Radiologic Changes in the Symphysis Pubis of Male Patients with Ankylosing Spondylitis

Bon San Koo, Yoonah Song, Kyung Bin Joo, Seunghun Lee, and Tae-Hwan Kim

ABSTRACT. ***Objective.*** We aimed to evaluate the involvement of the symphysis pubis in patients with ankylosing spondylitis (AS), and to assess the correlations between symphysis pubis changes and clinical findings.

Methods. We retrospectively evaluated a total of 222 male patients with AS who underwent pelvic and cervical/lumbar spine radiography at the Hanyang University Hospital for Rheumatic Diseases from August 2004 to February 2014. Radiographs were examined by 2 experienced radiologists, and radiographic damage was scored as follows: 0 (no damage), 1 (subtle irregularity and/or subchondral sclerosis), 2 (erosion), 3 (partial ankylosis), and 4 (total ankylosis). We evaluated the patients' clinical characteristics and analyzed their correlations with radiographic symphysis pubis changes.

Results. The mean patient age was 30.5 ± 8.3 years and mean disease duration was 7.1 ± 4.6 years; 105 patients (47.3%) exhibited radiologic damage in the symphysis pubis. Moreover, 75, 28, 0, and 2 patients had scores of 1, 2, 3, and 4, respectively. When comparing the normal (score 0) and abnormal (score 1–4) symphysis pubis groups, the latter had a longer symptom duration (10.1 ± 7.0 vs 7.6 ± 5.8 yrs, p = 0.004) and higher modified Stoke Ankylosing Spondylitis Spine Score (mSASSS; 18.6 ± 17.0 vs. 14.3 ± 13.4, p = 0.038). Moreover, a significant correlation was noted between the radiographic symphysis pubis damage score and mSASSS (r^2 = 0.147, p = 0.029).

Conclusion. Among male patients with AS, 47.3% exhibited symphysis pubis involvement. Moreover, a correlation was observed between the radiographic symphysis pubis and spine changes. (First Release December 15 2015; J Rheumatol 2016;43:330–4; doi:10.3899/jrheum.150711)

Key Indexing Terms:
SYMPHYSIS PUBIS ANKYLOSING SPONDYLITIS
MODIFIED STOKE ANKYLOSING SPONDYLITIS SPINE SCORE

Ankylosing spondylitis (AS) is characterized by the inflammation of the axial skeleton and peripheral joints, along with extraarticular manifestations such as the eyes, skin, and gastrointestinal tract[1]. The most characteristic feature of AS is ankylosis and fusion of the axial joints, including the sacroiliac (SI) joint.

The symphysis pubis is a nonsynovial fibrocartilaginous joint formed by the paired pubic bones and an interposed fibrocartilaginous disc[2]. Joint changes in the symphysis pubis lead to a widened, eroded, or damaged appearance, and have various causes such as degenerative changes in multiparous women and athletes, and occasionally, retropubic prostatectomy[3]. Tuberculosis and bacterial infection can also induce severe inflammatory changes in the symphysis pubis.

Such changes in the symphysis pubis have also been reported in rheumatic diseases, including AS, rheumatoid arthritis (RA), and osteoarthritis (OA)[4]; among these diseases, AS is known to more frequently involve the symphysis pubis. However, the involvement of the symphysis pubis in patients with AS has rarely been documented, given its low prevalence compared with the involvement of the spine or SI joint[5,6]. Nevertheless, a few studies suggest that symphysis pubis changes may frequently develop in patients with AS[4,6,7].

Previous attempts to classify radiographic symphysis pubis changes in AS have shown that scores assigned to these changes increased in patients with longer disease durations[4,8], suggesting that the development of symphysis pubis changes may be similar to that of axial spine changes. However, no previous studies have demonstrated a correlation between symphysis pubis and axial spine changes. In our present study, we aimed to investigate the prevalence of symphysis pubis involvement and its correlation with the clinical findings in patients with AS.

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MATERIALS AND METHODS

We retrospectively reviewed 222 male patients who had undergone followup pelvic radiography at the Hanyang University Hospital for Rheumatic Diseases from August 2004 to February 2014. All patients had been previously diagnosed with AS according to the modified New York criteria[9]. We excluded female patients because they may have exhibited symphysis pubis changes related to childbirth[3]. Our study was approved by the institutional review board of the Hanyang University Hospital (IRB permit number: 2014-04-010-006).

All clinical data were blinded, and radiographic changes were scored independently by 2 radiologists (SL, KBJ). Similar to SI joint grading according to the 1984 modified New York criteria[9], radiographic symphysis pubis changes were assigned scores of 0–4 (0 = no damage, 1 = subtle irregularity and/or subchondral sclerosis, 2 = erosion, 3 = partial ankylosis, and 4 = total ankylosis; Figure 1). The modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) was used for cervical and lumbar spine assessment on lateral radiographs; each anterior vertebral corner from the lower T12 to upper S1 level and lower C2 to upper T1 level was scored from 0 to 3 (0 = normal; 1 = erosion, sclerosis, or squaring; 2 = non-bridging syndesmophytes; and 3 = bridging syndesmophytes) to yield total scores ranging from 0 to 72. Because the interreader agreement regarding mSASSS was found to be very good in a previous study, with intraclass correlation coefficients (ICC) of 0.75 (95% CI 0.61–0.82) and 0.71 (95% CI 0.58–0.82) at different timepoints[10], the mSASSS was scored by a single radiologist in our present study.

Clinical characteristics were investigated, including age, sex, HLA-B27 positivity, juvenile-onset AS, disease duration, symptom duration, history of uveitis, peripheral arthritis, familial history of AS, and smoking. Tumor necrosis factor (TNF) inhibitor use and the nonsteroidal antiinflammatory drug (NSAID) index were reviewed[11]. The onset of symptoms in individuals aged ≤ 16 years was defined as juvenile-onset AS; all other cases were classified as adult-onset AS. Family history was defined as whether the subject had any first-degree relatives (parents, siblings, or offspring) diagnosed with AS.

We estimated the interreader agreement in the symphysis pubis radiographic change scores and mSASSS by using a κ statistic correlation. Clinical comparisons between the radiographic symphysis pubis change groups were performed by using Student t tests for normally distributed continuous measures. Mann-Whitney U tests were used for non-normally distributed continuous measures, and chi-square tests were used for categorical variables. A Spearman correlation analysis was conducted to examine the relationship between the symphysis pubis change score and mSASSS. A p value of < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 17.0 software (IBM).

RESULTS

A total of 222 patients underwent followup pelvic radiography. The patients had a mean age of 30.5 ± 8.3 years. The mean symptom duration (lower back pain) was 8.7 ± 6.5 years, and the mean disease duration (from the diagnosis of AS) was 7.1 ± 4.6 years. Moreover, 208 of the 214 patients (97.2%) who underwent HLA-B27 assessments indicated positive results. The mean NSAID index was 52.4 ± 32.6, and 82 patients (36.9%) used a TNF inhibitor.

In terms of radiologic analysis, the agreement between the 2 readers regarding the symphysis pubis change scoring was very good, with an ICC of 0.88 (95% CI 0.84–0.90). Among all patients, 117 (52.0%), 75 (33.3%), 28 (12.4%), 0 (0%), and 2 (0.9%) patients had scores of 0, 1, 2, 3, and 4, respectively. To evaluate factors associated with symphysis pubis changes, we divided patients into 2 groups according to symphysis pubis scores — patients with scores of 0 were classified into the normal group and those with scores of 1–4 were classified into the abnormal group. A comparison of the 2 groups (Table 1) revealed that, in terms of clinical characteristics, the mean symptom duration was significantly longer in the abnormal group than in the normal group (10.1 ± 7.0

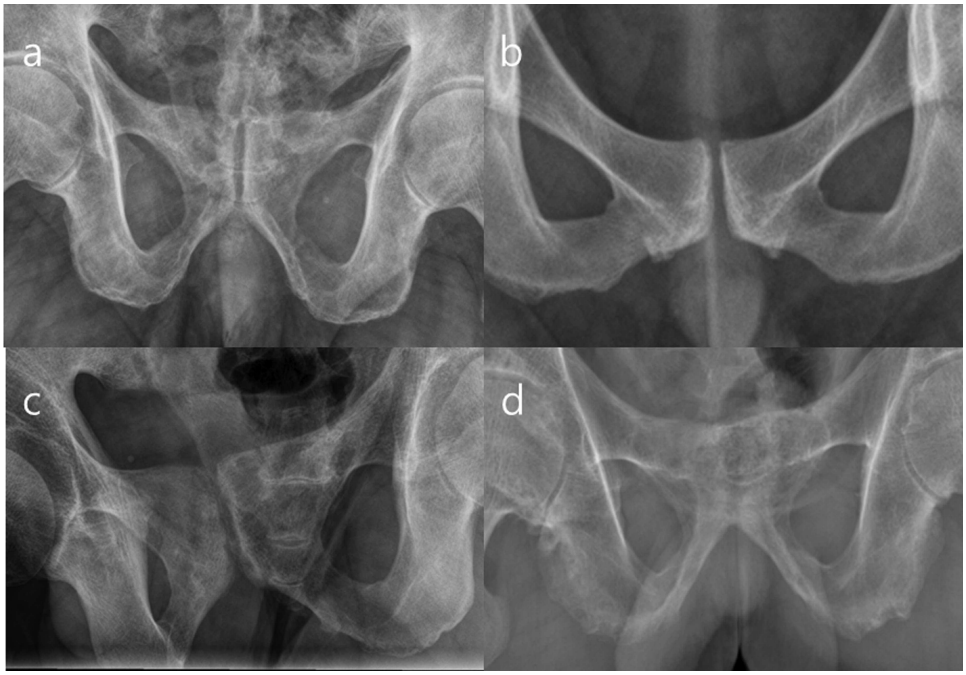

Figure 1. Radiographic changes in the symphysis pubis joint in patients with ankylosing spondylitis include (A) irregularity, (B) subchondral sclerosis, (C) erosion, and (D) total ankylosis.

Table 1. Comparison of the normal and abnormal symphysis pubis joint groups. Values are n (total, %) unless otherwise specified.

Characteristics	Normal Group, n = 117	Abnormal Group, n = 105	p
Age, yrs, mean ± SD	30.1 ± 8.0	31.1 ± 8.6	0.352
Symptom duration, yrs, mean ± SD	7.6 ± 5.8	10.1 ± 7.0	0.004
Disease duration, yrs, mean ± SD	6.7 ± 3.6	7.6 ± 5.5	0.124
HLA-B27 positivity	107 (112, 95.5)	101 (102, 99.0)	0.215
Juvenile-onset AS	19 (106, 17.9)	20 (96, 20.8)	0.721
History of uveitis	40 (117, 34.2)	40 (105, 38.1)	0.577
History of peripheral arthritis	40 (117, 34.2)	46 (105, 43.8)	0.168
Familial history of AS	12 (117, 10.3)	19 (105, 18.1)	0.120
Smoking, mean ± SD	7.2 ± 7.8	8.3 ± 10.2	0.611
NSAID index, mean ± SD	51.4 ± 32.2	53.6 ± 33.5	0.611
Use of TNF blocker	36 (117, 30.8)	46 (105, 43.8)	0.052
mSASSS, mean ± SD	14.3 ± 13.4	18.6 ± 17.0	0.038

AS: ankylosing spondylitis; NSAID: nonsteroidal antiinflammatory drugS; TNF: tumor necrosis factor; mSASSS: modified Stoke Ankylosing Spondylitis Spine Score.

vs 7.6 ± 5.8 yrs, p = 0.004). The mean mSASSS was also significantly greater in the abnormal group (18.6 ± 17.0 vs 14.3 ± 13.4, p = 0.038). As in Table 1, cases with a normal symphysis pubis and those with abnormalities such as subtle irregularity and/or subchondral sclerosis were compared with those with apparent changes, including erosion and ankylosis (Table 2). The symptom duration and mSASSS scores were significantly different between the group, including cases of normal symphysis pubis and minimal symphysis pubis abnormalities, and the group including cases with apparent changes. Moreover, the group with apparent changes had a greater number of cases with juvenile-onset AS and TNF blocker use. These results suggest that the symphysis pubis change score was associated with the progression of AS.

To confirm the correlation between symphysis pubis changes and radiographic progression in AS, we evaluated the correlation between symphysis pubis scores and mSASSS. A higher symphysis pubis change score was concomitantly observed with a higher mSASSS in most patients. Spearman correlation analysis indicated a significant correlation between the symphysis pubis score and the mSASSS score ($r^2 = 0.147$, p = 0.029).

To elucidate longitudinal radiographic symphysis pubis changes relative to mSASSS, the pelvic and spinal radiographs were compared with the followup symphysis pubis radiograph for each patient. The mean interval between the initial and followup radiographs was 4.3 ± 1.6 years. The mean mSASSS increased from the first measurement to the

Table 2. Comparison of the normal symphysis pubis cases and cases with minimal change to cases with apparent changes in the symphysis pubis joint groups. Normal symphysis pubis cases and cases with minimal changes include cases with a normal symphysis pubis and those with a subtle irregularity and/or subchondral sclerosis, whereas cases with apparent changes include those with erosion and ankylosis of the symphysis pubis. Values are n (total, %) unless otherwise specified.

Characteristics	Normal Cases and Cases with Minimal Changes, n = 192	Cases with Apparent Changes, n = 30	p
Age, yrs, mean ± SD	30.5 ± 8.1	31.1 ± 9.3	0.703
Symptom duration, yrs, mean ± SD	8.4 ± 6.3	11.2 ± 7.1	0.031
Disease duration, yrs, mean ± SD	7.0 ± 4.5	8.3 ± 5.3	0.153
HLA-B27 positivity	179 (185, 96.8)	29 (28, 100.0)	0.325
Juvenile-onset AS	30 (176, 17.0)	9 (26, 34.6)	0.034
History of uveitis	66 (192, 34.4)	14 (30, 46.7)	0.192
History of peripheral arthritis	70 (192, 36.5)	16 (30, 53.4)	0.075
Familial history of AS	25 (192, 13.0)	6 (30, 20.0)	0.305
Smoking, mean ± SD	7.7 ± 9.2	8.0 ± 8.0	0.895
NSAID index, mean ± SD	53.3 ± 32.6	47.0 ± 33.9	0.342
Use of TNF blocker	64 (192, 33.3)	18 (30, 60.0)	0.05
mSASSS, mean ± SD	15.3 ± 14.1	23.3 ± 20.6	0.008

AS: ankylosing spondylitis; NSAID: nonsteroidal antiinflammatory drug; TNF: tumor necrosis factor; mSASSS: modified Stoke Ankylosing Spondylitis Spine Score.

second measurement (16.3 ± 15.2 vs 19.9 ± 18.4, p = 0.001). In contrast, the mean symphysis pubis scores did not differ between timepoints (0.6 ± 0.7 vs 0.6 ± 0.7, p = 0.887), and 173 patients (77%) exhibited no changes in their symphysis pubis scores.

Twenty-five patients (11%) exhibited radiographic progression of symphysis pubis changes. Subtle irregularities with/without subchondral sclerosis developed (score 0 to 1) in 20 patients (9%), and erosion progressed (score 1 to 2) in 5 patients (2%). On the other hand, 24 patients (11%) exhibited decreases in radiograph scores. Bone erosion disappeared (score 2 to 1) in 7 patients (3%) and subchondral sclerosis and/or irregularity normalized (score 1 to 0) in 17 patients (8%). A Spearman analysis of the change in Δsymphysis pubis damage score and ΔmSASSS score did not indicate a significant correlation ($r^2 = –0.042$, p = 0.538).

DISCUSSION

Radiographic changes in the symphysis pubis have often been observed in patients with AS, although the prevalence rates differ among reports[3,8]. The male patients with AS in our cohort had a symphysis pubis involvement prevalence of 47%, which correlated with the mSASSS. This finding suggested that symphysis pubis involvement is a common manifestation of AS, and exhibits similar progression as the axial spine damage associated with AS, including bone erosion and formation.

Symphysis pubis damage was also classified in 2 previous studies[4,8]. Scott, *et al* classified patients with AS, RA, and OA into 5 grades based on the presence of sclerosis and symphysis pubis joint margin erosion. Among those patients, 10 of 40 patients with RA (25%) and 3 of 40 with OA (8%) exhibited symphysis pubis involvement; in contrast, all patients with AS exhibited grade 3 or 4 symphysis pubis changes[4]. Moreover, Jajić, *et al* studied 68 patients with AS (66 men) and found that 16 exhibited radiographic symphysis pubis changes[8]. Jajić, *et al* differentiated these radiologic changes into 4 stages — minimal, apparent destructive, reparation, and ankylosis — and suggested that patients with a longer disease duration exhibited a higher stage of symphysis pubis change. However, both previous studies mostly included patients in the ankylosis group[4] or demonstrated a uniform distribution at each stage[8]. In contrast, our study classified patients into 5 stages of symphysis pubis damage, similar to the sacroiliitis grading method that uses the modified New York criteria[9]. Compared with the 2 previous studies, most of our patients exhibited scores of 1 and 2, indicating early-phase sclerosis and/or symphysis pubis erosion, even though we adjusted for different classification criteria. Earlier diagnosis and more effective treatments (e.g., biologic therapy) in our present study, in comparison with the previous studies, might account for this discrepancy.

Interestingly, some patients (11%) exhibited decreased symphysis pubis scores on followup radiographs. The sequence of events leading to the development of ankylosis in the joints has not yet been established, but radiography suggests that ankylosis follows the resolution of erosions. A recent study suggested the following hypothesis: the resolution of inflammatory lesions in erosions is followed by the development of new tissue with the same high signal intensity as bone marrow fat metaplasia; this new tissue or fat lesion might subsequently develop into ankylosis, which the authors described as "backfill"[12]. Hence, we suggest that the decreased symphysis pubis scores observed in our present study might indicate ankylosis progression rather than healing.

Currently, the mSASSS is the most frequently used method for scoring spinal structural damage, given its good reliability and sensitivity for AS-related changes[13]. Accordingly, we used the mSASSS to determine whether the symphysis pubis changes and axial spine involvement are similar in patients with AS, and to identify the correlations with symphysis pubis damage scores. Our study revealed that patients with AS and advanced symphysis pubis damage scores also had high mSASSS. However, we did not find a correlation between the change in symphysis pubis damage score and the change in mSASSS, possibly because our symphysis pubis damage score classification did not properly reflect bone repair associated with AS progression.

Our study had some limitations. First, we did not evaluate AS disease activity indices such as the Bath Ankylosing Spondylitis Activity and Function indices. Therefore, we were unable to clarify the relationship between symptoms and radiograph changes. Second, because we only evaluated radiographs, we could not demonstrate active inflammatory joint lesions or enthesitis in the symphysis pubis and axial spine. Magnetic resonance imaging findings of enthesitis or inflammatory joints might provide additional information regarding the sequence of events, such as inflammation, reparation, or sclerosis in the symphysis pubis.

We found that 47% of male patients with AS in our cohort exhibited symphysis pubis involvement. Moreover, we suggest that an examination of symphysis pubis changes might provide valuable information regarding AS progression because symphysis pubis involvement appears to be correlated with axial spinal changes in patients with AS.

REFERENCES

1. Khan MA, van der Linden SM. A wider spectrum of spondyloarthropathies. Semin Arthritis Rheum 1990;20:107-13.
2. Budak MJ, Oliver TB. There's a hole in my symphysis — a review of disorders causing widening, erosion, and destruction of the symphysis pubis. Clin Radiol 2013;68:173-80.
3. Sequeira W. Diseases of the pubic symphysis. Semin Arthritis Rheum 1986;16:11-21.
4. Scott DL, Eastmond CJ, Wright V. A comparative radiological study of the pubic symphysis in rheumatic disorders. Ann Rheum Dis 1979;38:529-34.
5. Calin A, Elswood J. The relationship between pelvic, spinal and hip

involvement in ankylosing spondylitis—one disease process or several? Br J Rheumatol 1988;27:393-5.
6. Vinson EN, Major NM. MR imaging of ankylosing spondylitis. Semin Musculoskelet Radiol 2003;7:103-13.
7. Yilmaz MH, Ozbayrak M, Kasapcopur O, Kurugoglu S, Kanberoglu K. Pelvic MRI findings of juvenile-onset ankylosing spondylitis. Clin Rheumatol 2010;29:1007-13.
8. Jajić Z, Jajić I, Grazio S. Radiological changes of the symphysis in ankylosing spondylitis. Acta Radiol 2000;41:307-9.
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. Kim TJ, Lee S, Joo KB, Park DJ, Park YW, Lee SS, et al. The presence of peripheral arthritis delays spinal radiographic progression in ankylosing spondylitis: Observation Study of the Korean Spondyloarthropathy Registry. Rheumatology 2014;53:1404-8.
11. Dougados M, Simon P, Braun J, Burgos-Vargas R, Maksymowych WP, Sieper J, et al. ASAS recommendations for collecting, analysing and reporting NSAID intake in clinical trials/epidemiological studies in axial spondyloarthritis. Ann Rheum Dis 2011;70:249-51.
12. Maksymowych WP, Wichuk S, Chiowchanwisawakit P, Lambert RG, Pedersen SJ. Fat metaplasia and backfill are key intermediaries in the development of sacroiliac joint ankylosis in patients with ankylosing spondylitis. Arthritis Rheumatol 2014;66:2958-67.
13. Wanders AJ, Landewé RB, Spoorenberg A, Dougados M, van der Linden S, Mielants H, et al. What is the most appropriate radiologic scoring method for ankylosing spondylitis? A comparison of the available methods based on the Outcome Measures in Rheumatology Clinical Trials filter. Arthritis Rheum 2004;50:2622-32.