ORIGINAL ARTICLE

Degenerative Disc Pathology in Patients with Ankylosing Spondylitis: Frequency and Association with Disease Activity

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ABSTRACT

Objective: *To determine the frequency of degenerative disc pathology in patients with ankylosing spondylitis (AS) and explore its association with parameters of disease activity.*

Methods: *Patients between 15 and 65 years of age diagnosed with AS whose lumbar magnetic resonance imaging records were available in the registry database were enrolled. A total of 88 patients and 440 discs were evaluated. Modic classification was used for endplate degeneration, and the Pfirrmann scale, and the degree of disc herniation were analysed for disc degeneration. Aforementioned parameters were evaluated to determine whether they were associated with erythrocyte sedimentation rate, serum C-reactive protein (CRP) and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Values were expressed as frequencies and percentages for categorical variables. Spearman's test was used for correlation analysis.*

Results: *Among 440 discs examined, Modic changes were detected in 13% (person count [PC]: 30.7%) and Modic type 2 changes were the most common (disc count [DC]: 8.9%, PC: 25%). The most frequent Pfirrmann change was grade 1 degeneration (DC: 57.7%, 254 discs), and the most common form of disc herniation was bulging disc (DC: 21.7%, PC: 67%). A positive correlation was found between L1-L2 disc herniation and BASDAI activity and between L2-L3 disc herniation and CRP level (*$p < 0.05$*).*

Conclusion: *A high prevalence of Modic type 2 changes and bulging herniation was found. While this study may provide some insight for degenerative disc disease in AS, further studies involving a larger number of patients and a control group are needed.*

Keywords: Ankylosing spondylitis, disc degeneration, disc herniation, Modic changes.

INTRODUCTION

Ankylosing spondylitis (AS) is a member and also a prototype of the spondyloarthropathy (SPA) family of inflammatory disorders (1). The most common involvement is the involvement of the axial skeleton (2). The main clinical symptom is low back pain associated with the sacroiliac joint and spinal involvement (3). In AS, disease-specific vertebral changes include Romanus lesions, squaring of the vertebral bodies, syndesmophyte, 'bamboo spine' appearance, ankylosis, and Andersson lesions. In addition to these changes, disc degeneration and damage and destruction of vertebral endplates occur in patients with AS. These changes resemble those seen in severe degenerative disc disease (4, 5). Intervertebral disc degeneration is thought to be the first step in degenerative spinal changes. Furthermore, disc degeneration is considered to be one of the causes of several symptoms (neck pain or low back pain) (6).

Disc involvement plays a crucial role in the degenerative process that occurs in the axial spine. In AS, intervertebral disc involvement has been overshadowed by disease-specific pathologies, and in the present study, disc involvement in AS will be examined extensively. Usually, Andersson lesions, causing discovertebral erosion, has been the primary focus of studies in AS patients (7–13). There are few studies that explored the incidence

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of degenerative disc disease in AS, and these studies investigated solely endplate degeneration (14, 15). In a separate study that examined the SPA group of diseases as a whole, both endplate degeneration and disc degeneration were evaluated (16). However, as a result of our literature search, we did not identify any studies that investigated endplate degeneration, disc degeneration and disc herniation collectively in AS patients.

The purpose of the current study was to determine the frequency of degenerative disc pathology in AS patients and explore its association with parameters of disease activity.

SUBJECTS AND METHODS

The study was conducted retrospectively by examining the patient registry database. Before initiation of the study, approval was obtained from the Education Planning Committee and the Ethics Committee of Kayseri Research and Training Hospital. Patients between 15 and 65 years of age were enrolled. Study patients were selected from outpatients with examinations performed in the Kayseri Research and Training Hospital from December 2013 to January 2015. Patients diagnosed with AS according to the 1984 modified New York classification criteria and/or the 2009 Assessment of SpondyloArthritis international Society (ASAS) axial spondyloarthropathy classification criteria were studied (17, 18). Among those patients, patients with lumbar spine magnetic resonance imaging (MRI) records were included in the study.

Patients with other forms of spondyloarthropathy as well as AS, a past history of a surgical operation to the lumbar region, metallic implants that could impair image quality, a previous trauma or fracture to the lumbar region, spondylitis due to infectious diseases, or a metabolic bone disease affecting the degenerative process were excluded from the study. A flowchart diagram is provided in Fig. 1.

Magnetic resonance imaging evaluation

Lumbar MRI scans of patients were examined by three radiologists with an expertise in the musculoskeletal system. A total of 440 discs including L1-2, L2-3, L3-4, L4-5, and L5-S1 levels were examined at axial and sagittal T1 and T2 sequences. All images were evaluated using 21-inch high-resolution screens. For lumbar MRI scans, Modic classification was used for endplate degeneration, and Pfirrmann scale and the degree of disc herniation were analysed for disc degeneration.

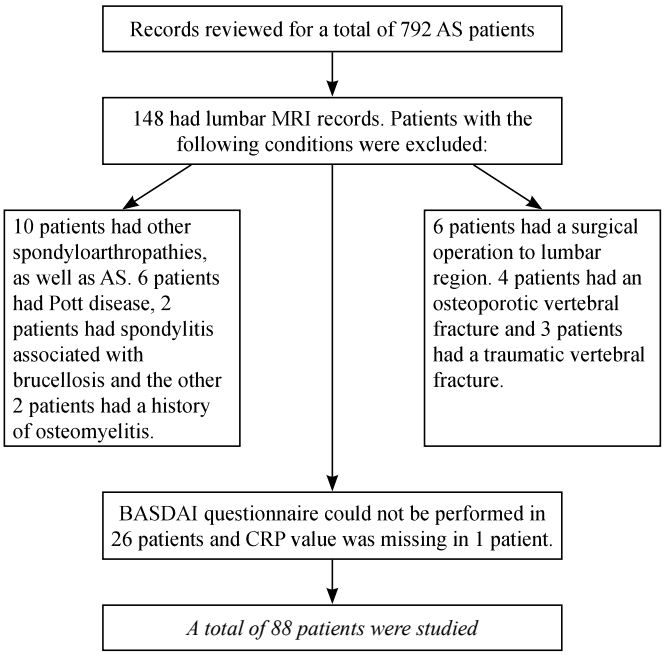

Fig. 1: Flowchart diagram. AS = ankylosing spondylitis; BASDAI= Bath Ankylosing Spondylitis Disease Activity Index; CRP = C-reactive protein; MRI = magnetic resonance imaging.

Modic changes

A formal classification was first provided by Modic *et al* in 1988 (19). Type 1 changes were hypointense on T1-weighted imaging (T1WI) and hyperintense on T2-weighted imaging (T2WI) and were shown to represent bone marrow oedema and inflammation (Fig. 2). Type 2 changes were hyperintense on T1WI and isointense or slightly hyperintense on T2WI and were associated with conversion of normal red haematopoietic bone marrow into yellow fatty marrow as a result of marrow ischaemia. Modic type 3 changes were

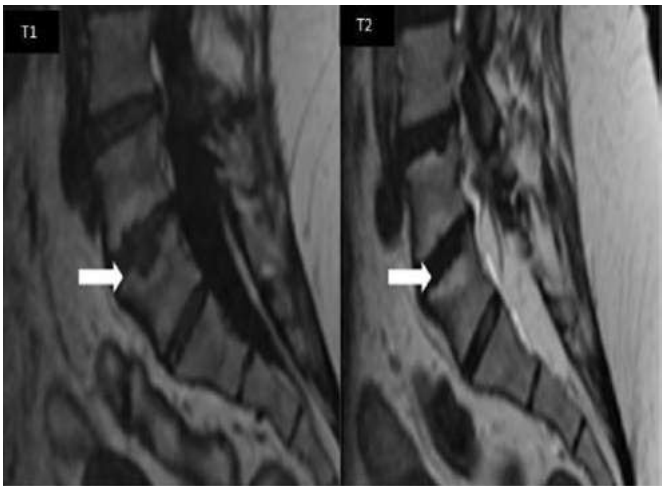

Fig. 2: Modic type 1 change observed in sagittal T1 and T2 sections.

subsequently described as hypointense on both T1WI and T2WI and were thought to represent subchondral bone sclerosis. Mixed-type 1/2 and 2/3 Modic changes have also been reported, suggesting that these changes can convert from one type to another and that they all represent different stages of the same pathologic process. The absence of Modic changes, a normal anatomic appearance, has often been designated as Modic type 0 (20). In the present study, oedema caused by a Romanus lesion or a Schmorl nodule was not included in the Modic classification.

Degree of disc herniation

The herniated disc was subdivided into bulging, subligamentous herniation and extrusion. Bulging was defined as displacement of the disc material greater than 50% of the disc circumference. When disc displacement was less than 50% of the disc circumference, the herniation was regarded as either protrusion (subligamentous herniation) or extrusion. The disc was defined as protrusion if the greatest distance between the edges of the disc material beyond the disc place was less than the distance between the edges of the base in any of the same planes. The extrusion was characterized as a greater diameter of the extruded fragment than of its base in any one plane (21).

Pfirrmann grading system

The degree of disc degeneration was graded on T2-weighted images with a modified Pfirrmann (22) scale as grade 1 (normal shape, no horizontal bands, distinction of nucleus and anulus is clear), grade 2 (non-homogeneous shape with horizontal bands, some blurring between nucleus and anulus), grade 3 (non-homogeneous shape with blurring between nucleus and anulus, anulus shape still recognizable), grade 4 (non-homogeneous shape with hypointensity, anulus shape not intact and distinction between nucleus and anulus impossible, disc height usually decreased; see Fig. 3), and grade 5 (same as grade 4, but collapsed disc space).

Laboratory parameters and disease activity

In order to assess the relationship between disc pathologies observed in lumbar MRI scans and laboratory parameters of patients, average erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values obtained in the previous year were analysed. To explore the association between disease activity and disc degeneration, patients were contacted via phone calls and the

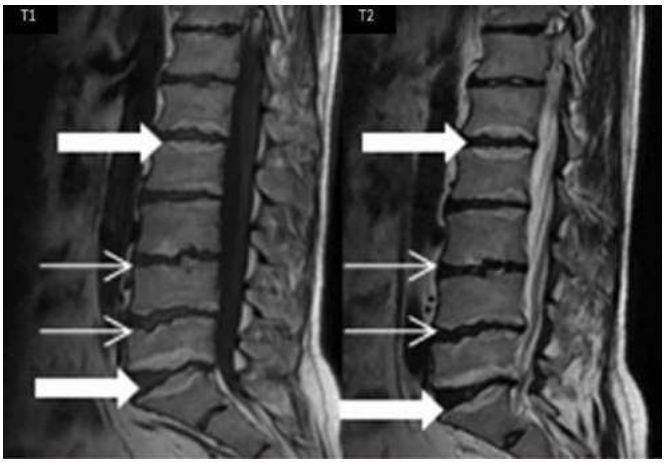

Fig. 3: Pfirrmann grade 4 degeneration (thin arrows) and Modic type 2 change (thick arrows) seen in sagittal T1 and T2 sequences.

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questionnaire was administered to patients during the calls.

Analysis of the prevalence of abnormal findings

The prevalence of the various abnormalities was calculated by disc count (DC) and person count (PC). Disc count is the number of discs, irrespective of the subjects (0–440), and PC is the number of subjects with disc degeneration (0–88).

Statistical analysis

Histogram and q–q plots were examined, and Shapiro–Wilk's test was performed to assess data normality. Values were expressed as frequencies and percentages for categorical variables, and mean and standard deviation or median and minimum–maximum statistics for continuous variables. Spearman's test was used for correlation analysis. Analysis was conducted using R 3.1.1 (www.r-project.org) software. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

Of 88 patients enrolled in the study, 38 (43.2%) were females and 50 (56.8%) were males. The mean (±SD) age of study patients was 40.34 ± 9.67 years. Clinical and demographic characteristics of patients are shown in Table 1. Table 2 summarizes the prevalence of Modic changes, disc bulging, protrusion, extrusion and disc degeneration levels in the MR studies. Table 3 shows the association of degenerative disc findings with ESR, CRP and BASDAI score.

Table 1: Patient characteristics

Variable	Statistics
Age (years)	40.34 ± 9.67
Gender	
Male	50 (56.8)
Female	38 (43.2)
Sacroiliac screening	
MRI sacroiliitis	66 (75.0)
Radiographic grade III sacroiliitis	14 (15.9)
Radiographic grade IV sacroiliitis	8 (9.1)
Laboratory values	
ESR	10.25 (2.00–58.00)
CRP	4.80 (3.30–46.40)
BASDAI	5.23 ± 2.12

Values are expressed as n (%), mean ± SD or median (min–max).
MRI = magnetic resonance imaging; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index.

Modic changes

Among 440 discs examined, Modic changes were detected in 13% (PC: 30.7%) but absent in 87% (PC: 64.7%). Modic type 1 change was observed in 13.6% of patients (DC: 3.6%). Modic type 2 was the most common pathologic Modic type affecting 25% of patients (DC: 8.9%). Both Modic type 1 and type 2 changes were observed in 5.7% of patients (DC: 1.1%), whereas Modic type 3 change was present in only 2 out of 440 discs. Modic changes were most commonly detected at L5-S1 disc (DC: 26.1%, 23 discs) with decreasing frequency towards the proximal disc. There was a significant association between Modic changes in L1-L2 and L3-L4 with CRP elevation ($p < 0.05$). Also, a significant relation was observed between Modic changes in L1-L2 disc and BASDAI ($p < 0.05$).

Table 2: Summary of the prevalence of disc bulging, protrusion, extrusion, disc degeneration levels and Modic changes in the MRI studies

Variable	Disc distance					
	L1-L2	L2-L3	L3-L4	L4-L5	L5-S1	Total
Modic						
Normal	82 (93.2)	83 (94.3)	80 (90.9)	73 (83.0)	65 (73.9)	383 (87)
Modic-I	2 (2.3)	1 (1.1)	2 (2.3)	3 (3.4)	8 (9.1)	16 (3.6)
Modic-II	4 (4.5)	4 (4.5)	5 (5.7)	12 (13.6)	14 (15.9)	39 (8.9)
Modic-III	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.5)
Pfirrmann						
Pfirrmann-I	70 (79.5)	64 (72.7)	51 (58.0)	34 (38.6)	35 (39.8)	254 (57.7)
Pfirrmann-II	9 (10.2)	15 (17.0)	26 (29.5)	36 (40.9)	26 (29.5)	112 (25.5)
Pfirrmann-III	3 (3.4)	8 (9.1)	8 (9.1)	16 (18.2)	21 (23.9)	56 (12.7)
Pfirrmann-IV	6 (6.8)	1 (1.1)	3 (3.4)	2 (2.3)	6 (6.8)	18 (4.1)
Disc prolapsus						
Normal	84 (95.8)	74 (84.1)	68 (77.3)	41 (46.6)	36 (40.9)	303 (68.9)
Bulging	4 (4.5)	12 (13.6)	17 (19.3)	35 (39.8)	27 (30.7)	95 (21.6)
Protrusion	0 (0.0)	1 (1.1)	3 (3.4)	12 (13.6)	25 (28.4)	41 (9.3)
Extrusion	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

Values are expressed as n (%).

Table 3: Spearman correlation coefficients among Modic changes, Pfirrmann scale, disc herniation and ESR, CRP and BASDAI

Variable	Disc distance				
	L1-L2	L2-L3	L3-L4	L4-L5	L5-S1
Modic					
ESR	–0.171	–0.170	–0.074	–0.002	0.086
CRP	0.034	–0.086	0.010	0.149	0.155
Basdai	0.025	0.131	0.141	0.064	0.100
Pfirrmann					
ESR	–0.191	–0.123	–0.119	–0.112	–0.010
CRP	–0.057	–0.099	–0.052	0.063	0.030
Basdal	0.117	0.219	–0.025	0.343	0.072
Disc prolapsus					
ESR	–0.262	0.082	–0.134	–0.007	–0.018
CRP	–0.129	0.023	–0.001	0.058	–0.128
Basdai	0.022	0.203	0.120	0.264	0.105

ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index.

Pfirrmann classification

The most common Pfirrmann change was grade 1 degeneration (DC: 57.7%, 254 discs), followed by grades 2, 3 and 4. None of the patients had grade 5 disc degeneration. Grades 2, 3 and 4 Pfirrmann changes were most frequently detected in L4-L5 and L5-S1 discs with decreasing frequency towards the proximal disc. Pfirrmann grade 4 disc degeneration was greater at L1-L2 and L5-S1 levels compared to other disc levels. L5-S1 disc degeneration showed a significant association with CRP ($p < 0.05$). At other disc levels, Pfirrmann scale did not show any association with ESR, CRP and BASDAI.

Disc herniation

Disc herniation was present in 137 discs out of 440 discs studied (DC: 31.1%, PC: 85.2%). Bulging was the most common form of disc herniation (DC: 21.7%, PC: 67%). Only one patient had disc extrusion, and sequestered discs were not found in any patient. Disc herniation mostly affected L4-L5 and L5-S1 discs with decreasing frequency towards the proximal disc. A positive correlation was found between L1-L2 disc herniation and BASDAI and between L2-L3 disc herniation and CRP ($p < 0.05$).

DISCUSSION

Modic changes

Substantial vertebral pathologies occur in the early and later stages of the disease in AS. This manifests itself clinically as low back pain. We think that degenerative disc disease affects AS patients to a greater extent and has some significance in contributing to low back pain in these patients.

There are several studies in literature that investigated Modic changes in asymptomatic subjects, the general population and patients with degenerative disc disease. A review of these studies revealed that Weishaupt *et al* found Modic type 1 changes in 2% of asymptomatic subjects, Modic type 2 in 7% and all types of Modic changes in 11% (23). In a separate study conducted with an asymptomatic population, Modic type 1 changes were found in 1.35% of the discs and Modic type 2 changes in 6.4% (24). A study on the general population showed that Modic changes were present in 6% of individuals 40 years of age and 9% of individuals 44 years of age (25).

Modic changes were studied more extensively in patients with degenerative disc disease or low back pain in comparison to asymptomatic patients. Modic *et al* studied patients with degenerative disc disease and found that Modic type 1 and 2 changes were present in 4% and 16% of patients, respectively (19). In a degenerative disc disease study by Toyone *et al*, the authors suggested that Modic type 1 changes could coexist with low back pain, whereas Modic type 2 changes could concurrently occur with stable degenerative disc disease (26). Kuisma *et al* showed Modic type 2 changes in 21% of discs in degenerative disc disease and found that Modic changes are a common phenomenon in degenerative disc disease (27). Kjaer *et al* reported a greater incidence of low back pain in a group of patients with both lumbar degenerative disc disease and Modic changes in comparison to the patient group with only degenerative disc disease without any Modic changes (28). This suggests that Modic changes might have a role in the development of low back pain. Although Jarvik *et al* did not identify an association between low back pain and Modic changes (29), other studies suggested that Modic changes might actually be associated with low back pain (27, 30–32). Additionally, in a review of 33 studies involving patients with low back pain, Modic type 2 changes were most commonly detected and a positive correlation between Modic changes and low back pain was demonstrated (33).

Only few studies are available which explored Modic changes in AS. In a 2009 study conducted by Nguyen *et al* that examined endplate degeneration in AS patients, 40 patients with a diagnosis of AS were evaluated for Modic changes. In that study, 15 out of 40 patients were found to have Modic 1 changes (PC: 37%). However, the same study focused specifically on Modic type 1 changes rather than examining other Modic changes individually (14). In the current study, all types of Modic changes (1, 2 and 3) were studied separately, and overall Modic changes were observed in 30.7% of patients. Of these changes, Modic type 1 changes were found in 13.6% (DC: 3.6%, 16 discs) and Modic type 2 in 25% (DC: 8.9%, 39 discs) of study patients. Similar to other study populations, Modic changes were most commonly observed in L4-5 and L5-S1 discs in the present study (27, 34–36).

In our study, the observed prevalence of Modic changes was greater in comparison to the prevalence in studies with asymptomatic patients or general population and similar to studies in patients with low back pain. Previous studies have shown a positive correlation between Modic changes and low back pain. We believe that the high prevalence of Modic changes that we observed in the present study might have significance in contributing to low back pain encountered in AS.

A significant association was found in the present study between Modic changes in L1-L2 and L3-L4 discs with elevated CRP ($p < 0.05$). Also, there was a significant association between Modic changes in L1-L2 disc with BASDAI ($p < 0.05$). This finding led us to think that Modic changes in upper lumbar levels might be correlated with parameters of disease activity. Thus, studies involving thoracic and thoracolumbar regions might be of value to assess the association of Modic changes with disease activity parameters.

Disc herniation

Many studies are available in the literature which examined disc herniation in asymptomatic subjects. Jensen *et al* found bulging in 52% and protrusion in 27% of patients without low back pain (37). Boden *et al* reported bulging and other types of hernia in 20% of patients younger than 60 years of age without low back pain (38). In Weinreb *et al*'s study, the corresponding rate was 54% among asymptomatic female patients (39). In the present study, it was 85.2% (DC: 31.1%). Bulging was identified in 67% (DC 21.7%) and protrusion in 35.2% (DC 9.4%) of our patients. Distribution of disc herniation by disc level was as follows: 4.5% for L1-L2, 15.9% for L2-L3 disc, 22.7% for L3-L4 disc, 52.3% for L4-L5 disc, and 59% for L5-S1 disc. In a study with 200 healthy volunteers, the corresponding rates were 0.5%, 3.5%, 6.5%, 25%, and 35%, respectively (40). Consistent with other studies, disc herniation most commonly affected L4-5 and L5-S1 disc levels in the current study (34, 41).

We did not identify a study that focused on disc herniation in AS patients. In the current study, we found an increased prevalence of disc herniation and specifically bulging in AS patients. We suggest that additional disc pathologies such as Modic changes might aggravate low back pain in AS. Similarly, Albert *et al* stated that disc herniation commonly occurs together with Modic changes and suggested that such coexistence might be closely associated with low back pain (30).

In the current study, a positive correlation was found between L1-L2 disc herniation and BASDAI and between L2-L3 disc herniation and CRP ($p < 0.05$). As with Modic changes, the association between disc herniation and parameters of disease activity was significant at upper lumbar levels. Thus, examination of upper vertebral segments would provide further insight while exploring an association between disc herniation and disease activity parameters.

Pfirrmann disc degeneration

There are few studies in the literature that assessed Pfirrmann disc degeneration. Frequency of disc degeneration varies across these studies. Pfirrmann *et al* evaluated 300 intervertebral discs in order to perform magnetic resonance classification of intervertebral disc degeneration. In that study, grade 1 Pfirrman degeneration was found in 4.6%, grade 2 in 27.3%, grade 3 in 24%, grade 4 in 22.6%, and grade 5 in 21.3% of the discs (22). Corresponding rates were 57.7%, 25.5%, 12.7%, 4.1%, and 0%, respectively, in our study. Takatalo *et al* found grade 3–5 disc degeneration in 13.4% of the discs in young patients with mechanical low back pain (34). We did not identify a study that specifically explored Pfirrmann disc degeneration in AS. We believe that further studies are needed to have a clear understanding of the link between AS and Pfirrmann disc degeneration.

CONCLUSION

In the present study, we observed a high prevalence of Modic type 2 changes and bulging herniation in AS patients. We think that this might contribute to low back pain observed in AS. Also, Modic changes and disc herniation in upper lumbar levels were positively correlated with parameters of disease activity. Thus, studies involving the thoracic spine would be of value to assess the association of degenerative disc disease with disease activity parameters. In conclusion, the present study might provide some insight for degenerative disc disease in AS. However, there is a need for studies involving the entire spine with a larger number of patients and a control group.

LIMITATION TO THE STUDY

The major limitation of the present study is the absence of a control group.

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