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Bone Mineral Density in Mild and Advanced Ankylosing Spondylitis

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To compare the bone mineral density (BMD) and determine the frequency of osteoporosis in mild and advanced ankylosing spondylitis (AS) cases.

Seventy three patients with AS were enrolled in this study. The BMD was analyzed at the lumbar spine and hip by dual energy X-ray absorptiometry. The patients were diagnosed as being "normal, osteopenia, or osteoporosis" according to the WHO classification. Using the BASRI-lumbar and BASRI-hip scores, the patients were grouped in mild and advanced AS categories.

The mean BMD in the lumbar spine and hip of patients with mild and advanced AS was similar ($p>0.05$). While 61.6% of the patients were found to have osteopenia or osteoporosis in the lumbar spine, 46.6% had osteopenia or osteoporosis in the total hip. Of the patients with advanced AS 54.3% had osteopenia or osteoporosis in the lumbar spine, 75% in the total hip. Of the patients with mild AS patients had 68.4% osteopenia or osteoporosis in the lumbar spine, and 42.3% in the total hip. The osteopenia or osteoporosis frequency of the mild and advanced cases of AS in the lumbar spine was similar ($p>0.05$). In the advanced AS patients, osteopenia or osteoporosis frequency was significantly higher in the total hip than in the mild AS patients ($p<0.05$).

In conclusion, there was evidence of osteoporosis in both the advanced AS and mild AS patients. The reason why the anteroposterior lumbar DXA results in the advanced AS patients were similar to the mild ones may be due to the existence of syndesmophytes and ligament calcification. In these cases, it is more convenient to use a hip DXA for assessing the extent of osteoporosis.

Key Words: Ankylosing spondylitis, bone mineral density, osteoporosis

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INTRODUCTION

Ankylosing spondylitis (AS) is a chronic disease characterized by inflammation at the enthesis in the spine and the peripheral skeleton, which may lead to a local bony erosion or juxtainsertional osteoporosis in the early stages. However, in latter stages, new bone formation and progressive ankylosis can occur.

Osteoporosis has long been recognized as a common finding in patients with AS. Osteoporosis in AS was noted as early as 1877 when Fagge described a patient with AS.[1] The presence of osteoporosis in AS patient has been confirmed by numerous researchers. In subsequent reports, the osteopenia or osteoporosis frequency ranged from 50 to 92%.[2-4]

In mild AS, the extent of osteoporosis has been assessed using dual photon absorptiometry (DPA) and dual energy x-ray absorptiometry (DXA).[5] Subsequently, many authors have reported osteoporosis in AS.[3,6-9] However, the time of onset and the pathogenesis of osteoporosis remains controversial.

The cause of osteoporosis in AS is most likely multifactorial. In early stage AS, the symptoms are spinal immobility caused by joint pain, stiffness and a restriction of motion. In late stage AS, bony ankylosis is responsible for the osteoporosis.[4,10] However, there is some controversy. Mitra et al.[5] reported that patients with mild AS had lower femoral and lumbar BMD values although the hip joints were normal. In addition, there was no spinal immobility and advanced spinal changing. Therefore, they proposed that spinal immobility does not play an important role

in the pathogenesis of osteoporosis. Will, et al.[6] and Mullaji et al.[7] reported that inactivity osteoporosis is not important in the pathogenesis because AS patients exercises more often than the controls and proposed that osteoporosis is a primary pathological event.

There are descriptions of the local or systemic osteopenic action of the bone cytokines produced in chronic inflammatory axial or peripheral joint AS lesions.[11] Other probable pathogenetic mechanisms are a genetic predisposition,[12] impaired calcium and vitamin D absorption related to chronic inflammatory intestinal lesions.[13] Non-steroid anti-inflammatory drugs (NSAID's) have not been shown to cause osteoporosis. As a result, their influence may be discounted.[7] Osteoporosis in AS was reported to be related to an increased bone resorption.[4] In contrast, Mitra[5] reported that the resorption indicators are no different from the controls.

However, mild AS patients were investigated in the majority of studies. In this study, we aimed to compare the BMD values and determine the osteoporosis frequency in both mild and advanced AS patients.

MATERIALS AND METHODS

Seventy-three patients (49 men whose mean ± SD age was 37.25 ± 9.45 and 24 premenopausal women whose mean age was 37.25 ± 8.21 years) with AS were enrolled in this study. All the patients fulfilled the modified New York criteria for AS,[14] and provided informed consent to participate this study, which was approved by the ethical committee. The disease duration was 12.47 ± 8.44 years (mean ± SD) in men and 10.42 ± 8.49 years in women ($p>0.05$) (Table 1). All the patients were taking NSAID's. None were taking glucocorticoids at the time of the study, nor had they ever taken such drugs.

Bone densitometry was measured by the DXA technique, using a Hologic QDR 4500 densitometer. The axial BMD was measured in the lumbar spine (L1-4) and the appendicular BMD was measured in the total hip. The World Health Organisation (WHO) classification recommended (normal, osteopenia, and osteoporosis) for quantifying the bone mass loss was used.

One radiologist evaluated radiographs of the pelvis and lumbar spine. The lumbar and hip involvements were assessed by the BATH ankylosing spondylitis radiology index (BASRI).[15] There were lumbar spine radiographs in all patients (n=73), but 64 of them had hip radiographs. The BASRI-hip scores and total-hip BMD could not be evaluated in 12 patients, as the hip radiographs were unavailable. All the patients were grouped according to the degree of their radiological lumbar and hip involvement (BASRI scores). According to this classification, the patients with BASRI lumbar scores between 0 and 1 were classed as being "mild", whereas those with scores of 2-4 were classed as having "advanced" lumbar involvement. Similarly, in assessing the hip joint, the patients were classified as having "mild" and "advanced" hip involvement. Sacroiliac involvement was graded according to the modified New York criteria.[14] The lumbar radiographs were evaluated for vertebral fractures using the method described by McCloskey.[16]

Statistical analysis

The results were analysed using the Statistical Package for Social Sciences (SPSS). The differences

Table 1. Age and Disease Duration for Male and Female Ankylosing Spondylitis Patients*

	Total (n=73)		Male (n=49)		Female (n=24)	
		range		range		range
Age (yr)	37.25 ± 9.00	18 - 60	37.25 ± 9.45	18 - 60	37.25 ± 8.21	23 - 53
Disease duration (yr)	11.79 ± 8.45	1 - 35	12.47 ± 8.44	1 - 35	10.42 ± 8.49	1 - 35

*Independent groups Student-t test, $p>0.05$.
Values are mean ± SD.

between the groups were tested for significance using the Student t-test or the Mann-Whitney U test for unpaired data. The Chi square or Fisher exact test were used for a comparison of the frequency. Correlations are presented as the Spearman's or Pearson's correlation coefficient. *P* values < 0.05 were considered statistically significant.

RESULTS

The BMD of male and female patients were similar ($p>0.05$) (Table 2). According to the BASRI-lumbar score, 38 patients (52%) had mild AS and 35 patients (48%) had advanced AS. In the patients with advanced AS, the mean age and mean disease duration were significantly higher than that of those with mild AS ($p<0.05$). There was no significant difference between the mild and advanced AS in terms of the BMD values in the lumbar spine ($p>0.05$) (Table 3). Vertebral fractures were observed in 4 out of 73 (5.5%) patients. The mean age, mean disease duration and mean lumbar BMD values in patients with or without vertebral fracture were similar ($p>0.05$).

According to the BASRI-hip score, 52 patients (81%) had mild AS and 12 patients (19%) had advanced AS. There was no significant difference in age between the mild and advanced AS patients ($p>0.05$). The mean disease duration was higher in the patients with advanced AS than those with mild AS, but the difference was not statistically significant ($p>0.05$). The mean BMD value of the total hip was lower in those with advanced AS than in those with mild AS, but the differences were also not significant ($p>0.05$) (Table 4).

The osteopenia or osteoporosis frequency was found to be 68.4% at the lumbar spine in the mild AS patients according to the t score defined by WHO. In the advanced AS patients, the osteopenia or osteoporosis frequency was found to be 54.3%, and at the total hip the frequency was 51.9% and 91.7%, respectively. There was no significant difference between patients with mild and advanced AS patients in the lumbar spine ($p>0.05$). However, but in the advanced AS patients, the frequency of osteoporosis in the total hip was significantly higher than in the mild AS patients in the total hip ($p<0.05$) (Table 5).

There was a significant positive correlation

Table 2. Lumbar Spine and the Total Hip BMD Values (g/cm^2) for Male and Female Ankylosing Spondylitis Patients*

	Total (n=73)	Male (n=49)	Female (n=24)
	mean ± SD	mean ± SD	mean ± SD
Lumbar spine	0.96 ± 0.16	0.96 ± 0.16	0.96 ± 0.17
Total hip	0.89 ± 0.15	0.91 ± 0.16	0.86 ± 0.12

*Independent groups Student-t test, $p>0.05$.

Table 3. Lumbar Spine BMD Values for Mild and Advanced Ankylosing Spondylitis Patients*

BASRI-lumbar	Mild (n=38)	Advanced (n=35)
	Mean ± SD	Mean ± SD
Age (yr)	33.95 ± 8.04	40.83 ± 8.71*
Disease duration (yr)	8.82 ± 6.15	15.03 ± 9.45*
Lumbar spine BMD (g/cm^2)	0.94 ± 0.14	0.99 ± 0.19

According to BASRI-hip score: 0-1 point signifieys "mild" patients, and 2-4 points signifies "advanced" patients.
Values are mean ± SD.
*Mann-Whitney U test $p>0.05$.

Table 4. Total Hip BMD Values for Mild and Advanced Ankylosing Spondylitis Patients*

BASRI-hip	Mild (n=52)	Advanced (n=12)
Age (yr)	37.56 ± 9.80	36.67 ± 5.94
Disease duration (yr)	10.87 ± 8.42	15.00 ± 8.93
Total hip BMD (g/cm^2)	0.90 ± 0.12	0.85 ± 0.24

According to BASRI-hip score: 0-1 point signifies mild patients, and 2-4 points signifies advanced patients.
Values are mean ± SD.
*Mann-Whitney U test $p>0.05$.

Table 5. Osteopenia/Osteoporosis Frequencies in Mild and Advanced Ankylosing Spondylitis (AS) Patients

	Mild AS		Advanced AS	
	normal	osteopenia + osteoporosis	normal	osteopenia + osteoporosis
	n (%)	n (%)	n (%)	n (%)
Lumbar spine	12 (31.6)	26 (68.4)	16 (45.7)	19 (54.3)
Total hip	25 (48.1)	27 (51.9)	1 (8.3)	11 (91.7)*

*Chi-square test, $p<0.05$.

Table 6. The Correlation between the BMD Values, the BASRI Scores and the Disease Duration (r/rs)

	Lumbar spine	Total hip	BASRI-lumbar	BASRI-hip
BASRI-lumbar score	0.139	-0.295*	1	0.296*
BASRI-hip score	-0.196	-0.296*	0.296*	1
Disease duration (yr)	0.336†	-0.260*	0.486†	0.147

Pearson correlations are between BMD and disease duration; Spearman correlations are between BMD, BASRI scores and disease duration; *$p<0.05$, †$p<0.01$.

between the disease duration and lumbar spine BMD and a significant negative correlation between the disease duration and the total hip BMD ($p<0.05$). The BASRI-lumbar score showed a positive correlation with the disease duration ($p<0.05$). No correlation was found between the disease duration and the BASRI-hip score ($p>0.05$). There was no correlation between the BASRI scores and the lumbar spine BMD. The BASRI scores showed a negative correlation with the total hip BMD (Table 6).

DISCUSSION

There have been different frequencies of osteoporosis reported in medical literature. When compared with control subjects, the total bone mass was 5.3% lower in AS patients.[17] Meirelles et al.[2] reported that the lumbar BMD was significantly lower than the controls. El Maghraoul et al.[4] reported 18.7% osteoporosis and 31.25% osteopenia in the lumbar spine, and 13.75% osteoporosis and 41.25 osteopenia in the femoral region. Meirelles et al.[2] found 50% osteoporosis or osteopenia in the lumbar spine and 86% in the total proximal femur. In this study, the osteoporosis frequency in mild AS patients was 68.4% in the lumbar spine and 51.9% in the total hip. The corresponding frequency was 54.3% and 91.7% in advanced AS patients, respectively. The variations in the frequency possibly resulted from

the insensitive measurement methods due to spinal changes.

Syndesmophytes can increase the spinal bone mineral content.[17] Mullaji et al.[7] proposed that a higher BMD value in advanced AS is due to serious enthesopathies and new bone formation in the spine. Devogelaer et al.[3] reported a significant decrease in the lumbar spine BMD in mild AS, but in advanced AS, the BMD values were similar to the normal controls. In advanced AS, it was thought that the normality with DPA and central osteopenia with quantitative computerized tomography (QCT) was the result of syndesmophytes and/or facet joint ankylosis.

There is a positive correlation between the disease duration and the lumbar spine and hip BMD values.[2] In many studies, the lumbar spine BMD was lower in patients with a short disease duration and a higher BMD in patients with a longer disease duration.[6,7,9,17] The positive correlation between the disease duration and the lumbar spine BMD values and the negative correlation between the BASRI scores and the total hip BMD values in our patients supports these proposals. However, some authors have reported no correlation between the BMD and the disease duration.[5,18]

Devogelaer et al.[3] attributed the 69% decrease in the lumbar BMD in men and 50% decrease in women to hormonal causes. Donnely et al.[9] found that the BMD was lower in men than women when comparing men and women with a similar disease duration and stage. Juanola et al.[18] found that inflammatory activity, immobilization, and bone resorption due to interleukins were smaller in women with AS than in men, and proposed that hormonal factors decrease the extent of osteoporosis in women with AS. Mullaji 7 could not find a difference between men and women. The BMD values in men and women were similar in our study.

Vertebral fractures are well-known complications of advanced AS.[19] It was thought that these fractures were the result of mechanical factors on a rigid spine or disuse osteoporosis. However, in recent years, osteoporotic compression fractures have gained increasing importance. When compared to normal control, fractures are more frequent in AS patients and even more common in advanced patients with large syndesmophytes.[6,8,19] Donnely 9 and Mitra 19 reported an increase in the fracture prevalence for AS patients. Although osteoporosis is common in AS, the fracture prevalence is not clear and a frequency between 1.25% and 16.7% has been reported.[4,19] In this study, the frequency was 5.5%. The mean age and lumbar spine or total hip BMD values in patients with or without fracture were similar but disease duration was significantly longer in patients with fractures.

The BMD is an important indicator of vertebral fractures in postmenopausal women but in AS, there is no correlation between the vertebral fractures and the BMD, which was attributed to the low sensitivity of the anteroposterior DXA measurement due to spinal changes.[9,19]

Fracture properties of our cases were similar and the mean age, disease duration, lumbar BMD in the cases with or without fractures were similar and there was no correlation between the BMD and vertebral fractures ($p>0.05$). However, only the lumbar spine radiographs were analysed in this study. Therefore, no conclusion on the vertebral fracture prevalence can be drawn.

It is believed that in patients with a longer disease duration, the lumbar spine BMD increase is misleadingly high because of calcification and ossification at the paravertebral bones and ligaments, and the measured value is higher than the real values. Because of these lumbar vertebrae artefacts, the sensitivity of a bone densitometer is low in patients with a prolonged disease duration. Therefore, it is more rational to evaluate the bone mass loss in the proximal femur.[2,4,9] Mitra et al.[5] proposed that a lateral spine densitometer is probably more sensitive in AS.

Lee et al.[20] studied 14 AS patients in the early and late stages and compared the DXA and QCT. They found that the BMD values in the late stage were higher with DXA and lower with QCT. They decided that QCT is more useful than an anteroposterior lumbar DXA in late stage AS patients.

As a result, the BMD values determined with DXA in the late stages, particularly with syndesmophytes and ligamentar calcifications at the lumbar regions, are not convenient to use for diagnosis. In this study, the BMD values of the late stage cases were no different from the early

stage values. However, when the insensitivity of DXA in the late stages is taken into account, these cases can be said to have lower BMD values and more severe osteoporosis than actually measured. Consequently, the anteroposterior lumbar DXA results can be misleading when evaluating the extent of osteoporosis, and treating late stage AS patients. In these patients, it is more convenient to use the hip DXA, the lateral lumbar DXA or the QCT results.

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