In patients with axial spondyloarthritis, inflammation on MRI of the spine is longitudinally related to disease activity only in men: 2 years of the axial spondyloarthritis DESIR cohort

The effects of inflammatory disease activity (DA) on radiographic progression in patients with axial spondyloarthritis (axSpA) are worse in men and smokers, but an explanation for this is lacking.[1] Recently, we have found a relationship between inflammatory lesions in the sacroiliac joints (SIJs) detected by MRI and clinical DA measures in male patients, which was absent in female patients.[2] Here, we investigate whether this gender-specific association between MRI-lesions and clinical DA extends to the spine.

The objectives of this study were: (i) to explore the relationship between inflammatory lesions of the spine on MRI and DA in patients with axSpA; (ii) to investigate if such a relationship is gender specific and (iii) to explore the influence of other patient-related factors on the relationship between MRI of the spine and DA.

Two-year follow-up data from 164 patients fulfilling Assessment of SpondyloArthritis international Society (ASAS) axSpA criteria in the DEvenir des Spondylarthopathies Indifférenciées Récentes (DESIR) cohort with at least two spine MRIs available during this period were analysed.[3 4]

The relationship between MRI-spine and DA (Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), patient's global DA, night pain, C reactive protein (CRP) and erythrocyte sedimentation rate (ESR)) was analysed by generalised estimating equations (GEEs) on absolute MRI-spine scores (Berlin method).[5] Interactions between DA and a set of characteristics, including age, gender, human leucocyte antigen B27 (HLA-B27), symptom duration, smoking status and current treatment with tumour necrosis factor inhibitors (TNFis), were examined one by one. In case of a relevant interaction, a stratified analysis was performed. If a relevant interaction was absent, relevant confounding was examined for the relationship between DA and MRI of the spine by comparing the crude model (non-adjusted model) with an adjusted model (adjusted for that specific factor).

Table 1 Characteristics of the patients with axial spondyloarthritis included in this study

	Total n=164	Men n=82 (50%)	Women n=82 (50%)
Age (years)	33.0±9.0	31.2±8.4	34.9±9.3
Male	82 (50)	–	–
Smoker	64 (39)	35 (43)	29 (35)
Fulfilling ASAS criteria			
Imaging arm only	31 (19)	12 (15)	19 (24)
Clinical arm only	58 (36)	23 (28)	35 (44)
Both arms	73 (45)	47 (57)	26 (32)
mNY criteria	46 (28)	33 (40)	13 (16)
Back pain duration (months)	17.9 ±10.7	16.4±9.5	19.3±11.7
HLA-B27 positive	134 (82)	71 (87)	63 (77)
ASDAS	2.6±1.0	2.6±1.1	2.6±0.9
BASDAI (0–10)	4.3±2.0	4.0±2.1	4.5±2.0
BASFI (0–10)	2.8±2.3	2.5±2.1	3.1±2.4
Night pain (0–10)	4.3±3.1	3.8±2.9	4.9±3.2
Pt's global disease (0–10)	4.9±2.6	4.7±2.6	5.1±2.6
ESR (mm/hour)	15.3 ±15.8	14.8±16.6	15.8±14.9
CRP (mg/L)	9.1±14.1	9.1±14.1	9.1±14.1
ASQoL (0–18)	8.8±5.0	7.7±4.9	10.0±4.9
MRI (0–69 Berlin; 0–72 SPARCC)			
Berlin (mean±SD)	1.4±2.9	2.2±3.7	0.5±1.2
Berlin (range)	0–22	0–22	0–8
Berlin≥1 unit	76 (11)	48 (59)	28 (34)
SPARCC-SIJs≥1 unit	87 (53)	53 (65)	34 (42)
Berlin≥1 unit and SPARCC-SIJs≥1 unit	47 (29)	33 (40)	14 (17)
Treatment (baseline)			
NSAID	159 (97)	78 (95)	81 (99)
Anti-TNFα	0	0	0
Treatment (at 24 months)			
NSAID	110 (67)	51 (62)	59 (72)
Anti-TNFα	58 (35)	30 (37)	28 (34)

Unless otherwise specified, the table shows mean±SD or absolute number (percentage) for all patients included in this analysis. Furthermore, the results are also stratified by gender.
Anti-TNFα, anti-tumour necrosis factor alpha therapy; ASAS, Assessment of SpondyloArthritis international Society; ASDAS, Ankylosing Spondylitis Disease Activity Score; ASQoL, Ankylosing Spondylitis Quality of Life; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; HLA-B27, human leucocyte antigen B27; mNY, modified New York; NSAIDs, non-steroidal anti-inflammatory drugs; pt's global: patient's global assessment for disease activity; SPARCC-SIJs, Spondyloarthritis Research Consortium of Canada scoring system for MRI of sacroiliac joints.

Baseline characteristics of the patients included in the study are presented in table 1.

Fifty per cent of patients were men, mean (SD) age was 33 (9) years, 39% were smokers, 82% carried HLA-B27 and mean symptom duration was 18 (11) months. Overall, baseline

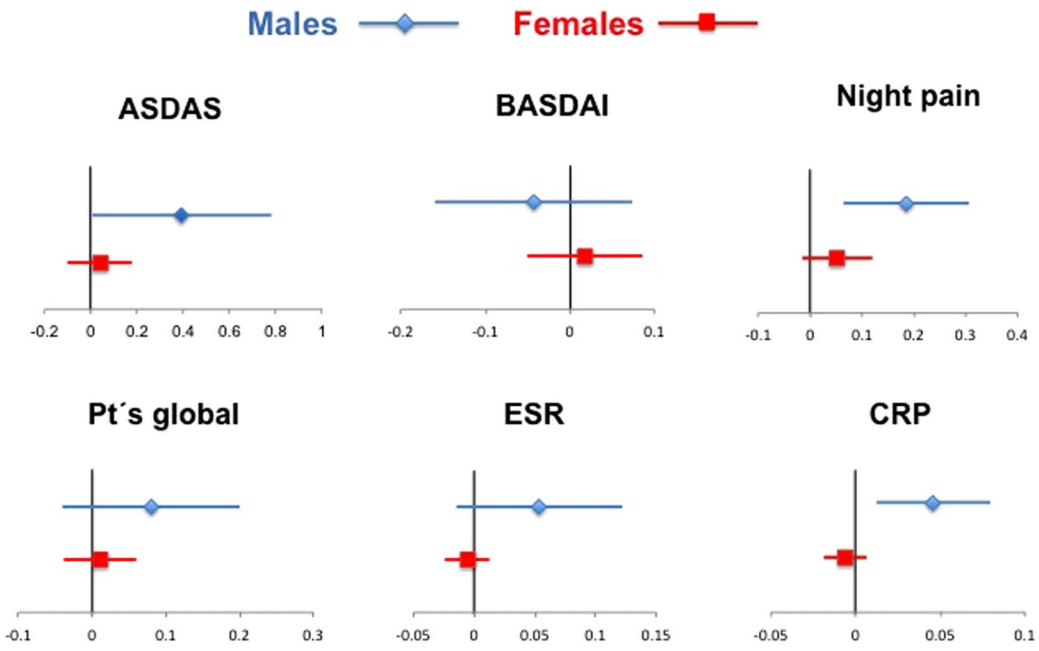

Figure 1 Longitudinal relationship between clinical disease activity (DA) measures and inflammation degree (Berlin score) on MRI of the spine stratified for gender. Each graph represents a separate model for the relationship between the specific clinical DA measure and spinal MRI-inflammation with a generalised estimating equation (GEE) model making use of data from baseline, 1year and 2 years of follow-up. All models were adjusted for current treatment with tumour necrosis factor alpha inhibitors and smoking status. Markers (diamond for men and square for women) represent the regression coefficient and the surrounding lines represent the 95% CIs. ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; pt's global disease, patient's global assessment for disease activity.

characteristics of included patients were similar to those of patients in the entire DESIR cohort.

Gender and DA had a relevant interaction on explaining variation in spinal MRI-scores (p=0.03 for ASDAS*gender); therefore, subsequent analyses were performed for men and women separately. In the fully adjusted GEE models, ASDAS, pain at night and CRP were statistically significantly related to inflammatory lesions on MRI in men, but not in women (figure 1). Beta values and 95% CIs for these DA in men were (β=0.392; 0.004 to 0.781), (β=0.185; 0.065 to 0.306) and (β=0.046; 0.012 to 0.080), respectively. In men, patient global assessment for DA (β=0.080; −0.040 to 0.200) and ESR (β=0.054; −0.015 to 0.122) showed a similar trend, but BASDAI did not have a relationship with MRI-spine, neither in male patients (β=−0.042; −0.159 to 0.074) nor in female patients. In addition, TNFi usage in men and smoking in women were associated with DA and with MRI-spine, and as such acted as confounders.

In conclusion, in patients with axSpA, DA and inflammatory lesions on spinal MRI are associated, but only in male patients, and not in female patients. This relationship was confounded by smoking (women) and TNFi usage (men) but remained intact after statistical adjustment. This finding confirms previous findings with MRI of the SIJ[2] and shows a different expression of axSpA between genders: that is, while in men clinical signs and symptoms coincide with MRI-positivity and with subsequent structural damage, in women symptoms attributed to axSpA (and measured by patient-reported outcomes) occur independently of MRI-inflammation and subsequent structural damage. The reasons for such gender-related uncoupling are unknown and deserve further research. Finally, within the possible limitations for this study, the lack of inflammation assessment at the posterolateral elements or axial enthesis and the presence of a floor effect need to be considered.

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