The Egyptian Rheumatologist 42 (2020) 297–301

Contents lists available at ScienceDirect

The Egyptian Rheumatologist

journal homepage: www.elsevier.com/locate/ejr

Bone mineral density in ankylosing spondylitis: Relation to disease activity, functional capacity, spinal mobility and radiological damage

Sahar Fakhreldin [a], Medhat Mohamed Abdallah [b], Mohamed Yasser Al-tohamy [c], Hania Salah Zayed [a,*]

[a] Rheumatology and Rehabilitation Department, Faculty of Medicine, Cairo University, Egypt
[b] Rheumatology Clinic, Air Force Hospital, New Cairo, Egypt
[c] Radiodiagnosis Department, Military Medical Academy, Cairo, Egypt

ARTICLE INFO

Article history:
Received 18 July 2020
Accepted 18 July 2020
Available online 6 August 2020

Keywords:
Ankylosing spondylitis
Bone mineral density
Disease activity
Functional capacity
Spinal mobility
Radiological damage

ABSTRACT

Aim of the work: To assess the bone mineral density (BMD) in Ankylosing Spondylitis (AS) patients and to investigate its relation to disease activity, functional capacity, spinal mobility and radiological damage.
Patients and methods: Thirty male AS patients (mean age 27.9 ± 6.2 and disease duration 4.2 ± 3.6 years) and thirty age-matched healthy controls were studied. Patients were assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), the Bath Ankylosing Spondylitis Metrology Index (BASMI) and the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) to quantify radiological damage. BMD of the lumbar spine and femoral neck were assessed by Dual Energy X ray Absorptiometry (DEXA).
Results: Patients had a lower BMD of the lumbar spine (1.13 ± 0.14 versus 1.22 ± 0.09 g/cm^2, p = 0.007) and femoral neck (0.89 ± 0.1 versus 1.05 ± 0.13 g/cm^2, p = 0.001) than controls. BMD of the lumbar spine was negatively correlated with the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), BASDAI, BASFI, BASMI and mSASSS (r = -0.6,-0.4, −0.5, −0.4, −0.5, −0.6; p = 0.001, 0.003, 0.01, 0.01, 0.004, 0.001, respectively) while BMD of the femoral neck was correlated negatively with the ESR,CRP, mSASSS (r = -0.5,-0.4,-0.5, p = 0.001, 0.004, 0.01) and positively with the modified Schöber test (r = 0.41, p = 0.02). On multiple regression analysis, the modified Schöber test, ESR and CRP were independent predictors of the BMD of the femoral neck (β = 0.45,-1.12, 0.58; p = 0.048, 0.02, 0.03, respectively).
Conclusion: BMD is reduced in AS patients and correlates with disease activity, functional capacity, spinal mobility and radiological damage.

1. Introduction

Ankylosing spondylitis is a common inflammatory rheumatic disease that mainly affects the axial skeleton, causing sacroiliitis, pain and stiffness of the spine and structural damage leading to limitation of spinal mobility. The condition may be associated with peripheral arthritis, enthesitis, anterior uveitis and less commonly cardiac manifestations [1] and may have considerable effects on the health-related quality of life [2].

In the AS spine, paradoxically, osteoproliferation and osteodestruction occur in parallel [3]. Osteoproliferation leads to syndesmophyte formation and limitation of spinal mobility and osteodestruction leads to osteoporosis with increased fracture risk [4,5]. Osteoproliferation is thought to be a consequence of the inflammatory process with contribution of molecular pathways that mechanically trigger new bone formation such as bone morphogenetic proteins, Wnt and hedhehog proteins [6]. Osteoporosis in AS can be secondary to immobility caused by pain, stiffness and ankylosis of the spine and the inflammatory process itself [3]. Abnormalities in sex hormones [7] and alterations in the parathyroid hormone- vitamin D hormonal axis and genetic factors such as vitamin D receptor gene polymorphisms can contribute to bone loss in AS [8].

The aim of this work was to assess the bone mineral density (BMD) in ankylosing spondylitis (AS) patients and to investigate its relation to disease activity, functional capacity, spinal mobility and radiological damage.

2. Patients and methods

Thirty male AS patients fulfilling the modified New York Criteria for classification of AS [9] and thirty age-matched healthy male

Peer review under responsibility of Egyptian Society of Rheumatic Diseases.
* Corresponding author.
E-mail address: hania.zayed@kasralainy.edu.eg (H.S. Zayed).

https://doi.org/10.1016/j.ejr.2020.07.009
1110-1164/

control subjects were included. Patients and control subjects were recruited from the rheumatology clinic at Agouza Rheumatology and Rehabilitation Centre for Armed Forces, Guizeh. They were all working military personnel. Patients less than 16 years old and those with complete bridging syndesmophytes on lumbar spine radiographs (bamboo spine), or those suffering from other seronegative sponyloarthropathies , chronic liver or kidney disease, thyroid or parathyroid disorders, malabsorption syndrome or taking drugs that may affect bone metabolism e.g. corticosteroids, diuretics, anticonvulsants, or antiresorptives were excluded. Consent was taken from all study participants. This work has been approved by the local Research Ethical Committee and is in accordance with the provisions of the Medical Association of Helsinki.

The patients were subjected to full history taking and clinical examination. The disease duration was calculated from the date of diagnosis of AS. Weight and height were obtained. The body mass index was calculated as the weight in kg / height in m^2. Cervical rotation, the tragus to wall distance, lumbar side flexion, modified Schöber test and intermalleolar distance were measured to calculate the Bath AS Metrology Index (BASMI); higher scores indicate more severe limitation of movement [10].

Assessment of disease activity was done by the Bath AS Disease Activity Index (BASDAI). It includes questions about pain in the spine, peripheral joints, tenderness and the level of morning stiffness in the last week; higher scores indicate more disease activity [11]. Assessment of mobility and ability to perform tasks of daily activities in the last week was done using the Bath AS Functional Index (BASFI); higher scores indicate more functional disability [12].

Laboratory assessment included a complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and testing for Human Leucocyte Antigen (HLA) B-27.

Radiological assessment: X-rays of the cervical, dorsal and lumbar vertebrae including antero-posterior and lateral views were obtained. The sacroiliac joints were evaluated on the antero-posterior view of the lumbar spine and graded as (grade I, some blurring of the joint margins –suspicious; grade II, minimal sclerosis with some erosion; grade III, definite sclerosis on both sides of the joint or severe erosion with widening of the joint space with or without ankylosis; grade IV, complete ankylosis [9].

Chronic AS related changes of the spine were estimated using the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS), which includes the anterior corners of vertebrae C2 to T1 and T12 to S1, which are graded with 0 to 3 points each (0 = normal, 1 = erosion, sclerosis or squaring (vertebral body squaring refers to loss of normal concavity of the anterior border), 2 = obvious syndesmophyte, 3 = bridging syndesmophyte). The remaining thoracic spine is not included in the score. The scoring scale ranges from 0 to 72 [13].

The BMD was measured for patients and controls at the L2-L4 lumbar spine (postero-anterior projection) and the left femoral neck by dual energy X-ray absorptiometry (DEXA) using a DPX-alpha machine (Lunar Corporation, USA). DEXA results were expressed as BMD (g/cm^2), as well as calculated T-score (number of standard deviations from the mean BMD of young adult normal individuals [14]. According to the World Health Organization (WHO), normal BMD was defined as a T score between 1 and −1, osteopenia as a T score < -1 to > -2.5 and osteoporosis as a T score $\leq$ -2.5 [15].

Statistical methods. The statistical program SPSS version 15 was used for statistical analysis. Results were expressed as mean ± standard deviation, or number and percentage. Student's *t*-test was used to compare continuous variables between AS patients and controls, and the Mann Whitney *U* test was used for comparisons between subgroups of AS patients. The chi-square test for categorical variables was performed when appropriate. The correlations between variables were presented as the Spearman's correlation coefficient (r). Multiple regression analysis was performed to identify predictors of BMD of the lumbar spine and femoral neck. The level of statistical significance was less than 0.05 (2-tailed).

3. Results

Thirty male AS patients and 30 age-matched healthy male control subjects were included in the present study. The ages of the control subjects ranged from 19 to 39 years, mean 27.7 ± 6.4 years and their BMI raged from 19 to 34, mean 24.63 ± 6.3. There were no statistically significant differences between patients and control group regarding age or BMI (p = 0.2 and 0.3, respectively). The characteristics of the studied patients are shown in table 1. Peripheral arthritis affected the hip in seven patients, the ankle in four, the knee in two and the shoulder in two patients. Eleven patients had extra-articular manifestations (10 patients had anterior uveitis and 5 patients had AS-associated inflammatory bowel disease). All patients were positive for HLA-B27. All patients had radiographic sacroliitis which was unilateral in 19 (63.3%) and bilateral in 11 (36.7%).

All patients were receiving treatment with non-steroidal anti-inflammatory drugs (NSAIDs). Twenty one (70%) of the patients were also treated with one tumor necrosis factor α antagonist (anti-TNF α), 14 patients were receiving infliximab and 7 patients etanercept. The duration of anti- TNF α use ranged from 2 to 24 months (mean 10.33 ± 6.86). Methotrexate was used by 4 patients (three patients received an anti- TNF α antagonist concomitantly). Also, 15(50%) of the patients were subjected to physical therapy in the form of hydrotherapy, range of motion exercises and extension strengthening exercises of the back muscles.

3.1. Bone mineral density in patients and controls

Assessment of BMD of AS patients and controls showed a significantly decreased BMD expressed in g/cm^2 at the lumbar spine and femoral neck in AS patients as compared to controls (p = 0.007 and 0.001, respectively). Eighteen of the AS patients had a normal BMD and 12 were osteopenic. All 12 patients had osteopenia of the

Table 1
Characteristics of studied AS patients.

	AS patients n = 30	
Age (y)	27.9 ± 6.2	(20–39)
Age at disease diagnosis (y)	23.8 ± 4.6	(19–35)
Disease duration (y)	4.2 ± 3.6	(1–16)
Duration before diagnosis (y)	1.97 ± 1.69	(1–6)
BMI (kg/m^2)	24.46 ± 6	(22.3–27.8)
Morning stiffness (min)	39.1 ± 36.8	(0–120)
ESR (mm/1. hour)	21.9 ± 8.2	(5–50)
CRP (mg/l)	11 ± 9.9	(6–45)
Tragus to wall distance (cm)	3.73 ± 1.91	0–7
Modified Schöber test (cm)	4.15 ± 1.29	1–7
Lumbar side flexion (cm)	6.57 ± 2.21	3–11
BASDAI	3.2 ± 1.6	(1.6–6.7)
BASFI	3.4 ± 1.6	(1.5–7)
BASMI	3.4 ± 1.8	(1–8)
Peripheral arthritis	13	43.33%
Extra-articular manifestations	11	36.7%
Sacroiliitis grades 2/3/4	6/19/5	
mSASSS	16.3 ± 11.6	5–43

Values are expressed as mean ± standard deviation (range) unless otherwise specified. Y, years ; BMI, body mass index; Bath Ankylosing Spondylitis Disease Activity Index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score

lumbar spine and seven patients (23.3%) had osteopenia of the femur in addition, while among the control group 2 were found to be osteopenic (table 2). Among the osteopenic patients, 8 had a disease duration less than 10 years, i.e. 8/30 (26.7%) AS patients had developed osteopenia during the first 10 years of the disease.

There were significant negative correlations between the BMD of the lumbar spine and ESR (p = 0.001), CRP (p = 0.003), BASDAI (p = 0.01), BASFI (p = 0.01), BASMI (p = 0.004), mSASSS (p = 0.001) and a positive correlation was found with the modified Schöber test (p = 0.04) and lumbar side flexion (p = 0.01). Significant negative correlations were also found between the BMD of the femoral neck and ESR (p = 0.001), CRP (p = 0.004), mSASSS (p = 0.01) and a positive correlation was found with the modified Schöber test (p = 0.02). On the other hand, no significant correlations were found between BMD of the lumbar spine or femoral neck and the age of the patients, age at disease diagnosis, disease duration, duration before diagnosis, BMI or the grade of sacroiliitis (table 3).

AS patients with peripheral arthritis, uveitis or inflammatory bowel disease did not differ in BMD of the lumbar spine or femoral neck from those who did not suffer from these manifestations. Concerning the effect of treatment, no statistically significant differences were found in mean BMD of the lumbar spine or femoral neck between patients who received an anti TNF-α antagonist or physical therapy and those who did not (table 4).

Multiple regression analysis revealed that the modified Schöber test (β = 0.45, p = 0.048), the ESR (β = -1.12, p = 0.02) and the CRP (β = 0.58, p = 0.03) were independent predictors of the BMD of the femur, while for BMD of the lumbar spine none of the independent variables was significant.

4. Discussion

Low bone mass occurs frequently in ankylosing spondylitis and may start early in the disease course [16,17].

Bone mineral density (BMD) of the lumbar spine or hip has been conventionally evaluated by DEXA in AS patients [17,18]. In normal subjects, BMD of the lumbar spine measured at the anteroposterior (AP) projection has twice the precision than the lateral projection [19], however, in AS patients the presence of syndesmophytes and calcification of the ligaments and zygapophyseal joints in severe cases may lead to a false increase in BMD results on AP DEXA scans [20–22]. Various alternative methods for assessing the vertebral bone status of AS patients have been investigated. It has been suggested that assessment of BMD on lateral vertebral projections on DEXA scans [18,20,23–25] or volumetric BMD assessment taking AP and lateral projections into account [24], or evaluation of the microarchitecture using the spinal trabecular bone score on DEXA scans [18,22,26]or quantitative computed tomography [26] may better reflect bone loss at the lumbar spine in patients with advanced disease. Also, proximal femur BMD may better reflect the bone loss in those patients [21,28,29].

In the present study, BMD of the lumbar spine and the femoral neck assessed on conventional AP DEXA scans were significantly lower in AS patients than in the control group. Low bone mass in the form of osteopenia affected 40% of the studied patients at the lumbar spine and 23.3% at the femoral neck while other studies revealed a prevalence of low bone mass at the lumbar spine in the form of osteopenia or osteoporosis in 20–68% of AS patients [18,27,28,30–33] and at the femoral neck in 15.8% – 73% [7,28,31–34]. None of our patients had osteoporosis. The active life style led by our patients which were all working military personnel could have mitigated their bone loss.

In the present study, BMD of the spine and femoral neck did not correlate with the age of the patients in agreement with other investigators [7,32] while Muntean et al. [33] found a positive correlation between lumbar spine BMD and age and Klingberg et al. [24] found an association between low bone mass and increasing age. We also found no correlation between BMD of the lumbar spine or femoral neck and disease duration, in agreement with other investigators [7,31–33], suggesting that bone loss in AS patients occurs in early disease. On the other hand, Klingberg et al. [24] found an association between low bone mass and longer disease duration.

The inflammatory process in AS is thought to contribute to bone loss in AS patients which has been documented in patients with preserved spinal mobility and absent or minimal radiographic changes of the hip and the lumbar spine [35]. Our results show negative correlations between BMD of the lumbar spine and femoral neck and the biological markers of inflammation, ESR and CRP. CRP and ESR were also found to independently predict the femoral neck BMD. These results are in agreement with some studies [23,24,31,34] but not with others [32,33,36]. We also found significantly negative correlations between BMD of the lumbar spine and BASDAI and BASFI. Several studies found associations between low bone mass at the lumbar spine and higher BASDAI [23,31,32], but others did not [33,36]. Sayed et al. [32] also found a negative correlation between lumbar spine BMD and BASFI, which was not confirmed by other investigators [31,33,36]. No correlation was found between femoral neck BMD and BASDAI or BASFI in the present study, in line with previous reports [7,32,33,36], while low BMD of the femoral neck was associated with a higher BASFI in some studies [25,31,33].

Bone loss in AS is generally considered to be caused by the immobilization associated with spinal ankylosis and rigidity [28]. In the present study, there was a significant correlation between the lumbar spine BMD and the modified Schöber test and a negative correlation with the BASMI; the latter is in agreement with Mermerci Başkan et al. [23] and Klingberg et al. [24] while Sayed et al. [32] found no correlation between lumbar spine BMD and the Schöber test. The present results also found a positive correlation between BMD of the femoral neck and the Schöber test, similar to other studies [28,33], moreover, the Schöber test was found to be an independent predictor of the femoral neck BMD.

Table 2
Bone mineral density in AS patients and controls.

	AS patients (n = 30)		Control (n = 30)		P-value
Lumbar spine BMD g/cm^2	1.13 ± 0.14	(0.9 – 1.4)	1.22 ± 0.09	(1.02 – 1.35)	0.007*
Lumbar spine T-score	−0.38 ± 0.99	(-2 – 1.3)	0.197 ± 0.96	(−1.8 – 1.9)	0.03*
Osteopenia of the lumbar spine	12	(40%)	1	(3.3%)	0.01*
Femoral neck BMD g/cm^2	0.89 ± 0.1	(0.7 – 1.2)	1.05 ± 0.13	(0.79 – 1.31)	0.001*
Femoral neck T-score	−0.69 ± 1.08	(-2.3 – 1.6)	−0.01 ± 0.7	(-1.8 – 1)	0.005*
Osteopenia of the femoral neck	7	(23.3%)	2	(6.6%)	0.02*

Values are expressed as mean ± standard deviation (range) or number (%). AS, ankylosing spondylitis; BMD, bone mineral density; *, statistically significant.

Table 3
Correlations between clinical, laboratory and radiological parameters and BMD of the spine and femoral neck in AS patients.

	BMD of the lumbar spine		BMD of the femoral neck	
	r	P-value	r	P-value
Age	0.31	0.09	−0.18	0.3
Age at disease diagnosis	0.15	0.4	−0.08	0.09
Disease duration	−0.21	0.4	−0.19	0.1
Duration before diagnosis	−0.132	0.1	−0.011	0.4
BMI	0.15	0.09	−0.07	0.08
Morning stiffness	−0.22	0.3	−0.3	0.1
ESR 1st hour	−0.6 *	0.001*	−0.5 *	0.001*
CRP	−0.4 *	0.003*	−0.4 *	0.004*
Tragus to wall distance	−0.28	0.14	−0.26	0.17
Modified Schöber test	0.37*	0.04*	0.41*	0.02*
Lumbar side flexion	0.45	0.01*	0.24	0.21
BASDAI	−0.5	0.01*	−0.2	0.4
BASFI	−0.4	0.01*	−0.2	0.3
BASMI	−0.5	0.004*	−0.3	0.1
mSASSS	−0.6	0.001*	−0.5	0.01*
Sacroiliitis **grade**	−0.3	0.2	−0.2	0.2

BMD, bone mineral density; BMI, body mass index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BASFI, Bath Ankylosing Spondylitis Functional Index, BASDAI, Bath Ankylosing Spondylitis Disease Activity Index, BASMI, Bath Ankylosing Spondylitis Metrology Index; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score

Table 4
Relation of bone mineral density in AS patients to peripheral arthritis, uveitis, inflammatory bowel disease and treatment.

	BMD of the lumbar spine	P-value	BMD of the femoral neck	P-value
Peripheral arthritis				
Yes (n = 13)	1.12 ± 0.43	0.34	0.82 ± 0.62	0.44
No (n = 17)	1.13 ± 0.59		1.04 ± 0.73	
Uveitis				
Yes (n = 10)	1.02 ± 0.23	0.29	0.74 ± 0.43	0.52
No (n = 20)	1.13 ± 0.49		1.03 ± 0.64	
Inflammatory bowel disease				
Yes (n = 5)	1.13 ± 0.4	0.4	0.78 ± 0.6	0.39
No (n = 25)	1.22 ± 0.68		1.12 ± 0.67	
TNF-α antagonist use				
Yes (n = 21)	1.12 ± 0.63	0.4	0.86 ± 0.54	0.35
No (n = 9)	1.13 ± 0.43		1.13 ± 0.64	
Physical therapy				
Yes (n = 15)	1.12 ± 0.46	0.23	0.88 ± 0.63	0.4
No (n = 15	1.13 ± 0.43		1.12 ± 0.68	

BMD, bone mineral density; TNF-α, tumor necrosis factor alpha; NSAID, non-steroidal anti-inflammatory drug

No correlations were found between the femoral neck BMD and the tragus to wall distance or BASMI in the present study while other investigators found significant negative correlations between BMD of the femoral neck and the BASMI [22,24] or the chin to chest and occiput to wall distances [32].

Regarding the association between bone loss and radiographic damage, our results showed negative correlations between the BMD of the lumbar spine and femoral neck and the chronic AS-related changes of the cervical and lumbar spine quantified by the mSASSS but not with the grade of sacroiliac joint involvement. Klingberg et al. [37] also found an association between low BMD of the femoral neck and mSASSS after adjustment for age. Kim et al. [18] found that mSASSS was negatively correlated with lateral lumbar spine BMD and lumbar spine trabecular bone score. Associations between the presence of syndesmophytes and a lower lumbar BMD assessed on lateral vertebral projections [25] and a low hip BMD [38] have been reported, while another study found no significant difference between BMD values at the lumbar spine or femoral neck in AS subjects with or without syndesmophytes [36].

Some investigators reported a lower BMD at the lumbar spine and/or the femoral neck in AS patients with history of hip arthritis [24,34], however, this observation was not confirmed in the present study, in agreement with Muntean et al. [33].

In patients with AS and axial spondyloathropathies, bone density can be improved with TNF inhibitors [39]. The effect on bone is mediated by their anti-inflammatory effects as demonstrated by reduction of ESR and CRP [40] and BASDAI [41]. AS patients receiving anti TNF α were found to have significantly higher femoral neck and lumbar BMD than those naïve to this therapy [34] however, we could not confirm this association. Ivanova et al. [22] also found no effect of therapy (including TNF α antagonists, methotrexate and sulfasalazine) on BMD of the lumbar spine or femoral neck.

The small number of studied patients is an important limitation of this study, however, they constituted a relatively homogeneous group, all male, younger than 40 years and physically active due to their recruitment from military personnel. The discrepancies found between different studies could be attributed to differences in the characteristics of the studied patients and study design.

In conclusion, bone mineral density is frequently reduced in AS patients and correlates with disease activity, functional capacity, spinal mobility and radiological damage. The inflammatory markers, ESR and CRP, and the modified Schöber test independently predict the BMD of the femoral neck.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Braun J, Sieper J. Ankylosing spondylitis. Lancet 2007;369:1379–90.
[2] Sallam RA, Elbahnasawy AS. Health related quality of life (HRQoL) in ankylosing spondylitis patients: Relation to clinical features, disease activity and radiographic damage. The Egyptian Rheumatologist 2020;42(4):287–90. doi: https://doi.org/10.1016/j.ejr.2020.02.006.
[3] Briot K, Roux C. Inflammation, bone loss and fracture risk in spondyloarthritis. RMD Open. 2015 14;1(1):e000052.
[4] Ghozlani I, Ghazi M, Nouijai A, Mounach A, Rezqi A, Achemlal L, et al. Prevalence and risk factors of osteoporosis and vertebral fractures in patients with ankylosing spondylitis. Bone 2009;44:772–6.
[5] Geusens P, De Winter L, Quaden D, Vanhoof J, Vosse D, van den Bergh J, et al. The prevalence of vertebral fractures in spondyloarthritis: relation to disease characteristics, bone mineral density, syndesmophytes and history of back pain and trauma. Arthritis Res Ther. 2015;17:294.
[6] Gheita TA. Inflammation and new bone formation: The long lasting debate in axial spondyloarthritis. J Rheumatol Arthritic Dis 2016;1:1–2.
[7] Aydin T, Karacan I, Demir SE, Sahin Z. Bone loss in males with ankylosing spondylitis: its relation to sex hormone levels. Clin Endocrinol (Oxf). 2005;63:467–9.
[8] Dischereit G, Lange U. Rheumatism and bone metabolism. Orthopade. 2019; 48:911-916. German.
[9] van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum. 1984;27:361–8.
[10] Jenkinson TR, Mallorie PA, Whitelock HC, Kennedy LG, Garrett SL, Calin A. Defining spinal mobility in ankylosing spondylitis (AS). The Bath AS Metrology Index. J Rheumatol. 1994;21:1694–8.
[11] Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol. 1994;21:2286–91.
[12] Calin A, Garrett S, Whitelock H, Kennedy LG, O'Hea J, Mallorie P, et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. J Rheumatol. 1994;21:2281–5.
[13] Creemers MC, Franssen MJ, van't Hof MA, Gribnau FW,. van de Putte LB, van Riel PL. Assessment of outcome in ankylosing spondylitis: an extended radiographic scoring system. Ann Rheum Dis. 2005;64:127–9.
[14] Saag KG. Osteoporosis. A. Epidemiology and clinical assessment. In Klippel JH, Stone JH, Crofford LJ, White PH ,editors. Primer on the rheumatic diseases. 13th ed. New York: Springer Science + Business Media, LLC; 2009, p.576-83.
[15] . World Health Organ Tech Rep Ser. 1994;843:1–129.
[16] van der Weijden MA, Claushuis TA, Nazari T, Lems WF, Dijkmans BA, van der Horst-Bruinsma IE. High prevalence of low bone mineral density in patients within 10 years of onset of ankylosing spondylitis: a systematic review. Clin Rheumatol. 2012;31:1529–35.
[17] Kilic E, Ozgocmen S. Bone mass in axial spondyloarthritis: A literature review. World J Orthop. 2015;6:298–310.
[18] Kim JW, Chung MK, Lee J, Kwok SK, Kim WU, Park SH, et al. Low bone mineral density of vertebral lateral projections can predict spinal radiographic damage in patients with ankylosing spondylitis. Clin Rheumatol. 2019;38:3567–74.
[19] Del Rio L, Pons F, Huguet M, Setoain FJ, Setoain J. Anteroposterior versus lateral bone mineral density of spine assessed by dual X-ray absorptiometry. Eur J Nucl Med 1995;22:407–12.
[20] Gilgil E, Kaçar C, Tuncer T, Bütün B. The association of syndesmophytes with vertebral bone mineral density in patients with ankylosing spondylitis. J Rheumatol. 2005;32:292–4.
[21] Kaya A, Ozgocmen S, Kamanli A, Ardicoglu O. Bone loss in ankylosing spondylitis: does syndesmophyte formation have an influence on bone density changes?. Med Princ Pract. 2009;18(6):470–6.
[22] Ivanova M, Manolova I, Boyadzhieva V, Stoilov R, Dimitrov N, Stoilov N, et al. Relationship between physical function, disease activity, spinal mobility and bone parameters (trabecular bone score and bone mineral density) in ankylosing spondylitis patients. Biotechnol Biotechnol Equip 2015;29: 956–62.
[23] Mermerci Başkan B, Pekin Doğan Y, Sivas F, Bodur H, Ozoran K. The relation between osteoporosis and vitamin D levels and disease activity in ankylosing spondylitis. Rheumatol Int. 2010;30:375–81.
[24] Klingberg E, Lorentzon M, Mellström D, Geijer M, Göthlin J, Hilme E, et al. Osteoporosis in ankylosing spondylitis - prevalence, risk factors and methods of assessment. Arthritis Res Ther. 2012;14:R108.
[25] Ulu MA, Çevik R, Dilek B. Comparison of PA spine, lateral spine, and femoral BMD measurements to determine bone loss in ankylosing spondylitis. Rheumatol Int. 2013;33:1705–11.
[26] Richards C, Hans D, Leslie WD. Trabecular Bone Score (TBS) Predicts Fracture in Ankylosing Spondylitis: The Manitoba BMD Registry. J Clin Densitom. 2020, pii: S1094-6950(19)30218-5. doi: 10.1016/j.jocd.2020.01.003. [Epub ahead of print]
[27] Klingberg E, Lorentzon M, Gothlin J, Mellstrom D, Geijer M, Ohlsson C, et al. Bone microarchitecture in ankylosing spondylitis and the association with bone mineral density, fractures, and syndesmophytes. Arthritis Res Ther. 2013;15:R179.
[28] Baek HJ, Kang SW, Lee YJ, Shin KC, Lee EB, Yoo CD, et al. Osteopenia in men with mild and severe ankylosing spondylitis. Rheumatol Int. 2005;26:30–4.
[29] Deminger A, Klingberg E, Lorentzon M, Geijer M, Göthlin J, Hedberg M, et al. Which measuring site in ankylosing spondylitis is best to detect bone loss and what predicts the decline: results from a 5-year prospective study. Arthritis Res Ther. 2017;19:273.
[30] Dos Santos FP, Constantin A, Laroche M, Destombes F, Bernard J, Mazières B, et al. Whole body and regional bone mineral density in ankylosing spondylitis. J Rheumatol. 2001;28:547–9.
[31] Grazio S, Kusić Z, Cvijetić S, Grubišić F, Balenović A, Nemčić T, et al. Relationship of bone mineral density with disease activity and functional ability in patients with ankylosing spondylitis: a cross-sectional study. Rheumatol Int. 2012;32:2801–8.
[32] Sayed S, Darweesh H, Fathy K, Mourad AM. Clinical significance of bone mineral density in ankylosing spondylitis patients: Relation to disease activity and physical function. The Egyptian Rheumatologist 2015;37:35–9.
[33] Muntean L, Rojas-Vargas M, Font P, Simon SP, Rednic S, Schiotis R, et al. Relative value of the lumbar spine and hip bone mineral density and bone turnover markers in men with ankylosing spondylitis. Clin Rheumatol. 2011;30:691–5.
[34] Feki A, Fourati H, Sellami I, Gassara Z , Ghorbel A, Ezzeddine M, et al. Bone mineral density and bone remodelling in Tunisian patients with ankylosing spondylitis: A cross-sectional study. The Egyptian Rheumatologist 2020;42 (4):281–86. https://doi.org/10.1016/j.ejr.2019.06.004.
[35] Will R, Palmer R, Bhalla AK, Ring F, Calin A. Osteoporosis in early ankylosing spondylitis: a primary pathological event?. Lancet 1989;2:1483–5.
[36] Vasdev V, Bhakuni D, Garg MK, Narayanan K, Jain R, Chadha D. Bone mineral density in young males with ankylosing spondylitis.Int. J Rheum Dis. 2011;14:68–73.
[37] Klingberg E, Nurkkala M, Carlsten H, Forsblad-d'Elia H. Biomarkers of bone metabolism in ankylosing spondylitis in relation to osteoproliferation and osteoporosis. J Rheumatol. 2014;41:1349–56.
[38] Karberg K, Zochling J, Sieper J, Felsenberg D, Braun J. Bone loss is detected more frequently in patients with ankylosing spondylitis with syndesmophytes. J Rheumatol. 2005;32:1290–8.
[39] Ashany D, Stein EM, Goto R, Goodman SM. The Effect of TNF Inhibition on Bone Density and Fracture Risk and of IL17 Inhibition on Radiographic Progression and Bone Density in Patients with Axial Spondyloarthritis: a Systematic Literature Review. Curr Rheumatol Rep. 2019;21:20.
[40] Kang KY, Lee KY, Kwok SK, Ju JH, Park KS, Hong YS, et al. The change of bone mineral density according to treatment agents in patients with ankylosing spondylitis. Joint Bone Spine. 2011;78(2):188–93.
[41] Dischereit G, Tarner IH, Müller-Ladner U, Lange U. Infliximab improves bone metabolism and bone mineral density in rheumatoid arthritis and ankylosing spondylitis: a prospective 2-year study. Clin Rheumatol. 2013;32:377–81.