Spondyloarthritis : recognition, imaging, treatment

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Percentage of patients with spondyloarthritis in patients referred because of chronic back pain and performance of classification criteria: experience from the SpondyloArthritis Caught Early (SPACE)-cohort

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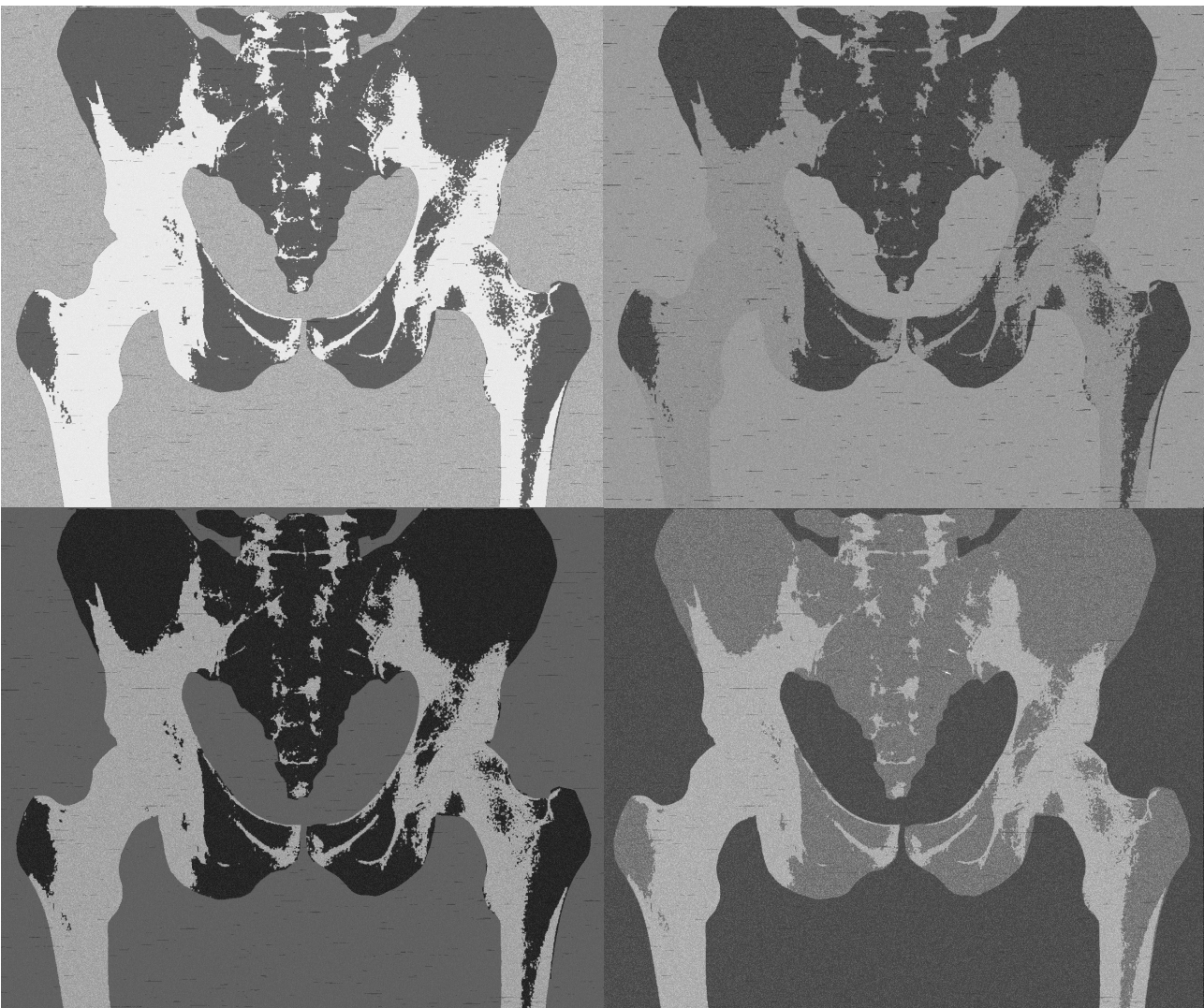

Abstract

Objectives

The objectives of the study are to describe the Spondyloarthritis Caught Early (SPACE) cohort, present the performance of various SpA classification criteria and compare patients fulfilling the imaging arm with patients fulfilling the clinical arm of the Assessment of Spondyloarthritis international Society (ASAS) axSpA criteria on demographics, presence of SpA-features and level of disease activity.

Methods

Patients with back pain (≥3 months but ≤2 years, onset <45 years) visiting the rheumatology outpatient clinic of the Leiden University Medical Center were included in the SPACE-cohort. Patients were classified according to the modified New York (mNY), ESSG, Amor and ASAS axSpA criteria. The sensitivity and specificity of criteria were tested against a rheumatologist's diagnosis.

Results

In total, 157 patients were included; 92 patients fulfilled any criteria, 11 fulfilled the mNY (sensitivity 16.9%, specificity 100%), 68 the ESSG (sensitivity 64.6%, specificity 71.7%), 48 the Amor (sensitivity 47.7%, specificity 81.5%) and 60 the ASAS axSpA criteria (sensitivity 84.6%, specificity 94.6%). Of those 60 patients, 30 fulfilled the imaging arm and 30 the clinical arm. Patients in the imaging arm are statistically significantly more often male, have a longer symptom duration and less often a positive family history for SpA than patients fulfilling the clinical arm. Patients in both arms are very similar regarding all other SpA-features and level of disease activity.

Conclusion

The inclusion criteria of the SPACE-cohort yield the same high numbers of SpA patients compared with referral strategies like inflammatory back pain, HLA-B27+ or sacroiliitis, yet are easier to apply. The ASAS axSpA criteria outperformed the other criteria; 38.2% fulfilled the ASAS axSpA criteria. Patients fulfilling the clinical arm of the ASAS axSpA reflect a group of patients similar to those fulfilling the imaging arm.

Introduction

SpA comprises a group of interrelated rheumatic diseases, including AS, PsA and arthritis associated with IBD [1]. The diagnosis is challenging because of the lack of diagnostic criteria for (early) SpA.

Over the years, several criteria sets have been developed to classify patients with SpA. The modified New York (mNY) criteria are available to classify patients with AS [2], however, they are of limited use in early disease or other subtypes of SpA [3]. The ESSG and the Amor criteria are widely used to define the whole concept of SpA [4, 5]. More recently, the Assessment of Spondyloarthritis international Society (ASAS) developed criteria to classify patients with predominantly axial SpA (axSpA) and criteria to classify patients with predominantly peripheral SpA [6, 7]. It is possible to classify patients as having axSpA according to the imaging arm if they have sacroiliitis on radiographs and/or MRI plus at least one additional SpA feature, or according to the clinical arm based on HLA-B27 positivity in combination with at least two other SpA-features [6]. Yet the question arose of whether patients fulfilling the clinical arm reflect a group of patients similar to those fulfilling the imaging arm.

The ASAS axSpA criteria should be applied in patients with back pain (almost daily for ≤3 months, onset <45 years) of unknown origin, which is considered to be the leading symptom of axSpA [8]. However, it is difficult to recognize axSpA in an early stage among the enormous number of patients with back pain, since the clinical presentation of axSpA is very heterogeneous and there is no single shared distinguishing feature [9]. Hence some have stated that not just chronic back pain, but specific inflammatory back pain (IBP) is typical of axSpA [10]. Therefore IBP is often proposed as one of the referral parameters [11, 12]. However, there is increasing evidence that not all patients with axSpA have IBP, and vice versa, which is also evident from the relatively low sensitivity and specificity of IBP criteria (e.g. 79.6% and 72.4%, respectively, for the ASAS IBP criteria) [3, 13-16].

The SpondyloArthritis Caught Early (SPACE) cohort in the Leiden University Medical Center (LUMC) in Leiden, the Netherlands, uses chronic back pain (≥3 months but ≤2 years, onset <45 years) as the only inclusion criteria. These inclusion criteria are, to our knowledge, unique for a SpA cohort. Other early back pain cohorts like ESPAC (the Early SPondyloArthritis Clinic) and DESIR (DEvenir des Spondylarthropathies Indifférenciées Récentes) included only patients with IBP [17, 18].

The goal of this study is to give a description of the characteristics of the patients included in the SPACE-cohort. The percentage of patients fulfilling at least one of the classification criteria sets for SpA is given. Second, the performance of the various classification criteria for SpA is tested. Furthermore, demographics, number of SpA-features and level of disease activity in patients fulfilling the imaging arm and patients fulfilling the clinical arm of the ASAS axSpA criteria are compared.

Patients and methods

Patients

The SpondyloArthritis Caught Early (SPACE) cohort started in January 2009 and is an ongoing project. General practitioners as well as other specialists such as ophthalmologists and gastroenterologists were informed about the start of the SPACE-cohort and about the inclusion criteria. Patients aged 16 years and older with chronic (almost daily) back pain for ≥3 months but ≤2 years with the onset before the age of 45 years referred to the rheumatology outpatient clinic of the LUMC were included after signing informed consent. The SPACE study protocol was approved by the local medical ethics committee of the LUMC. Patients could not be included if other painful conditions not related to SpA could interfere with the evaluation of disease activity or if any reason was present that was likely

to invalidate informed consent or limit the ability of the subject to comply with the protocol requirements.

Assessments and visits

All patients underwent a diagnostic workup at baseline; descriptions of the performed diagnostic workup follow below. Thereafter only patients with definite or possible SpA were included for follow-up visits after 3, 12 and 24 months. Definite axSpA is defined as a patient fulfilling the ASAS axSpA criteria. Possible SpA is defined as the presence of at least one of the following specific SpA-features [high likelihood ratio (LR+) [6, 14]: HLA-B27 positivity, positive family history for SpA, sacroiliitis (MRI or radiographs), acute anterior uveitis] or at least two of the following less-specific SpA-features [lower LR+: IBP (ASAS definition [16]), (heel) enthesitis, peripheral arthritis, psoriasis, IBD, good response to NSAIDs or elevated levels of ESR or CRP], but not fulfilling any of the classification criteria. Annual visits after the first 2 years were scheduled for patients with definite axSpA (ASAS criteria). Unless otherwise specified, all measurements were performed by one of the researchers (RvdB or MdH) during every visit.

Physical examination

In total, 68 joints were examined for tenderness and 66 for swelling. Entheses were examined according to the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) index [19]. Spinal mobility was assessed by measuring chest expansion, occiput to wall distance, modified Schober test, cervical rotation, lateral spinal flexion and intermalleolar distance as described in the ASAS handbook [20]. The tragus-to-wall distance was derived from the OWD by adding 8 cm to the OWD score. By doing so, the value of zero in the OWD corresponds to a score of zero in the calculation of the BASMI [21]. Based on these measurements, the BASMI was calculated [21].

Patient-reported questionnaires

Patients completed the BASDAI [22] and BASFI [23].

Other parameters

Overall assessment of disease activity was done by the physician on an 11-point numerical rating scale (NRS), 0 representing inactive disease and 10 extremely active disease. The presence (past or current) of extra-spinal and extra-articular manifestations (acute anterior uveitis, urethritis, balanitis, cervicitis, IBD and psoriasis, enthesitis) and a positive family history of SpA (AS, reactive arthritis, psoriasis, IBD, uveitis) all according to the definition of the ASAS criteria [6] was recorded. Treatment with NSAIDs, DMARDs and biologic therapies was recorded. NSAID intake is recorded according to the ASAS recommendations [24]. A good response of back pain to a full dose of NSAID was defined as not present anymore or much better [6]. Furthermore, the Ankylosing Spondylitis Disease Activity Score (ASDAS) was calculated [25]. More information about performed measurements during the visits can be found in the supplementary data, available at Rheumatology Online.

Laboratory assessment

The laboratory assessment during each visit consisted of measurements of ESR (Westergren method in mm/1 h) and CRP (ELISA in mg/l). HLA-B27 was only typed at baseline.

Imaging assessment

MR imaging was performed on a 1.5T (Philips Medical Systems, Best, Netherlands) T1 weighted turbo spin echo (T1TSE) (TR 550/TE 10) and short tau inversion recovery (STIR) (TR 2500/TE 60) sequences were acquired, coronal oblique of the SI joints (MRI-SI). The slice thickness was 4 mm. Radiographs of the pelvis (anterior-posterior view) were performed at baseline, after 1 and 2 years, and thereafter every second year.
SI joints, both on MRI and on radiograph, were independently scored by two trained readers (MdH and RvdB). MRI-SIs were scored on the presence of bone marrow edema (BME) according to the ASAS/OMERACT definition [26], according to the Spondyloarthritis Research Consortium of Canada (SPARCC) score [27] and on the presence of capsulitis/enthesitis. All radiographs of the SI joints (X-SIs) were scored according to the modified mNY criteria [2]. In case the first two readers disagreed on an image [MRI (ASAS/OMERACT definition) or radiograph], a third trained reader (VN) served as adjudicator. If two of three readers scored positive, the image was marked positive. Moreover, all positive X-SIs were checked by a senior rheumatologist (DvdH) who gave a final judgement about the X-SI. All readers were blinded for clinical and laboratory data as well as the results of the other imaging modality.

Diagnosing the patients

A rheumatologist experienced in the field of SpA diagnosed all patients as predominantly axSpA, both axSpA and peripheral SpA, or no SpA based on all collected information, including imaging and HLA-B27 status. For this analysis, patients with only axSpA were used. In the case of no SpA, the rheumatologists filled out another suitable diagnosis. Furthermore, the rheumatologist marked the level of confidence about the diagnosis, either SpA or no SpA, on an 11-point NRS from 0 (not confident at all) to 10 (very confident).

Classification of patients

All patients were classified according to the Amor, ESSG, mNY and ASAS axSpA criteria [2, 4-6]. In addition, both the ESSG and AMOR criteria were modified by judging active sacroiliitis on MRI similarly to radiographic sacroiliitis.

Data analysis

For the present analysis, only data of the baseline visit were used. First, it was investigated how many patients fulfilled at least one of the classification criteria sets for SpA, shown in Venn diagrams.
Next, the number of patients diagnosed as axSpA according to the rheumatologist was described. The diagnosis of the rheumatologist served as external standard to test the performance of the various classification criteria. The performance was determined by calculating sensitivity, specificity, positive likelihood ratio (LR+) and negative likelihood ratio (LR-). For further analyses, the ASAS axSpA criteria set was selected to differentiate between SpA and no SpA patients. Characteristics of the patients were described using t-tests and χ^2-tests. In a following step, the ASAS axSpA criteria were studied in more detail. Patients fulfilling the clinical arm and patients fulfilling the imaging arm were compared on demographics, the presence of SpA-features and level of disease activity. Furthermore, within the imaging arm, patients with sacroiliitis on radiograph were compared with patients with sacroiliitis on MRI only, also by t-tests and χ^2-tests.
Missing values for the presence of SpA-features were interpreted as being absent. All analyses were performed using SPSS version 17. P-values <0.05 were considered significant.

Results

Performance of classification criteria

In total, 157 patients were included in the SPACE-cohort. The mean age at inclusion was 31.2 (SD 12.6) years, the mean symptom duration was 13.5 (SD 7.2) months and 33.1% were male. Of the 157 patients, 92 (58.6%) fulfilled any classification criteria set at baseline. Sixty (38.2%) patients fulfilled the ASAS axSpA criteria; this percentage has been similar over the years the SPACE-cohort has been running (40.4% in 2009, 36.2% in 2010, 38.9% in 2011 and 34.1% in 2012). Thirty-nine of these 60 patients fulfilled at least one other criteria set as well. Sixty-eight (43.3%) patients fulfilled the ESSG criteria; 53/68 fulfilled at least one other criteria set as well. Forty-eight (30.6%) patients fulfilled the Amor criteria; the majority of the patients (45/48) also fulfilled another criteria set. Eleven (7.0%) patients fulfilled the mNY criteria; all fulfilled at least one other classification criteria as well. Nine patients fulfilled all four criteria sets, 15 patients fulfilled three criteria sets (14 the combination of ASAS axSpA, ESSG and Amor and 1 the combination of ASAS axSpA, Amor and mNY) and 38 patients fulfilled two criteria sets (16 both ASAS axSpA and ESSG, 7 both ASAS axSpA and Amor, 14 both ESSG and Amor and 1 both ASAS axSpA and mNY) (figure 1).

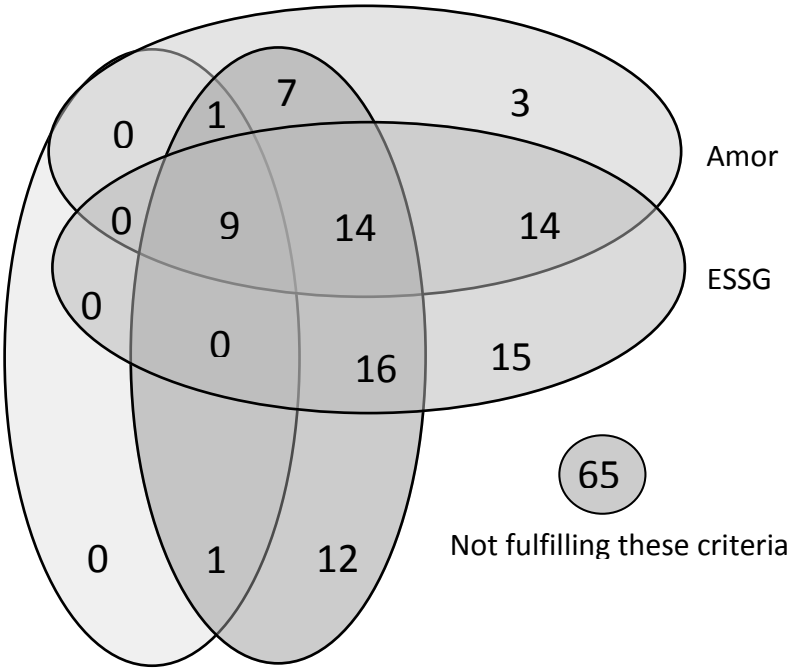

Figure 1: Venn-diagram representing the overlap between the various classification criteria for axial SpA.

To calculate the performance of the various classification criteria, the diagnosis of the rheumatologist was used as external standard. The rheumatologist diagnosed 65 patients (41.4%) as axSpA and 92 patients as no SpA. The mean level of confidence about the diagnosis is similar for patients fulfilling the ESSG, Amor and ASAS axSpA criteria (6.2-6.7 out of 10), but higher for patients fulfilling the mNY criteria (7.8 out of 10) (table 1). The mNY criteria showed the lowest sensitivity (16.9%) but highest specificity (100%). The Amor criteria

showed a sensitivity of 47.7%, which increased to 67.7% in the modified version, without a decrease in specificity (71.7%). The ESSG criteria showed a sensitivity of 64.6%, which increased to 75.4% in the modified version without a decrease in specificity (81.5%). The ASAS axSpA criteria outperformed all other classification criteria, including the modified Amor and modified ESSG criteria, in terms of sensitivity (84.6%), specificity (94.6%), LR+ (15.6) and LR- (0.16) (table 1). For all further analyses we used the ASAS axSpA criteria for the definition if a patient fits into the category axSpA or no SpA. This criterion is exactly defined and reproducible for readers, while the diagnosis by the rheumatologist is not.

Table 1: Performance of the various classification criteria for axial spondyloarthritis with the diagnosis and the level of confidence about the diagnosis of axSpA of rheumatologist as external standard for axSpA versus no SpA.

axSpA patients versus no axSpA patients	axSpA patients (n=65), N positive (sensitivity)	no axSpA patients (n=92), N negative (specificity)	LR+	LR
ASAS axSpA	55 (84.6)	87 (94.6)	15.6	0.16
mNY	11 (16.9)	92 (100)	15.6	0.99
ESSG	42 (64.6)	66 (71.7)	2.3	0.49
Amor	31 (47.7)	75 (81.5)	2.6	0.64
Modified ESSG (with MRI)	49 (75.4)	66 (71.7)	2.7	0.34
Modified Amor (with MRI)	44 (67.7)	75 (81.5)	3.7	0.40

ESSG, European Spondylarthropathy Study Group; ASAS, Assessment of SpondyloArthritis international Society (ASAS); mNY, modified New York; LR+, positive likelihood ratio; LR-, negative likelihood ratio. Level of confidence about the diagnosis SpA on an 11-point NRS from 0 (not confident at all) to 10 (very confident).

Patient characteristics

The majority of the patients referred to the SPACE-cohort were from the Leiden area; over the years, 17.0%, 7.3%, 10.2% and 17.7% of the referrals in 2009, 2010, 2011 and 2012, respectively, were from outside the Leiden area.

Thirty-three patients were not included for follow-up because of the lack of specific SpA-features; 13 patients did not have any SpA-features and the remaining 20 patients had only one less specific SpA feature (1 patient with peripheral arthritis only, 1 patient with heel enthesitis only, 6 patients with a good response to NSAIDs only, 12 patients with IBP only). Of the patients included for follow-up, 64 had possible SpA and the remaining 60 patients fulfilled the ASAS axSpA criteria.

Patients classified as axSpA according to the ASAS axSpA criteria were compared with the group of noaxSpA patients including possible SpA patients and patients excluded for follow-up, revealing some statistically significant differences. AxSpA patients are more frequently male (p=0.001), more often have a positive family history for SpA (p=0.001), IBP (p=0.001), a good response to NSAIDs (p=0.004) and sacroiliitis on radiograph (p<0.001) and MRI (p<0.001), and are more often HLA-B27 positive (p<0.001) compared with no axSpA patients. Furthermore, there was a trend that axSpA patients more often have uveitis (p=0.07) and higher levels of ESR (p=0.08) (table 2).

Table 2: Baseline characteristics of axSpA patients versus no axSpA patients, according to the ASAS axSpA criteria.

	axSpA patients, n=60	no axSpA patients, n=97	P-values axSpA versus no axSpA patients
Age (years) at inclusion, mean ± SD	29.5 ± 8.7	32.3 ± 14.4	0.17
Male, n (%)	29 (48.3)	23 (23.7)	0.001
Duration of back pain (months), mean ± SD	13.4 ± 7.7	13.6 ± 6.9	0.88
HLA-B27 positive, n (%)	47 (79.7)	6 (6.2)	<0.001
Pos. Fam. History SpA, n (%)	31 (51.7)	25 (25.8)	0.001
IBP, n (%)	50 (83.3)	55 (56.7)	0.001
Psoriasis, n (%)	8 (13.3)	8 (8.2)	0.31
Dactylitis, n (%)	3 (5.0)	3 (3.1)	0.55
Enthesitis, n (%)	8 (13.3)	17 (17.5)	0.49
Uveitis, n (%)	9 (15.0)	6 (6.2)	0.07
IBD, n(%)	3 (5.0)	6 (6.2)	0.76
Preceding infection, n (%)	1 (1.7)	1 (1.0)	0.73
CRP (mg/l), mean ± SD	8.4 ± 11.9	5.8 ± 6.9	0.12
ESR (mm/h), mean ± SD	14.4 ± 16.7	10.1 ± 10.6	0.08
Alternating buttock pain, n (%)	16 (26.7)	17 (17.5)	0.17
Good response to NSAIDs, n (%)	29 (48.3)	25 (25.8)	0.004
Elevated CRP/ESR, n (%)	16 (26.7)	15 (15.5)	0.09
Asymmetric lower limb arthritis, n (%)	8 (13.3)	15 (15.5)	0.71
Sacroiliitis radiograph, n (%)	11 (18.3)	1 (1.1)	<0.001
Sacroiliitis MRI, n (%)	25 (41.7)	2 (2.1)	<0.001

IBP, Inflammatory Back Pain; IBD, Inflammatory Bowel Disease; age, age at baseline; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HLA-B27, Human Leukocyte Antigen; preceding infection can be balinitis, urethritis, cervicitis and/or acute diarrhea.

ASAS imaging arm versus clinical arm

The comparison of patients fulfilling the imaging arm with patients fulfilling the clinical arm revealed that patients in the imaging arm are more often male (p=0.02), have a longer symptom duration (p=0.04) and less often have a positive family history for SpA (p=0.001) than patients fulfilling the clinical arm. However, patients fulfilling the clinical arm reflect a group of patients similar to those fulfilling the imaging arm with respect to the presence of other SpA-features and level of disease activity (table 3). Nevertheless, the mean level of confidence about the diagnosis axSpA in patients fulfilling the clinical arm of the ASAS axSpA criteria (4.9 ± 1.5) is lower in comparison to the level of confidence about the diagnosis in patients fulfilling the imaging arm (7.7 ± 0.8). Within the imaging arm, patients with and without sacroiliitis on radiographs were compared. Remarkably, there was no difference in symptom duration (table 3).

Table 3: Characteristics of patients in the clinical arm compared to patients in the imaging arm of the ASAS axSpA criteria.

	Imaging arm, n=30			Clinical-arm, n=30	P-value imaging arm vs clinical arm
	mNY+, n=11	mNY-, n=19	Total, n=30		
Age (years) at inclusion, mean ± SD	28.6 ± 9.6	32.9 ± 8.7	31.2 ± 9.0	28.2 ± 8.4	0.14
Male, n (%)	8 (72.7)	11 (57.9)	19 (63.3)	10 (33.3)	0.02
Duration of back pain (months), mean ± SD	15.6 ± 8.5	16.0 ± 6.9	15.5 ± 7.6	11.4 ± 7.3	0.04
HLA-B27 positive, n (%)	6 (54.5)	11 (61.1)	17 (58.6)	30 (100)	<0.001
Pos. Fam. History SpA, n (%)	4 (36.4)	5 (26.3)	9 (30.0)	22 (73.3)	0.001
IBP, n (%)	9 (81.8)	14 (73.7)	23 (76.7)	27 (90.0)	0.17
Psoriasis, n (%)	2 (18.2)	2 (10.5)	4 (13.3)	4 (13.3)	1
Dactylitis, n (%)	0 (0.0)	2 (10.5)	2 (6.7)	1 (3.3)	0.55
Enthesitis, n (%)	2 (18.2)	2 (10.5)	4 (13.3)	4 (13.3)	1
Uveitis, n (%)	1 (9.1)	1 (5.3)	2 (6.7)	7 (23.3)	0.07
IBD, n(%)	2 (18.2)	1 (5.3)	3 (10.0)	0 (0.0)	0.08
Preceding infection, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)	0.31
CRP (mg/l), mean ± SD	6.9 ± 7.2	7.6 ± 8.6	7.3 ± 8.0	15.6 ± 18.9	0.58
ESR (mm/h), mean ± SD	11.4 ± 13.9	14.2 ± 14.8	13.2 ± 14.3	9.4 ± 14.9	0.50
Alternating buttock pain, n (%)	6 (54.5)	5 (26.3)	11 (36.7)	5 (16.7)	0.08
Good response to NSAIDs, n (%)	6 (54.5)	10 (52.6)	16 (53.3)	13 (43.3)	0.44
Elevated CRP/ESR, n (%)	4 (36.4)	5 (26.3)	9 (30.0)	7 (23.3)	0.56
Asymmetric lower limb arthritis, n (%)	0 (0.0)	4 (21.1)	4 (13.3)	4 (13.3)	1
Sacroiliitis radiograph, n (%)	11 (100)	-	11 (36.7)	-	-
Sacroiliitis MRI, n (%)	6 (54.5)[†]	19 (100)[†]	25 (86.2)	-	-
BASDAI	3.7 ± 1.8	4.0 ±2.5	3.9 ± 2.3	3.9 ± 1.9	0.97
ASDAS	2.4 ± 0.7	2.5 ± 0.9	2.4 ± 0.8	2.4 ± 0.9	0.94
BASFI	3.3 ± 1.9	2.4 ± 2.2	2.7 ± 2.1	2.3 ± 2.2	0.50
BASMI	1.9 ± 0.7	1.6 ± 0.5	1.7 ± 0.6	1.6 ± 0.8	0.51
NSAID use, n (%)	9 (81.8)	15 (78.9)	24 (80.0)	22 (73.3)	0.54
DMARD use, n (%)	1 (9.1)	1 (5.3)	2 (6.7)	1 (3.3)	0.55
Biological use, n (%)	0 (0.0)	1 (5.3)	1 (3.3)	0 (0.0)	0.31
Confidence diagnosis axSpA, mean ± SD	7.8 ± 1.1	7.5 ± 0.6	7.7 ± 0.8	4.9 ± 1.5	<0.001

† Statistically significant difference between patients fulfilling the modified New York criteria and patients not fulfilling the modified New York criteria within the total imaging arm. IBP, Inflammatory Back Pain; IBD, Inflammatory Bowel Disease; age, age at baseline; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HLA-B27, Human Leukocyte Antigen; preceding infection can be balinitis, urethritis, cervicitis and/or acute diarrhea; mNY, modified New York criteria; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; ASDAS, Ankylosing Spondylitis Disease Activity Score; NSAID, Non-Steroidal Anti-Inflammatory Drug; DMARD, Disease Modifying AntiRheumatic Drug. Level of confidence about the diagnosis SpA on an 11-point NRS from 0 (not confident at all) to 10 (very confident).

Discussion

The SPACE-cohort consists of patients with chronic back pain (≥3 months, but ≤2 years, onset <45 years). The only available numbers about the prevalence of chronic back pain (≥3 months duration) in the Netherlands stem from the mid-90s and show a prevalence of 20.8% [28]. The majority of these patients (90%) have non-specific back pain [29]. Hence Dutch rheumatologists in general, and likewise rheumatologists in our department, feared that outpatient clinics would be overloaded by patients with non-specific back pain by using the above-described criteria as the sole referral symptom, although we showed that this fear is unfounded in at least the setting of a tertiary hospital, since ~60% of the patients in the SPACE-cohort fulfill one or more axSpA classification criteria at baseline and 41.4% of patients are directly diagnosed as SpA by the rheumatologist. Moreover, in the light of these results, the value of the numbers about prevalence of chronic back pain from the mid-90s is questionable, thereby indicating that more up-to-date numbers are needed. Furthermore, this percentage of SpA is similar to the percentage of 41.8% found by a muticenter study using a referral strategy consisting of the presence of either IBP or HLA-B27 or sacroiliitis on imaging (MRI and/or radiograph) [11] and the 35.1% found in a study using IBP or a good response to NSAIDs as referral symptom [12]. Although the test result for the presence of HLA-B27 is not difficult to interpret, it is challenging for referring physicians to interpret back pain as inflammatory or not and to detect sacroiliitis, as demonstrated by the low agreement between general practitioners and rheumatologists [11].

It could be argued that our observed prevalence of axSpA is influenced by referral bias; e.g. that due to increased awareness among referring physicians about the SPACE-cohort over time, patients from areas other than the Leiden area are referred to the LUMC or that only patients with a high suspicion of axSpA are referred. However, the percentage of axSpA among all referred patients over the years was similar, and the percentage of referrals from outside the Leiden area was also similar over time. Moreover, 33 of the 157 patients (21.0%) included at baseline had none or only one less specific SpA feature. This indicates, but does not prove, that there is no referral bias, thereby suggesting that the observed prevalence of axSpA could be generalized to primary care. In addition, other studies should investigate the prevalence of SpA among patients with chronic back pain >2 years previously not recognized as SpA.

Around 80% of the axSpA patients in the SPACE-cohort have IBP, thereby confirming that IBP is not present in all SpA patients [13]. Moreover, IBP is frequently (56.7%) present in no SpA patients in the SPACE-cohort, which is consistent with the 45.1% found in another study [11]. These results show that IBP is not a strong discriminating feature and that if IBP was used as an inclusion criterion instead of chronic back pain, 20% of the SpA patients would have been missed.

Depending on the presence and type of SpA-features, patients fulfill various classification criteria. The performance of the Amor, ESSG and ASAS axSpA criteria was better than the mNY criteria at the time of presentation of patients to rheumatologists. This can be explained by the fact that it takes several years before patients develop radiographic sacroiliitis [30].

Moreover, the ASAS axSpA criteria outperformed the Amor and ESSG criteria, even after adding active sacroiliitis (MRI) to the list of SpA-features. These results are in contrast with the results found in a more established cohort [the Cochin Spondyloarthritis (COSPA) cohort] where the ASAS axSpA criteria (fulfilled by 90% of the patients) did not have additional value in comparison to the Amor (fulfilled by 96% of the patients) and ESSG criteria (fulfilled by 83% of the patients) [31]. A possible explanation for these contrasting results is that the longer the symptom duration, the more chance that (extra-articular) features develop. To fulfill the Amor criteria, a patient needs to have at least 6 points representing three to four items. This is quite difficult to reach, especially for patients early in the disease, as in the SPACE-cohort, reflected by the fact that only 31% of these patients fulfilled the Amor criteria. Patients in the COSPA cohort, however, had a mean symptom duration of 16 years (range 8-27 years) and therefore fulfill the Amor criteria more easily.

To fulfill the ESSG criteria, a patient needs to have either IBP or synovitis (asymmetric or predominantly in the lower limbs) and at least one additional feature. The focus of the SPACE-cohort is towards axSpA and not peripheral SpA, and therefore the number of patients with peripheral complaints (synovitis) is low. Furthermore, IBP is only present in about 80% of the axSpA patients in the SPACE-cohort. Therefore it is not possible for some patients to fulfill the ESSG criteria.

It could be argued that the good performance of the ASAS axSpA criteria might be biased by the fact that patients are diagnosed by only one rheumatologist accustomed to work with the ASAS axSpA. However, this bias is unlikely when looking at the level of confidence about the diagnosis, which is similar for patients fulfilling the ESSG, Amor and ASAS axSpA criteria, and when looking at the small numbers of misclassifications by the ASAS axSpA criteria compared with the diagnoses yielded by the modified Berlin algorithm, which is a diagnostic tool [32]. The ASAS axSpA criteria yield 3.8-6.1% of wrongly diagnosed patients as SpA and 7.6-10.2% of missed diagnoses compared with the modified Berlin algorithm. It might even support the rationale to use the ASAS axSpA criteria as diagnostic criteria in this type of setting with referrals to rheumatologists based on chronic back pain starting before the age of 45.

Within the ASAS axSpA criteria, it was questioned whether patients fulfilling the clinical arm of the ASAS axSpA criteria reflect the same disease as patients fulfilling the imaging arm. We found that patients in the SPACE-cohort fulfilling the clinical arm were remarkably similar to patients fulfilling the imaging arm with respect to the presence of most SpA-features and level of disease activity. Another study (ABILITY I trial) found the same results [33]. However, the difference in level of confidence about the diagnosis indicates that the judgement by the rheumatologist is heavily weighted by positive imaging. Furthermore, within the imaging arm of the ASAS axSpA criteria, patients with sacroiliitis on radiographs have the same level of disease activity and symptom duration as patients with sacroiliitis on MRI only.

In conclusion, the inclusion criteria used for the SPACE-cohort, almost daily chronic back pain of short duration (≤2 years) starting before the age of 45 years (in accordance with the entry criteria for the ASAS axSpA criteria), yield the same high number of patients with SpA compared with other referral strategies such as IBP, HLA-B27+ or sacroiliitis, yet are easier to apply. Furthermore, the ASAS axSpA criteria outperformed the other classification criteria; almost 40% fulfilled the ASAS axSpA criteria. Patients fulfilling the clinical arm of the ASAS axSpA reflect a group of patients similar to those fulfilling the imaging arm.

Supplementary data

Supplementary data are available at Rheumatology Online.

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