Prevalence and risk factors of low bone mineral density in spondyloarthritis

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Abstract

Background: *Osteopenia* is a common bone disorder that is the most prevalent underlying cause of fractures. One of the causes of secondary osteopenia is spondyloarthritis. The rate of bone loss in patients with spondyloarthritis is relatively high in the early stages of the disease. **Objectives:** This study is evaluated the prevalence and risk factors of low bone mineral density by Dual Energy X-ray Absorptiometry (DEXA) in spondyloarthritis. **Material and Methods:** A cross-sectional description combined to retrospective with control group. The spondyloarthritis group included 40 patients at the Department of General Internal Medicine-Endocrinology-Rheumatology, Hue University of Medicine and Pharmacy Hospital. The group of patients with 40 healthy people had their bone mineral density measured at the Department of Functional Exploration - Hue University of Medicine and Pharmacy Hospital. **Results:** Spondyloarthritis is common in men, accounting for 67.5%, with onset in young patients. In spondyloarthritis patients, the average bone mineral density in the lumbar spine was 0.908 ± 0.193 g/cm², at the femoral neck was 0.910 ± 0.208 g/cm², at the total hip was 0.910 ± 0.208 g/cm², much lower than the control group with statistical significance ($p<0.05$). The rate of osteopenia in the lumbar spine is 22.5%, in the femoral neck and the total hip is 5%. When comparing the mean bone mineral density of the spondyloarthritis group with the control group, in the lumbar spine, the average bone mineral density of lumbar vertebrae L4 decreased the most by 12.7%. Bone mineral density in the lumbar spine positively correlates with age, age of disease onset, disease duration, and BMI (body mass index), with no correlation with CRP value, erythrocyte sedimentation rate, disease activity level, lesions sacroiliac joint injury on X-ray. Bone mineral density at the femoral neck was not associated with sex, age, age of onset, disease duration, BMI, CRP, erythrocyte sedimentation rate, disease activity level, sacroiliac joint damage on X-ray, and treatment. **Conclusions:** Osteopenia is common in patients with spondyloarthritis, especially in the lumbar spine. Bone mineral density in the lumbar spine was positively correlated with age, age of disease onset, disease duration, and BMI.

Keywords: *spondyloarthritis, osteoporosis, bone mineral density, osteopenia, Vietnam*.

1. INTRODUCTION

Osteoporosis is a bone disorder characterized by decreased bone strength that increases the fracture risk. Bone strength is reflected by bone density and bone quality. Osteoporosis is the most common underlying cause of fractures and accounts for approximately 1.5 million fractures in the United States each year. In addition, each year, there are more than 500,000 hospitalizations, more than 2.6 million medical visits, more than 800,000 emergency hospital admissions, and approximately 180,000 people enrolled in nursing homes in the US. It is predicted that by 2040, the cost of treating osteoporosis and its complications will increase from 100% to 200% [1].

Based on the cause, osteoporosis is divided into two main groups: primary and secondary osteoporosis [2]. One of the causes of secondary osteoporosis is spondyloarthritis. Decreased bone mineral density and osteoporotic vertebral fractures are known complications of spondylitis, especially in ankylosing spondylitis. A reduction in bone density has been reported as high as 47% in the lumbar and femoral spine, even in patients with early-stage spondyloarthritis [3]. Patients with ankylosing spondylitis may be at increased risk of bone loss due to high levels of disease activity, proinflammatory cytokines, mechanical factors (i.e., spinal stiffness, vertebral deformity), and reduced physical activity or mineralization defects associated with inflammatory bowel conditions [4].

Therefore, it is essential to evaluate the risk factors for reduced bone density and osteoporosis and predict the risk of fracture in patients with spondyloarthritis, from which there are treatment and preventive measures to reduce the risk of fracture

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in patients. So, we conducted a study on the topic: ***"Prevalence and risk factors of low bone mineral density in spondyloarthritis"*** with the research objective: *Evaluation the prevalence and risk factors of low bone mineral density by Dual Energy X-ray Absorptiometry (DEXA) in spondyloarthritis*

2. SUBJECTS AND METHODS

2.1. Research subjects

A cross-sectional descriptive study with retrospective comparison was performed on 40 patients diagnosed with spondyloarthritis according to ASAS 2009 criteria [5], being treated at the Department of General Internal Medicine-Endocrinology- Rheumatology - Hue Central Hospital from June 2019 to November 2021 and the control group were 40 people without spondyloarthritis and other diseases affecting to bone mineral density.

2.1.1. Criteria for selecting disease groups: The patient was diagnosed with spondyloarthritis according to the Assessment of Spondylo Arthritis International Society - ASAS 2009 criteria [5]. The patient had no physical, mental, or physical disabilities or ability to communicate influence when answering questions.

2.1.2. Criteria for selecting a control group: The control group is those who went to the hospital for medical examination at the Hue University Hospital and did not have spondyloarthritis or diseases that affect the results of BMD, such as diabetes, kidney failure, hyperthyroidism, or hyperparathyroidism.

2.1.3. Exclusion criteria: It is crucial to note that some patients did not provide their consent to participate in the study. The patient is currently battling an acute illness. Additionally, the patient has undergone bilateral hip replacement. It's important to consider that some patients may have contraindications to DEXA bone density measurement, such as pregnant women or those who have recently undergone gastrointestinal contrast and nuclear medicine testing. These patients are advised to wait at least 72 hours before measuring bone mineral density, or 7 days for long-lived units such as gallium.

2.2. Research methods

A cross-sectional descriptive study with retrospective comparison

2.3. Analyzing data

The data were collected and processed using SPSS 26.0 software

3. RESULTS

3.1. General characteristics of the study group

3.1.1. Comparison of anthropometric characteristics of the spondyloarthritis group and the control group

Table 1. Anthropometric characteristics of the spondyloarthritis group and the control group

Factorial		SpA group (n = 40)	Control group (n = 40)	p
Gender	Male	27	27	
	Female	13	13	
Age	≤ 30 years	31	30	0.000
	>30 years	9	10	0.942
	Medium	25.78 ± 8.51	29.58 ± 6.45	0.027
BMI	Underweight	17.07 ±1.34	17.18 ± 1.28	0.879
	Normal	20.54 ± 1.34	21.10 ± 1.35	0.173
	Overweight	24.88 ± 1.61	24.78 ± 1.35	0.902
	Medium	20.17 ± 3.01	21.53 ± 2.64	0.035

- The SpA group and the control group had a similar gender distribution.

- The mean age of the SpA group and control group was different between the two groups ($p<0.05$). Notably, the number of subjects under 30 years old dominated in both groups.

- There was no difference in body mass index (BMI) between the underweight, normal, and overweight groups ($p>0.05$).

3.1.2. Clinical and sub-clinical characteristics of patients with spondyloarthritis

The spondyloarthritis group includes 40 subjects, of which 67.5% are male. The age of disease onset was 22.48 ± 7.61 years old. The mean duration of disease was 43.30 ± 56.37 months. Family factors account for 7.5%.

Table 2. Clinical and sub-clinical characteristics of patients with spondylarthitis

	Median	SD	Min-Max
CRP (mg/l)	30.78	58.44	0.31 - 300.57
ESR (mm/h)	30.95	26.47	6 - 109
HLA-B27	5/6 (83.3%)		
ASDAS-CRP	2.49	1.16	0.87-5.86
Sacroiliitis on x-ray	Stage 0:10 (25%)	Not qualified clinical criteria New York: 14 (35%)	Qualification clinical NewYork: 16 (40%)
MRI of sacroiliac joints	No damage: 2/29 (6.9%)	Active inflammation lesions: 19/29 (65.5%)	Chronic inflammation lesions: 8/29 (27.6%)
Classification	Ankylosing spondylitis: 16 (40%)	Non-radiographic axial spondyloarthritis: 24 (60%)	Peripheral SpA: 0%
Treatment	Nontreatment: 25 (62.5%)	*cDMARDs: 2 (5%)	**bDMARDs: 13 (32.5%)

**: conventional disease-modifying antirheumatic drugs*

***: biologic disease-modifying antirheumatic drugs*

- Sacroiliitis on x-ray qualification New York criteria accounts for only 40%.
- an MRI of the sacroiliac joints was performed on 29 patients. In which 93.1% of patients have sacroiliac joint abnormalities, active inflammatory lesions account for 65.5%.
- All patients belong to the axial spondyloarthritis group, 40% have ankylosing spondylitis and 60% have non-radiographic axial spondyloarthritis.
- Most patients with spondyloarthritis have not been treated, accounting for 62.5%. The treatment group consisted of cDMARD (5%) and bDMARDs (32.5%).

3.2. Bone mineral density in spondyloarthritis

3.2.1. Prevalence of low bone mineral density of study subjects according to Z-score

Table 3. Prevalence of low bone mineral density by Z-score (Z-score ≤ -2)

Position	SpA group (n = 40)		Control group (n = 40)	
	N	%	N	%
Lumbar spine	9	22.5	0	0
Femoral neck	2	5.0	0	0
Total hip	2	5.0	0	0
Any site	9	22.5	0	0

- There was no decrease in bone density in the control group.
- With the SpA group, the overall reduction in bone density was 22.5%, 22.5% in the lumbar spine, and 5% at the femoral neck and the total hip.

3.2.2. Mean bone mineral density of spondyloarthritis group and control group

Table 4. Mean bone mineral density of spondyloarthritis group and control group

Position		SpA group (n=40)	Control group (n=40)	p
L1	BMD	0.839 ± 0.184	0.956 ± 0.130	0.001
	Z-score	-0.412 ± 1.870	0.722 ± 1.193	0.002
L2	BMD	0.912 ± 0.196	1.026 ± 0.126	0.003
	Z-score	-0.412 ± 1.989	0.658 ± 1.161	0.005
L3	BMD	0.936 ± 0.201	1.064 ± 0.126	0.001
	Z-score	-0.655 ± 2.021	0.590 ± 1.133	0.001

L4	BMD	0.934 ± 0.206	1.070 ± 0.117	0.001
	Z-score	-1.130 ± 2.112	0.180 ± 1.135	0.001
Lumbar spine	BMD	0.908 ± 0.193	1.032 ± 0.117	0.001
	Z-score	-0.695 ± 1.981	0.505 ± 1.064	0.001
Femoral neck	BMD	0.910 ± 0.208	1.056 ± 0.210	0.003
	Z-score	0.483 ± 1.697	1.615 ± 1.463	0.002
Total hip	BMD	0.970 ± 0.185	1.112 ± 0.163	0.001
	Z-score	-0.240 ± 1.221	0.665 ± 0.922	0.000

- The average BMD of the lumbar spine and femur of the SpA group was statistically significant (p<0.05) lower than that of the control group.

3.2.3. Bone mineral density of the spondyloarthritis group and the control group by age

Table 5. Bone mineral density of the study group by age

BMD	SpA group	Control group	p
Age ≤ 30 years	n = 31	n = 30	
Lumbar spine	0.869 ± 0,160	1.037 ± 0.131	0.000
Femoral neck	0.887 ± 0,202	1.061 ± 0.208	0.002
Total hip	0.948 ± 0,189	1.116 ± 0.173	0.001
Age > 30 years	n = 9	n = 10	
Lumbar spine	1.042 ± 0.246	1.019 ± 0.061	0.788
Femoral neck	0.989 ± 0.221	1.042 ± 0.227	0.616
Total hip	1.044 ± 0.162	1.097 ± 0.137	0.454

- Age ≤ 30 years: The BMD of the spondyloarthritis group was lower than that of the control group, with statistical significance in both lumbar spine, femoral neck, and total hip (p<0.05).

3.2.4. Bone mineral density of spondyloarthritis group and control group according to BMI

Table 6. Bone mineral density of study subjects according to BMI

BMD	SpA group	Control group	p
BMI < 18,5	n = 13	n = 5	
Lumbar spine	0.830 ± 0.148	0.938 ± 0.052	0.134
Femoral neck	0.833 ± 0.183	0.924 ± 0.087	0.307
Total hip	0.902 ± 0.168	0.971 ± 0.061	0.391
18.5 ≤ BMI < 22.9	n = 20	n = 25	
Lumbar spine	0.898 ± 0.162	1.024 ± 0.073	0.004
Femoral neck	0.944 ± 0.240	1.046 ± 0.201	0.127
Total hip	0.990 ± 0.215	1.098±0.146	0.064
BMI ≥ 23	n = 7	n = 10	p
Lumbar spine	1.081 ± 0.259	1.101 ± 0.183	0.849
Femoral neck	0.957 ± 0.108	1.148 ± 0.248	0.078
Total hip	1.037 ± 0.061	1.215 ± 0.183	0.015

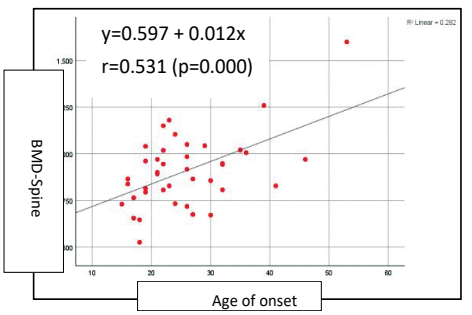
- Underweight group: There was no difference in BMD between the spondyloarthritis group and the control group (p>0.05).

- Normal group: the BMD in the lumbar spine of the spondyloarthritis group was statistically significant compared with the control group (p=0.004), and there was no significant difference in the BMD in the femoral neck and the total hip in the two groups (p>0.05).

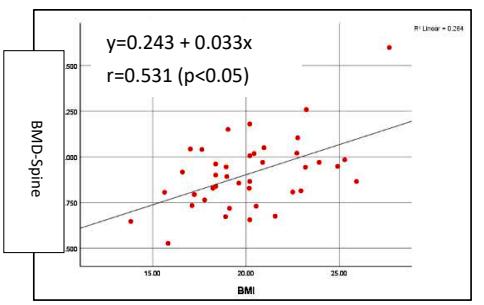
- Overweight group, there was no difference in BMD in the lumbar spine and femoral neck between the two groups of spondyloarthritis and the control group. Meanwhile, BMD at the total hip of the spondyloarthritis group was statistically significantly lower than that of the control group (p<0.05).

3.3. The relationship between BMD between patients with spondyloarthritis and factors

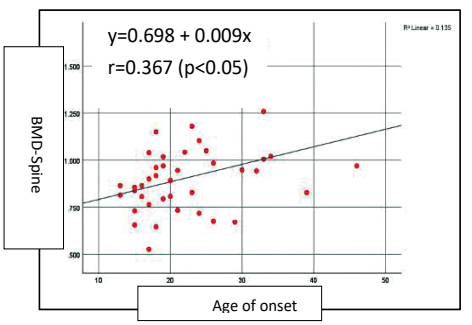
Our comprehensive study has thoroughly investigated the associations between the BMD of the lumbar spine and key factors such as age, age at onset of disease, duration of disease, and BMI. We found no significant associations with gender, CRP, ESR, sacroiliitis on X-ray, and treatment of disease. The BMD at the femoral neck and the total hip was also found to be unrelated to these factors.



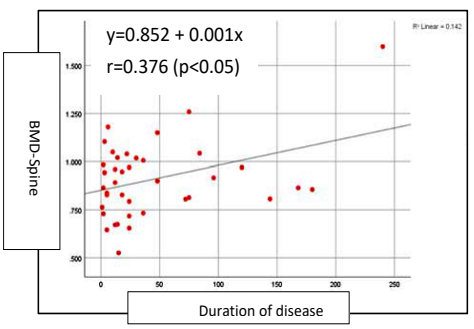
Chard 1. Correlation between BMD of lumbar spine and age



Chard 2. Correlation between BMD of lumbar spine and BMI



Chard 3. Correlation between BMD of lumbar spine with age of onset



Chard 4. Correlation between BMD of lumbar spine with duration of disease

4. DISCUSSION

4.1. Bone mineral density in patients with spondyloarthritis

Through the study of BMD in 40 SpA patients with an average age of 25.78 ±8 .51 compared with 40 subjects without SpA with gender and age homogeneity (group age ≤30 years old and >30 years old had similarity in numbers, especially with age >30 years old in the two groups there was no difference), the BMD of SpA patients at lumbar spine was 0.908 ± 0.193 g/cm², and at the femoral neck was 0.910 ± 0.208 g/cm², at the total hip was 0.970 ± 0.185 g/cm², lower than the control group with a statistically significant difference (p<0.05). The reduction rate in overall BMD in the SpA group was 22.5%, mainly in the lumbar spine at 22.5%, the femoral neck, and the total hip at 5%. The BMD at each vertebra of SpA patients was lower than that of the control group; the lowest was at the L4 position (average BMD decreased 12.7% compared to the control group). Thus, in our study, the BMD of SpA patients decreased more at the lumbar spine. This is also understandable when all spondyloarthritis subjects in our study were axial spondyloarthritis, with predominant expression at the spinal position. Furthermore, in patients with spondyloarthritis, one

of the features of local bone changes is damage to the spinal location [6].

The results of Table 6 confirm that the BMD of the lumbar spine in underweight patients (BMI<18.5) is significantly lower than in the control group. Even among SpA patients with a normal BMI (BMI: 18.5-22.9), the average BMD was lower than the control group, with a particularly pronounced difference in the lumbar spine (p<0.05). This further solidifies the fact that SpA patients consistently have low BMD. The presence of low BMD is also evident in the age group with peak bone mass. The BMD of the young group at the lumbar spine was not only lower than the control group of the same age (Table 5) but also lower than the patient group over the age of 30. At the femoral neck, the vertebral column in patients under 30 years old was lower than in the control group, but when compared with the age group over 30 years old, there was no difference between the two age groups (p>0.05).

Some studies on BMD of SpA patients in the world and in Vietnam have shown low bone density. According to Mullaji AB et al. (1994), when studying BMD on 33 patients with ankylosing spondylitis. Ankylosing spondylitis (27 men and 6 women) and 41 healthy people using the DEXA method showed an increase in lumbar spine BMD in the late stage and a decrease in BMD in the early stage of the disease. Thus, bone loss occurs very early in the disease stage, and there is no limitation of spinal movement [7]. A decrease in BMD was also observed in the study of author Toussirot E et al. 2001, in 71 ankylosing spondylitis patients with 71 healthy people of the same age, showing that the BMD at the lumbar spine was 1.08 ± 0.17 g/cm², BMD at the vertebral column was 0.97 ± 0.16 g/cm², which was statistically significantly lower than the control group [8]. These findings underscore the importance of early screening and intervention in ankylosing spondylitis patients to prevent or mitigate bone loss.

4.2. The relationship between BMD and clinical and sub-clinical factors

The relationship between BMD and sex

Our study has revealed that gender is an independent risk factor affecting bone, and we found no significant difference in mean BMD between women and men (p>0.05). This independence of gender as a risk factor is a unique aspect of our study. In the study of the author Dao Xuan Thanh (2017), the average BMD in the lumbar spine and femoral neck in women is statistically significantly higher than in men [9]. The mean age in our study is 25.78 ± 8.51 years, which is younger than the average age in Dao Xuan Thanh's study, which is 32.56 ± 13.68 years.

The relationship between BMD and age

The study's findings on BMD variation with age have significant implications for bone health. Notably, during puberty, BMD experiences a rapid increase, reaching its peak between the ages of 20 and 30. The results of Table 5 indicate that SpA groups under 30 years old have a lower BMD at TL 0.869 ± 0.160 g/cm², and CF 0.887 ± 0.202 g/cm² compared to the control group of the same age (p<0.05). Furthermore, the BMD at the lumbar spine of SpA patients under 30 years old is lower than that of patients over 30 years old. These findings suggest that at the age of under 30 years, there is a peak bone mass. However, the results of the SpA study of patients with low SpA in both lumbar spine and femoral neck compared with controls. The variation in BMD by age group shows that at the lumbar spine, the BMD increases gradually with age group, possibly due to the ossification of the ligament around the vertebrae and the limitation of the DEXA method of measuring BMD in the posterior-anterior dimension. The BMD at the femoral neck does not increase with the age group. Thus, age has an impact on BMD in the lumbar spine, which has significant implications for bone health.

The relationship between BMD and age of disease onset

Our analysis of the correlation between the age of onset and BMD at the lumbar spine and femoral neck revealed some interesting findings. We found that BMD at the lumbar spine had a positive correlation with the age of onset of the disease (r=0.367, p=0.02). The bone at the femoral neck did not show any correlation with the age of disease onset. When compared with the study of Nguyen Thi Minh Tam (2008), we found a reassuring similarity: BMD in the lumbar spine had a positive correlation with the age of onset of the disease (r=0.253; p=0.006), and no correlation was observed between BMD at the femoral neck and age of disease onset [10]. In the study of Maltere L et al. (2005) on 59 patients with AS, including 37 males, the mean age was 40.2 ± 13.8 years, the mean age of onset was 31.12 ± 11.1 years, higher than our study, and Mai Thi Minh Tam showed that there was a correlation between the age of onset of the disease and the BMD of both lumbar spine and femoral neck (p<0.05) [6, 11].

The relationship between BMD and BMI

The results of chart two show that the BMD of the lumbar spine correlates with the body mass index: The BMD at the lumbar spine has a positive

correlation with the BMI of the research subjects with the coefficient r=0.531 (p<0.05), which means that the higher the BMI, the higher the patient's bone density. There is no correlation between the BMD at CKD and the BMI of the study subjects. Of particular interest is the comparison with the research results of Phung Duc Tam (2016) and Mai Thi Minh Tam (2008), which also found a positive correlation between BMD in the lumbar spine and BMI, but an additional positive relationship between BMD at the femoral neck and BMI [11, 12].

The relationship between BMD and sacroiliitis

In our study, we rigorously examined 16 patients who met the clinical criteria New York, 14 who did not, and ten patients who showed no signs of sacroiliitis on x-ray. When we compared the bone mineral density (BMD) in these groups, we found no statistically significant difference in BMD. This suggests that the stage of sacroiliitis on straight pelvic radiographs is not a reliable indicator of decreased BMD in patients with SpA. Our thorough methodology and robust findings provide confidence in the results of this study.

The relationship between BMD and treatment

In our study, all patients belonged to the axial spondyloarthritis group. The essential treatment consisted of using conventional DMARDs (Sulfasalazine) or biologic drugs such as Infliximab (Remicade), Adalimumab (Humira), Fraizeron (Secukinumab). When evaluating the relationship between BMD and treatment, it can be seen that there is no difference in BMD in both lumbar spine and femoral neck between the three groups that have not been treated or treated with DMARDs or biologics with p>0.05. However, there are many cases of patients receiving essential treatment who receive treatment infrequently, in waves, and only receive essential treatment for a few months to 1 year while the disease has progressed for a few years. Some have received treatment with biological drugs, but due to economic conditions, which can significantly impact their treatment, or stable disease status, the treatment dose is extended. This may be why there is no statistically significant difference in BMD in the treated and untreated groups or because the sample size of our study was not large enough to evaluate this difference.

5. CONCLUSION

The mean bone mineral density of patients with spondyloarthritis was statistically significantly lower than that of the control group. The prevalence of low bone mineral density was 22.5%. The greatest decrease was in the lumbar spine with 22.5%, especially the L4 vertebra. The low bone mineral density at the femoral neck and the total hip is 5%.

Bone mineral density in the lumbar spine has a positive correlation with age, age of disease onset, disease duration, and BMI; it does not correlation with CRP value, erythrocyte sedimentation rate, disease activity level, or lesions of sacroiliac joint injury on X-ray.

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