Multiparametric Large Field of View Rheumatology Imaging for Axial Spondyloarthropathy Detects Enthesitis in Setting of Inactive Sacroiliac Joint Disease and Impacts Clinical Diagnosis

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Aim: To test the diagnostic efficacy of a multiparametric rheumatology lumbosacral magnetic resonance (MR) imaging protocol in detection and characterization of axial spondylarthritis (SpA) and compare it with serology and clinical findings.

Methods: A consecutive series of multiparametric rheumatology lumbosacral MR imaging examinations performed on 3T MR scanner. Three-dimensional inversion recovery turbo spin echo, precontrast and postcontrast fat-suppressed T1-weighted images, as well as diffusion-weighted images were used to detect active erosions and enthesitis using established criteria. Pearson χ^2 was used for categorical variables. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were measured for magnetic resonance imaging (MRI) and serology, based on the final diagnosis from rheumatologists. An alpha error below 0.05 was considered statistically significant.

Results: The final study sample included 130 consecutive patients (80 women and 50 men; mean ± SD 44 ± 13 and 45 ± 14 years, respectively). Seventy-eight subjects were diagnosed with axial SpA and 52 with non-SpA arthropathy. In the non-SpA group, 27 patients were diagnosed with osteoarthritis, 6 had unremarkable imaging, whereas 19 were considered as clinically undetermined. There was positive correlation between positive MRI results and SpA diagnosis ($P < 0.00001$). No correlation existed between positive serology alone and SpA diagnosis ($P = 0.0634$). Although MRI and serology proved equally sensitive in detecting SpA, the specificity and overall accuracy of MRI were significantly higher. Inflammatory activity was detected in 45 (57.7%) cases, in the pelvic enthesis in 29 (37.2%) cases, in the lumbosacral spine in 16 (20.5%) cases, in the hip joints in 15 (19.2%) cases, and in the pubic symphysis in 5 (6.4%). Inactive sacral disease was seen in 7 of 35 enthesitis patients (20.0%), and in 2 SpA cases, there were no sacral lesions.

Conclusions: The results suggest that in patients with suspected SpA, MRI should not be limited to the sacroiliac joints, but also include enthesitis sites and other joints of the axial skeleton. The multiparametric rheumatology protocol increases the efficacy of MRI in detecting enthesitis and joint inflammatory disease, thereby offering additional information to the clinician and assisting in the early diagnosis/detecting disease activity.

Key Words: axial spondyloarthritis, enthesitis, sacroiliitis, MRI, DWI

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Spondyloarthritis (SpA) is a heterogeneous group of chronic inflammatory diseases primarily affecting the axial skeleton. Although the well-known representative is ankylosing spondylitis (AS), the grouping includes reactive arthritis (including Reiter syndrome), psoriatic arthritis, arthropathy associated with inflammatory bowel disease, and undifferentiated spondyloarthropathy. The overall prevalence of these entities is estimated between 0.23% and 1.8%.[1] If undiagnosed and untreated, SpA may lead to permanent joint and bone damage and lifelong disability.[2]

Early diagnostic criteria (Rome, 1961 and New York, 1966) used only clinical features and were limited for the diagnosis of AS. In later years, the criteria progressively evolved to include many inflammatory entities and incorporated both clinical and imaging features.[3–9] In 2009, the Assessment of SpondyloArthritis International Society established classification criteria to better identify the patients with SpA.[10,11] An important addition was the inclusion of magnetic resonance imaging (MRI) findings positive for sacroiliitis as a major diagnostic criterion. However, SpA not only involves the sacroiliac (SI) joints but also affects various entheses sites and other major joints[12–15] connected to the axial skeleton, all of which are amenable to imaging in the larger field of view protocol.[9] The detection of such sites could extend the diagnostic efficacy of MRI for SpA and timely treatment of the active disease.[16,17]

In our tertiary care institution, we have been using a multiparametric rheumatology lumbosacral MR imaging (MRLI) protocol to evaluate the involvement and inflammatory activity of several joints and entheses sites in the same field of view, eg, SI joints, hip joints, pubic symphysis, lumbosacral spine and pelvis. We performed a retrospective study to test the diagnostic efficacy and characterization of this protocol in SpA and compared it with serology and clinical findings. Our hypothesis was that the comprehensive MRLI protocol will detect a greater number of cases and more active sites than imaging of SI joints alone.

MATERIALS AND METHODS

Patient Population

After institutional review board approval was granted and informed consent was waived for this Health Insurance Portability and Accountability Act-compliant study, the imaging database of our institution was searched for MRLI examinations performed from August 2015 to March 2020 for suspected SpA. All cases clinically suspected of SpA who underwent MRLI were included in the study. The search yielded 135 studies, 3 of which were excluded due to incomplete imaging and/or motion artifacts, and were excluded as the respective patients had prior infection and/or underlying malignancy.

The final study sample included 130 consecutive patients (80 women and 50 men, mean ± SD 44 ± 13 and 45 ± 14 years, respectively). In 109 (83.84%—72 SpA and 37 non-SpA patients) subjects, serology tests (acute phase response indicators, erythrocyte

TABLE 1. The Imaging Protocol Employed in the Study

Sequence	TR (ms)	TE (ms)	Voxel (mm)	FOV Read	TA (s)	Turbo Factor
Coronal 3D SPAIR/STIR (AP)	2000	78	1.5 × 1.5 × 1.5	400	8:40	80
Axial T2W (AP)	4200	94	0.6 × 0.6 × 3.5	200	3:57	15
Sagittal STIR (P)	2500	29	0.5 × 0.5 × 3.5	300	3:37	15
Sagittal T1W (P)	600	9.6	0.5 × 0.5 × 3.5	300	4:06	3
Sagittal T2W (P)	4000	95	0.5 × 0.5 × 3.5	300	3:54	21
Axial DWI (AP)	12,200	79	2.0 × 2.0 × 4.0	300	5:17	*B* 50,400,800 s/mm^2
Coronal precontrast and postcontrast VIBE-Dixon (AP)	7.0	1.35/2.58	1.2 × 1.2 × 1.2	350	5:06	

3D indicates 3-dimensional; SPAIR, spectral adiabatic inversion recovery; STIR, short tau inversion recovery; DWI, diffusion-weighted imaging; FOV, field of view; TA, time of acquisition; TE, echo time; TR, repetition time; VIBE, volume interpolated breath-hold examination; AP, abdomen and pelvis; P, pelvis.

sedimentation rate, and/or C-reactive protein) were available within 12 weeks of the imaging study.

Imaging Technique and Study Analysis

Imaging was performed on a 3 Tesla scanner (Skyra, Siemens, Erlangen) using the protocol shown in Table 1. T1-weighted (T1W), T2-weighted (T2W) and fat-suppressed (fs) T2W images were used to establish chronic fatty changes, erosions, and sclerosis.[18] Three-dimensional inversion recovery turbo spin echo, precontrast and postcontrast fat-suppressed T1-weighted images, as well as diffusion-weighted images were used to detect active erosions and enthesitis using established criteria.[16,19–29]

The studies were interpreted by 3 expert musculoskeletal radiologists with interest in rheumatologic imaging as part of routine patient care and the reporting followed a structured format outlining the involvement of different joints and enthesis sites in the lumbosacral area (Fig. 1). A musculoskeletal fellow reviewed all 130 studies again and rechecked the findings in consensus with a senior musculoskeletal radiologist. Final consensus imaging findings blinded to the clinical findings and diagnosis were input in the Excel file (Excel 2016; Microsoft, Seattle, WA) for the assessment of diagnostic efficacy and calculating correlation analysis.

An MRI study was considered positive when there was an imaging evidence of active, chronic or acute on chronic inflammatory activity in the SI joints, hip joints, pubic symphysis, lumbosacral spine, and/or pelvis. In the SI joints, hip joints, and pubic symphysis, features indicating active disease included bone marrow edema with or without erosions (Fig. 2), cartilage erosion, joint effusion, synovitis, capsulitis, and widened joint space. Findings suggesting chronic disease included well-defined erosions with no marrow edema, ankylosis, and subchondral fatty marrow (Fig. 3). In the lumbosacral spine, features indicating active disease included vertebral corner marrow edema with or without erosion (Fig. 4), endplate erosions with marrow edema and facet marrow edema with or without associated erosions or perifacet soft tissue edema. Findings suggesting chronic disease included endplate fatty marrow (Modic II) changes, sclerotic (Modic III) changes, and vertebral corner erosions without underlying marrow edema. In the pelvis, sites of potential enthesitis included the anterior and

EXAM: MR MSK RHEUMATOLOGY LUMBOSACRAL

HISTORY:

TECHNIQUE: High resolution MRI of the lumbosacral spine and MRI of the pelvis was performed for the purposes of lumbosacral rheumatology evaluation employing 2D and 3D techniques on a Tesla system. Contrast material was not administered.

COMPARISON: None.

FINDINGS:
Joints:

Lumbosacral spine:
Alignment: Normal
Spinal Canal: Developmental stenosis absent.
End plate changes:

L1-L2: Central canal:
Neural foramina: Right Normal Left Normal
L2-L3: Central canal:
Neural foramina: Right Normal Left Normal
L3-L4: Central canal: Patent
Neural foramina: Right Normal Left Normal
L4-L5: Central canal: Patent
Neural foramina: Right Normal Left Normal
L5-S1: Central canal: Patent
Neural foramina: Right Normal Left Normal

Sacroiliac joints: mild degenerative arthritis.
Pubic symphysis: mild degenerative arthritis.
Hip joints:

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Enthesopathy sites:
ASIS: Normal.
PSIS: Normal.
AIIS: Normal.
Pubic bone: Normal.
Supraspinatus ligament: Normal.
Others: Normal.

Muscles/Tendons
Psoas major: Bulk: Normal. Intramuscular signal: Normal.
Piriformis: Bulk: Normal. Intramuscular signal: Normal.
Gluteal: Bulk: Normal. Intramuscular signal: Normal.
Hamstring tendons: Normal.
Adductors:

Marrow signal: Otherwise normal.

Nerves: Normal.

Vessels: Within normal limits

Masses: None

Other findings: None

IMPRESSION:

FOLLOW-UP RECOMMENDATIONS: Per clinical team.

FIGURE 1. The structured template for reporting multiparametric MRI studies in rheumatology patients.

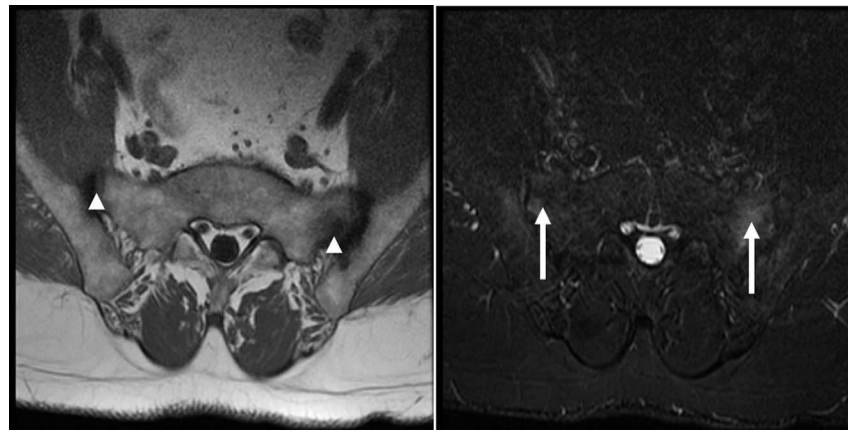

FIGURE 2. Axial T1 and fsT2W- Bilateral SI joints with erosive changes (white arrowheads) and edema (white arrows).

posterior superior iliac spines, the anterior inferior iliac spine (AIIS), the greater trochanters and the ischial tuberosities. In these locations, enthesitis (Fig. 5, Fig. 6, Fig. 7, and Fig. 8) was established upon the presence of subchondral or flame-shaped bone marrow and/or fascial edema with or without associated tendon or ligament thickening. The presence of enhancement on contrast imaging was considered as an ongoing activity despite chronic findings. The final diagnosis was decided by the rheumatologists based on the clinical criteria and MRLI findings.

Statistical Analysis

Pearson χ^2 was used for categorical variables. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were measured for MRI and serology, based on the final diagnosis from rheumatologists. An alpha error below 0.05 was considered statistically significant. All data were stored on an Excel spreadsheet, and analysis was performed using a commercially available statistical package (MedCalc 8.0; Mariakerke, Belgium).

RESULTS

In the study sample, 78 subjects were diagnosed with axial SpA and 52 with non-SpA arthropathy. The imaging and serology results of the subgroup of cases, in which serology tests that were available are demonstrated in Table 2. The diagnoses of the SpA group and their relation to positive MRI and serology studies are shown in Table 3. In the non-SpA group, 27 patients were diagnosed with osteoarthritis, 6 had unremarkable imaging, whereas 19 were considered as clinically undetermined, because they had questionable imaging findings, such as mild perifacet edema or greater trochanteric bursitis, and lacked specific (serology and clinical) features of SpA or osteoarthritis.

There was a correlation between positive MRI results and SpA diagnosis, both in the complete study group ($P < 0.00001$) and in the subgroup of subjects with available serology ($P < 0.00001$). No correlation existed between positive serology alone and SpA diagnosis ($P = 0.0634$). In the subgroup of subjects with available serology tests, there was no significant relationship with MRI results ($P = 0.28$).

Although MRI and serology proved equally sensitive in detecting SpA, the specificity and overall accuracy of MRI were significantly higher. Regarding the types of SpA (although the number of each type was small), MRI was more sensitive in detecting AS, whereas serology was more sensitive in detecting idiopathic SpA and psoriatic arthritis. The 2 methods proved equally sensitive in detecting lupus erythematosus arthritis (Table 4).

In the study group, inflammatory activity was detected in 45 (57.7%) cases, in the pelvic enthesis in 29 (37.2%) cases, in the lumbosacral spine in 16 (20.5%) cases, in the hip joints in 15 (19.2%) cases, and in the pubic symphysis in 5 (6.4%) (Table 5).

Most common enthesitis site was anterior superior iliac spine (ASIS) in 22 of 35 patients (62.9%), followed by posterior superior iliac spine, Romanus lesions, supraspinous ligament, AIIS and pubic symphysis (Table 6). Inactive sacral disease was seen in 7 of 35 enthesitis patients (20.0%), and in 2 SpA cases, there were no sacral lesions (Table 7).

DISCUSSION

Spondylarthritis are entities with continuum of long-term disease process and related symptoms. Because patients usually

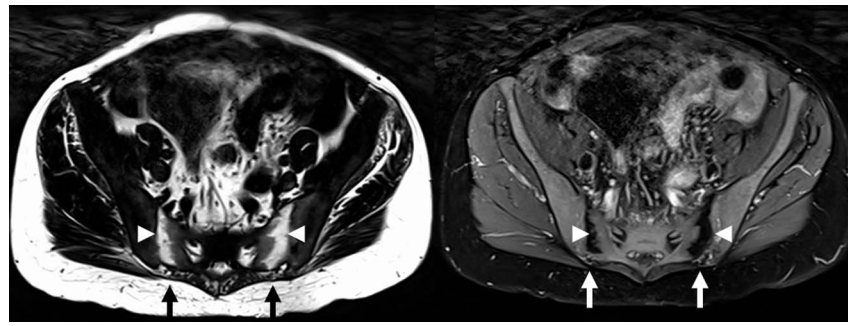

FIGURE 3. T1 and fsT2W showing fatty metamorphosis (white/black arrows) and complete ankylosis (white arrows) of the SI joints depicting chronic enthesitis.

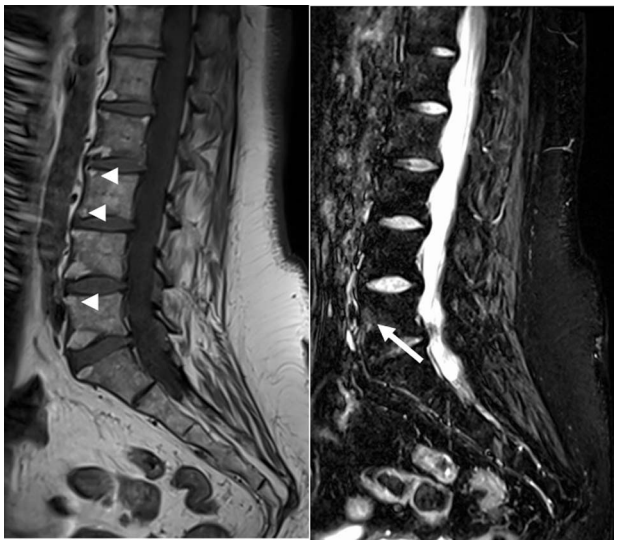

FIGURE 4. Chronic romanus lesions with fatty metamorphosis (white arrowheads) and active acute on chronic romanus (white arrow).

demonstrate a wide variety of clinical features and there is no standardized laboratory test protocol, the diagnosis of SpA is rarely straightforward. Serum and plasma biomarkers have recently undergone extensive examination. Although human leukocyte antigen remains relevant,[30–32] other biomarkers for systemic inflammation, such as C-reactive protein and erythrocyte sedimentation rate, which are usually used in clinical practice,[16,17,33–39] are often unable to assess disease activity.[29,34,35,37,40–44] Because early treatment can reduce the disease burden in SpA patients and disease-related costs, developing other tests, which can assist in the early diagnosis of SpA, has become an important undertaking.[2]

Positive MRI of the SI joints has been added as major criterion[11] in diagnosing SpA, but ignores inflammatory activity in entheses and other joints of the axial skeleton, which may exist while the SI joints are normal. An extended imaging coverage of the axial skeleton could detect this activity and assist in the diagnosis. We tested the efficacy of a multiparametric MRI protocol,[19] which covers not only the SI joints but also the hip joints, pubic symphysis, lumbosacral spine, and pelvic regional enthesopathy sites, in diagnosing SpA.

It is interesting that in 33 of 78 patients with SpA, the SI joints were normal at MRI. In these cases, an MRI study limited

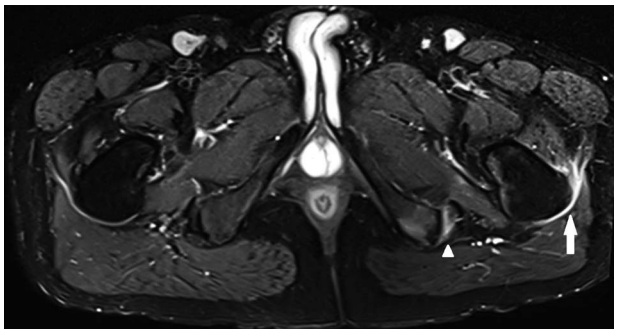

FIGURE 5. Axial fsT2W image shows left ischial tuberosity enthesitis (white arrowhead) and greater trochanteric bursitis (white arrow).

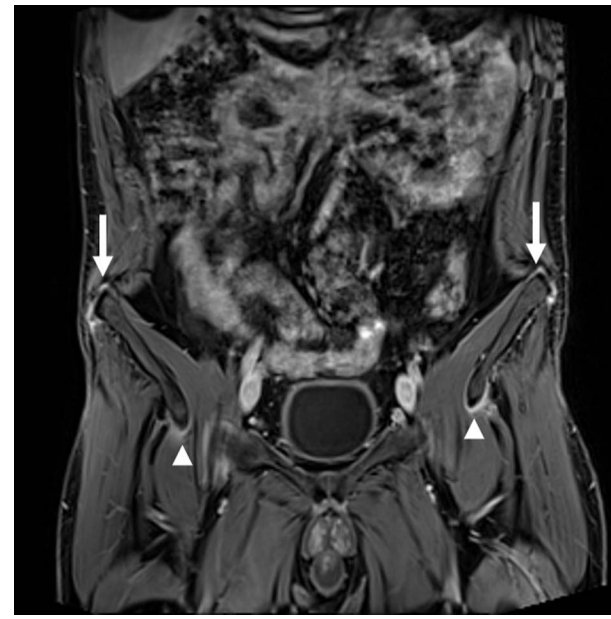

FIGURE 6. Postcontrast fs3DT1W images show bilateral ASIS (white arrows) and AIIS (white arrowheads) enthesitis.

to the SI joints would show no suspicion of SpA, and the result could misguide the clinician and delay the diagnosis. Another advantage of this protocol is that it covers all potential joint inflammatory sites in a single study, thereby avoiding 2 or more separate examinations, which could be performed at a questionable intervening time.

The study included consecutive series of patients suspected of axial SpA. Thus, it included both positive (78 subjects) and negative (52 subjects) studies. Magnetic resonance imaging showed higher accuracy and specificity than serology. Serology alone did not prove accurate in detecting SpA. This is in agreement to

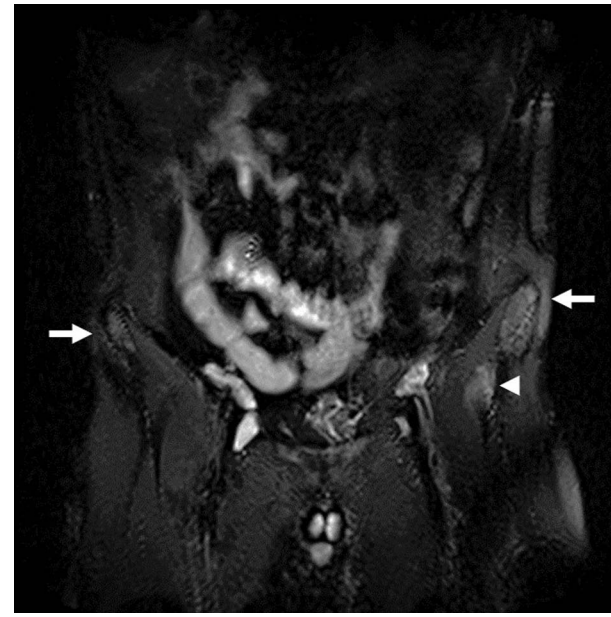

FIGURE 7. 3D-STIR images in the same case showing ASIS (white arrows) and AIIS (white arrowhead) enthesitis.

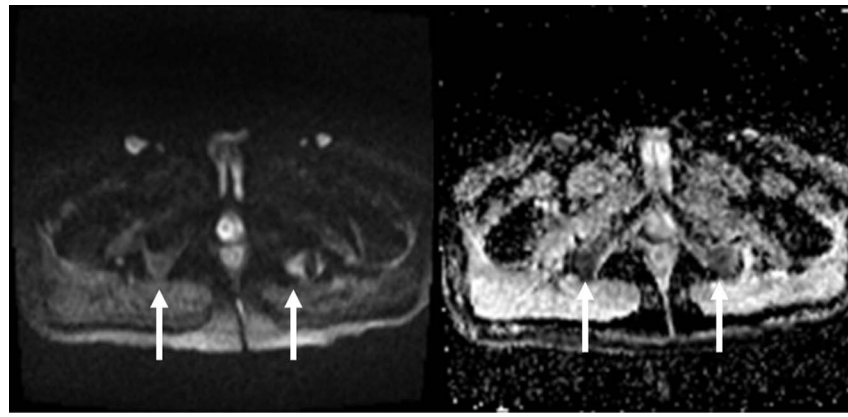

FIGURE 8. Axial DWI and ADC images in the same case also show bilateral ischial tuberosity enthesitis (white arrows) with good background suppression, not evident on fsT2W images.

previous studies, which have shown that serology markers may be elevated in non-SpA arthritis and even in normal individuals.

In our study, enthesitis, which was second most common finding next to sacral involvement, but the most common finding in active patients (37.2% in enthesitis vs 19.2% in sacroiliitis) more common than active sacral lesions. Therefore, giving us crucial information about disease activity needed to treat patients. Although enthesitis is known to occur in various other locations, including chest wall and peripheral locations,[45–47] not many studies have been done to show their usefulness in diagnosing SpA except whole body MR imaging.[48,49] Also it would be a cost burden on patient if other additional imaging of different location in the body is done to prove disease activity. To the best of our knowledge, this is the only study with a large number of patients identified for enthesitis, especially in pelvic region due to the new MRI protocol covering abdomen and pelvis for the most common sites of pelvic enthesitis.

This study had several limitations. First, we did not account the effect of treatment on serology or MRI positivity. Second, the role of other serology markers (except for acute phase reactants) was not assessed. Third, radiologists were aware of the serology results at the time of MRI interpretation, therefore their reports could have been influenced. Finally, the findings were assessed in consensus and no interreader analysis was obtained although moderate-excellent interreader performance using this kind of protocol has been shown previously in the literature.[19]

These examinations are billed as 2 current procedural terminology codes (MRI of lumbar spine with and without contrast and MRI of pelvis with and without contrast). Although the cost is higher than isolated SI joint imaging, the benefits of finding other active sites with negative or inactive SI joint disease and a comprehensive approach of evaluating all possible active sites in abdomen and pelvis overscore the costs of repeat imaging, fragmented approach of imaging various sites at different

TABLE 2. The Imaging and Serology Results of the Subgroup of Cases, in Which Serology Tests Were Available

	Positive MRI	Negative MRI	Positive Serology	Negative Serology
SpA	50	22	50	22
Other joint disease	1	36	19	18
Total	51	58	69	40

Numbers indicate patients.

TABLE 3. The Diagnoses of the Spondyloarthritis Group and Their Relation to Positive MRI and Serology Studies

	Patients (n)	Positive MRI, n (%)	Positive Serology, n (%)
AS	16	15 (93.8)	11/15 (73.3)
Idiopathic	23	14 (60.8)	17/23 (73.9)
Rheumatoid arthritis	8	5 (62.3)	5/8 (62.5)
Psoriatic arthritis	6	3 (50.0)	3/5 (60.0)
Lupus erythematosus	3	3 (100.0)	3/3 (100.0)
Mixed connective tissue disease	18	12 (66.7)	11/15 (73.3)

TABLE 4. The Diagnostic Efficacies of MRI and Serology in Detecting Spondyloarthritis

	MRI, %	Serology, %
Sensitivity	69.23	69.44
Specificity	98.08	48.65
Positive predictive value	98.18	72.46
Negative predictive value	68.00	45.00
Accuracy	80.77	62.39

TABLE 5. The Joints Showing Inflammatory Activity in the MRI Studies Related to the Diagnoses

	SpA		Other Joint Disease	
	Positive MRI	Negative MRI	Positive MRI	Negative MRI
SI joints	45	33	0	52
Pelvis	29	49	1	51
Lumbosacral spine	16	62	0	52
Hip joints	15	63	0	52
Pubic symphysis	5	73	0	52

TABLE 6. Common Enthesitis Locations in MRLI Positive SpA

	ASIS	PSIS	Acute Romanus	Supraspinous Ligament	AIIS	Pubic Symphysis
Acute/active enthesitis (35 cases)	22 (62.9% enthesitis)	11	6	6	5	5

TABLE 7. MRLI Findings Subgroups in MRLI Positive SpA Focusing on Enthesitis

	With Acute Sacral Lesions	With Acute on Chronic Sacral Lesions	With Only Chronic Sacral Lesions	Only (Without Sacral Lesions)	With Degenerative Sacral Changes Without Classic Sacral Lesions
Acute/active enthesitis (35 cases)	10	8	7	2	8

times points, leading to expedited patient treatment. Similar protocol is also commonly used for MR neurography with addition of diffusion tensor imaging and 3D processing.

In conclusion, our results suggest that in patients with suspected SpA, MRI should not be limited to the SI joints but also include enthesitis sites and other joints of the axial skeleton. We propose a multiparametric rheumatology protocol, which increases the efficacy of MRI in detecting enthesitis and joint inflammatory disease, thereby offering additional information to the clinician and assisting in the early diagnosis/detecting disease activity.

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