Factors Associated with Radiological Hip Joint Involvement in Patients with Ankylosing Spondylitis

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Research article

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Abstract

Background: The associated factors for hip involvement in patients with ankylosing spondylitis (AS) are poorly known. This study was to analyze the clinical data of patients with AS and to explore the potential associated factors of AS-related radiological hip joint.

Methods: This was a cross-sectional study of patients diagnosed with AS and treated at the Beijing Jishuitan Hospital between 01/2013 and 12/2019. A BASRI-hip score ≥ 2 was defined as radiological hip joint involvement. Univariable and multivariable logistic regression analyses were performed to analyze the factors associated with radiological hip joint involvement.

Results: A total of 350 AS patients were included. Patients with radiological hip joint involvement (BASRI-hip ≥2) accounted for 50.6% (177/350). The proportion of men was 83.7% (293/350). The mean age was 35.0±12.7 years old. The mean duration of the disease was 10.8±8.6 years. The HLA-B27 positive rate was 90.9% (318/350). The multivariable analysis showed that the juvenile onset (OR=4.955, 95%CI: 2.464-9.961, P<0.001), bone mass lower than peers (OR=2.862, 95%CI: 1.593-5.142, P<0.001), BMI <18.5 kg/m2 (OR=2.832, 95%CI: 1.321-6.069, P=0.007), BASFI (OR=1.278, 95%CI: 1.069-1.527, P=0.007), and continuous NSAIDs treatment (OR=0.400, 95%CI: 0.200-0.799, P=0.009) were independently associated with radiological hip joint involvement in patients with AS.

Conclusion: AS with radiological hip joint involvement had worse body function and lower bone density. The associated factors with radiological hip joint involvement in AS patients included juvenile-onset, thin body size. The prognosis of patients with AS who received continuous NSAIDs drug treatment might be improved.

Background

Ankylosing spondylitis (AS) is a chronic inflammatory disease that mainly damages the central axis joints [1]. It is more common in young men and has an incidence of 0.1%-0.5% [1]. The main features are inflammatory low back pain, attachment point inflammation, sacroiliitis, new bone formation in the spine, and high correlation with the HLA-B27 genetic marker [1]. The complications of AS are low bone density, osteoporosis, and fracture [1]. The majority of patients AS report the chronic use of various types of pain killers [1].

Previous studies reported that the proportion of AS-related hip involvement is high and that about 25%-33% of patients with AS also have hip joints damage [2]. About 5% of patients with AS will need hip arthroplasty [2]. In humans, the hip joints are the full-motion joints with the greatest weight-bearing demand. It is the most important joint for maintaining body balance and limb movements. Hip joint damage is also one of the main causes of disability in AS [3]. The methods for evaluating AS-related hip joint involvement include clinical symptoms, joint examination, and imaging results (X-ray radiography and magnetic resonance imaging). Among them, the Bath Ankylosing Spondylitis Radiology Index (BASRI)-hip score based on X-rays is commonly used in the studies of AS-related hip joint damage, and

the score is relatively objective [4]. While new bone formation is mainly involved in AS-related damage in the spine, AS-related hip damage mainly involves synovial inflammation, bone erosion, and joint space narrowing [5].

A previous study showed that a high body mass index (BMI) and advanced hip arthritis at baseline were associated with hip arthroplasty in patients with AS [5]. Another study showed that the use of anti-tumor necrosis factor (anti-TNF) decreased the rate of hip arthroplasty by 40% [6]. Notwithstanding, the associated factors for hip involvement in patients with AS are not well known, and exploring the associated factors of AS-related hip joint involvement could guide not only clinical work but also help basic research.

Therefore, the aim of this retrospective study was to analyze the clinical data, including the BASRI-hip score, of patients with AS and to explore the potential risk factors of AS-related radiological hip joint. The results could help identify the patients who might require a closer follow-up because they might require hip arthroplasty.

Methods

Patients

This was a cross-sectional study of patients diagnosed with AS and treated at the rheumatology department of Beijing Jishuitan Hospital between January 2013 and December 2019. The inclusion criteria were: 1) >18 years of age; 2) met the modified New York criteria (1984) for AS classification; and 3) duration of disease ≥1 year. The exclusion criteria were: 1) incomplete data; 2) bone tumor, bone metastasis, or hematological cancer; or 3) other rheumatic diseases, such as rheumatoid arthritis, gouty arthritis, or infectious arthritis.

The study was approved by the Ethics Committee of Beijing Jishuitan Hospital (No: 202003-13). The need for individual consent was waived by the committee because of the retrospective nature of the study.

Data collection

The variables included sex, age, age at onset, duration of disease, smoking history, family history, BMI (classified into <18.5 kg/m^2 and ≥18.5 kg/m^2) [7], Schober's test, peripheral arthritis (physician found swelling or tenderness in peripheral joints or joint effusion and synovitis on imaging examination), and iritis (diagnosed by an ophthalmologist). The BASDAI and BASFI scores of all patients were recorded [8,9]. The erythrocyte sedimentation rate (ESR) was recorded (Italian ALIFAX Test-1 automatic rapid erythrocyte sedimentation rate analyzer; normal reference range, 0-20 mm/h), as well as C-reactive protein (CRP) (Beckman IMAGE800 analyzer and matching kit, immunoturbidimetry; normal reference range, 0-8 mg/L), HLA-B27 status, and bone mass. Bone mass was determined at the calcaneus using an

Ultrasonic bone intensity meter (GE Healthcare, Waukesha, WI, USA). A Z-value ≤-2 was defined as bone mass lower than that of peers. The drugs (anti-TNF, non-steroid anti-inflammatory drugs (NSAIDs), sulfasalazine, methotrexate, thalidomide, and glucocorticoids) were recorded. All indicators were collected by the specialists at the department of rheumatology and immunology.

Outcomes

The outcome index was the radiographic hip joint involvement assessed by the BASRI-hip score [10]. The BASRI-hip score ranges from 0 to 4 points: 0) normal, i.e., no radiological hip joint damage; 1) suspected hip joint damage, i.e., limited joint space stenosis; 2) mild hip joint damage, i.e., with an obvious hip joint lesion, but the hip joint space >2 mm; 3) moderate hip joint damage, with a definite hip joint lesion, hip joint space ≤2 mm and articular bony interface ≤2 cm; and 4) severe hip joint damage, i.e., with hip joint fusion or articular bony interface ≥2 cm, or indication for total hip replacement. A BASRI-hip score ≥2 was defined as radiological hip joint involvement.

Statistical analysis

SPSS 22.0 (IBM, Armonk, NY, USA) was used for all analyses. Continuous data were tested with the Kolmogorov-Smirnov test for normal distribution. Normally distributed continuous data are expressed as means ± SD, and non-normally distributed continuous data are expressed as medians (Q1, Q3). Categorical variables were presented as frequencies. Normally distributed continuous data were tested using the Student t-test, while non-normally distributed continuous data were analyzed by the Mann-Whitney U test. Univariable and multivariable (forward (LR) method) logistic regression analyses were performed to analyze the factors associated with radiological hip joint involvement. The variables with $P<0.1$ in the univariable analyses were included in the multivariable analysis. Two-sided P-values <0.05 were considered statistically significant.

Results

Characteristics of the patients

A total of 350 AS patients were included. The basic information, medical history information, and objective examination results are shown in Table 1. The patients with radiological hip joint involvement (BASRI-hip ≥ 2) accounted for 50.6% (177/350). The proportion of men was 83.7% (293/350). The mean age was 35.0 ± 12.7 years. The mean duration of disease was 10.8 ± 8.6 years; 21.4% (75/350) of the patients had a juvenile-onset (age ≤ 16 years). Patients with iritis accounted for 8.9% (31/350). The proportion of patients with a family history was 15.1% (53/350). The HLA-B27 positive rate was 90.9% (318/350). The mean BMI was 23.0 ± 4.4 kg/m^2. The mean value of BASDAI was 4.0 ± 2.1, and the mean value of BASFI was 3.6 ± 2.7. The proportion of patients with TNFi treatment > 3 months was 14.9% (52/350). The proportion of patients with continuous NSAIDs treatment was 16.6% (58/350).

Table 1
The clinical data of the included patients with AS (n = 350)

	Total (n = 350)
Male, n (%)	293 (83.7)
Age (years), mean ± SD (range)	35.0 ± 12.7 (18–79)
BMI (kg/m^2), mean ± SD, (range)	23.0 ± 4.4 (14.8–39.2)
BMI < 18.5 kg/m^2, n (%)	57 (16.3)
Duration of disease (years), median(Q1,Q3)	9 (5,15)
Juvenile onset (age ≤ 16 years old), n (%)	75 (21.4)
Iritis, n (%)	31 (8.9)
Achilles tendinitis, n (%)	47 (13.4)
Peripheral arthritis, n (%)	163 (46.6)
Smoking history, n (%)	178 (50.9)
Family history, n (%)	53 (15.1)
Schober test (positive), n (%)	176 (50.3)
HLAB27 (positive), n (%)	318 (90.9)
Bone mass lower than peers (Z≤-2), n (%)	90 (25.7)
CRP (mg/dl), median(Q1,Q3)	22.9(11.0,54.0)
ESR (mm/h), median(Q1,Q3)	40(19,63)
BASDAI, median(Q1,Q3)	3.6 (2.2,5.6)
BASFI, median(Q1,Q3)	3.1 (1.2,5.5)
TNFi > 3 months, n (%)	52 (14.9)
Continuous NSAIDs, n (%)	58 (16.6)
Sulfasalazine > 6 months, n (%)	81 (23.1)
Methotrexate > 6 months, n (%)	34 (9.7)
Thalidomide > 6 months, n (%)	29 (8.3)
Glucocorticoids > 2 weeks, n (%)	33 (9.4)

BMI: body mass index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; TNFi: tumor necrosis factor inhibitor; NSAIDs: non-steroidal anti-inflammatory drugs; BASRI: Bath Ankylosing Spondylitis radiological index.

	Total (n = 350)
BASRI-hip score, n (%)	
≥ 2	177 (50.6)
≤ 1	173 (49.4)

BMI: body mass index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; TNFi: tumor necrosis factor inhibitor; NSAIDs: non-steroidal anti-inflammatory drugs; BASRI: Bath Ankylosing Spondylitis radiological index.

Univariable analyses

The results of the univariable analyses are shown in Table 2. Compared with patients without radiological hip joint involvement, the patients with radiological hip joint involvement were younger (31.5 ± 11.2 vs. 38.6 ± 13.3, P < 0.001), had a higher rate of juvenile-onset (age ≤ 16 years old) (32.8% vs. 9.8%, P < 0.001), had a lower BMI (21.8 ± 4.2 vs. 24.2 ± 4.3, P < 0.001), a higher rate of bone mass was lower than peers (Z≤-2) (38.2% vs. 14.7%, P < 0.001), higher BASFI values (4.6 ± 2.9 vs. 2.8 ± 2.3, P = 0.001), and a higher rate of TNFi treatment > 3 months (20.6% vs. 9.2%, P = 0.004).

Table 2
Univariable logistic regression analyses for BASRI-hip ≥ 2

	BASRI-hip ≤ 1 (n = 173)	BASRI-hip ≥ 2 (n = 177)	OR	95%CI	P
Male, n (%)	139 (80.3)	154 (87)	1.638	0.920–2.916	0.094
Age (years), mean ± SD (range)	38.6 ± 13.3	31.5 ± 11.2	0.953	0.935–0.971	**< 0.001**
BMI (kg/m^2), mean ± SD (range)	24.2 ± 4.3	21.8 ± 4.2	0.87	0.824–0.919	**< 0.001**
BMI < 18.5 kg/m^2, n (%)	13(7.5)	44(24.9)	4.046	2.091–7.830	**< 0.001**
Duration of disease (years), median(Q1,Q3)	9(4,16)	9(5,14)	0.991	0.976–1.016	0.484
Juvenile onset (age ≤ 16 years old), n (%)	17 (9.8)	58 (32.8)	4.473	2.477–8.075	**< 0.001**
Iritis, n (%)	10 (5.8)	21 (11.9)	2.194	1.001–4.808	0.05
Achilles tendinitis, n (%)	24 (13.8)	23 (13.2)*	0.882	0.476–1.634	0.689
Peripheral arthritis, n (%)	77 (44.5)	86 (49.7)	1.232	0.808–1.881	0.333
Smoking history, n (%)	80 (46.2)	98 (56.6)	1.519	0.994–2.321	0.053
Family history, n (%)	32 (18.5)	21 (11.9)	0.593	0.327–1.076	0.086
Schober test (positive), n (%)	82 (48.2)	94 (54.7)	1.293	0.846–1.978	0.236
HLAB27 (positive), n (%)	157 (91.3)	161 (94.2)	1.538	0.671–3.527	0.309
Bone mass lower than peers (Z≤-2), n (%)	24 (14.7)	66 (38.2)	3.572	2.101–6.074	**< 0.001**
CRP (mg/dl), median(Q1,Q3)	20.6(9.7,53.9)	25.4(12.1,54.1)	1.001	0.995–1.006	0.808

*, missing data for 3 patients.

BASRI: Bath Ankylosing Spondylitis radiological index; OR: odds ratio; CI: confidence interval; BMI: body mass index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; TNFi: tumor necrosis factor inhibitor; NSAIDs: non-steroidal anti-inflammatory drugs.

	BASRI-hip ≤ 1 (n = 173)	BASRI-hip ≥ 2 (n = 177)	OR	95%CI	P
ESR (mm/h), median(Q1,Q3)	37(18,60)	41(24,65)	1.004	0.997–1.010	0.283
BASDAI, median(Q1,Q3)	3.7(2.3,5.7)	3.6(1.7,5.6)	0.974	0.818–1.160	0.766
BASFI, median(Q1,Q3)	2.5(1,4.3)	4(1.9,7.3)	1.288	1.103–1.503	**0.001**
TNFi > 3 months, n (%)	16 (9.2)	36 (20.6)	2.541	1.351–4.779	**0.004**
Continuous NSAIDs, n (%)	35 (20.2)	23 (13.0)	0.597	0.336–1.060	0.078
Sulfasalazine > 6 months, n (%)	37 (21.5)	44 (25.1)	1.266	0.744–2.018	0.424
Methotrexate > 6 months, n (%)	14 (8.1)	20 (11.4)	1.456	0.710–2.986	0.305
Thalidamide > 6 months, n (%)	13 (7.6)	16 (9.1)	1.215	0.566–2.610	0.617
Glucocorticoids > 2 weeks, n (%)	15 (8.7)	18 (10.3)	1.208	0.588–2.481	0.607
*, missing data for 3 patients.					
BASRI: Bath Ankylosing Spondylitis radiological index; OR: odds ratio; CI: confidence interval; BMI: body mass index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; TNFi: tumor necrosis factor inhibitor; NSAIDs: non-steroidal anti-inflammatory drugs.					

There was no significant difference in sex, duration of disease, iritis, Achilles tendinitis, peripheral arthritis, smoking history, family history, positive Schober test, HLA-B27 positive rate, CRP, ESR, BASDAI, continuous NSAIDs treatment, Sulfasalazine > 6 months, Methotrexate > 6 months, Thalidamide > 6 months and Glucocorticoids > 2 weeks between the two groups.

Multivariable analysis

The multivariable analysis of the factors associated with radiological hip joint involvement is shown in Table 3. The variables with $P < 0.1$ in the univariable analyses were included in the multivariable analysis. After adjusting for sex, iritis, smoking history, family history, and TNFi > 3 months, the results showed that the juvenile onset (age ≤ 16 years old) (OR = 4.955, 95%CI: 2.464–9.961, $P < 0.001$), bone mass lower than peers ($Z \leq -2$) (OR = 2.862, 95%CI: 1.593–5.142, $P < 0.001$), thin body size (BMI < 18.5 kg/m^2) (OR = 2.832, 95%CI: 1.321–6.069, P = 0.007), BASFI (OR = 1.278, 95%CI: 1.069–1.527, P = 0.007), and

continuous NSAIDs treatment (OR = 0.400, 95%CI: 0.200-0.799, P = 0.009) were independently associated with radiological hip joint involvement in patients with AS.

Table 3
Multivariable logistic regression analysis for BASRI-hip ≥ 2

	OR	95%CI	P
Juvenile onset (age ≤ 16 years old)	4.955	2.464–9.961	< 0.001
Bone mass lower than peers (Z≤-2)	2.862	1.593–5.142	< 0.001
BMI < 18.5	2.832	1.321–6.069	0.007
BASFI	1.278	1.069–1.527	0.007
Continuous NSAIDs	0.4	0.2-0.799	0.009
BASRI: Bath Ankylosing Spondylitis radiological index; BMI: body mass index; BASFI: Bath Ankylosing Spondylitis Functional Index.			
Adjusted variables: sex, iritis, smoking history, family history, TNFi > 3 months.			

Discussion

The results strongly suggest that AS with radiological hip joint involvement had worse body function and lower bone density. The independently associated factors with radiological hip joint involvement in patients with AS included juvenile-onset, bone mass lower than peers, thin body size, BASFI, and continuous NSAIDs drug treatment.

The results of the multivariable analysis showed that a juvenile-onset, bone mass lower than peers, and thin body size were associated with radiological hip joint involvement. The occurrence rate of radiological hip involvement in AS with juvenile-onset was 5.0 times that of non-juvenile onset. A study pointed out that a juvenile-onset of AS might be more serious, the occurrence rate of radiological hip joint damage might be higher, and the requirements for total hip replacement could be increased [11]. Another previous study indicated that spinal arthritis with onset during childhood was less likely to affect the axial bones, but it was more likely to involve the hip joints [12]. Another study divided AS patients into three groups according to the age of onset and found that the degree of radiological hip joint damage in patients with AS and juvenile onset was significantly more severe than that in AS patients with adult-onset [13]. Therefore, the patients could be required to be screened for hip joint damage, and the physicians should pay attention to the progression of hip joint damage during follow-up.

Osteoporosis is a common complication of AS, and the occurrence of both low bone mass and osteoporosis is high in AS patients [14, 15]. Of all the 350 AS patients in this study, patients with low bone mass accounted for 25.7% (90/350). Exercise could induce osteoclast differentiation to initiate bone reconstruction, which might increase bone mass [16].

The BASFI of patients with AS and radiological hip joint involvement in this study was significantly higher than in those without radiographic hip joint involvement. Compared with healthy people, AS patients have a fat-free mass (FFM) of 3 kg lower than the mean value, and appendicular lean mass (ALM) of 1 kg/m less than the mean value [17]. The data in this study showed that the mean BMI of all 350 AS patients was 23.0 ± 4.4 kg/m^2, which was lower than the mean level of Chinese adults (24.7 ± 3.5 kg/m^2) [18]. The multivariate analysis also showed that lean body shape (BMI < 18.5 kg/m^2) was an independent risk factor for radiological hip joint involvement in patients with AS.

The results of this study showed that the cumulative use of slow-acting drugs such as sulfasalazine, methotrexate, and thalidomide for more than 6 months was not protective for radiological hip joint damage in patients with AS. Some studies also reported that anti-TNF could slow the progression of hip joint damage in patients with AS [19, 20]. One study even reported that six AS patients with radiological hip joint involvement had increased hip joint space after anti-TNF treatment, and the BASRI score of these six patients decreased from 3 to 2 points [21], but the sample size was small. The present study showed that the usage rate of anti-TNF in AS patients with radiological hip joint damage was 19.7%, which was higher than that of 9.5% in AS patients without radiological hip joint damage, but the multivariable analysis showed that anti-TNF was not a protective factor for AS radiological hip joint damage. The therapeutic effect of NSAIDs on AS had been confirmed by many studies, and the 2019 American College of Rheumatology (ACR) update on AS and non-radiographic axial spondyloarthritis recommended continuous usage of NSAIDs in patients with AS [1]. A 2-year follow-up randomized controlled study showed that continuous non-steroidal anti-inflammatory drug treatment could reduce the progression of spine imaging in patients with AS [22]. Previous studies also reported that continuous NSAID treatment could reduce the risk of fracture in patients with AS [23].

In this study, the BASRI-hip score was used to evaluate AS-related hip joint damage. BASRI-hip ≥ 2 was defined as radiological hip joint involvement. This method was relatively objective based on the X-ray examination, but the radiological hip joint damage assessed by this method is already in a more advanced stage [24], which could not be considered because of the retrospective nature of the study. In addition, only the variables that were routinely collected in the clinical setting could be analyzed. In addition, the sample size was relatively small and limited to a single center.

Conclusions

In conclusion, patients with AS and radiological hip joint involvement had worse body function and lower bone density. The risk of radiological hip joint involvement in patients with AS and juvenile-onset and thin body size could be significantly increased. Screening and monitoring of hip joint damage should be conducted in patients with AS and these characteristics. Continuous NSAIDs drug treatment was a protective factor for radiological hip joint involvement in patients with AS. It might be recommended that NSAID treatment should be continued if the patients are without contraindications.

Abbreviations

AS: Ankylosing spondylitis; BASRI: Bath Ankylosing Spondylitis Radiology Index; BMI: body mass index; anti-TNF: anti-tumor necrosis factor; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; NSAIDs: non-steroid anti-inflammatory drugs; ACR: American College of Rheumatology.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Beijing Jishuitan Hospital (No: 202003-13). The need for individual consent was waived by the committee because of the retrospective nature of the study.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

WL, SM, Hi and PD carried out the studies, participated in collecting data, and drafted the manuscript. WL, HS and SM performed the statistical analysis and participated in its design. WL, HS, SM, HL and PD participated in acquisition, analysis, or interpretation of data and drafted the manuscript. All authors read and approved the final manuscript.

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