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Research Article

Radiographic axial versus non-radiographic axial spondyloarthritis: Comparison of the disease activity parameters and the disease activity and functional scores: RBSMR study

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Background: A new terminology based on the Assessment of SpondyloArthritis International Society (ASAS) 2009 classification criteria has been proposed to describe the phenotype of patients with axial spondyloarthritis (axSpA). This classification defines two subgroups: radiographic axial spondyloarthritis (r-axSpA) patients and non-radiographic axial spondyloarthritis (nr-axSpA) patients.

Methods and findings: The aim of this study is to describe and analyse the differences and the similarities between r-axSpA and nr-axSpA concerning the demographic and clinical characteristics of patients and the disease features according to the Moroccan registry of biological therapies in rheumatic diseases RBSMR (Registre des Biothérapies de la Société Marocaine de Rhumatologie) database. A cross-sectional, multicenter and analytical study based on the RBSMR registry database, which included 194 patients with SpA, among them 186 patients had axSpA fulfilling the 2009 ASAS criteria with 170 patients having r-axSpA and 16 patients having nr-axSpA. The demographic characteristics and the disease features were compared using descriptive statistics. Among 186 patients having axSpA, 91.4% had r-axSpA and 8.6% had nr-axSpA. The two subgroups shared respectively similar demographic characteristics with a mean age at 39 versus 38.5 years and had male gender predominance. We didn't find significant differences between the two subgroups concerning the disease features which are the disease duration, the HLA B27, the family history of SpA, the extra-articular manifestations (uveitis and inflammatory bowel disease), the peripheral arthritis, the visual analogue scale for fatigue (VAS-F), the Schober's test, the radiographic and ultrasonographic coxitis, except for the psoriasis which was significantly more frequent in patient with r-axSpA (p=0.027). We didn't note significant differences between the two subgroups concerning the disease activity (erythrocyte sedimentation rate, C-reactive protein) parameters and the disease activity (BASDAI, ASDAS-CRP) and functional (BASFI) scores.

Conclusions: Our study didn't find significant differences in the demographic, clinical characteristics of the patients and the disease features between the two subgroups r-axSpA versus nr-axSpA included in the Moroccan biotherapy registry RBSMR except for the psoriasis which was significantly more frequent in r-axSpA patients. These results differ from those reported in the literature because the registry included only the severe forms of SpA, which were referred to tertiary centers for treatment by biotherapy.

Keywords: comparison • radiographic axial spondyloarthritis • non-radiographic axial spondyloarthritis • RBSMR registry

Abbreviations: ASAS: Assessment of SpondyloArthritis International Society; axSpA: Axial spondyloarthritis; r-axSpA: Radiographic axial spondyloarthritis; nr-axSpA: Non-radiographic axial spondyloarthritis; RBSMR: Registre des Biothérapies de la Société Marocaine de Rhumatologie; SpA: Spondyloarthritis; HLA B27: Human Leukocyte Antigen B27; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score-CRP; BASFI: Bath Ankylosing Spondylitis Disease Functional Index; AS: Ankylosing Spondylitis; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; VAS-F: Visual Analogue Scale for Fatigue; PRESPOND: PREcision medicine in SPONdyloarthritis for Better Outcomes and Disease Remission; HRQOL: Health-Related Quality of Life; GESPIC: German Spondyloarthritis Inception Cohort

Introduction

Spondyloarthritis (SpA) is a heterogeneous group of chronic rheumatic diseases having in common a genetic predisposition and specific clinical characteristics [1,2]. The spectrum of SpA includes Ankylosing Spondylitis (AS), psoriatic

arthritis, arthritis related to inflammatory bowel disease, reactive arthritis and undifferentiated SpA. They share common clinical features, extra-articular manifestations and a strong association with the human leukocyte antigen B27 (HLA B27) [2-4]. The SpA can be categorized into axial SpA (axSpA) when the symptoms are dominated by inflammatory back pain and into peripheral SpA when the symptoms are dominated by peripheral joint involvement [5,6]. AS is the prototype disease of axSpA. The sacroiliac radiographic changes, fulfilling the modified New York criteria, have long been a major criterion for the diagnosis of AS [7,8]. However, many patients had similar axial symptoms with active sacroiliitis signs detected by Magnetic Resonance Imaging (MRI) in the absence of definite sacroiliac joint changes on pelvic X-rays [8,9]. In 2009, the ASAS developed new classification criteria for axSpA including MRI as an appropriate diagnostic tool to allow the recognition and the treatment of patients with early axial disease [3].

This classification had introduced a new concept, which is the nr-axSpA [2,4,10]. The patients classified as having nr-axSpA are those with a chronic back pain and onset before the age of 45 years as entry criteria, in the absence of radiographic sacroiliitis. They satisfy either the imaging arm with MRI findings of active sacroiliitis and at least one another SpA feature or the clinical arm with HLA B27 positivity combined to at least two other SpA features [8,11,12].

Actually, there is a discussion about these two subgroups of SpA, supposing that both r-axSpA and nr-axSpA present the continuum of the disease. Diverse studies reported that 10% to 40% of patients with nr-axSpA progress to r-axSpA over the term of two to ten years, reinforcing the hypothesis that the two entities are considered as different aspects of the same disease [13,14].

Multiple studies have compared subjects with r-axSpA versus nr-axSpA. In Morocco, there is a lack of information concerning the characteristics of each subgroup. Thus, the present study aims to describe the differences and similarities between the two subgroups and to compare the outcomes to the literature.

Methods

The RBSMR registry

The RBSMR (Registre des Biothérapies de la Société Marocaine de Rhumatologie) is a registry of biological therapies in rheumatic diseases of the Moroccan Society of Rheumatology. It is an historical, prospective and multicenter registry, which includes 10 departments of rheumatology in university medical centers. The patients recruited in the registry, had an age over than 18 years. They were diagnosed for Rheumatoid Arthritis (RA) or spondyloarthritis (SpA) and treated by biotherapy (initiation or ongoing biotherapy) in different university medical centers in Morocco. The inclusion period was from May 2017 to January 2019 and the follow-up was 3 years. The number of the included patients was 440 patients; which 419 patients were validated (225 RA/194 SpA). The primary objective of the RBSMR registry was to assess the tolerability of the patients with RA or SpA treated by biotherapy in rheumatology. The secondary objectives were to identify the most common side effects in daily practice, to evaluate the effectiveness of biotherapies in rheumatology and to evaluate the impact of biotherapies on the patients' quality of life. The details of the data collected have been published previously [15].

The study

We performed a cross-sectional, multicenter and analytical study using the RBSMR registry database, which included 194 patients followed for SpA with 186 patients having axSpA fulfilling the 2009 ASAS criteria. The objectives of this study are to describe and analyze the differences and the similarities between r-axSpA and nr-axSpA concerning the demographic and clinical characteristics of patients and the disease features and to compare our results to previous published studies.

The statistical analysis

The statistical study was conducted according to the database frozen in January 2019. The statistical analysis was performed using SPSS software, version 13.0. Data for patients were presented as medians and interquartile ranges for continuous variables and as numbers and percentages for categorical variables. The comparisons between the two subgroups r-axSpA versus nr-axSpA were examined using the Mann-Whitney test for continuous variables with non-normal distribution and using the Chi-squared test or Fischer's exact test for categorical variables. p values less than 0.05 were considered statistically significant.

Table 1. The comparison of demographic, clinical characteristics and disease features between the two subgroups: r-axSpA versus nr-axSpA.

Parameters	r-axSpA (n=170)	nr-axSpA (n=16)	p value
Age (years)[1]	39 [28.7-51.2]	38.5 [25-50.5]	0.719
Gender (male)[2]	112 (65.9)	9 (56.3)	0.44
Disease duration (weeks)[1]	574 [365-835]	494.5 [248-613]	0.134
HLA B27 positive[2]	33 (66)	1 (50)	0.641
The family history of SpA[2]	24 (15.3)	2 (14.3)	0.92
Uveitis[2]	23 (14.2)	3 (18.8)	0.623
Psoriasis[2]	8 (4.9)	3 (18.8)	0.027
Inflammatory bowel disease[2]	19 (11.7)	1 (6.3)	0.512
Peripheral arthritis[2]	112 (67.5)	13 (81.3)	0.256
VAS-F[1]	6.75 [5-8]	7.5 [6.2-8]	0.274
Schober's test[1]	3 [2-4]	3.2 [2-4]	0.693
Radiographic coxitis[2]	74 (43.5)	3 (20)	0.076
Ultrasonographic coxitis[2]	20 (21.7)	1 (12.5)	0.538

HLA B27: Human leukocyte antigen B27; VAS-F: Visual analogue scale for fatigue; [1]Medians and interquartile ranges; [2]Numbers and percentages. Results according to available data.

Table 2. The comparison of the disease activity parameters, the disease activity and functional scores between the two subgroups: r-axSpA versus nr-axSpA.

Scores	r-axSpA (n=170)	nr-axSpA (n=16)	p value
ESR (mm)	17 [8-35]	16 [6.5-37.5]	0.824
CRP (mg/l)	6 [2.1-18.6]	5 [0.6-12.2]	0.221
BASDAI	3 [1.7-4.8]	3.3 [2-4.7]	0.93
ASDAS-CRP	1.9 [0.9-3.1]	2 [1.3-3]	0.901
BASFI	3.2 [1.2-5]	2.5 [1.3-4.1]	0.426

ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score-CRP; BASFI: Bath Ankylosing Spondylitis Functional Index. Results are expressed as medians and interquartile ranges. Results according to available data.

Results

Among 194 patients with SpA, 186 patients had axSpA with 170 (91.4%) r-axSpA and 16 (8.6%) nr-axSpA. The two subgroups shared similar demographic and clinical characteristics with a mean age of 39 versus 38.5 years and had male gender predominance 112 (65.9%) versus 9 (56.3%). No significant differences were found concerning the disease features which are the disease duration, the HLA B27, the family history of SpA, the extra-articular manifestations (uveitis, inflammatory bowel disease), the peripheral arthritis, the VAS-F, the Schober's test, the radiographic and ultrasonographic coxitis, except for the psoriasis which was significantly frequent in the r-axSpA patients (p=0.027) (Table 1).

The two subgroups had similar disease activity parameters (ESR: Erythrocyte Sedimentation Rate, CRP: C-Reactive Protein) and similar activity (BASDAI: Bath Ankylosing Spondylitis Disease Activity Index and ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score-CRP) and functional (BASFI: Bath Ankylosing Spondylitis Disease Functional Index) scores. We noted in our population study low medians of BASDAI, ASDAS-CRP and BASFI scores (Table 2).

Discussion

Since the new ASAS classification criteria for axSpA have been published, a number of studies have compared subjects with r-axSpA and nr-axSpA for the various axSpA-related variables. In Morocco, our study is the first study based on data collected from 10 departments of rheumatology in all Moroccan university medical centers that compared demographic, clinical characteristics of patients and disease features in these two subgroups receiving anti-TNFα as a treatment, to characterize the profile of each entity. Among 186 axSpA patients recruited in the study, 91.4% had r-axSpA and 8.6% had nr-axSpA. Comparing this prevalence to those reported in the literature, the number of

nr-axSpA patients available for the analysis was low which seems to be limited by the criterion of patients undergoing biotherapy, reflecting the small number of nr-axSpA patients receiving biotherapy in our country.

We didn't find significant differences in the demographic and clinical characteristics respectively in r-axSpA versus nr-axSpA subgroups. The mean age was 39 versus 38.5 years with male gender predominance in the two subgroups contrasting with several studies that reported the higher proportion of women in the nr-axSpA subgroup while more men were affected in r-axSpA subgroup [2,6,9,11,16]. Our data demonstrated that r-axSpA patients presented relatively a longer disease duration, which is compatible with all previous studies. Concerning the disease features, we didn't note significant differences in the HLA B27, the family history of SpA, the peripheral arthritis, the VAS-F, the Schober's test, the radiographic and ultrasonographic coxitis. The comparison of the outcomes to the literature found some differences. A multi-ethnic Asian cohort using the data from PRESPOND (PREcision medicine in SPONdyloarthritis for Better Outcomes and Disease Remission) registry in Singapore General Hospital found that patients with AS are more likely to be HLA B27 positive [17]. The previous studies [6,11,18] showed that the peripheral arthritis was more prevalent in nr-axSpA subgroup with female gender predominance contrasting with a meta-analysis of de Winter JJ et al. showing similar prevalence in peripheral manifestations including arthritis, enthesitis and dactylitis [19]. Bubova K et al. and Akasbi N et al. reported that hip involvement was more frequent in r-axSpA patients especially in men [6,16]. Some studies have showed that the hip disease is more prevalent in patients with a younger disease onset and can be associated with more severe axial disease [20,21].

Concerning the extra-articular manifestations, uveitis and inflammatory bowel disease were similar in the two subgroups except for psoriasis, which was significantly frequent in r-axSpA patients. Prior studies [6,18] showed an equal prevalence in all extra-articular manifestations in the two subgroups contrasting with the meta-analysis of de Winter JJ et al. which reported that the uveitis was slightly more prevalent in r-axSpA [19].

In our study population, no significant differences were found comparing the two subgroups in the disease activity parameters (ESR, CRP) and the disease activity (BASDAI, ASDAS-CRP) and functional (BASFI)scores with low medians of all scores. In the literature, patient-reported outcomes demonstrate in some studies similar levels of disease activity, overall physical impairment and Health-Related Quality Of Life (HRQOL) [9,11,13,22,23]. In other studies, the patients with r-axSpA presented higher disease activity as defined by ASDAS and acute phase reactants compared with the patients with nr-axSpA [6,24,25]. The ASDAS-CRP is the preferred measure of disease activity in axSpA because the BASDAI reflects subjective perceptions of the disease. Bubova K et al. and the GESPIC (German Spondyloarthritis Inception Cohort) data reported that nr-axSpA patients had better functional values than r-axSpA patients due to advanced structural changes, which may lead to spine ankylosis in r-axSpA patients [6,9,11].

In our study, the small sample of the patients with nr-axSpA seems to be related to the inclusion criterion, which is axSpA patients undergoing anti-TNFα treated in tertiary medical centers. A large sample size might have been necessary to confirm these results.

Conclusions

Since the concept of nr-axSpA has been validated by the ASAS, several studies have compared the two subgroups of axSpA with the aim to characterize the profile of each entity. In our study, based on the data of the RBSMR registry, the two subgroups have shared similar demographic, clinical characteristics and similar disease activity parameters, disease activity and functional scores except for the psoriasis, which was significantly more frequent in the r-axSpA patients.

Ethical approval and consent to participate

The protocol for the original RBSMR study was reviewed and approved by local institutional review boards and the national ethic committee.

Consent for publication

Written informed consent for publication was obtained from the patients.

Availability of data and material

The datasets are available from the RBSMR registry of the Moroccan Society of Rheumatology.

Competing interests

The authors declare that they have no Competing interests.

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Authors' contributions

SB drafted this manuscript and reviewed the literature. BA, IE, IH, SR and RB reviewed critically the manuscript. The scientific committee of the RBSMR study has reviewed and approved the final manuscript.

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