Results: *NLRP12* expression was significantly lower in PBMC isolated from SLE patients compared to healthy donors. The inverse correlation was observed in *NLRP12* and *IFNA* gene expression as well as *NLRP12* expression and amount of double-stranded DNA autoantibody in SLE patients. *NLRP12* expression showed negative correlations with IFN-α treatment, as well as herpes simplex virus-1 (HSV-1) infection. Results from ChIP and EMSA analysis indicated a potential transcription factor 1 (TF-1) regulating NLRP12 promoter activity. TF-1 lead to transcriptional suppression of *NLRP12* in SLE PBMC, and it was gradually induced after IFN treatment. Recruitment of TF-1 to NLRP12 promoter in SLE PBMC compared to the healthy PBMC was detected, and increased when treating with IFN. Human CD14+ monocytes collected from lupus and healthy control stimulating with different type of nucleic acids revealing significant increasing level of *IFN-α* and *IL-6* in lupus patients. Among animal models, both pristine induced mice and Fas^{lpr} mice revealed increasing autoantibodies production and severity of glomerulonephritis in *Nlrp12-/-* group in comparison with *Nlrp12+/+* ones, indicating the role of NLRP12 in maintaining positive interferon signature as well as disease activity.

Conclusion: Expression level of *NLRP1.2* has been demonstrated to be a biomarker of disease activity in SLE patients. The NLRP12 was involved in the interferon signature, which was also negatively regulated by TF-1. Both clinical samples and animal models revealed NLRP12 in maintaining the positive interferon signature, indicating the possible role of exacerbating factor for lupus disease activity.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4215

Clinical aspects of axial spondyloarthritis – science meets daily practice

OP0046

CAN PATIENTS WITH AXIAL SPONDYLOARTHRITIS INDICATE WHETHER PAIN IS MAINLY RELATED TO INFLAMMATION OR STRUCTURAL DAMAGE?

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Background: Patients with axial spondylarthritis (axSpA) mainly rate disease activity on experienced symptoms such as pain (1). Pain is also included in the assessments (ASDAS and BASDAI) used to monitor disease activity in axSpA. However, besides disease activity, also other factors including the presence of structural damage may be related to experienced pain and discomfort.

Objectives: To explore to what extent axSpA patients relate their experienced pain in neck, back and hips to inflammation and/or structural damage.

Methods: Patients from the Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort visiting the out-patient clinic between May 2016 and October 2019 were included in this cross-sectional analysis. Patients filled out two additional questions related to question 2 of the BASDAI: To what extent do you think pain in your neck, back and hips is related to: 1. inflammation caused by axSpA?, 2. damage of spine and joints caused by axSpA? These questions were answered on a NRS from 0 (none) to 10 (very much). A difference of ≥2 points was considered as clinically relevant. Patients who differentiated the cause of their pain were allocated to an inflammation or damage group, in favour of their highest score. Furthermore, patient characteristics and clinical assessments were compared between the inflammation and damage groups.

Results: In total, 688 axSpA patients were included, 62.4% were male, mean age was 47.9 years, median symptom duration was 19 years, 77.9% were HLA-B27+, mean BASDAI was 3.9 and mean $ASDAS_{CRP}$ was 2.3. Respectively 13% and 14% of the patients reported a score of 0 on the additional questions about inflammation or damage.

In total, 517 (75%) patients could not differentiate between inflammation or damage. 102 (15%) patients interpreted experienced pain as mainly related to inflammation and 69 (10%) patients interpreted their pain as mainly related to structural damage.

Patients who interpreted pain as mainly related to inflammation were significantly younger, had shorter symptom duration, were more frequently diagnosed as non-radiographic axSpA and had higher $ASDAS_{CRP}$, which was driven by the patient-reported questions as the objective marker CRP was not significantly different between both groups (Table 1).

Table 1. Patients characteristics and clinical assessments of axSpA patients who related pain mainly to inflammation versus to structural damage.

	Inflammation group (n = 102)	Structural damage group (n = 69)	P-value
Age (years)	39.5 ± 12.4	48.9 ± 12.4	<0.001
Symptom duration (years)	12 (6 – 20)	28 (17 – 35)	<0.001
Diagnosis non-radiographic axSpA	39 (40%)	8 (13%)	<0.001
Male gender	60 (59%)	44 (64%)	0.627
BASDAI	4.2 ± 1.8	3.9 ± 2.0	0.371
BASDAI – Q2	6 (3 – 7)	4 (2 – 6)	0.005
Patient global disease activity	4 (3 – 7)	3 (2 – 5)	<0.001
$ASDAS_{CRP}$	2.6 ± 0.9	2.2 ± 0.8	0.003
CRP	3.0 (2.0 – 8.0)	2.5 (2.0 – 4.4)	0.094
Occiput wall distance (cm)	0.0 (0.0 – 4.0)	4.0 (0.0 – 10.0)	<0.001
Chest expansion (cm)	5.8 (4.0 – 7.0)	4.0 (3.0 – 6.0)	0.006
Modified Schober test (cm)	14.0 ± 1.6	13.5 ± 1.6	0.052
Lateral flexion mean (cm)	15.3 ± 6.5	12 ± 5.9	0.001
Cervical rotation mean (degrees)	80 (70 – 90)	70 (45 - 81)	<0.001
mSASSS *	3.0 (0.0 – 9.0)	8.0 (1.8 – 26.0)	0.061

* only available in a subgroup of patients. Inflammation group (n=31), structural damage group (n=39).

Patients who reported their pain as mainly related to structural damage showed significantly worse spinal mobility on almost all spinal mobility tests. In the subgroup of patients with available mSASSS data, there was also a trend towards more spinal radiographic damage (Table 1).

Conclusion: In our large observational cohort of axSpA patients, the vast majority (75%) could not rate whether experienced pain in neck, back and hips was more related to inflammation or structural damage. However, if patients were able to relate pain to inflammation or damage, it seems in accordance with the outcome of their clinical assessments.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.293

OP0047

IDENTIFICATION OF CLINICAL PHENOTYPES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS, PERIPHERAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS ACCORDING TO PERIPHERAL MUSCULOSKELETAL MANIFESTATIONS: A CLUSTER ANALYSIS IN THE INTERNATIONAL ASAS-PERSPA STUDY

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Background: Patients with a diagnosis of Spondyloarthritis (SpA) and Psoriatic Arthritis (PsA) may have predominant axial or peripheral symptoms, and the frequency and distribution of these symptoms may determine the clinical diagnosis by the rheumatologist ("clinical clusters"). Clustering analysis represents an unsupervised exploratory analysis which tries to identify homogeneous groups of cases ("statistical clusters") without prior information about the membership for any of the cases.
Objectives: To identify "statistical clusters" of peripheral involvement according to the specific location of these symptoms in the whole spectrum of SpA and PsA (without prior information about the diagnosis of the patients), and to evaluate whether these "statistical clusters" are in agreement with the "clinical clusters".
Methods: Cross-sectional and multicentre study with 24 participating countries. Consecutive patients considered by their treating rheumatologist as suffering from either PsA, axial SpA (axSpA) or peripheral SpA (pSpA) were enrolled. Four different cluster analyses were conducted: the first one using information about the specific location from all the peripheral musculoskeletal manifestations (i.e., peripheral arthritis, enthesitis and dactylitis), and thereafter a cluster analysis for each peripheral manifestation individually. Multiple correspondence analyses and k-means clustering methods were used. Distribution of peripheral manifestations and clinical characteristics were compared across the different clusters.
Results: 4465 patients were included in the analysis. Two clusters were found with regard to the *location of all the peripheral manifestations* (Fig. 1). Cluster 1 showed a low prevalence of peripheral manifestations in comparison with cluster 2; however, when peripheral involvement appeared in cluster 1, this was mostly represented by arthritis of hip, knee and ankle, as well as enthesitis of the heel. Patients from cluster 1 showed a higher prevalence of males (63% vs 44%), HLA-B27 positivity (69% vs 38%) and axial involvement (80% vs 52%), as well as more frequent diagnosis of axSpA (66% vs 21%) and more frequently fulfilling the ASAS axSpA criteria (69% vs. 41%). Patients from cluster 2 showed a higher prevalence of psoriasis (63% vs 25%), a more frequent diagnosis of PsA (61% vs 19%), and they fulfilled more frequently the peripheral ASAS (26% vs 11%) and the CASPAR criteria (57% vs 19%).

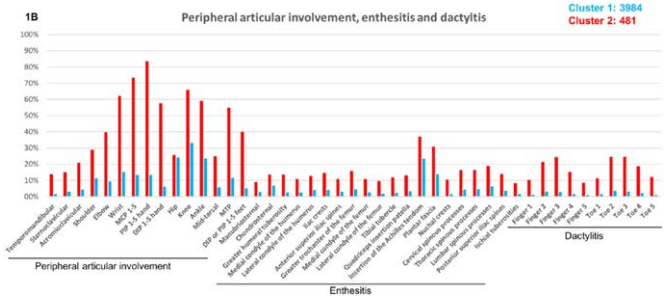

Figure 1. Distribution of the peripheral involvement across clusters

Three clusters were found with regard to the *location of the peripheral arthritis.* Clusters 2 and 3 showed a high prevalence of peripheral joint disease, although this was located more predominantly in the lower limbs in cluster 2, and in the upper limbs in cluster 3. Cluster 1 showed a higher prevalence of males, HLA-B27 positivity, axial involvement, a lower presence of psoriasis, a more frequent diagnosis of axSpA and fulfilling the ASAS axSpA criteria in comparison with clusters 2 and 3, respectively. Clusters 2 and 3 showed a higher prevalence of enthesitis and dactylitis in comparison with cluster 1, a more frequent diagnosis of PsA and fulfillment of the CASPAR criteria. Information about the *location of enthesitis* exhibited three groups: cluster 1 showed a very low prevalence of enthesitis, while cluster 2 and 3 showed a high prevalence of enthesitis, with a predominant involvement of axial enthesis in cluster 2 and peripheral enthesitis in cluster 3.
Finally, the *analysis of dactylitis* also exhibited three clusters that showed a very low prevalence of dactylitis, predominantly toes and predominantly fingers involvement, respectively.
Conclusion: These results suggest the presence of heterogeneous patterns of peripheral involvement in SpA and PsA patients without clearly defined groups, confirming the clear overlap of these peripheral manifestations across the different underlying diagnoses.
Acknowledgements: This study was conducted under the umbrella of ASAS with unrestricted grant of Abbvie, Pfizer, Lilly, Novartis, UCB, Janssen and Merck.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.805

OP0048

DIAGNOSING AXIAL SPONDYLOARTHRITIS: ESTIMATION OF THE DISEASE PROBABILITY IN PATIENTS WITH A PRIORI DIFFERENT LIKELIHOODS OF THE DIAGNOSIS

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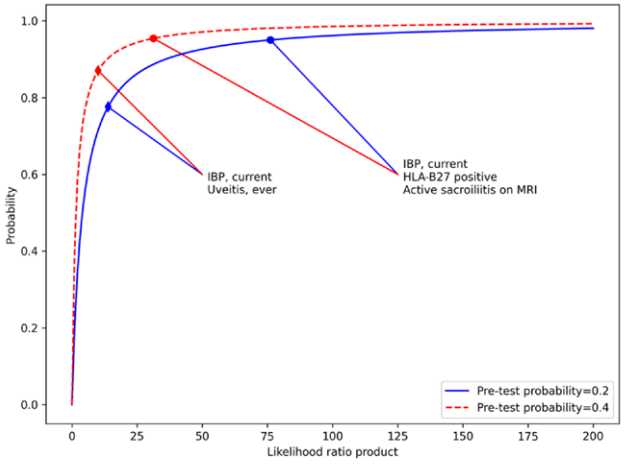
Background: The diagnostic approach in axial spondyloarthritis (SpA) relies on a estimation of the post-test disease probability that is based on evaluation of positive and negative results of diagnostic tests in the context of the pre-test disease probability.
Objectives: To evaluate the diagnostic value of SpA parameters and their combination for the diagnosis of axial SpA in patients with an *a priori* different probability of the diagnosis.
Methods: A total of 361 patients with chronic back pain and suspicion of axial SpA (181 referred by primary care physicians or orthopaedists, 180 recruited via an online screening tool) received a structured rheumatologic examination as a part of the OptiRef study [1], which resulted into a diagnosis or exclusion of axial SpA. The prevalence of axial SpA indicating the pre-test probability was 40% in the physician-referred subgroup and 20% in the online screening subgroup. Sensitivities, specificities, and likelihood ratios (LRs) for SpA features were determined in both subgroups and the respective post-test probabilities of axial SpA were calculated.
Results: The relative diagnostic value of single SpA features varied substantially between the groups with different referral pathways – see the online disease probability calculator http://www.axspa.de/calculator.html. It can be seen that the diagnostic values of the SpA parameters vary substantially between the groups. For instance, HLA-B27 positivity increased the probability of the presence of axial SpA by 35% to 55% in online-screened patients and by 22% to 62% in physician-referred patients. Furthermore, the absence of HLA-B27 resulted in a sharp decrease in the probability of the presence of axial SpA in physician-referred patients (from 40% to 6%). This decrease was less sharp in the online screening group (from 20% to 10%). Furthermore, combinations of parameters performed differently in the studied subgroups. Figure 1 illustrates that the observed differences in the diagnostic values of the SpA parameters in different subgroups were only clinically relevant in the presence of a low number of positive test results. For instance, combining IBP with anterior uveitis increased the post-test probability for axial SpA to 78% in the online screening group and to 87% in the physician-referred group, whereas using HLA-B27 positivity and active sacroiliitis on MRI in combination with IBP resulted in a surge in the post-test probability of the presence of axial SpA to around 95% in both groups.

Figure 1. The relationship between the likelihood ratio product and the post-test probability of axial SpA in patients with different pre-test disease probability.



The relationship between the likelihood ratio product and the post-test probability of axial SpA is depicted for patients referred via an online screening tool (pre-test probability of axial SpA = 20%) and in patients referred via a physician-based referral tool (pre-test probability of axial SpA = 40%).

IBP: inflammatory back pain; MRI: magnetic resonance imaging; SpA: spondyloarthritis.