Magnetic Resonance Imaging in Early Diagnosis of Seronegative Spondyloarthritis

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ABSTRACT

BACKGROUND

Seronegative spondyloarthritis (SpA) is a group of joint diseases having common immunopathologic mechanisms. Early diagnosis and prompt treatment are essential for avoiding structural damage and functional impairment in patients having these conditions. The aim of this study was to assess the severity of spondyloarthritis using Spondyloarthritis Research Consortium of Canada (SPARCC) Magnetic Resonance Imaging Spinal Inflammation Index. Further we correlated SPARCC MRI score with Ankylosing Spondylitis Disease Activity Score (ASDAS).

METHODS

50 diagnosed patients of spondyloarthritis were taken up for this study. The patients were initially evaluated clinically and ASADAS-CRP and ASDAS-ESR scores were calculated. Then the patients were subjected to MR Imaging and SPARCC spinal inflammation score was calculated. The findings of SPARCC spinal inflammation score and ASADAS-CRP and ASDAS-ESR scores were statistically analysed.

RESULTS

Our study results suggest that as the disease activity was increasing, SPARCC scores of the patients were also increasing. The correlation of SPARCC Score with ASDAS ESR was found to be statistically significant. The correlation of SPARCC Score with ASDAS CRP was also found to be statistically significant.

CONCLUSIONS

Early spondyloarthritis is often difficult to assess and diagnose clinically. Magnetic resonance imaging is the best imaging modality to diagnose early spondyloarthritis and it is highly sensitive for picking up inflammatory as well as structural changes of spondyloarthritis.

KEYWORDS

Spondyloarthritis, Disease Activity Score, C-Reactive Protein, Erythrocyte Sedimentation Rate, Magnetic Resonance Imaging

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DOI: 10.18410/jebmh/2020/257

Financial or Other Competing Interests: None.

How to Cite This Article:
Udaybhanu K, Jain NK, Grewal DS, et al. Magnetic resonance imaging in early diagnosis of seronegative spondyloarthritis. J. Evid. Based Med. Healthc. 2020; 7(25), 1203-1208. DOI: 10.18410/jebmh/2020/257

Submission 17-05-2020,
Peer Review 21-05-2020,
Acceptance 06-06-2020,
Published 21-06-2020.

BACKGROUND

Seronegative spondyloarthritis (SpA) is a group of musculoskeletal conditions having common clinical features and immunopathologic mechanisms.[1] Seronegative spondyloarthritis are classified into five subgroups, which include ankylosing spondylitis, psoriatic arthritis, reactive arthritis, arthritis associated with inflammatory bowel disease and undifferentiated spondyloarthritis.[2]

Imaging of the spine and the sacroiliac (SI) joints plays an important role in diagnosis, classification and follow up of patients with Seronegative spondyloarthritis. Different kinds of inflammatory lesions are seen in spondyloarthritis because of anatomic complexity of vertebral column. Magnetic resonance imaging (MRI) can pick up inflammation at spine and SI joints in early stage even before the disease manifestations are seen on plain radiographs.[3]

The options for treating patients with severe forms of spondyloarthritis have been limited in the past.[4] Nonsteroidal anti-inflammatory drugs are widely used and rigorous physical therapy played a key role in preserving mobility of spine.[5] For some time now tumor necrosis factor (TNF)– inhibitors have been used for treating spondyloarthritis and many studies have reported good results with them.[6] Early diagnosis and prompt treatment is essential for avoiding structural damage and functional impairment in patients having these conditions.

The Spondyloarthritis Research Consortium of Canada (SPARCC)[7] developed a systematic program of MRI-based scoring inflammation and structural damage in both the spine and sacroiliac joints. The aim of this study was to assess the severity of spondyloarthritis using Spondyloarthritis Research Consortium of Canada Magnetic Resonance Imaging Spinal Inflammation Index. Further we correlated SPARCC MRI score with Ankylosing Spondylitis Disease Activity Score (ASDAS).

METHODS

The study was conducted in the Department of Radiodiagnosis and imaging of a tertiary care hospital from Oct 2018 to March 2020. It was an observational study and included 50 diagnosed cases of spondyloarthritis between 18 and 60 years of age. Patients having rheumatoid arthritis, overlap syndrome and other non-articular rheumatism were excluded from the study. All patients were initially clinically assessed and then underwent relevant investigations. Approval was taken from institutional ethical committee for the study. Informed consent was taken from all the participants of the study.

Clinical Assessment

The clinical assessment of the patient was done using ASDAS- C-reactive protein (CRP) score and ASDAS-erythrocyte sedimentation rate (ESR) score. Parameters used for the ASDAS were back pain, patient global disease activity, peripheral pain/swelling and duration of morning stiffness. CRP and ESR were determined for all patients. For CRP, the blood sample was coagulated and centrifuged. The serum was taken and kept at 4°C. CRP levels were measured using a Roche Cobas 6000 c501 automatic analyser based on an immune turbidimetry method using the reagents and instructions provided by the manufacturer.

The ASDAS-CRP was calculated according using the formula-

0.12 x Back pain + 0.06 x Duration of morning stiffness + 0.11 x Patient global disease activity + 0.07 x Peripheral pain/swelling + 0.58 x Ln (CRP + 1)

The ASDAS-ESR was calculated according using the formula-

0.08 x Back pain + 0.07 x Duration of morning stiffness + 0.11 x Patient global disease activity + 0.09 x Peripheral pain / swelling + 0.29 X $\sqrt{ESR)}$

Patients with ASDAS-CRP score and ASDAS-ESR score of <1.3 were considered to be having inactive disease, those with 1.3-2.1 having moderate disease activity, those with 2.1-3.5 having high disease activity and patients having score >3.5 were considered to be having very high disease activity.

Imaging

Plain radiography was performed using Philips digital diagnostic digital radiography system. All patients underwent radiographs of whole spine in antero-posterior and lateral projections. Radiographs of SI joints were performed in short axis postero-anterior (SAPA) projection.

MRI was performed with 1.5 Tesla Siemens MR Scanner (Siemens, Erlangen, Germany) using appropriate surface coils. Sequences were obtained in sagittal orientation with 4-mm slice thickness and 12–15 slices acquired. Spine sequences were T1-weighted spin echo (time to recovery (TR) 517–618 m sec, time to echo (TE) 13 m sec) and STIR (TR 2,720–3,170 m sec, time to inversion 140 m sec, TE 38–61 m sec).

SPARCC MRI Scoring

After scanning the entire spine, 6 disco-vertebral units (DVU) were selected for scoring. These levels were chosen as representing the 6 most abnormal levels on STIR sequence. Only abnormalities on the STIR sequence were scored. T1 SE images were used for anatomical reference (Figure 1). After selecting levels, three consecutive sagittal slices were chosen for scoring at each level representing the most abnormal slices for that level. Each discovertebral unit was divided into four quadrants: upper anterior endplate, upper posterior end plate, lower anterior endplate and lower posterior endplate. The presence of increased signal in each quadrant was recorded for each of the three sagittal slices.

Maximum score per discovertebral level was 12 and hence maximum score for 6 levels was 72.

A score for intense oedema was assigned to each level on each slice. High signal from cerebrospinal fluid was taken as a reference for assigning signal intensity. A score of 1 was assigned if "intense" signal was seen in any quadrant on a single slice. Therefore maximum score per slice was 1, per level was 3 and for 6 levels was 18. (Figure 2).

A score for deep was assigned to each level on each slice. A lesion was graded as "deep" if there was homogeneous and unequivocal increase in signal extending over a depth of at least 1 cm from the surface of endplate. A score of 1 was assigned if "deep" signal was seen in any quadrant on a single slice. Therefore maximum score per slice was 1, per level was 3 and for 6 levels was 18. (Figure 3).

All the above were combined to get a total score as under:

Presence of "bone marrow oedema" =72
Presence of "intense oedema" =18
Presence of "deep oedema" =18
Total maximum score is =108

Statistical analysis of the data has been done using SPSS version 19.

RESULTS

Out of the 50 patients included in the study, 43(86%) were males and 7 (14%) patients were females. The maximum age was 49 years and the minimum age was 20 years with mean age of 33 years. 24 (48%) patients had disease duration less than 10 months, 21 (42%) patients had disease duration of 11-17 months and 5 (10%) patients had disease duration between 17-24 months.

ESR of 20 (40%) patients was <20 mm/hr. 12 (24%) patients had ESR between 21-40 mm/hr and 18 patients had ESR >41 mm/hr. 23 (46%) patients had CRP of less than 07 mg/l, 04 (08%) patients had CRP value between 8-14 mg/l and 23 (46%) patients had CRP value of more than 28 mg/l. 42 (84%) patients were HLA B27 positive and 8 (16%) patients were HLA B27 negative.

2 (4%) patients had ASDAS ESR score less than 1.3; suggestive of inactive disease. 17 (34%) patients had ASDAS ESR score between 1.3-2.1; suggestive of moderate disease activity. 12 (24%) patients had ASDAS ESR score between 2.2-3.5; suggestive of high disease activity and 19 (38%) patients had ASDAS ESR score of more than 3.5; suggestive of very high disease activity. 2 patients had ASDAS CRP score of less than 1.3; suggestive of inactive disease. 18 (36%) patients had ASDAS CRP score between 1.3-2.1; suggestive of moderate disease activity. 10 (20%) patients had ASDAS CRP score between 2.2-3.5; suggestive of high disease activity and 20 (40%) patient had ASDAS CRP score of more than 3.5; suggestive of very high disease activity.

17 (34%) patients had bone marrow oedema score between 0-24. 32 (64%) patients had bone marrow oedema score between 25 – 48 and 1 (2%) patient had score between 49-72. 33 (66%) patients had intense bone marrow oedema score between 0 – 6 and 17 (34%) patients had intense bone marrow oedema score between 7-12. None of the patients had intense bone marrow oedema score greater than 12. 49 patients had deep bone marrow oedema score of 0 (Zero). Only 1 patient had deep bone marrow oedema score of 2 (two).

19 (38%) patients had SPARCC Score between 0-27, 28 (56%) patients had SPARCC score between 28- 54 and 3 (6%) patients had SPARCC Score between 55-81. None of the patients had SPARCC Score above 82 (Table 1). 18 patients had SPARCC Score between 27-54 and their ASDAS-CRP Score was >3.5. 3 patients had SPARCC Score 55-81 out of which 2 of patients had ASDAS-CRP >3.5. These study results imply that as the disease activity was increasing, SPARCC scores of the patients were also increasing. The correlation of SPARCC Score with ASDAS ESR was found to be statistically significant (Table 2). The correlation of SPARCC Score with ASDAS CRP was also found to be statistically significant (Table 3).

SPARCC Score	No. of Patients	%
0-27	19	38
28-54	28	56
55-81	3	6
82-108	0	0
Total	50	100

Table 1. Distribution of SPARCC Score

SPARCC Score	<1.3		1.3-2.1		2.1-3.5		>3.5		Grand Total		P-Value
	Patients	%	Patients	%	Patients	%	Patients	%	Patients	%	
0-27	2	10.5	15	78.9	2	10.5	0	0.0	19	100	0.001
27-54	0	0.0	2	7.1	9	32.1	17	60.7	28	100	
55-81	0	0.0	0	0.0	1	33.3	2	66.7	3	100	
82-108	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
Grand Total	2	4.0	17	34.0	12	24.0	19	38.0	50	100.0	

Table 2. Correlation of SPARCC Score with ASDAS ESR Score

* The Chi-square statistic is significant at 0.05 level

SPARCC Score	<1.3		1.3-2.1		2.1-3.5		>3.5		Grand Total		P-Value
	Patients	%	Patients	%	Patients	%	Patients	%	Patients	%	
0-27	2	10.5	15	79.0	2	10.5	0	0.0	19	100	0.001
27-54	0	0.0	3	10.7	7	25.0	18	64.3	28	100	
55-81	0	0.0	0	0.0	1	33.3	2	66.7	3	100	
82-108	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
Grand Total	2	4.0	18	36.0	10	20.0	20	40.0	50	100	

Table 3. Correlation of SPARCC Score with ASDAS CRP Score

*. The Chi-square statistic is significant at the 0.05 level

DISCUSSION

Chronic back pain affects up to 10% of general population with a significant cost to affected individuals and society at large. Spondyloarthritis is a common cause of back pain and Ankylosing spondylitis is its commonest subgroup.[8]

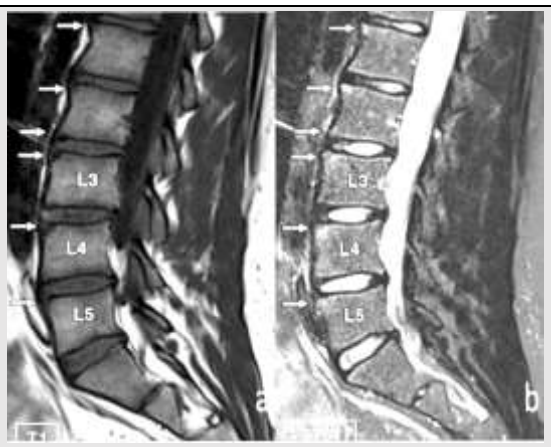

Figure 1

1a. Sagittal T1-weighted image of lumbosacral spine shows hypointense areas in anterior aspects of lumbar vertebral endplates (arrows).
1b. Sagittal STIR image of lumbosacral spine shows florid hyperintense Romanus lesions in lumbar vertebrae (arrows). Patient's ASDAS CRP score was 3.5.

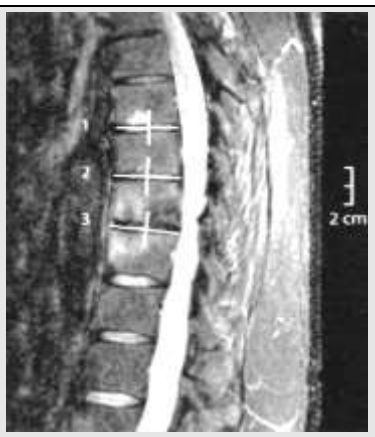

Figure 2

Sagittal STIR image of dorsal spine showing calculation of SPARCC spinal inflammation score. Level 1: score = 2 (antero-superior quadrant plus 1 for intensity); Level 2: score = 1 (postero-inferior quadrant); Level 3: score = 4 (antero-superior and both inferior quadrants plus 1 for depth). Total score = 7.

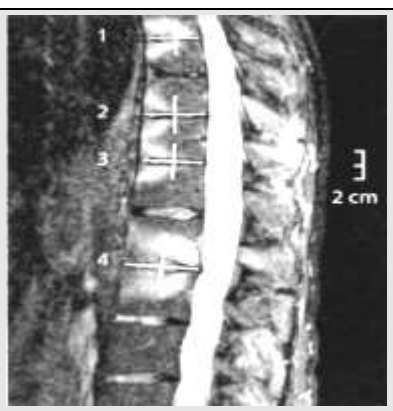

Figure 3

Sagittal STIR image of dorsal spine showing calculation of SPARCC spinal inflammation score. Level 1: score = 5 (3 quadrants plus 1 each for depth and intensity); Level 2: score = 4 (2 quadrants plus 1 each for depth and intensity); Level 3: score = 4 (2 quadrants plus 1 each for depth and intensity); Level 4: score = 6 (4 quadrants plus 1 each for depth and intensity). Total score = 19.

Diagnostic evaluation and management of SpA is more problematic than most other forms of inflammatory arthritis.[9] This is because physical findings are typically confined to later stages of disease. Laboratory investigations are essentially limited to acute phase reactants and HLAB-27, which alone have limited diagnostic value.[10] Plain radiographic abnormalities occur late, are insensitive to change, and depict structural abnormalities only.[11,12] With the availability of biological therapies that are highly efficacious in treatment of SpA with an acceptable safety profile, capacity to alleviate signs and symptoms and improve the quality of life of the patients, there is need to diagnose these disorders at an early stage, before the structural damage has occurred.[13]

The advent of MRI has proven to be a milestone in the evaluation of SpA through its ability to depict objective features of active inflammation, thereby facilitating earlier diagnosis and ongoing management, and permitting quantitative assessment of extent and severity of spinal inflammation.[14,15]

In our study, there was significant correlation between SPARCC inflammation score and ASDAS ESR (p=0.001) and CRP (p=0.001). Based on linear regression analysis, SPARCC spine scores were significantly associated with symptom duration. The most frequently involved DVUs with bone marrow oedema on MRI were found in the lower thoracic and lumbar spine. The findings described in our report confirm previously published data and add new insights to the growing body of literature on MRI in axial SpA.[16,17,18] The distribution of DVU involvement along the spine in our study population confirms previous findings that the thoracic and lumbar regions of the spine are the areas most frequently affected by inflammation in axial SpA.[19,20,21]

One of the studies tried to correlate MRI and clinical disease activity score (DAS) in a axial SpA outpatient population to assess the difference in MR DAS in individuals with high and low clinical DAS. The study concluded that MR DAS provided information about disease activity not provided by the current standard of clinical DAS and may be considered as a useful adjunct in clinical practice.[22] In another study correlation was done between clinical and MRI disease activity scores in axial SpA. The study concluded that ASDAS was the preferred clinical measure of disease activity in SpA and of all MRI assessments, change in SPARCC sacroiliac joint inflammation seemed most closely aligned with changes in ASDAS, CRP and BASDAI, though the correlations were modest.[23] In another study the SPARCC scoring method was used to compare treatment methods in patients with SpA. MRI abnormalities in bone marrow oedema (BME) were compared before and after treatment in order to compare the efficacy of anti-TNF-α and DMARD, alone or in combination. After treatment, ASDAS and SPARCC scores, ESR and CRP were significantly improved ($P < 0.05$) in the anti-TNF-α monotherapy and combination groups. SPARCC showed a correlation with ASDAS score pre-treatment. The study concluded that SPARCC can be used to assess severity of disease pre-treatment.[24] Our study results are in concordance with above studies.

Our results indicate that MRI provides the best objective and complementary evidence for diagnosis of SpA. It was positive in 48 out of 50 patients. MRI picked up abnormalities in patients who had normal spinal radiography. Plain radiography is least sensitive for detection of early SpA. In our study group fatty deposition and ankylosis were not seen in any of the patients on MRI. Enthesitis was not detected in any of the patients under study, probably because of non-administration of contrast. As shown by various studies, the use of dynamic contrast-enhanced MRI could be of value in reflecting inflammatory activity. But the same could not be used in our study because of cost factor.

Our study had some limitations. Only sagittal images of the spine were scored. Therefore, some lesions that may be evident only on coronal planes may have been missed. MRI findings were evaluated and the most probable single diagnosis was given based on these findings. Therefore, the possibility of coexisting conditions was not taken into account. Finally, the present Spondyloarthritis cohort had established disease. The sample size was small and the timing of MRI examinations was not similar for all patients. There was also no group of patients without axial SpA who served as a control for this exercise. In our study MRI was done early in the disease and only bone marrow oedema was taken into consideration for SPARCC scoring. Other changes like Spondylodiscitis, enthesitis, insufficiency fracture changes were not taken into consideration.

CONCLUSIONS

Early spondyloarthritis is often difficult to assess and diagnose clinically. The diagnosis frequently depends on radiological evaluation. Plain radiographs have a limited role in early diagnosis. MRI is the best imaging modality to diagnose early spondyloarthritis. It is highly sensitive for picking up inflammatory as well as structural changes of SpA and the changes are apparent as early as 3 months.

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