA, OP involvement in different parts of the skeleton may vary according to disease status and duration. Some characteristics of SpA's themselves also pose challenges to the diagnosis of OP. It has been reported that in early stages of the disease, inflammation causes losses in vertebral BMD, which may in part be explained by bone marrow edema, however in later stages, ligament calcifications vertebral sclerosis may cause false negative results in lumbar DXA examination (5). In our patient population who had a mean disease duration of 15 years, significant differences were detected in the femoral BMD measurements while in most patients, lumbar BMD measurements were in the normal range, in some patients, even in the presence of radiographically diagnosed vertebral fractures. This finding is in agreement with the literature, in that highest risk for osteoporotic fractures have been reported in those patients with low BMD at the femoral neck or distal forearm (11).

AS patients were reported to have a fracture risk almost twice as high as those without AS (11). In this patient group, consequent vertebral fractures further exacerbate the spinal deformity that is the characteristic feature of this disease. Pain resulting from fractures also limit subjects' mobility and poorly affect muscle mass and function. Vitamin D levels were overall below normal values in all subjects. We could not detect the effect of low vitamin d on BMD since both groups had insufficiency. Median BASDAI scores for the study population was found to be 3 (range: 0-8). Chronic untreated inflammatory conditions, through the effects of IL-6, IL-1 and TNF- $\alpha$  exacerbate OP (12). Subjects included in this study were receiving treatment and most were in the chronic stages of the disease. We detected no correlation between disease activity score and BMD values. A low disease activity score may explain the relative lack of correlation between BMD and other disease parameters.

## Study Limitations

Because this is a retrospective cross-sectional study, data were obtained from patients who had already had X-rays and DXA taken. That may have caused an imbalance in favor of patients with higher disease activity than the general patient population since patients with more active symptoms may have received

**Table 3. Comparison of patients with and without osteoporosis**

	Osteoporosis/penia present (n=48)	Osteoporosis/penia not present (n=52)	p-value
Age, years, mean ± SD	53.4±9.5	42.7±10.3	0.03 <sup>+</sup>
Sex, male, n (%)	23 (47.9)	31 (59.6)	0.04 <sup>§</sup>
Lumbar spine DXA			
T-score	-0.72±1.6	0.58±1.2	0.13 <sup>+</sup>
BMD	1.090±0.171	1.272±0.279	
Femoral neck			
T-score	-1.31±1.06	-0.79±1.32	0.009 <sup>***</sup>
BMD	0.810±0.092	0.917±0.152	
Hip total			
T-score	-0.6±0.94	0.2±1.33	0.049 <sup>+</sup>
BMD	0.842±0.135	0.1002±0.099	
BASDAI, median (min-max)	4 (0-8)	3 (0-7)	0.82 <sup>#</sup>
Vitamin D, ng/mL, mean ± SD	20.3±5.9	16.2±13.7	0.59 <sup>+</sup>
Disease duration, years, mean ± SD	19±8.9	14±6.1	0.03 <sup>*</sup>
Anti TNF-α use, n (%)	5	9	0.68 <sup>§</sup>
NSAID use, n (%)	40	41	0.62 <sup>§</sup>
n: Number, SD: Standard deviation, BMD: Bone mineral density, BASDAI: Bath Ankylosing Spondylitis Disease Activity index, NSAID: Non-steroidal anti-inflammatory drug, anti TNF-α: Anti tumor necrosis alpha, <sup>+</sup> p<0.05, <sup>**</sup> p<0.01, <sup>*</sup> Independent samples T-test, <sup>§</sup> Chi-square test, <sup>#</sup> Kruskal-Wallis test			

more robust laboratory testing. Also, nearly half of our subjects were females, which is a higher ratio than usually observed in other studies about AS. This may be explained by the relative selectiveness of physicians for ordering OP tests from female patients.

## Conclusion

In this retrospective cross-sectional study, we have found the prevalence of OP in an AS population to be higher than previously reported. AS, in addition to causing OP, may also decrease physical exercise capacity and cause muscle weakness, further making patients susceptible to falls. In order to prevent fractures and related complications, all physicians caring for patients with AS be aware of this heightened risk for OP.

## Ethics

**Ethics Committee Approval:** Ethics approval was obtained from the Ethics Committee of Ege University Medical Research on 18.05.2022 with the approval number 22-5T/62.

**Informed Consent:** Retrospective study.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: E.Ç., Y.K., D.K., G.K., Concept: E.Ç., Y.K., D.K., G.K., Design: E.Ç., Y.K., D.K., G.K., Data Collection or Processing: E.Ç., Y.K., D.K., G.K., Analysis or Interpretation: E.Ç., Y.K., D.K., G.K., Literature Search: E.Ç., Y.K., D.K., G.K., Writing: E.Ç., Y.K., D.K., G.K.

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