Fibromyalgia in patients with ankylosing spondylitis: prevalence and utility of the measures of activity, function and radiological damage

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ABSTRACT

Objectives. *To determine the prevalence of fibromyalgia (FM) in ankylosing spondylitis (AS). To evaluate the effect of FM on the measures of activity in AS. To analyse predictive factors in order to identify this group of patients.*

Patients and methods. *A cross-sectional study based on 462 patients with definite ankylosing spondylitis included in the REGISPONSER. Sociodemographic data, clinical features, Bath AS disease activity index (BASDAI), Bath AS functional index (BASFI), Bath AS radiology index (BASRI), Stoke modified index (Sasss-m), laboratory data, Short-Format 12 (SF-12), AS specific quality of life (ASQoL), Fibromyalgia Impact Questionnaire (FIQ) and treatments used were all documented. To diagnose FM, the ACR 1990 criteria had to be fulfilled. All statistical tests were performed using STATA.*

Results. *The prevalence of fibromyalgia in all AS was 4.11%. Among the women with AS, the prevalence of FM increased to 10.83%. The BASDAI, BASFI and total BASRI were strongly influenced by the presence of FM. The inverse relationship between BASDAI or BASFI and total BASRI was taken to generate a ratio. Accordingly, if the patient presented BASDAI/BASRI ≥1.5 or BASFI/BASRI ≥1.08, the probability of having FM was very high.*

Conclusion. *There is an increased risk of FM in females with AS. The fact of having FM distorts the measures of activity and functional damage of AS. As a result, it is possible that some patients with AS and FM are being overtreated. The BASDAI/BASRI and BASFI/BASRI ratios are very useful to identify these patients.*

Introduction

Ankylosing spondylitis (AS) is a chronic rheumatic inflammatory disease of unknown etiology and likely autoimmune pathogenesis (1). It predominantly affects the axial skeleton, pelvis, spine and chest, with a male-to-female ratio of 3–4 to 1. Involvement of the sacroiliac joints is a constant feature, and enthesopathy, arthritis and peripheral extraarticular disease can occur at any time during the development of AS (2).

Fibromyalgia (FM) is a syndrome of unknown etiology characterised by chronic widespread pain, fatigue, sleep disturbances and painful palpation at certain specific areas of the musculoskeletal system. It is prevalent in the general population that varies between 2–4%. Patient age at onset varies from 30–50 years, and the disorder is predominantly observed among females (80–90% of all cases). FM is classified among the muscle and soft tissue conditions without being able to demonstrate inflammation or tissue injury at any level (3). It is important to establish the differential diagnosis of FM with other rheumatic diseases or neurological or endocrine symptoms with which they share the symptoms of widespread pain or of fatigue. In some cases, FM can be associated with rheumatic inflammatory processes or systemic diseases such as rheumatoid arthritis, systemic lupus erythematosus or Sjögren's syndrome, which complicate interpretation of the origin of the symptoms (4, 5).

Patients with FM experience continuous pain and a higher level of fatigue and intensity of pain than patients with rheumatoid arthritis or AS (6). In addition, health status is worse in patients with FM than in patients with AS (7). Through PET (Problem Elicitation

Technique) questionnaires, it has also been possible to identify more problems in patients with FM than in patients with AS (8).

BASDAI is the main index used to assess activity in AS. BASDAI is based on the subjective assessment of fatigue, stiffness and pain – all symptoms that are also present in FM. This is why in patients in whom AS and FM coexist, it is so difficult to determine the degree of activity and functional capacity associated with each disease separately, and why many doubts arise at the time of diagnosis, the assessment of disease activity, the selection of patients for trials, and ascertaining response to treatment – this being especially relevant in the use of biological therapies.

To help the physician make decisions in patients with the two coexisting conditions, our group decided to undertake a study of the prevalence of FM in patients diagnosed with AS. Additionally, we aimed to analyse the factors that best characterise these patients, to assess to what extent FM affects the measures of disease in AS, and to search for parameters that are useful in identifying patients with both disorders.

Patients and methods

Design and patient selection

This is a cross-sectional study of 462 patients classified as having AS according to the modified New York Criteria AS (9). Patients were selected at random from the initial 10 centres participating in the Spanish Society of Rheumatology National Registry of Spondyloarthropathies (REGISPONSER). The design, sampling and recruitment of patients in the registry have all been previously published (10, 11). Patients entering REGISPONSER were all consecutive patients attending the participating rheumatology clinics and who fulfilled the European Spondyloarthropathies Criteria (ESSG) during the recruitment period. All patients gave informed consent to participate in the study, which was approved centrally by the Ethics Committee of Reina Sofia Hospital (Córdoba, Spain).

Case definition and measurements

At each centre, all patients were evaluated by the same rheumatologist who had been previously trained in a standardisation session. FM has been defined according to the 1990 American College of Rheumatology (ACR) classification criteria (3).

Data collection forms were designed to retrieve information on sociodemographic variables, employment-related variables, habits, exercise, family history, duration of AS, clinical form of AS and on extra-articular disease manifestations.

For the evaluation of disease status, the following anthropometrical measures were included: occipital-to-wall distance (OWD), modified Schöber test, lateral flexion of lumbar spine (LLF), thoracic expansion (TE), lateral cervical rotation (CR), and finger-to-floor distance (FFD) (10). Additionally, the following measures were included: night pain scored by a 0 (no pain) to 10 (maximum pain) Visual Analogue Scale (VAS); physician and patient global assessment of disease activity, also scored by a 0 (very well) to 10 (very bad) VAS; number of swollen peripheral joints; number of tender enthesis rated by the Maastricht Ankylosing Spondylitis Enthesis Score (MASES) (12), the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) from 0 (no activity) to 10 (maximum activity) (13), and functional capacity as scored by the Bath Ankylosing Spondylitis Functional Index (BASFI) (14) from 0 (no disability) to 10 (maximum disability).

Damage was accrued by two radiological indexes: the Bath Ankylosing Spondylitis Radiology Index (BASRI) (15), both for spine and total (BASRI spine+BASRI hips), and the modified Stoke AS Spine Score (mSASSS) (16).

Quality of life was evaluated by two questionnaires: the specific questionnaire of quality of life in spondyloarthritis (ASQoL) (17), in which lower values indicate a better quality of life, and by the generic SF-12 (18), in which higher values indicate a better quality of life. Additionally, patients in which FM criteria were present completed the Fibromyalgia Impact Questionnaire (FIQ) (19), which consists of 11 questions on physical functioning (physical impairment score) and 7 VAS for evaluating ability to work, diffuse pain, anxiety, depression, fatigue, tiredness on awakening, and stiffness (19), with higher values indicating a poorer quality of life.

Laboratory tests included erythrocyte sedimentation rate (ESR: normal 0–20mm/h), C-reactive protein (CRP: normal 0–5 mg/l), and human leukocyte antigen (HLA B27) status.

Current treatment, including nonsteroidal anti-inflammatory drugs (NSAIDs), corticoids, disease-modifying antirheumatic drugs (DMARDs), and biological therapies was also recorded. The effectiveness of NSAIDs in relieving pain was defined as reduction of pain within 48 hours after introducing them, or as rapid worsening within 48 hours after discontinuing the medication.

Statistical analysis

The prevalence of FM in AS with the corresponding 95% confidence interval (95%CI) was estimated. We studied the correlation of sociodemographic, clinical and quality of life-related variables to the presence of FM criteria by using the statistical tests suited to the distribution of the variables. We tested the correlation of sociodemographic and clinical factors to the presence of FM by means of the appropriate statistical test, depending on the distribution of the variable (parametric or nonparametric). In the case of binomial variables we also obtained odds ratios (ORs) and 95%CI from contingency tables. We likewise analysed the effect of FM on the measures of disease through linear regression models. In such models the dependent variable varied: modified Schöber test, FFD, TE, OWD, LLF, CR, VAS evaluation by the physician, BASDAI, BASFI, BASRI-spine, total BASRI, m-SASSS, ESR and CRP. From the models we estimated the beta-coefficient of the factor "presence of FM" and its 95%CI for each of the measures. Multiple regression models were also constructed to analyse the existence of factors that may interfere in the relationship between FM and the measures of AS. Additionally, we aimed to analyse the discriminative value of significantly associated measures or combinations of meas-

ures to identify patients with AS and FM through Receiver Operating Curve (ROC) analyses. Areas under the curve were obtained for the complete ROC analyses and for specific cutoff values. All analyses were performed with the statistical software Stata 10.0 (StataCorp LP, College Station, TX, USA).

Results

We studied 462 patients with AS, of which 342 (75%) were males and 120 (26%) females, with a mean age (±SD) of 50±12. Nineteen patients met criteria for FM, which corresponds to an estimated prevalence of FM in AS of 4.1% (95%CI: 2.3–5.9). Among the women with AS, the prevalence of FM increased to 10.8% (95%CI: 5.2–16.5), versus only 1.8% in males (95%CI: 0.4–3.15). The sociodemographic and clinical characteristics, including the mean scores in measures of the disease, of the patients with AS fulfilling or not fulfilling the criteria for FM, are presented in Tables I and II. Besides being more frequently women (OR_{women} 6.8 (95%CI: 2.5–18.3)), patients with FM scored significantly higher in the BASDAI, BASFI and ASQoL, and had greater FFD–though curiously patients with FM did not have arthritis in their lower limbs, and the total BASRI index and m-SASSS cervical score were significantly lower, in the same way as the serum CRP levels. Patients with FM had a lesser response to NSAIDs compared to patients without FM.

Focusing on women only, the presence of FM was associated with the same variables as in men. Additionally, women with FM criteria showed significantly shorter OWD than women without FM (0cm *vs*. 1.5±3.4 cm; $p<0.01$). Interestingly, the number of sacroiliac MRI scans performed in females with FM was significantly larger than among women without FM (30% *vs*. 0%; $p<0.0001$).

Various multiple linear regression models were constructed to see the effect of FM on measures of spondylitic disease (Table III). We noticed that meeting criteria for FM was associated with a significant increase in the BASDAI and BASFI scores, and a likewise statistically significant decrease in the total BASRI score. All this led us to propose two parameters that would allow us to discriminate between patients with and without FM in the context of AS. Such parameters were the ratios BASDAI / total BASRI and BASFI / total

Table I. Sociodemographic and clinical characteristics of AS patients with and without FM.

	AS (n=443)	AS+FM (n=19)	*p*-value
Females, n (%)	107 (24)	13 (68)	<0.001*
Age (years), m ± SD	51 ± 13	48 ± 7	NS
Age at initial symptoms (years), m ± SD	28 ± 12	27 ± 8	NS
Disease duration (years), m ± SD	22 ± 13	21 ± 10	NS
Diagnosis delay (years), m ± SD	7 ± 9	8 ± 7	NS
Work disability (yes/no), n (%)	133 (37)	3 (16)	NS
Family history of AS, n (%)	89 (20)	2 (11)	NS
Exercise practice (yes/no), n (%)	161 (38)	12 (63)	NS
Enthesitis (yes/no), n (%)	21 (5)	1 (5)	NS
Peripheral arthritis arms, n (%)			
Upper limbs	34 (8)	–	NS
Lower limbs	77 (17)	–	0.03*
Psoriasis, n (%)	50 (13)	1 (5)	NS
Inflammatory bowel disease, n (%)	18 (5)	1 (6)	NS
Uveitis, n (%)	89 (22)	2 (11)	NS

AS: ankylosing spondylitis; FM: fibromyalgia; m±SD: mean ± standard deviation.
*$p<0.05$. NS: not significant.

Table II. Measures of disease in AS, according to the presence of FM criteria.

Measures	AS (n=443)	AS+FM (n=19)	*p*-value
VAS of night pain (cm)	3.5 ± 2.7	6 ± 3	<0.001*
VAS patient's global assessment (cm)	4.2 ± 2.6	6.4 ± 2.4	<0.001*
VAS physician's global assessment (cm)	2.7 ± 1.9	4.2 ± 2.9	NS
BASDAI (cm)	3.7 ± 2.2	6.5 ± 2.2	<0.001*
BASDAI > 4 (n)%	168 (44)	16 (84)	0.001*
BASFI (cm)	3.9 ± 2.7	6.4 ± 2.4	<0.001*
BASFI > 4 (n)%	175 (46)	15 (79)	0.004*
BASRI spine	7.2 ± 3.6	5.3 ± 2.7	0.05*
BASRI total	8.2 ± 4.6	5.6 ± 3.3	0.02*
Sasss-m cervical	8.8 ± 10.3	2.9 ± 4.8	0.02*
Sasss-m lumbar	6.3 ± 9.8	1.9 ± 3.9	NS
Chest expansion (cm)	4 ± 2	3.6 ± 1.5	NS
Modified Schöber (cm)	3.2 ± 2	2.9 ± 1.2	NS
Occipital-wall distance (cm)	4.6 ± 6.2	2.7 ± 6.5	NS
Finger-floor distance (cm)	19.4 ± 14.4	27.2 ± 14.8	0.02*
Lumbar lateral flexion (cm)	20 ± 18	21 ± 19	NS
Erythrocyte sedimentation rate (mm/h)	15.2 ± 13.6	15 ± 9.8	NS
C-Reactive protein (mg/dl)	8.8 ± 16	3.3 ± 3.4	<0.001*
HLA B27, n (%)	298 (85)	15 (79)	NS
ASQoL	6.4 ± 4.8	12.7 ± 4.6	<0.001*
SF-12 physical component	34.2 ± 12.4	33.3 ± 5.1	NS
SF-12 mental component	46.7 ± 14.8	48.2 ± 4.9	NS
FIQ	32.7 ± 22	65.6 ± 23.4	<0.001*
Sacroiliac joint, MRI (n)%	11 (2)	2 (10)	NS
NSAIDs, n (%)	282 (73)	14 (74)	NS
Methotrexate, n (%)	13.4 (73)	–	NS
Salazopyrin, n (%)	34 (9)	2 (11)	NS
Infliximab, n (%)	49 (13)	2 (11)	NS
Etanercept, n (%)	37 (10)	2 (11)	NS
Adalimumab, n (%)	13 (93)	1 (7)	NS
Response to NSAIDs, n (%)	313 (96)	14 (4)	0.01*

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); Bath Ankylosing Spondylitis Functional Index (BASFI); Bath Ankylosing Spondylitis Radiology Index (BASRI). ASQoL: specific questionnaire of quality of life in spondyloarthritis; SF-12: 12-Item Short-Form Health Survey. FIQ: Fibromyalgia Impact Questionnaire.
*$p<0.05$. NS: not significant.

Table III. Multiple linear regression analyses to see the effect of FM on measures of AS, adjusted for age and gender.

Variables FM	t	Beta-coefficient	95%CI	*p*-value
VAS physician's global assessment (cm)	2.83	1.4	(0.4 – 2.3)	0.005*
BASDAI	4.89	2.5	(1.4 – 3.6)	0.0001*
BASFI	4.47	2.7	(1.5 – 4)	0.0001*
BASRI spine	-0.82	-7.1	(-2.4 – 0.9)	NS
BASRI total	-1.01	-1.1	(-3.3 – 1)	0.0001*
Sasss-m cervical	-0.48	-1.3	(-7 – 4.2)	NS
Sasss-m lumbar	-0.4	-1.15	(-6.8 – 4.5)	NS
Chest expansion (cm)	-1.25	-0.58	(-1.5 – 0.3)	NS
Modified Schöber (cm)	-1.96	-0.8	(-1.7 – 0.002)	NS
Occipital-wall distance (cm)	0.28	0.37	(-2.2 – 2.9)	NS
Finger-floor distance (cm)	3.47	11.4	(4.9 – 17.8)	0.001*
Lumbar lateral flexion (cm)	0.07	0.32	(-8.2 – 8.8)	NS
Cervical rotation	-0.42	-0.26	(-1.4 – 0.95)	NS
Erythrocyte sedimentation rate (mm/h)	-0.5	-1.6	(-7.8 – 4.6)	NS
C-Reactive protein (mg/dl)	-1.38	-5.2	(-12.7 – 2.2)	NS
FIQ	5.01	32.9	(19.9 – 45.8)	0.0001*

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); Bath Ankylosing Spondylitis Functional Index (BASFI); Bath Ankylosing Spondylitis Radiology Index (BASRI). Modified Stoke AS Spine Score (mSASSS). FIQ: Fibromyalgia Impact Questionnaire.
*$p<0.05$. NS: not significant.

Table IV. Receiver Operating Curve (ROC) analyses for the utility of the BASDAI / total BASRI and BASFI / total BASRI ratios in identifying FM in AS.

	AUC	Cut-off value	Sensitivity	Specificity	LR+	LR-
BASDAI / total BASRI ratio	0.8	(≥0 – 0.209)	100%	12.04%	1.13	0
		(≥0.21 – 0.34)	100%	31.02%	1.4	0
		(≥0.346 – 0.525)	93.75%	50.73%	1.9	0.1
		(>0.525 – 0.78)	87.5%	67.8%	2.7	0.1
		(≥0.8 –1.45)	75%	83.94%	4.6	0.2
		(≥1.5– >5)	12.5%	95.99%	3.1	0.9
BASFI / total BASRI ratio	0.86	(≥0 – 0.19)	100%	12.04%	1.13	0
		(≥0.2 – 0.33)	100%	29.2%	1.4	0
		(>0.33 – 0.51)	93.75%	43.07%	1.64	0.1
		(>0.51 – 0.68)	87.5%	59.49%	2.1	0.2
		(>0.68 – 1.04)	87.5%	77.37%	3.8	0.1
		(≥1.05 – >4.7)	50%	91.61%	5.7	0.5

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); Bath Ankylosing Spondylitis Functional Index (BASFI); Bath Ankylosing Spondylitis Radiology Index (BASRI), Area under the curve (AUC); Likelihood ratio (LR).

BASRI. Before analysing the discriminatory value of these ratios, we aimed to examine the effect of other factors on the association between FM and such ratios. To this effect, we generated multiple linear regression models with the ratios as dependent variables, and excluded variables other than the presence of FM, which was fixed in the models, in a stepwise fashion from the most saturated model. The only other factor that increased the association between the ratios BASDAI / total BASRI and FM (beta-coefficient 0.09; 95%CI (0.05 to 0.13); $p<0.001$) and BASFI / total BASRI and FM (beta-coefficient 0.07; 95%CI (0.04 to 0.11); $p<0.001$) was the physician's global impression of the disease.

Table IV shows the result of the ROC analyses of the utility of the proposed ratios BASDAI or BASFI / total BASRI in properly classifying patients with FM and AS. If a patient presents a BASDAI / total BASRI ratio greater than or equal to 1.5, the probability of having FM is high, with an area under the curve of 0.8, a positive likelihood ratio of 5.9, a sensitivity of 43.8% and a specificity of 92.7%. All patients with AS meeting FM criteria, and 7 patients without FM had a ratio equal to or greater then 1.5. On the other hand, a BASFI / total BASRI ratio greater than or equal to 1.4 also has a high discriminatory value in detecting the presence of FM, since the area under the curve was 0.86, the positive likelihood ratio 17.1, sensitivity 6.3% and specificity 99.6%.

Since the BASRI worsens with time from diagnosis, both ratios were analysed in different groups of patients according to the length of AS. The BASDAI / total BASRI ratio was very useful in those patients with a disease duration between 10–20 years, in whom a ratio equal to or greater than 1.5 yielded a likelihood ratio of 9.8. In the group of patients with a disease duration between 30–40 years a BASDAI / BASRI ratio equal to or greater than 2.3 showed a likelihood ratio of 21.5 (Table V). Regarding the BASFI / total BASRI ratio, it was seen to be very useful for those patients with a disease duration between 10–20 years who had a ratio equal to or greater than 1.5 with a likelihood ratio of 13.1, and also for those patients with a duration of AS between 20–30 years, where a ratio equal to or greater than 1.6 implied a likelihood ratio of having FM of 9.6. Finally, in the group of patients with a duration of AS of 30–40 years a BASFI / BASRI ratio equal to or greater than 2.2 yielded a likelihood ratio of 21.5 (Table VI).

The utility of having a poor response or no response to NSAIDs was also analysed by ROC curves to examine whether this parameter might help to properly classify patients with AS and FM, but the area under the curve was only 0.3 and thus was not regarded as a good parameter.

Finally, we assessed whether there was a correct use of anti-TNF-alpha therapies or overtreatment in patients with AS and FM. After analysing the percentage use of infliximab, etanercept and adalimumab in our sample, we found no statistically significant differences when comparing patients with AS who met criteria of FM compared to those who did not (Table II). Similar results were found when evaluating the use of biological therapies in terms of having or not having a BASDAI / total BASRI ratio greater or equal to 1.5 (in-

Table V. ROC analyses of the utility of the BASDAI / total BASRI ratio in identifying FM in AS, based on the duration of AS.

BASDAI/total BASRI ratio	AUC	Cut-off value	Sensitivity	Specificity	LR+	LR-
0–10 years	0.77	(≥0 – ≥0.6)	100%	32.69%	1.4	0
		(≥0.66 – >5)	50%	76.92%	2.1	0.6
>10–20 years	0.92	(≥0 – ≥0.56)	100%	27.12%	1.3	0
		(≥0.58 – >4.4)	100%	83.05%	5.9	0
>20–30 years	0.77	(≥0 – ≥0.42)	100%	29.87%	1.4	0
		(≥0.48 – >4.4)	75%	80.52%	3.8	0.3
>30–40 years	0.86	(≥0 – ≥0.43)	100%	27.91%	1.38	0
		(≥0.45 – >2.5)	75%	77.91%	3.3	0.3

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); Bath Ankylosing Spondylitis Radiology Index (BASRI); Area under the curve (AUC); Likelihood ratio (LH).

Table VI. ROC analyses of the utility of the BASFI / total BASRI ratio in identifying FM in AS, based on the duration of AS.

BASFI / total BASRI ratio	AUC	Cut-off value	Sensitivity	Specificity	LR+	LR-
0-10 years	0.86	(≥0 – ≥0.54)	100%	36.54%	1.5	0
		(>0.54 – >3.5)	100%	82.69%	5.7	0
>10-20 years	0.94	(≥0 – ≥0.55)	100%	35.59%	1.5	0
		(≥0.58 – >4.05)	83.3%	84.75%	5.4	0.1
>20-30 years	0.76	(≥0 – ≥0.52)	100%	28.57%	1.4	0
		(≥0.53 – >4.7)	75%	81.82%	4.1	0.3
>30-40 years	0.81	(≥0 – ≥0.58)	100%	26.74%	1.3	0
		(>0.58 – >3.05)	75%	80.23%	3.7	0.3

Bath Ankylosing Spondylitis Functional Index (BASFI); Bath Ankylosing Spondylitis Radiology Index (BASRI); Area under the curve (AUC); Likelihood ratio (LH).

fliximab: 8.3% *vs*. 17.03%; etanercept: 12.5% *vs*. 10.6%: adalimumab: 0% *vs*. 3.96% $p>0.05$)

Discussion

Fibromyalgia (FM) may exist as a primary syndrome or coexist with a variety of rheumatic diseases. FM is frequently found in rheumatoid arthritis (17%), systemic lupus erythematosus (10–47%), Sjögren's syndrome (22%), Behçet's disease (10–37%), and in psoriatic arthritis (24%) (20-26). Studies on the association between FM and ankylosing spondylitis (AS) are limited. There is only one such study in which FM was reported in up to 25% of the patients with AS (27). This figure contrasts sharply with the prevalence of 4.1% that we found in our AS patients, which is the prevalence that would be expected in a population in their forties (28). In our experience, and despite the fact that FM and AS share pain and axial involvement as key symptoms, one should not expect too high a prevalence of FM in AS. The finding of an increased prevalence of FM in women compared with men in our patients is consistent with other FM studies in rheumatic diseases (25, 27, 29, 30, 31). As stated above, FM and AS share many symptoms. The diagnosis of AS is based on the presence of chronic back pain accompanied by morning stiffness - complaints that are often prominent in FM (32). The association of FM and AS may pose diagnostic dilemmas and also may lead to misinterpretation of treatment failure or disease relapse. Moreover, AS indexes have a high component of subjectivity, as happens with most measures in rheumatology, and FM may influence them greatly. BASDAI was developed to evaluate disease activity in AS, and is based on patient perception of fatigue, stiffness, pain and tenderness – all well-known symptoms of FM. In our study, BASDAI and BASFI scores were both higher in patients with AS and coexisting FM. It is this subjectivity implied in the measurements that makes the differentiation of both diseases so complicated. Such differentiation is extremely important, as it is the BASDAI score that ultimately drives the decision to start biological therapy in AS – a treatment that has no indication whatsoever in FM. Other studies support the finding of high scores in functional and activity indexes in patients with coexisting FM. Aloush *et al*. (27) concluded that the presence of FM is associated with higher disease activity indexes (BASDAI and BASFI), and is not related to the severity of the physical findings or to ESR. Heikkila *et al*. (29) showed mean BASDAI to be significantly greater in FM than in AS, but they did not find any correlation between FM and BASFI. Mengshoel *et al*. (33) demonstrated that FM patients report more pain and fatigue than those with AS. We found that women with AS and FM had a significantly lower OWD, in agreement with a previous study (27). In addition, the scores of the FIQ and ASQoL questionnaires were significantly higher in our patients with AS and FM than in those without FM criteria. Mas *et al*. found that persons fulfilling FM criteria show impaired functioning and quality of life (34).

Coexisting FM in the context of AS may occasionally lead to the administration of anti-TNF-alpha therapies. We analysed this fact in our patients with AS and FM, and did not find that they were receiving more anti-TNF-alpha treatments than patients without FM. Naranjo *et al*. (30) found that patients with rheumatoid arthritis and FM had received DMARDs more frequently than patients without FM. Accordingly, Wolfe *et al*. have shown increased use of corticosteroids, biological agents and COX-2 inhibitors in patients with rheumatoid arthritis and FM, as well as greater medical costs (20). In our work, women with AS and FM were ordered sacroiliac joint MRI scans with greater frequency than in women without FM.

Another aspect to take into account is that these patients also show a poor response to NSAIDs. Somatisation, which is a feature frequently related to FM, has been shown to be a good predictor of non-response to biologi-

cal therapy in patients with rheumatoid arthritis (35). Probably, this may be the case with other treatments such as NSAIDs in AS.

Other reports also describe the discordance between self-reporting questionnaires and observed functional disability as the most striking feature in FM (25, 27, 29, 30, 36-37). In our study, for example, the level of an objective parameter, such as C-reactive protein, was lower in patients meeting FM criteria than in patients not meeting them. Also, the total BASRI score and the m-SASSS cervical score were lower in this group of patients. Our study thus demonstrates the fact that having FM distorts the measures of activity and function in patients with AS but not the objective measures – a finding that can be effectively used in clinical practice. The inverse relationships between BASDAI or BASFI (subjective indexes) and total BASRI (objective index) were used for the creation of two ratios. Interestingly, these ratios show a good discriminatory ability in identifying patients with FM, with likelihood ratios of over 8. Nevertheless, and given that BASRI may not be especially deteriorated in early disease, we would recommend application of the cut-off values for specific disease durations. Essentially, we found that both proposed ratios were most useful in patients with duration of AS over 10 years.

It can be argued that the cut-off values proposed for the ratios have a rather low sensitivity. We prefer using likelihood ratios as the decision driving parameters, since likelihood ratios are directly related to changes in post-test probability (38). Furthermore, we consider it more important to over-classify AS without FM than to over-classify FM. If we classified more patients with FM than there were in reality, we might be under-treating those patients who may have worse structural damage. On the other hand, we are not recommending that the ratios should be the only parameter for basing the decision to treat or not to treat a given patient.

From the data of this study it seems possible to draw a number of conclusions: 1) The occurrence of FM in AS is similar to that seen in the general population; 2) there is an increased risk of FM in females with AS; 3) the fact of having FM distorts the measures of activity and function; 4) the abilities of BASDAI to assess inflammatory disease activity and of BASFI to assess function capacity in AS with FM are poor; and 5) the BASDAI/BASRI and BASFI/BASRI ratios can be very useful in identifying patients with coexisting FM, and may thus help physicians decide the most appropriate treatment.

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