SATURDAY, 15 JUNE 2019

To image or not to image in spondyloarthritis?_____

OP0343

LONGITUDINAL ASSESSMENT OF MRI OF THE SACROILIAC JOINTS IN THE ASAS CLASSIFICATION COHORT: EVOLUTION OF DIAGNOSTIC FEATURES AND PREDICTIVE UTILITY FOR AXIAL SPONDYLOARTHRITIS:

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Background: Follow up of the ASAS Classification Cohort (CC) indicated a high positive predictive value for the ASAS classification criteria derived from baseline patient and imaging data¹. Moreover, diagnosis of axSpA was changed by the rheumatologist in only 11.2% of patients after 4.4 years. This has raised potential concerns regarding diagnostic ascertainment bias.

Objectives: To determine the evolution of MRI features of axSpA in ASAS-CC cases by central readers, whether this reflects diagnostic assignment by the rheumatologist, and the predictive utility of baseline MRI features of axSpA.

Methods: MR images were available from 108 cases in the ASAS-CC at baseline and follow up (mean 4.4 years) and also had a rheumatologist diagnosis at both time points. Eight readers from the ASAS MRI group recorded MRI lesions that comprised global assessment (MRI indicative of axSpA (yes/no), active and/or structural lesion typical of axSpA (yes/no) according to ASAS definitions), ASAS definition of positive MRI, and detailed scoring of lesions per SIJ quadrant (SPARCC SIJ method). MRI data from ≥ 2 readers and from the majority of readers ($\geq 5/8$) was used to calculate positive and negative predictive values (PPV, NPV).

Table 1

Rheumatologist's diagnosis	MRI is indicative of axSpA (≥ 2 readers)			
	Yes at baseline and yes at follow up (N = 48)	Yes at baseline and no at follow up (N = 4)	No at baseline and yes at follow up (N = 6)	No at baseline and no at follow up (N = 50)
SpA yes at baseline and follow up (N= 82)	46 (56.1%)	2 (2.4%)	4 (4.9%)	30 (36.6%)
SpA yes at baseline and no at follow up (N = 4)	1 (25%)	1 (25%)	0 (0%)	2 (50%)
SpA no at baseline and yes at follow up (N = 5)	1 (20%)	0 (0%)	1 (20%)	3 (60%)
SpA no at baseline and no at follow up (N = 17)	0 (0%)	1 (5.9%)	1 (5.9%)	15 (88.2%)

Table 2

MRI scan at baseline	Rheumatologist Diagnosis of axSpA at follow up n=108			
	Sensitivity	Specificity	PPV (%)	NPV (%)
Active lesions typical of axSpA (≥ 2 readers)	48.3 (37.4-59.2)	100.0 (83.9-100.0)	100.0	31.8
Active lesions typical of axSpA ($\geq 5/8$ readers)	40.2 (29.9-51.3)	100.0 (83.9-100.0)	100.0	28.8
Structural lesions typical of axSpA (≥ 2 readers)	48.3 (37.4-59.2)	90.48 (69.6-98.9)	95.5	29.7
Structural lesions typical of axSpA ($\geq 5/8$ readers)	31.0 (21.5-41.9)	95.2 (76.2-99.9)	96.4	25.0
ASAS positive MRI (≥ 2 readers)	46.0 (35.2-57.0)	100.0 (83.9-100.0)	100.0	30.9
ASAS positive MRI ($\geq 5/8$ readers)	40.23 (29.9-51.3)	100.0 (83.9-100.0)	100.0	28.8
MRI indicative of axSpA (≥ 2 readers)	56.3 (45.3-66.9)	85.7 (63.7-97.0)	94.2	32.1
MRI indicative of axSpA ($\geq 5/8$ readers)	50.6 (39.6-61.5)	100.0 (83.9-100.0)	100.0	32.8

Results: MRI was considered diagnostic of axSpA in 52/108 (48.1%) cases at baseline and in 47/86 (54.7%) diagnosed at baseline as axSpA by the rheumatologist. Change in MRI diagnosis was recorded in 10/108 (9.3%) of cases (2 from yes to no, and 4 from no to yes for axSpA) according to agreement by ≥ 2 readers and in only 3 cases according to $\geq 5/8$ readers (Table 1). Change in rheumatologist diagnosis was recorded in 9/108 (8.3%), 2 of which had a change in MRI diagnosis. Baseline MRI lesions considered typical of axSpA had very high PPV for follow up diagnosis of axSpA (Table 2).

Conclusion: The infrequent change in diagnostic ascertainment of rheumatologists over follow up of the ASAS-CC is supported by this central reader evaluation of MRI scans. A positive MRI at baseline had very high PPV for a follow up diagnosis of axSpA.

REFERENCE:

[1] Sepriano et al. ARD 2016;75:1034-42

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OP0344

WHICH MAGNETIC RESONANCE IMAGING LESIONS OF THE SACROILIAC JOINTS ARE OF DIAGNOSTIC VALUE FOR AXIAL SPONDYLOARTHRITIS?

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Background: Classification of patients as having axial spondyloarthritis (axSpA) by the imaging arm of the ASAS criteria relies partly on the detection of bone marrow edema (BME) suspicious of SpA on magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ). Fatty lesions (FL) and erosions on SIJ-MRI have been suggested to be genuinely related to SpA in the context of interpretation of a 'positive' MRI in case of doubtful BME cases (1).

Objectives: Evaluate the role of different SIJ-MRI lesions for diagnosing axSpA in daily routine practice.

Methods: Consecutive patients with chronic back pain (duration >3 months) starting before age 45 and clinical suspicion of axSpA underwent a complete diagnostic workup including SIJ-MRI. All clinical, laboratory and imaging data were available to experienced rheumatologists for diagnosing axSpA or not (non-SpA). In parallel, two experienced readers, blinded to all patients' information and diagnosis, evaluated the MRIs and made a diagnostic judgement based only on imaging. Furthermore, radiologists quantitatively assessed MRIs for BME (Berlin Score), FL, erosions, sclerosis and ankylosis.

Results: A total of 300 consecutive patients were recruited. AxSpA was diagnosed by the rheumatologist in 131 patients (43.7%) with mean age of 34.5 $\pm$ 7.2 years, 73% HLA-B27+, mean symptom duration 58.6 $\pm$ 69.5 months, vs. 169 non-SpA patients with mean age of 34.5 $\pm$ 7.4 years, 21.3% HLA-B27+, mean symptom duration 33.9 $\pm$ 45.1 months. The ASAS classification criteria were fulfilled by 99/131 patients diagnosed with axSpA (75.6%) vs. 70/169 patients diagnosed vs. non-SpA non-SpA (41.4%).

In 97/162 patients, rheumatologists and radiologists agreed on a diagnosis of axSpA and non-SpA (overall agreement: 86.3%). However, 34/131 (28.1%) patients were diagnosed with axSpA by rheumatologists but not by radiologists. According to radiologists, BME alone was critical for diagnosis in only 7/97 patients (7.2%) with axSpA as agreed by both, rheumatologists and radiologists, in contrast to chronic lesions alone (30/97, 30.9%) or the combination of both lesion types (60/97, 61.9%).

While the sensitivity of BME for diagnosing axSpA did not change, the specificity improved when chronic lesions were also present (Tab.1). In addition, based on rheumatologists' diagnosis, the respective odds ratio (OR) for identifying axSpA by MRI was higher when chronic lesions were present (Tab.1). MRI scores were significantly higher in axSpA vs. non-SpA patients, indicating that axSpA is associated with deeper BME or chronic lesions (Tab.2).

Table 1. Odds ratios for MRI lesions and combinations used for diagnosing axSpA.

Lesion type	Sensitivity	Specificity	OR	95% CI	p-value
BME	72.5%	63.3%	4.6	2.8-7.5	0.001
BME + any chronic lesion	71.8%	72.8%	16.0	7.5-34.0	0.001
FL	56.5%	89.3%	10.9	6.0-19.8	0.001
Erosion	59.5%	88.8%	11.6	6.4-21.0	0.001
Sclerosis	81.7%	43.2%	3.4	2.0-5.8	0.001
Ankylosis	12.2%	99.4%	23.4	3.1-178.7	0.002
BME+FL	36.6%	95.3%	11.6	5.3-25.7	0.001
BME+Erosion	48.9%	94.1%	15.2	7.4-31.4	0.001
BME+Sclerosis	64.1%	75.1%			0.001
BME+Ankylosis	5.3%	99.4%	9.5	1.2-78.1	0.036

Table 2. Mean/median Berlin SIJ scores $\pm$ standard deviation for inflammatory and chronic lesions.

	Lesion type	axSpA	non-SpA	p-value
Mean	Total score	14.8	2.7 $\pm$ 3.4	p<0.001
$\pm$ SD		$\pm$ 10.8		
	BME (0-24)	3.3 $\pm$ 3.6	0.8 $\pm$ 1.3	
	FL (0-24)	5.2 $\pm$ 6.8	0.5 $\pm$ 1.9	
	Erosions (0-24)	4.5 $\pm$ 5.4	0.4 $\pm$ 1.4	
Median	Sclerosis or Ankylosis (0-2)	0	0	—

Conclusion: The combination of structural changes and BME lesions as assessed by MRI performed best in the process of diagnosing axSpA in consecutive patients in a real-life setting presenting to our center. The discrepancy in diagnosis between rheumatologists and radiologists reflects the increasing insecurity of including only BME of SIJ as the major criterium for diagnosing axSpA.

REFERENCE:

[1] Lambert R et al. Ann Rheum Dis 2016

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How low should you go? What is the relevant target in T2T in rheumatoid arthritis?

OP0345

DOES IMMUNOLOGICAL REMISSION, DEFINED AS DISAPPEARANCE OF AUTOANTIBODIES, OCCUR WITH CURRENT TREATMENT STRATEGIES? A LONG-TERM FOLLOW-UP STUDY IN RHEUMATOID ARTHRITIS PATIENTS WHO ACHIEVED A SUSTAINED DMARD-FREE STATUS

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Background: Sustained disease modifying antirheumatic drug (DMARD)-free status, the sustained absence of synovitis after cessation of DMARD-therapy, is infrequent in autoantibody-positive RA, but approximates cure (i.e. disappearance of signs and symptoms). It was recently suggested that immunological remission, defined as disappearance of anticitrullinated protein antibodies (ACPA) and rheumatoid factor (RF), underlies this outcome.¹ However, the association between seroreversion and cure of disease has not been extensively studied before.

Objectives: To determine in a long-term observational study if autoantibodies disappear in RA-patients who achieved sustained DMARD-free remission.

Methods: We studied 95 ACPA- and/or RF-positive RA-patients who achieved DMARD-free remission after median 4.8 years and kept this status for the remaining follow-up (median 4.2 years). Additionally, 21 autoantibody-positive RA-patients with a late flare, defined as recurrence of clinical synovitis after a DMARD-free status of ≥ 1 year, and 45 autoantibody-positive RA-patients who were unable to stop DMARD-therapy (during median 10 years) were studied. Anti-CCP2 IgG, IgM and RF IgM levels were measured in 587 samples obtained at diagnosis, before and after achieving DMARD-free remission.

Results: 12.8% of anti-CCP2 IgG positive RA-patients had seroreverted when achieving remission. In RA-patients with a late flare and with persistent disease this was 8.3% and 5.7%, respectively (p=0.63, Figure). For anti-CCP2 IgM and RF IgM similar results were observed. Evaluating the estimated slope of serially measured levels revealed that RF-levels decreased more in patients with than without remission (p<0.001); the course of anti-CCP2 levels was not different (p=0.66).

Figure Reversion to anti-CCP2 IgG (A) and RF IgM (B) seronegativity in autoantibody positive RA-patients who achieved sustained DMARD-free remission, who had a late flare and in patients with persistent RA

Conclusion: Sustained DMARD-free status in autoantibody-positive RA was not paralleled by an increased frequency of reversion to autoantibody-negativity. This form of immunological remission should therefore not be a treatment target.

REFERENCE:

[1] Schett G, Emery P, Tanaka Y, et al. Tapering biologic and conventional DMARD therapy in rheumatoid arthritis: current evidence and future directions. *Ann Rheum Dis* 2016;**75**:1428–37. doi:10.1136/annrheumdis-2016-209201