Radiographic Hip Involvement in Ankylosing Spondylitis: Factors Associated with Severe Hip Diseases

Jinzhao Zhao, Wei Zheng, Chao Zhang, Jia Li, Denghui Liu, and Weidong Xu

ABSTRACT. Objective. To determine the factors associated with severe radiographic hip involvement in patients with ankylosing spondylitis (AS).

Methods. A cross-sectional retrospective study was performed. The patients were classified into 3 groups based on the Bath Ankylosing Spondylitis Radiology Hip Index (BASRI-hip): minimal hip disease, moderate hip disease, and severe hip disease. Demographic, clinical, radiographic, and laboratory data were collected and analyzed. To identify factors associated with severe hip disease, ordinal regression analyses were performed.

Results. A total of 256 patients were involved in the study. There were differences in the age at onset, delay in diagnosis, bilateral hip involvement, sacroiliitis, Schober's index, and occiput-to-wall distance among the 3 groups (p < 0.05). The patients with severe hip disease had lower C-reactive protein and erythrocyte sedimentation rate levels than did the minimal group (p < 0.05). The functional status based on the Bath Ankylosing Spondylitis Functional Index and the Harris Hip Score showed significant differences (p < 0.05). The results of the ordinal regression analyses showed that bilateral hip involvement, sacroiliitis, delay in diagnosis, age at onset, and spinal involvement were associated with a higher BASRI-hip (p < 0.05).

Conclusion. Bilateral hip involvement, severe sacroiliitis, longer delay in diagnosis, early disease onset, and spinal involvement are associated with severe hip disease in patients with AS. The severity of hip involvement is associated with the functional status in AS. (First Release Nov 1 2014; J Rheumatol 2015;42:106–10; doi:10.3899/jrheum.140428)

Key Indexing Terms: ANKYLOSING SPONDYLITIS | HIP INVOLVEMENT | RADIOGRAPHIC
MATERIALS AND METHODS

Study subjects. A total of 256 patients with AS who were referred to our orthopedics outpatient clinics from December 2010 to December 2013 were included in a cross-sectional, retrospective study. All of the patients met the modified New York criteria for AS (5) and had radiographic hip involvement according to the BASRI-hip (6). Written informed consent was obtained from all the subjects, and the study was approved by the local ethics committee of Changhai Hospital (Shanghai, PR China). The subjects’ characteristics are given in Table 1.

Clinical data. The following clinical data were collected from all patients: age, sex, disease duration, initial symptoms of AS (low back pain, hip involvement, enthesitis, and others), age at disease onset, delay in diagnosis, family history of AS, treatment history [the usage of tumor necrosis factor (TNF) blockers]. Clinical examinations were performed by the same observer and included Schober’s index and the occiput-to-wall distance.

Disease assessment. The Bath Ankylosing Spondylitis Functional Index (BASFI) (7), Harris Hip Score (8), and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (9) were used to assess the functional status, hip function, and disease activity, respectively.

Radiological assessment. The BASRI-hip was used to assess radiographic hip involvement. The BASRI-hip is a reliable method for grading hip radiographic changes in AS (9). It was graded as follows: 0 = no disease (no change), 1 = suspicious disease (possible focal joint space narrowing), 2 = minimal disease (definite narrowing, leaving a circumferential joint space > 2 mm), 3 = moderate disease (narrowing but with circumferential joint space ≤ 2 mm or bone-on-bone apposition of < 2 cm), 4 = severe disease (bone deformity or bone-on-bone apposition > 2 cm or total hip replacement). Radiographic hip involvement was defined as a BASRI-hip score of at least grade 2. Bilateral hip involvement was defined as BASRI-hip scores of both hips ≥ 2. Anteroposterior pelvic radiographs were scored separately by 2 trained independent readers. When there was disagreement between the 2 readers, a senior physician made the final decision. The patients were classified into 3 categories based on their BASRI-hip scores: minimal hip disease (score of 2), moderate hip disease (score of 3), and severe hip disease (score of 4). Sacroiliitis was graded on the anteroposterior pelvic radiograph, according to the New York scale (10). Imaging studies were performed on the same day as the patient reported.

Laboratory measurements. The HLA-B27 status, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were evaluated and recorded in all subjects.

Statistical analysis. The subjects’ characteristics were described as the means (SD) for quantitative data and as proportions for qualitative data. To compare differences of continuous data, we used a 1-way ANOVA test. If there was a violation of variance homogeneity, Kruskal-Wallis 1-way ANOVA-rank was used. Categorical data were compared with Pearson chi-square analyses. To identify factors that are associated with severe hip disease, ordinal regression analyses were performed. The statistical analyses were conducted using SPSS 21.0. P ≤ 0.05 was considered statistically significant.

RESULTS

Description of study subjects’ characteristics. The demographics, clinical characteristics, laboratory, and radiographic data of 256 patients with AS with radiographic hip involvement are shown in Table 1. Based on the BASRI-hip, 107 patients (41.80%) had minimal hip disease (BASRI-hip = 2), 73 (28.51%) had moderate hip disease (BASRI-hip = 3), and 76 (29.69%) had severe hip disease (BASRI-hip = 4). The average age of the patients with AS was 34.00 years (8.26). The mean disease duration was 11.01 years (5.60). The age at onset was 22.99 years (5.50). The delay in diagnosis was 3.86 years (2.04). Of the 256 patients, 226 (88.28%) were male, and the ratio of males to females was 7.53:1. A total of 245 patients (95.70%) had bilateral hip involvement. The BASRI-hip was 2.59 (0.85) and the hip radiographic changes was 15.59 (6.17). The mean ESR was 5.80 (3.16) and the mean CRP was 3.16 mg/dl (1.01).

Comparison of patient characteristics among 3 subgroups. Table 2 shows the differences in patient characteristics among the 3 groups of hip-involved patients with AS. ANOVA analyses were used to compare differences in mean

Table 1. Demographic and clinical characteristics, and laboratory and radiographic data of 256 AS patients with radiographic hip involvement.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs, mean (SD)</td>
<td>34.00</td>
<td>17.10–63.00</td>
</tr>
<tr>
<td>Disease duration, yrs, mean (SD)</td>
<td>11.01</td>
<td>5.50–39.00</td>
</tr>
<tr>
<td>Age at onset, yrs, mean (SD)</td>
<td>22.99</td>
<td>5.50–47.00</td>
</tr>
<tr>
<td>Delay in diagnosis, yrs, mean (SD)</td>
<td>3.86</td>
<td>2.04–10.00</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>226</td>
<td>(88.28)</td>
</tr>
<tr>
<td>Male/female, ratio</td>
<td>7.53</td>
<td>1</td>
</tr>
<tr>
<td>HLA-B27+, n (%)</td>
<td>236</td>
<td>(92.20)</td>
</tr>
<tr>
<td>Family history, n (%)</td>
<td>28</td>
<td>(10.94)</td>
</tr>
<tr>
<td>TNF blockers, n (%)</td>
<td>50</td>
<td>(19.5)</td>
</tr>
<tr>
<td>Initial symptom at disease onset</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low back pain, n (%)</td>
<td>155</td>
<td>(60.55)</td>
</tr>
<tr>
<td>Hip joint, n (%)</td>
<td>42</td>
<td>(11.41)</td>
</tr>
<tr>
<td>Enthesitis, n (%)</td>
<td>27</td>
<td>(10.55)</td>
</tr>
<tr>
<td>Others, n (%)</td>
<td>31</td>
<td>(12.11)</td>
</tr>
<tr>
<td>Bilateral hip, n (%)</td>
<td>245</td>
<td>(95.70)</td>
</tr>
<tr>
<td>Schober’s index, cm, mean (SD)</td>
<td>2.59</td>
<td>0.85–5.00</td>
</tr>
<tr>
<td>Occiput-to-wall distance, cm,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (SD)</td>
<td>15.59</td>
<td>6.17–43.00</td>
</tr>
<tr>
<td>Sacroiliitis score, mean (SD)</td>
<td>3.22</td>
<td>0.65–6.13</td>
</tr>
<tr>
<td>BASFI, mean (SD)</td>
<td>6.13</td>
<td>1.33–9.30</td>
</tr>
<tr>
<td>BASDAI, mean (SD)</td>
<td>5.09</td>
<td>0.97–8.00</td>
</tr>
<tr>
<td>Harris Hip Score, mean (SD)</td>
<td>45.52</td>
<td>12.11–83.00</td>
</tr>
<tr>
<td>CRP, mg/dl, mean (SD)</td>
<td>3.16</td>
<td>1.01–5.80</td>
</tr>
<tr>
<td>ESR, mm/h, mean (SD)</td>
<td>5.80</td>
<td>3.16–60.00</td>
</tr>
<tr>
<td>BASRI-hip</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2, n (%)</td>
<td>107</td>
<td>(41.80)</td>
</tr>
<tr>
<td>3, n (%)</td>
<td>73</td>
<td>(28.51)</td>
</tr>
<tr>
<td>4, n (%)</td>
<td>76</td>
<td>(29.69)</td>
</tr>
</tbody>
</table>

AS: ankylosing spondylitis; TNF: tumor necrosis factors; BASFI: Bath Ankylosing Spondylitis Functional Index; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; BASRI-hip: Bath Ankylosing Spondylitis Radiology Hip Index.
age, age at onset, delay in diagnosis, Schober’s index, BASDAI, BASFI, CRP, and ESR among the 3 groups. If there was a violation of variance homogeneity, Kruskal-Wallis 1-way ANOVA-rank was used to compare differences in disease duration, occiput-to-wall distance, and Harris Hip Score. The results showed that there were differences in the age, age at onset, and delay in diagnosis among the 3 subgroups (p = 0.004, p = 0.001, and p = 0.001). Disease activity status measured by the BASDAI, the functional measures based on the BASFI score, and the Harris Hip Score showed significant differences (p = 0.048, p = 0.001, and p < 0.001, respectively). Schober’s index and the occiput-to-wall distance were significantly different among the 3 groups. Patients with more severe hip disease had lower CRP and ESR levels than the minimal group. Sacroiliitis score was significantly different among the 3 groups (p < 0.001). No differences were found in disease duration (p = 0.464). Pearson chi-square analyses were used to measure difference in sex, HLA-B27 positivity, family history, initial symptom at onset, treatment history, and bilateral hip involvement among groups. No differences were found in sex distribution, family history of AS, initial symptom at onset, use of TNF blockers, and percentage of HLA-B27 carriers. Bilateral hip involvement was significantly different among groups (p = 0.005).

Factors associated with higher BASRI-hip score. Separate regression analyses were performed to determine baseline risk factors for severe hip disease. OR (95% CI) were calculated. For the initial selection of multivariate risk factors, univariate risk factors with a p value < 0.20 were chosen. Finally, bilateral hip involvement, sacroiliitis, occiput-to-wall distance, delay in diagnosis, age at onset, and Schober’s index were included in the regression model (Table 3). Multivariate ordinal regression analyses were performed.

The results showed that bilateral hip involvement was the most significant factor associated with severe hip disease (OR 14.25, 95% CI 2.56–73.44, p = 0.002). It was followed by sacroiliitis (OR 4.93, 95% CI 3.12–7.79, p < 0.001), occiput-to-wall distance (OR 3.04, 95% CI 1.95–4.75, p < 0.001), delay in diagnosis (OR 2.35, 95% CI 1.36–4.08, p = 0.002), age at onset (OR 0.46, 95% CI 0.29–0.72, p = 0.001), and Schober’s index (OR 0.14, 95% CI 0.05–0.40, p < 0.001).

DISCUSSION
Our study confirmed that the severity of hip involvement is associated with a more impaired functional status (BASFI and Harris Hip Score) in AS and more limited spinal mobility measured by the occiput-to-wall distance and Schober’s index. We determined that the severity of radiographic hip disease in AS is associated with age at

<table>
<thead>
<tr>
<th>No. Patients</th>
<th>Minimal Hip Disease, BASRI-hip = 2</th>
<th>Moderate Hip Disease, BASRI-hip = 3</th>
<th>Severe Hip Disease, BASRI-hip = 4</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs, mean (SD)</td>
<td>35.99 (8.36)</td>
<td>32.67 (8.30)</td>
<td>32.47 (7.59)</td>
<td>0.004</td>
</tr>
<tr>
<td>Age at onset, yrs, mean (SD)</td>
<td>24.33 (5.22)</td>
<td>22.77 (4.93)</td>
<td>21.32 (5.97)</td>
<td>0.001</td>
</tr>
<tr>
<td>Disease duration, yrs, mean (SD)</td>
<td>11.66 (6.28)</td>
<td>9.90 (5.33)</td>
<td>11.16 (6.48)</td>
<td>0.464</td>
</tr>
<tr>
<td>Delay in diagnosis, yrs, mean (SD)</td>
<td>3.46 (2.00)</td>
<td>3.68 (2.04)</td>
<td>4.59 (1.91)</td>
<td>0.001</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>98 (91.59)</td>
<td>63 (86.30)</td>
<td>65 (85.53)</td>
<td>0.374</td>
</tr>
<tr>
<td>HLA-B27+, n (%)</td>
<td>98 (91.59)</td>
<td>63 (86.30)</td>
<td>65 (85.53)</td>
<td>0.374</td>
</tr>
<tr>
<td>Family history, n (%)</td>
<td>14 (13.08)</td>
<td>8 (10.69)</td>
<td>6 (7.89)</td>
<td>0.541</td>
</tr>
<tr>
<td>TNF blockers, n (%)</td>
<td>21 (19.6)</td>
<td>18 (24.7)</td>
<td>11 (14.5)</td>
<td>0.293</td>
</tr>
<tr>
<td>Initial symptom at disease onset</td>
<td>70 (65.42)</td>
<td>43 (58.90)</td>
<td>42 (55.26)</td>
<td>0.861</td>
</tr>
<tr>
<td>Low back pain, n (%)</td>
<td>70 (65.42)</td>
<td>43 (58.90)</td>
<td>42 (55.26)</td>
<td>0.861</td>
</tr>
<tr>
<td>Hip joint, n (%)</td>
<td>14 (13.08)</td>
<td>13 (17.81)</td>
<td>15 (19.74)</td>
<td>0.861</td>
</tr>
<tr>
<td>Enthesitis, n (%)</td>
<td>12 (11.22)</td>
<td>10 (13.70)</td>
<td>10 (13.16)</td>
<td>0.861</td>
</tr>
<tr>
<td>Others, n (%)</td>
<td>11 (10.28)</td>
<td>7 (9.59)</td>
<td>9 (11.84)</td>
<td>0.861</td>
</tr>
<tr>
<td>Bilateral hip, n (%)</td>
<td>98 (91.59)</td>
<td>71 (97.26)</td>
<td>76 (100)</td>
<td>0.005</td>
</tr>
<tr>
<td>Sacroiliitis, mean (SD)</td>
<td>2.96 (0.61)</td>
<td>3.22 (0.61)</td>
<td>3.59 (0.57)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Schober’s index, cm, mean (SD)</td>
<td>2.83 (0.88)</td>
<td>2.52 (0.79)</td>
<td>2.30 (0.77)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Occiput-to-wall distance, cm, mean (SD)</td>
<td>13.69 (4.73)</td>
<td>14.41 (4.35)</td>
<td>19.38 (7.66)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BASFI, mean (SD)</td>
<td>5.81 (1.25)</td>
<td>6.15 (1.30)</td>
<td>6.55 (1.36)</td>
<td>0.004</td>
</tr>
<tr>
<td>BASDAI, mean (SD)</td>
<td>4.91 (0.91)</td>
<td>5.23 (0.93)</td>
<td>5.17 (1.02)</td>
<td>0.048</td>
</tr>
<tr>
<td>CRP, mg/dl, mean (SD)</td>
<td>3.33 (1.09)</td>
<td>3.13 (0.89)</td>
<td>2.94 (0.95)</td>
<td>0.036</td>
</tr>
<tr>
<td>ESR, mm/h, mean (SD)</td>
<td>35.93 (9.94)</td>
<td>31.40 (9.29)</td>
<td>28.03 (10.61)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

TNF: tumor necrosis factors; BASFI: Bath Ankylosing Spondylitis Functional Index; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; BASRI-hip: Bath Ankylosing Spondylitis Radiology Hip Index.

Table 2. Comparison of clinical, laboratory, and radiographic data between 3 groups based on BASRI-hip scores in hip-involved patients with ankylosing spondylitis.
did not have longer disease duration. A delay in diagnosis
in hip arthroplasty in AS. In our study, we determined that
involvement had a longer duration of diagnosis delay but
have more hip involvement, and this is associated with total
factor of developing more severe radiographic hip disease
in AS. The age at onset (per 10 yrs) is a protective
study, patients with AS who had more severe hip disease
had more severe sacroiliitis, spinal involvement, longer
delay in diagnosis, and early onset.

We found a strong correlation between severity of
radiographic hip damage and BASFI scores in patients with
AS, and more severe radiographic hip involvement contributed
to higher BASFI scores. The same result was found in
terms of the Harris Hip Score. The hip joint plays an
important role in bipedalism and movement function in
human beings. Previous reports have shown that patients
with clinical or radiological hip involvement have worse
BASFI scores than those without hip involvement, and this
could lead to impaired physical functioning. For the individuals
with more severely involved hips and those with worse
functional status, total hip arthroplasty was considered.

In our study, the severity of hip involvement was associated with
limitations of spinal mobility, such as low Schober’s index
and occiput-to-wall distance, indicating that hip involvement
patients have more severe axial damage, making them susceptible to a decline in physical function. These results are
consistent with previous studies. For the individuals
with more severely involved hips and those with worse
functional status, total hip arthroplasty was considered.

This demonstrates the necessity of preventing the deterioration
of hip involvement and taking early measures to allow these patients to have a better functional status.

Some reports indicate that patients with juvenile onset
have more hip involvement, and this is associated with total
hip arthroplasty in AS. In our study, we determined
that younger age at onset is closely related to severe hip
disease in AS. The age at onset (per 10 yrs) is a protective
factor of developing more severe radiographic hip disease
(OR 0.46, 95% CI 0.29–0.72, p = 0.001).

Disease duration has been shown to be associated with
hip involvement, but we found no association between disease
duration and more severe hip disease in AS. In our study, patients with AS who had more severe hip disease
involvement had a longer duration of diagnosis delay but
did not have longer disease duration. A delay in diagnosis
indicates misdiagnosis and inappropriate treatment in early stages. This result indicates that it is important to make the
diagnosis early and implement the appropriate therapeutic strategy for reducing the occurrence and development of
severe hip involvement in hip-involved patients with AS.

The susceptibility of AS has a strong association with
young males and the HLA-B27 genotype. In our study, the presence of HLA-B27, a family history of AS, and sex
distribution were not different among patients with different severities of hip involvement. These results were consistent with the study by Burki, et al. That study showed that genetic factors might play a minor role in the processing of
hip disease in hip-involved patients with AS. Regarding
initial symptoms, inflammatory back pain was the most commonly affected site, followed by enthesitis and the hip
joints. There was no difference in initial symptoms among the subgroups.

TNF blockers are effective in relieving symptoms and
improving disease status. However, it is unclear whether TNF blockers could prevent structural damage in
AS. Some studies reported that TNF inhibitors fail to
substantially slow new bone formation in AS; some studies show it appears to be associated with increased
structural damage, and some studies showed a potential
benefit of TNF blockers on radiographic progression in AS.
In some studies, the effect of longterm treatment with the TNF blocker infliximab (IFX) on radiographic progression of hip arthritis in AS was studied, and the authors found that radiographic progression of hip arthritis in AS may be arrested during IFX treatment. We
reviewed the clinical data on use of TNF blockers in our study and found no significant difference among the 3
groups (p = 0.293).

The levels of laboratory inflammatory biomarkers, such as
CRP and ESR, were different among the 3 groups in our study. Minimal hip disease is associated with a higher level of
CRP and ESR; these elevations did not occur in the more
severely affected groups. This result confirmed that the
main pathological features of AS are different in different
disease stages; inflammation lesions are predominant in the early stage, and tissue repair or ossification are predominant in advanced stages. This finding indicates that appropriate indicators should be used in certain stages of disease in AS for evaluating the severity of the disease.

There are limitations to our study. It is a retrospective
cross-sectional study, and a prospective cohort study should be performed to confirm the risk factors for severe hip
disease in AS. The subjects in our study, who were patients
referred to an outpatient orthopedic clinic, might represent a
severely affected group. All study subjects agreed to partici-
pate, and there might be selection bias.

More severe hip involvement is associated with a worse
functional status in AS. Bilateral hip involvement, severe
sacroiliitis, longer delay in diagnosis, early disease onset,
and spinal involvement are associated with severe hip disease in patients with AS. Disease duration, sex, HLA-B27, and family history showed no association with the severity of hip disease. Inflammatory biomarkers, such as ESR and CRP, cannot reflect disease severity in advanced stages. To improve the quality of life of hip-involved patients with AS, the diagnosis and treatment of hip disease should be done in the early stage, especially in patients with AS diagnosed at an early age, those who have bilateral hip involvement, and patients with severe sacroiliitis.

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REFERENCES


