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Factors associated with radiographic lesions in early axial spondyloarthritis. Results from the DESIR cohort

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Abstract

Objective. To assess whether factors such as inflammation by laboratory tests and MRI differ between early axial SpA with and without radiographic lesions.

Methods. Cross-sectional analysis of baseline data from Devenir des Spondylarthropathies Indifferenciées Récentes (DESIR) cohort patients having recent-onset inflammatory back pain and meeting Assessment of SpondyloArthritis international Society criteria. The baseline evaluation included radiographs and MRI of the SI joints (SIJs) and spine. Patients were classified as having radiographic lesions if they had at least one obvious sacroiliitis, grade 2 for at least one vertebral corner or grade 1 for at least two vertebral corners (at the cervical or lumbar level, according to the modified Stoke Ankylosing Spondylitis Spine Score). Associations between baseline characteristics and the presence of radiographic lesions were evaluated by estimating multi-adjusted odd ratios (aORs) and their 95% CIs using a logistic regression model.

Results. Of 475 patients, 180 (37.9%) had radiographic lesions. Factors positively associated with radiographic lesions were alcohol use (aOR 2.42; 95% CI 1.31, 4.44; $P = 0.005$), CRP level (aOR 1.44; 95% CI 1.13, 1.84; $P = 0.003$) and SIJ inflammation by MRI (aOR 2.25; 95% CI 1.40, 3.60; $P = 0.001$); negative associations occurred with good NSAID responsiveness (aOR 0.44; 95% CI 0.24, 0.81; $P = 0.008$); spinal MRI inflammation was associated with radiographic lesions only in smokers (aOR 1.99; 95% CI 1.01, 3.92; $P = 0.048$).

Conclusion. Alcohol use, poor responsiveness to NSAIDs, CRP elevation, SIJ MRI inflammation and spinal MRI inflammation in smokers were independently associated with radiographic lesions in early axial SpA.

Key words: spondyloarthritis, MRI, inflammation, radiographic lesions, axial spondylorarthritis, epidemiology.

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Introduction

AS is a chronic inflammatory disease with a prevalence of 0.5% [1] and is the most common subtype of SpA. The modified New York criteria for AS require at least bilateral grade II or unilateral grade III radiographic changes in the SI joints (SIJs) [2]. Because the radiographic changes in AS progress slowly, the development of grade II or III radiographic sacroiliitis requires considerable time, contributing to the diagnostic delay of 5–10 years in AS [3]. Therefore, it has been suggested that all cases of predominantly axial SpA be considered as belonging to a single

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disease continuum of axial SpA, irrespective of the presence or absence of radiographic changes [4]. In keeping with this suggestion, new classification criteria for axial SpA were recently developed by the Assessment of SpondyloArthritis international Society (ASAS) [5, 6]. Patients with back pain for more than 3 months and symptom onset before the age of 45 years are classified as having axial SpA if they exhibit sacroiliitis by either radiography or MRI and at least one typical SpA feature or if they are HLA-B27-positive with at least two typical SpA features [5, 6]. Nevertheless, among patients on the SpA continuum, some experience rapid disease progression within the first decade after disease onset [7], whereas others have little or no radiographic changes throughout the course of their disease [8]. Few data are available about potential differences between these two patient groups at the very early stage of axial SpA in terms of demographic, clinical and laboratory characteristics and of inflammation detected by MRI. A previous study in patients with recent-onset SpA or AS, issued from the German Spondyloarthritis Inception Cohort (GESPIC), found no differences in the main demographic and clinical features except for a higher CRP level in the group with sacroiliitis [4]. However, these results require confirmation, if possible in patients with even shorter disease durations. In addition, differences must be sought not only in the clinical and laboratory parameters of disease activity but also in MRI inflammation, particularly as studies have shown a link between spinal MRI inflammation and current or subsequent ossification [9, 10].

We hypothesized that some factors such as inflammation by laboratory tests and MRI differed between patients with early axial SpA with and without radiographic lesions. To assess this hypothesis, we conducted a cross-sectional analysis of baseline data from a prospective longitudinal cohort, the Devenir des Spondylarthropathies Indifferenciées Récentes (DESIR) cohort.

Methods

Study design

DESIR is a prospective longitudinal cohort study conducted in France in 25 rheumatology centres and 708 patients [11]. The DESIR cohort fulfilled current good clinical practice and has obtained the approval of the appropriate ethics committee (clinicaltrials.gov NCT01648907). Participants in the study gave their written informed consent for collection of their personal data for further analyses. The aim of DESIR is to collect comprehensive data on the natural course and prognosis of SpA starting at symptom onset. Here, we conducted a cross-sectional analysis of baseline data from a subgroup of the DESIR cohort.

Patients

As previously described [11], consecutive patients between 18 and 49 years of age were included in the DESIR cohort between October 2007 and April 2010 if they had inflammatory back pain in the thoracic spine, lumbar spine or buttock area for at least 3 months but less than 3 years duration and symptoms suggestive of SpA according to a rheumatologist (score $\geqslant 5$ on a 0–10 rating scale, where 0 was not suggestive and 10 was very suggestive of SpA). Inflammatory back pain was defined according to the criteria of Calin *et al.* [12] or Berlin criteria [13]. Patients were not included if they had a definite diagnosis of non-SpA back pain, conditions that might interfere with the validity of informed consent and/or with optimal compliance (e.g. alcoholism or psychiatric disorder) or a history of treatment with TNF-α antagonists. Corticosteroid intake was permitted only with prednisone doses of <10 mg/day with no change in the past 4 weeks. Details of the protocol and the case record form are available on the website (www.lacohortedesir.fr). The present study was conducted in the DESIR cohort patients who met ASAS criteria for axial SpA at baseline [5, 6].

Data collection

Patients in the DESIR cohort are evaluated every 6 months for the first 2 years and then once a year. For the present study, we used only the data collected at the first visit, which included age, ethnicity, smoking history, alcohol use, date of IBP onset and site of IBP, date of peripheral arthritis onset, presence of other SpA features, relevant family history, medication including use of NSAIDs and DMARDs and number of patient-reported missed work days in the past year. For NSAID intake, we used the ASAS NSAIDs score, recently recommended by ASAS, accounting for both dose and duration/regimen of drug intake (0, no NSAIDs intake at all; 100, daily NSAIDs intake in a dose equivalent to diclofenac 150 mg over the whole period of interest) [14]. Patients were asked about their NSAID responsiveness as defined in the ASAS criteria [5, 6]. Patients were considered as smokers if they were smokers at baseline or previous smokers; no quantitative data on smoking were taken into account. For alcohol consumption, the case record form (CRF) only provided a yes or no answer with no further quantitative assessment. Axial symptom duration was defined as the time from the first axial symptom to the baseline interview. The intensity of IBP was reported by the patients using a 0–10 rating scale. Patients were also asked to complete the BASDAI [15], BASFI [16] and BAS-G. A physical examination was performed to assess the Ritchie articular index (53 joints), cervical rotations, Schöber's test and chest expansion. Extra-articular manifestations of SpA were collected.

Blood tests were performed at the regional rheumatology centres and included the serum CRP level and presence of the HLA-B27 antigen. The CRP level was used to compute the Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) [17], a recently validated tool for assessing disease activity in AS [18]. Health-related quality of life (HRQoL) was assessed using the Short Form-36 Health Survey (SF-36) and AS Quality of Life (ASQoL) questionnaire [19, 20]. The SF-36 is a generic health status instrument that yields two summary scores, the Physical Component Summary score and the Mental

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Component Summary score. Component scores range from 0 to 100, with higher scores reflecting better health. The ASQoL is an AS-specific instrument that can produce scores in the 0–18 range, with lower scores indicating better HRQoL.

Radiographs and MRI scans were evaluated by the local radiologist or rheumatologist. In the DESIR cohort, SIJ radiographs were locally graded as follows: 0, normal; 1, doubtful sacroiliitis; 2, obvious sacroiliitis and 3, fusion; indeed, for that local reading, with practitioners from real life and not expert readers, it was considered as more robust to pool mild and moderate sacroiliitis according to the modified New York criteria in one grade, i.e. obvious sacroiliitis. Unilateral radiographic sacroiliitis was then defined as the presence of grade 2 or 3 lesions. Spinal radiographs were scored using the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) [21]. T1-weighted fast spin echo and short τ inversion recovery MRI scans of the entire spine and both SIJs were performed, using a 1–1.5 Tesla machine, to assess inflammatory and structural lesions. MRIs were classified as showing definite, doubtful or absent inflammatory lesions (bone oedema) at the spine and/or SIJs. In our analysis we defined the presence of radiographic lesions as at least one sacroiliitis, a syndesmophyte on at least one vertebral corner (mSASSS grade 2) or grade 1 changes (sclerosis, squaring or erosion) in at least two vertebral corners (at the cervical or lumbar level according to the mSASSS). Doubtful MRI images were classified as normal.

Statistical analysis

Qualitative data are descibed as *n* (%) and quantitative data as mean (S.D.) or median (quartile1–quartile3) as appropriate. CRP was log-transformed for statistical testing. The primary endpoint was the presence of axial radiographic lesions (at the SIJs and/or spine).

First, baseline characteristics were compared between patients with and without axial radiographic lesions, using the *t*-test or Wilcoxon–Mann–Whitney test for continuous variables as appropriate and the Pearson χ^2 test for categorical variables. Second, associations between baseline characteristics (demographics, physical findings, laboratory test results, disease activity and imaging) and the presence of axial radiographic lesions were evaluated by building a logistic regression model to estimate the odds ratios (ORs) and their 95% CIs. Variables yielding *P* values <0.15 by univariate analysis were considered for the multivariate analysis. We also looked for interactions between variables kept in the multivariate model. Interactions were assessed one at a time and those yielding *P* values <0.10 were taken into account.

We conducted a sensitivity analysis by comparing baseline characteristics of patients with and without radiographic abnormalities of the SIJs, irrespective of the presence or absence of radiographic lesions of the spine. All analyses were two-sided and *P* values <0.05 were considered significant. STATA software version 11 (College Station, TX, USA) was used for the statistical analyses.

Results

Of the 708 patients in the DESIR cohort, 475 patients met ASAS criteria and were included in the analysis. Mean age was 33 ± 8.6 years, 239 (50.3%) patients were men and 395 (83.2%) patients were HLA-B27-positive. Of the 180 (37.9%) patients who met our definition of axial radiographic lesions, 66 (36.6%) had radiographic lesions confined to the SIJs, 62 (34.4%) had radiographic lesions confined to the spine and 52 (28.8%) had radiographic lesions of both the SIJs and spine. Missing data are reported in Table 1.

As shown in Table 1, where all tested features are presented, demographic and clinical characteristics were largely similar in the groups with and without axial radiographic lesions. However, the group with axial radiographic lesions had lower values for chest expansion and higher proportions of patients with alcohol use, current smoking, Crohn's disease and enthesitis. The group with radiographic lesions also had a higher median CRP level and contained fewer good responders to NSAIDs. The group with axial radiographic lesions had a higher proportion of patients having both SIJ and spinal inflammation by MRI. In the spine, MRI inflammation occurred with similar frequency in the thoracic and lumbar spine in both groups (data not shown).

After full adjustment, factors yielding *P* values <0.15 by univariate analysis that were associated with axial radiographic lesions were alcohol use, higher CRP level, poor responsiveness to NSAIDs, spinal MRI inflammation and SIJ MRI inflammation (Table 2). An interaction of borderline significance was found between smoking and spinal MRI inflammation ($P = 0.08$); spinal MRI inflammation was associated with radiographic lesions only in smokers (Table 2).

When doubtful MRIs were classified as abnormal, the associations between MRI inflammation and axial radiographic lesions remained significant (data not shown).

In the sensitivity analysis taking only the SIJ radiographic lesions into account to define the radiographic group, i.e. the AS patients, the results were similar. However, a significant association emerged between BMI and SIJ radiographic lesions and, in contrast, no significant association was found with NSAID responsiveness and SIJ radiographic lesions (Table 3).

Discussion

In 475 patients of the DESIR cohort who met ASAS criteria at baseline, the main demographic and clinical characteristics were largely similar in the groups with and without axial radiographic lesions, and factors having independent positive associations with baseline radiographic lesions of the SIJs and/or spine were alcohol use, poor responsiveness to NSAIDs, CRP elevation, SIJ MRI inflammation and spinal MRI inflammation in smokers.

Some of the variables associated with radiographic lesions in our study were also identified in previous studies. However, our patients were seen at an earlier stage of the disease (symptoms for less than 3 years, with a mean of 18 months). Thus, our data further suggest that

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Table 1 Main baseline features in patients with axial spondyloarthropathy, the DESIR cohort

	Overall ($n = 475$)	Radiographic abnormalities ($n = 180$)	No radiographic abnormalities ($n = 295$)	*P* value[a]	Missing data
Male gender, *n* (%)	239 (50.3)	96 (53.3)	143 (48.6)	0.32	1
Age, mean (s.d.), years	33 (8.6)	33.2 (9.1)	32.8 (8.3)	0.62	2
Caucasians, *n* (%)	429 (90.3)	160 (88.9)	269 (91.2)	0.55	0
Symptom duration, mean (s.d.), years	1.5 (0.9)	1.55 (0.87)	1.53 (0.93)	0.78	35
Manual labourer, *n* (%)	68 (14.4)	36 (18)	32 (11.8)	0.06	4
Past or current smoker, *n* (%)	188 (39.7)	82 (45.8)	106 (36.5)	0.03	2
Alcohol consumption (Y/N), *n* (%)	80 (17)	41 (23.2)	39 (13.3)	0.006	5
Height, mean (s.d.), cm	169.9 (10.1)	170.2 (9.4)	169.8 (10.5)	0.62	3
Weight, mean (s.d.), kg	68.9 (13.3)	70.1 (1.04)	68.2 (0.75)	0.11	4
BMI, mean (s.d.), kg/m^2	23.9 (4.8)	24.2 (4.5)	23.7 (4.9)	0.28	6
Current clinical manifestations					
Thoracic pain, *n* (%)	268 (56.4)	96 (53.3)	172 (58.3)	0.29	0
Lumbar pain, *n* (%)	421 (88.6)	159 (88.3)	262 (88.8)	0.87	0
Buttock pain, *n* (%)	355 (74.7)	137 (76.1)	218 (73.9)	0.59	0
Chest expansion, mean (s.d.), cm	5 (4–7)	5 (4–7)	6 (4–7)	0.04	1
Schöber's index, mean (s.d.)	3.78 (1.4)	3.62 (1.33)	3.89 (1.48)	0.07	2
Cervical rotation, median (IQR), cm	77 (63–85)	75 (60–85)	79 (67–85)	0.05	9
Ritchie articular index, median (IQR)	1 (0–4)	1 (0–4)	1 (0–4)	0.32	1
Peripheral arthritis, *n* (%)	261 (55.1)	109 (54.5)	152 (55.5)	0.83	1
Enthesitis, *n* (%)	227 (47.8)	85 (42.3)	142 (51.8)	0.04	0
Chest wall pain, *n* (%)	225 (47.4)	93 (46.3)	132 (48.2)	0.68	0
Dactylitis, *n* (%)	64 (13.5)	28 (13.9)	36 (13.1)	0.8	0
Uveitis, *n* (%)	46 (9.7)	22 (11)	24 (8.7)	0.43	0
Psoriasis, *n* (%)	76 (16)	34 (16.9)	42 (15.3)	0.64	0
Crohn's disease, *n* (%)	15 (3.2)	11 (5.5)	4 (1.5)	0.01	0
Ulcerative colitis, *n* (%)	7 (1.5)	3 (1.5)	5 (1.5)	0.98	0
HLA-B27-positive, *n* (%)	395 (83.3)	144 (80.4)	251 (85.1)	0.41	1
CRP[b], median (IQR)	4.4 (2.25–10)	6 (3.1–15)	4 (1.7–8)	<0.0001	83
Back pain (0–10), median (IQR)	5 (2–7)	5 (2–7)	5 (2–7)	0.47	1
BASDAI (0–10), median (IQR)	27 (16–35)	26 (15–36)	27 (16–35)	0.63	5
BASFI (0–10), median (IQR)	27 (12–48)	27 (14–53)	27 (10–47)	0.35	10
ASDAS, median (IQR)	2.84 (2.1–3.47)	2.87 (2.1–3.6)	2.78 (2.1–3.3)	0.11	85
BAS-G (week) (0–10), median (IQR)	5 (3–7)	5 (2–7)	5 (3–7)	0.07	4
HAQ AS, median (IQR)	1.42 (1.14–1.85)	1.57 (1.14–1.85)	1.42 (1.14–1.86)	0.4	50
SF-36[a] MCS[c], median (IQR)	58.1 (40–72.4)	58.7 (41–71.5)	57.5 (38.3–73)	0.98	19
SF-36[a] PCS[d], median (IQR)	54.5 (43.8–62.3)	56.3 (45.3–62.4)	54.2 (43.2–62.0)	0.39	19
ASQoL[e], median (IQR)	9 (5–14)	9 (5–14)	10 (5–13)	0.76	12
Missed work days, median (IQR)	5 (0–28)	8 (0–30)	4 (0–25)	0.25	67
MRI inflammatory lesions					
SIJ MRI inflammatory lesions, *n* (%)	225 (50.2)	124 (65.6)	101 (38.4)	<0.0001	23
Spinal MRI inflammatory lesions, *n* (%)	118 (26.2)	61 (36.3)	57 (20.2)	<0.0001	25
Treatment					
NSAID use, *n* (%)	452 (95.4)	171 (95.5)	281 (95.2)	0.89	1
ASAS NSAIDs score, median (IQR)	49 (22–84)	53.9 (25.3–90.4)	45.3 (19.6–78.7)	0.09	13
Self-reported good response to NSAIDs (Y/N), *n* (%)	401 (84.8)	144 (80)	257 (87.7)	0.02	2
DMARD use, *n* (%)	67 (14.1)	26 (14.5)	41 (13.9)	0.85	1

Categorical variables are expressed as *n* (%) and continuous variables as mean (s.d.) when normally distributed and median (Q1–Q3) otherwise. Categorical variables were compared using the Pearson χ^2 test and continuous variables using the *t* test if normally distributed and the Wilcoxon–Mann–Whitney test otherwise. [a]Data from the Short Form 36 Health Survey. [b]Serum CRP levels were log-transformed for statistical testing. [c]Physical Component Summary score. [d]Mental Component Summary score. [e]AS-specific instrument for assessing health-related quality of life.

studies of these variables may shed light on the mechanisms underlying the radiographic progression of AS. In the GESPIC, CRP elevation at baseline was associated with radiographic sacroiliitis (OR 1.85; 95% CI 0.96, 3.56; $P = 0.07$) and one or more syndesmophytes (OR 2.59; 95% CI 1.23, 5.54; $P = 0.01$) at baseline [4]. Data obtained in the same cohort 2 years later showed that baseline CRP elevation strongly predicted progression of radiographic sacroiliitis, in patients both with and without radiographic evidence of sacroiliitis at baseline (ORs 3.65 and 5.08, respectively; $P < 0.05$) [22]. Since mean symptom duration was three times shorter in our study, the association of CRP elevation and the ossification process appears to be a very early phenomenon that reinforces the link between systemic inflammation and ossification in SpA and raises the question of the potential impact of attempting to normalize CRP level when treating early SpA patients in order to prevent further ossification.

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Table 2 Baseline factors associated with spine or SIJ radiographic abnormalities[a]

Axial radiographic lesions	OR[b] (95% CI)	*P* value[c]
Alcohol use	2.42 (1.31, 4.44)	0.005
NSAID responsiveness	0.44 (0.24, 0.81)	0.008
CRP[d]	1.44 (1.13, 1.84)	0.003
Non-smokers without spinal MRI inflammation	1.00	–
Smokers without spinal MRI inflammation	0.70 (0.39, 1.25)	0.23
Non-smokers with spinal MRI inflammation	1.02 (0.49, 2.09)	0.96
Smokers with spinal MRI inflammation	1.99 (1.01, 3.92)	0.048
SIJ MRI inflammation	2.25 (1.40, 3.60)	0.001

[a]Spine or SIJ radiographic abnormalities were defined by the presence of radiographic lesions as either at least one obvious sacroiliitis or a syndesmophyte on at least one vertebral corner (mSASSS grade 2) or grade 1 changes (sclerosis, squaring, or erosion) in at least two vertebral corners (at the cervical or lumbar level according to the mSASSS). [b]ORs were calculated using logistic regression models. [c]Wald test. [d]Serum CRP levels were log-transformed for statistical testing.

Table 3 Baseline factors associated with radiographic abnormalities of the sacroiliac joints[a]

Radiographic abnormalities	OR[b] (95% CI)	*P* value[c]
Alcohol	2.30 (1.19, 4.44)	0.013
BMI	0.90 (0.83, 0.97)	0.007
CRP[d]	1.46 (1.11, 1.91)	0.007
Non-smokers without spinal MRI inflammation	1.00	–
Smokers without spinal MRI inflammation	0.99 (0.50, 1.95)	0.97
Non-smokers with spinal MRI inflammation	1.45 (0.64, 3.27)	0.37
Smokers with spinal MRI inflammation	3.23 (1.57, 6.62)	0.001
SIJ MRI inflammation	3.44 (1.94, 6.10)	<0.001

[a]SIJ radiographic abnormalities were defined by the presence of at least one obvious sacroiliitis. [b]ORs were calculated using logistic regression models. [c]Wald test. [d]Serum CRP levels were log-transformed for statistical testing.

Recent studies demonstrated that MRI inflammation at the SIJs and spine was associated with the subsequent development of radiographic lesions [9, 23–25]. Recent additional MRI data reported from 100 consecutive patients with axial SpA showed that both CRP and MRI inflammation were associated with the AS subgroup in comparison with the non-radiographic subgroup [10]. We found that MRI inflammation was associated with radiographic lesions independently from CRP elevation. Thus it appears that even in the very early stages of the disease, MRI inflammation at the spine and/or SIJs is a factor independently associated with the presence of radiographic lesions.

We also found an association between NSAID responsiveness and axial radiographic lesions. Patients with greater responsiveness to NSAIDs were less likely to have early axial radiographic lesions. This finding supports earlier evidence that NSAIDs might protect against spinal ossification, particularly as NSAID responsiveness was not associated with radiographic lesions specifically located at the SIJs, indicating that the link mainly involved spinal lesions. In a randomized clinical trial comparing continuous *vs* on demand use of the NSAID celecoxib, the mean mSASSS increase after 2 years of follow-up was smaller in the continuous treatment group (0.4 ± 1.7 *vs* 1.5 ± 2.5, $P < 0.002$) [23]. A recent report on a subgroup of GESPIC AS patients for whom data on NSAID intake over 2 years were available also suggested greater radiographic progression in patients with lower NSAID intakes as assessed by the ASAS NSAID index [24]. However, in our study, there was no significant association between the ASAS NSAID score and early axial radiographic lesions. It may be hypothesized that the individual NSAID responsiveness is more important in slowing the ossification process than the amount of NSAID intake. Follow-up data from the DESIR patients should help to clarify the role for NSAIDs in the development of structural damage.

Besides the associated factors we found, we have also shown that all the clinical characteristics of the disease as well as its burden were not associated with an early ossification process. Those data strongly suggest that, even in very early disease development, forms with radiographic ossification are clinically (phenotype, symptoms, activity, function, quality of life) similar to the non-radiographic forms.

In our population, after multiple adjustments, the association of axial radiographic lesions with smoking was no longer significant, whereas that with alcohol use was significant. In a previous study in the 647 DESIR patients

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meeting at least one set of SpA criteria, smoking was closely associated with MRI inflammation of the spine and/or SIJs and with higher mSASSS values [25]. The 2-year follow-up study of 210 GESPIC patients showed a significant association between current smoking and spinal radiographic progression, with an OR of 2.52 (95% CI 1.06, 5.99) [26]. In the current study, MRI spinal inflammation was associated with radiographic lesions only in smokers, suggesting that the combination of these two factors might promote the development of structural spinal damage and that the association between smoking and radiographic lesions evidenced in previous studies might be chiefly mediated by spinal inflammation. One hypothesis to explain the association between alcohol use and radiographic lesions in our population is that symptoms associated with the development of structural damage lead to alcohol use. However, neither disease activity nor quality-of-life impairments were greater in the subgroup with axial radiographic lesions. A recent study of stored serum samples obtained at the stage of preclinical rheumatoid arthritis from participants in the US Nurses' Health Study showed that alcohol intake was associated with markers of inflammation, including serum IL-6 and soluble TNF receptor II levels [27]. However, in our study, the association between alcohol use and axial radiographic lesions was independent of CRP level, i.e. the main marker of systemic inflammation. Thus the mechanism underlying the association between alcohol use and radiographic lesions remains unclear, and further studies with quantitative evaluation of alcohol consumption are needed to confirm, or not, this association.

The absence of radiographic lesions of the SIJs was slightly associated with BMI, whereas no significant association was apparent when all axial radiographic lesions were considered. This finding also remains to be confirmed in other studies.

HLA-B27 was not significantly associated with radiographic lesions in our population, in contradiction with another study of the DESIR cohort [28]. However, the earlier study included the entire DESIR cohort, whereas we confined our analysis to patients meeting ASAS criteria [5, 6]. This is possibly explained by the fact that all patients who are HLA-B27 negative in the DESIR cohort had to fulfil the imaging arm of the ASAS criteria in our study, meaning they had radiographic or MRI sacroiliitis, which are associated with ossification, as we have shown. In keeping with our results, in the cross-sectional baseline GESPIC study, HLA-B27 was not associated with radiographic sacroiliitis or syndesmophytes [4]. Consequently, the association between HLA-B27 and the ossification process is not yet been established as it has for CRP elevation and axial MRI inflammation.

It should be emphasized that we considered as radiographic forms not only, as usual, patients with radiographic sacroiliitis, but also patients with some evidence of ossification of the spine even without radiographic sacroiliitis [syndesmophyte on at least one vertebral corner (mSASSS grade 2) or mSASSS grade 1 changes in at least two vertebral corners]. Thus we considered 62 more patients as radiographic patients than those with purely AS disease, i.e. patients who had radiographic lesions confined to the spine. We thought that this approach was more relevant when focusing on the ossification process. Indeed, it may be too restrictive and lead to loss of relevant data to consider as radiographic forms only those with radiographic sacroiliitis and not also those with overt ossification of the spine. When, in Table 3, we considered only patients with radiographic sacroiliitis as radiographic forms, we lost the association with NSAID responsiveness, which seems to be a relevant parameter in the ossification process. Considering as radiographic forms those with at least one syndesmophyte of the spine, whatever the SIJ status, could be an interesting approach, in the diagnosis of axial SpA, which needs further validation.

Our study has several limitations. The cross-sectional design precluded an evaluation of potential causal links between patient characteristics and radiographic lesions. Since many variables were self-reported, there may have been some degree of misclassification. Moreover, the images were not analysed in a centralized manner, although they were read and classified by trained rheumatologists and radiologists at each study site. The strengths of our study include the multicentre design with 450 patients who were routinely investigated using MRI of the spine and SIJs. Moreover, IBP duration was less than 3 years, indicating that our patients were at the very early stages of their disease. Detailed interviews, physical examinations and laboratory tests were performed, allowing full adjustment for demographic characteristics, lifestyle factors, laboratory parameters, treatments and HLA-B27 status.

In summary, this study showed that, among patients with early axial SpA, those without axial radiographic lesions did not differ from those with axial radiographic lesions regarding the main disease characteristics. However, both systemic inflammation and SIJ MRI inflammation were associated with axial radiographic lesions. Alcohol use was also associated with axial radiographic lesions, as well as smoking in patients with spinal MRI inflammation. Furthermore, poor NSAID responsiveness was also associated with radiographic lesions, reinforcing the interest recently given to NSAIDs in the ossification process.

Rheumatology key messages

- Radiographic and non-radiographic forms of early axial SpA do not differ in most of their features.
- Systemic and axial MRI inflammations are associated with a radiographic pattern in early axial spondyloarthritis.

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