BRIEF REPORT

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Axial psoriatic arthritis: the impact of underdiagnosed disease on outcomes in real life

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Abstract

Psoriatic arthritis (PsA) may affect different joints, including the spine. The prevalence of spinal involvement is variable depending on the definition and a subset of patients have been identified in cohorts that do not have clinical features of axial disease and yet have imaging findings. Still, there is not a consensus on how and when to screen axial disease. In this study, we aimed to investigate factors associated with being underdiagnosed for axial psoriatic arthritis (axPsA) and its impacts on outcomes. Disease features and outcomes of axPsA according to the physician ($n = 415$) were compared with patients with imaging findings only (sacroiliitis fulfilling the modified New York criteria, $n = 112$), using data from a real-life PsA registry. Patients with imaging findings only were more frequently women (83/220 (37.7%) vs 29/122 (23.8%); $p = 0.008$). This group also had higher peripheral disease activity (imaging only vs clinical AxPsA: mean (SD) tender joint count 5.3 (6.1) vs 3.3 (4.7), swollen joint count 1.9 (2.9) vs 1.2 (2.4); $p < 0.001$ for both comparisons) and was less often treated using TNF inhibitors (16.1 vs 38.2%; $p < 0.001$) than patients who were classified as axPsA. Patient-reported outcomes were similar in both groups. PsA patients, especially women with more severe peripheral disease, have a higher risk of being underdiagnosed for axPsA. The severity of peripheral symptoms may be a risk factor to mask the spinal features of PsA.

Keywords Axial disease · Psoriatic arthritis · Radiography

Introduction

Psoriatic arthritis (PsA) is a heterogenous disease with different subtypes of joint disease [1, 2]. The frequency of axial involvement is 24–78% of PsA, depending on the definition of axial disease [3–5]. Subclinical axial involvement with spondylitic changes/sacroiliitis in the absence of clinical features is around 20–25% [5–8]. However, there is not a consensus on how to perform radiological screening in PsA. In our experience, most of the physicians do not perform routine imaging with the argument that subclinical disease has no effects on management decisions.

In this study, we aimed to clarify which group of patients had underdiagnosed axial PsA (axPsA) and its clinical implications in real life including patient- (PROs) and physician-reported outcomes and treatment choices. If underdiagnosed axPsA has any impacts on the outcomes and therapies, this would highlight the importance of routine screening by imaging methods.

Methods

Psoriatic Arthritis Registry of Turkey (PsART) was established in 2014 and includes 32 rheumatology centers. Ethics approval was obtained from Hacettepe University Ethics Board (GO 14/578) and all patients gave informed consent prior recruitment. PsART data are collected using a web-based system (www.trials-network.org) following the recommendations of a survey led by Group for Research and Assessment of

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Psoriasis and PsA (GRAPPA) [9]. The details of the registry including how missing data was handled had been previously explained in detail [10]. In brief summary demographics, disease characteristics for psoriasis and PsA, PROs and physician-reported outcomes, comorbidities, and treatments have been collected. The presence of axial involvement was based on inflammatory back pain but a positive imaging finding suggestive of sacroiliitis and/or spondylitis was not a requirement. There are no specific imaging requirements for PsART beyond local practice for individual centers. Plain radiographs were sent for central reading, whenever available.

Images were scored by one experienced investigator (SZA), blinded to the clinical data. Radiological classification of sacroiliitis was made according to definitions used in the modified New York criteria for AS [11]. Although erosions, squaring, and sclerosis are included in composite scores, due to the low frequency and the poor reliability of detecting these lesions, spinal radiographs were only assessed for the presence of syndesmophytes [12].

Statistical analysis

Descriptive statistics were given as frequencies (percentages) for categorical and mean (standard deviation (SD)) values for continuous variables. Comparisons were made using a chi-square test or Mann-Whitney U test, as appropriate. Demographics and disease features of patients with or without axPsA and the impact of axPsA by imaging on PROs and physician-reported outcomes were analyzed. Reliability for central reading for radiographs was tested in patients where both cervical and lumbar spine x-rays were available ($n = 72$) and on 28 patients for sacroiliac joints (SIJs) in 2 separate sessions, being 3 months apart. Kappa values and complete agreement rates were calculated for the presence of syndesmophytes and for the degree of sacroiliitis. In addition, interreader agreement with a second reader was analyzed using kappa agreement for the SIJs ($n = 25$), cervical spine ($n = 17$), and lumbar spine ($n = 18$).

SPSS V-24 was used for analysis (SPSS Inc., Chicago, IL, USA).

Results

Clinical features of patients with or without axial disease

In October 2016, 1195 patients were recruited to the registry and 1186 had data on clinical subtypes for arthritis and were included in the analysis. Within these, 415 (35%) were classified as having axPsA by the physician, either alone or in combination with other subtypes (Fig. 1). Subjects with axPsA were more frequently men, were younger, were more frequently smokers, were more likely to be on TNF inhibitors (TNFis), and had more nail involvement (Table 1).

Imaging findings

SIJs Of 395 SIJ radiographs, a*symmetrical* sacroiliitis (grade 2-3-4 on one side) was seen in 70 (17.7%) patients and 246 (62.3%) had *symmetrical* sacroiliitis (grade ≥ 2 on both sides). Two hundred and eighty-three (71.6%) patients fulfilled the sacroiliitis criteria required for classifying the patient as having AS according to the modified NY criteria [11].

The spine assessment The prevalence of syndesmophytes in the cervical spine was higher than that in the lumbar spine [45/96 (46.9%) vs 47/150 (31.3%)]. Within 80 patients that had both cervical and lumbar spine radiographs available for central reading, 25 (31%) had syndesmophytes at either cervical or lumbar spine only. Data from 157 patients where both sacroiliac findings and spine radiographs were available showed that patients that fulfilled the mNY criteria had more frequent syndesmophytes compared to patients that did not fulfil the criteria [58/121 (47.9%) vs 10/36 (27.8%); $p = 0.04$]. Overall, only 10 in 157 patients had syndesmophytes in the absence of significant sacroiliitis.

Among 71 patients that had syndesmophytes, 20 patients (28.2%) were not classified as having axPsA according to the physician. This was higher for women (15/42, 35.7%) than for men (5/29, 17.2%).

Characteristics of patients with underdiagnosed axPsA and implications in management

One hundred and twelve patients had sacroiliitis fulfilling the modified NY criteria, despite not being categorized as axPsA. These were mostly women [83/220 (37.7%) vs 29/122 (23.8%); $p = 0.008$] and were less likely to be on TNFis (16.1 vs 38.2%; $p < 0.001$). They also had higher tender and swollen joint counts (Table 2). PROs and physician's global assessment for disease activity were similar in both groups, suggesting a comparable degree of disease activity according to the patients and physicians. As not all patients had routine screening by imaging, a percentage for underdiagnosed axPsA was not calculated.

Reliability

The complete agreement for detecting syndesmophytes in 2 separate readings was 70/72 (97.2%, kappa 0.971) for the cervical spine and 58/72 (80.6%, kappa 0.641) for the lumbar spine. The kappa value for the grading of sacroiliitis from 0 to 4 was 0.791 with a complete agreement in the score in 34/56
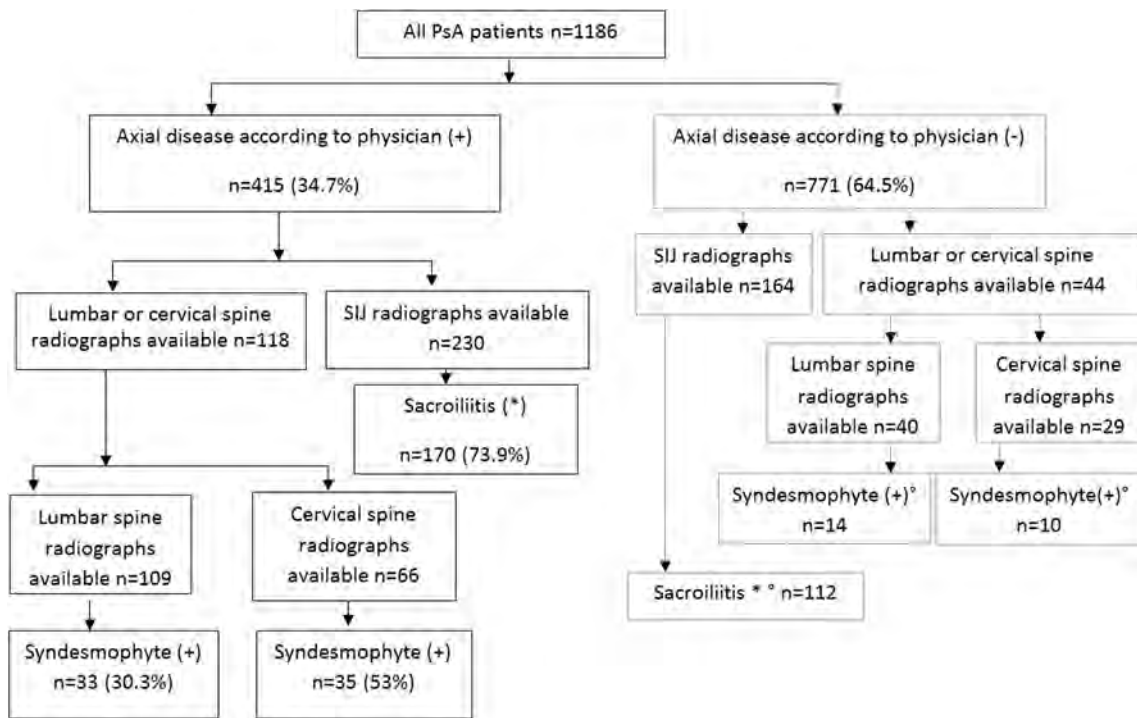
Fig. 1 Number of PsA patients with available data and positive for axial disease according to the clinician. The number of radiographs corresponds to the radiographs of which the quality was sufficient to be scored by the central reader, after excluding 36 sacroiliac joint (SIJ) and 5 lumbar spine radiographs. *Sacroiliitis ≥ grade 3 unilateral or ≥ grade 2 bilateral. °A percentage was not calculated for these radiographs as routine imaging was not performed to all patients

SIJs. The second reading resulted in 6/28 patients to be classified differently for modified NY criteria. The interreader agreement to detect grade 2 or higher sacroiliitis showed moderate agreement (kappa 0.451). The interreader kappa values for syndesmophytes were 0.806 for the lumbar spine and 0.870 for the cervical spine.

Table 1 Demographics of the whole group and patients with or without axial disease according to the physician. Comparisons between patients with or without axial disease were significant at the following levels: *$p < 0.001$, **p 0.04, ***p 0.01, [+]p 0.006, [++]p 0.03, [+++]p 0.001. The data are given as mean (SD) if not mentioned otherwise

	Physician's assessment for axial disease	
	Axial PsA ($n = 415$)	Non-axial PsA ($n = 771$)
Age	44.4 (12.2)*	47.9 (13)*
Gender: women, n (%)	248 (59.8%)[+]	523 (67.8%)[+]
Disease duration (for arthritis) (months since diagnosis)	68.7 (83.2)	66.6 (80)
Disease duration (for psoriasis) (months since the onset)	178.6 (132.6)	181.8 (139)
Nail disease, n (%)	207 (49.9)[++]	333 (43.2)[++]
Smoking (current or past), n (%)	185 (44.6%)*	263 (34.1%)*
Body mass index	27.6 (5.1)**	28.2 (5.1)**
TNF inhibitors, n (%)	137/369 (37.1%)***	197/670 (29.4%)***
Symmetrical polyarthritis	129 (31.1)*	343 (44.5)*
Asymmetrical oligoarthritis/monoarthritis	145 (34.9)[+++]	345 (44.8)[+++]
Axial		
Distal interphalangeal joint disease	42 (10.1)	155 (20.1)
Arthritis mutilans	3 (0.7)	6 (0.8)
Plaque psoriasis	191 (69.2)	383 (74.1)
Flexural	2 (0.7)	5 (1)
Inverse	1 (0.4)	3 (0.6)
Pustular	72 (26.1)	106 (20.5)
Erytrodermic	10 (3.6)	20 (3.9)

Table 2 Comparison of patient-reported outcomes and physician-based assessments in patients with axial disease according to the clinician and axial disease by imaging only. *BASDAI*, Bath Ankylosing Spondylitis Disease Activity Index; *BASFI*, Bath Ankylosing Spondylitis Function Index. Numbers are given as mean (SD)

	Axial disease according to the clinician ($n = 415$)	Axial disease by imaging only ($n = 112$)	p
Patient global assessment ($n = 408$)*	46 (24.9)	49 (21)	0.1
Pain ($n = 429$)*	45.4 (28.7)	50.5 (22.3)	0.08
Fatigue ($n = 427$)*	47.3 (27.6)	52.9 (22.5)	0.2
BASDAI ($n = 345$)*	4.5 (2.5)	3.8 (2.3)	0.1
BASFI ($n = 331$)*	3.4 (2.5)	3.1 (2.3)	0.5
Physician's global assessment ($n = 378$)*	37.9 (23)	39.8 (18.2)	0.08
Tender joint count ($n = 503$)*	3.3 (4.7)	5.3 (6.1)	< 0.001
Swollen joint count ($n = 504$)*	1.2 (2.4)	1.9 (2.9)	< 0.001
Leeds enthesitis index ($n = 453$)* Body surface area	0.3 (0.8)	0.4 (1)	0.1

*Number of patients with available data

Discussion

PsA is a heterogeneous disease and the complexity of the clinical presentation makes it difficult to accurately classify patients. It is likely that there is a subset of patients with more tender and swollen joints that have imaging findings for axPsA, without clear clinical manifestations of axial disease to help the physicians for diagnosis, which is more frequent in women. In case of having other disease features, like active peripheral arthritis, both patients and physicians may be disregarding the involvement of the spine. Additionally, as recently been shown by our group, the IBP questionnaires only have moderate sensitivity in axPsA, which can be another reason for missing the axial disease [13].

In patients who had sacroiliitis on imaging despite not being classified as axPsA by the physician, the same magnitude of disease burden according to the patients was reflected by the PROs, which made us to describe as "underdiagnosed" instead of "subclinical" axPsA. This is an important difference as subclinical disease may not need screening unless long-term impacts on outcomes are shown. On the other hand, underdiagnosed is terminology that would suggest the need for better screening methods. In addition to the impacts on the PROs, our data show that diagnosis of axial disease not only is an academically relevant question but also may have an impact on the treatment. The treatment recommendations by GRAPPA and EULAR suggest that patients with axPsA and peripheral disease require different treatment approaches such as peripheral disease being more responsive to conventional DMARD therapies whereas biological therapies are the next medical treatment steps after the nonsteroidal anti-inflammatory drugs for axial disease [14, 15]. On the other hand, patients with axial disease according to the physician have similar disease burden with patients with axPsA by imaging only according to PROs, and yet treated less with TNFis.

Another question is which imaging modality needs to be used and which site(s) need be screened. For the SIJs, radiograph is the initial screening method for economic concerns and for being widely available. The presence of syndesmophytes was not a part of axPsA in this study; however, 6% of patients in our data had syndesmophytes without any sacroiliitis, which was less frequent than a recent study by Jadon et al. [5]. Screening only the lumbar or cervical spine would have led to underdiagnosing 11.3% of our patients. Routine screening of SIJ and spine at least once would give a better understanding of the spectrum of the disease.

Our study has some limitations. PsA patients were consecutively recruited to the registry with no specific inclusion criteria; therefore, a selection bias was not applicable at the stage of recruitment. However, this is an observational study and radiographs were ordered in the discretion of the recruiting physician and there might have been a selection bias for the group of patients that had radiographs. There is not a widely accepted definition for axPsA for radiographs or where to draw the threshold for a positive finding. Although there are controversies on the effect of HLAB27 on the disease progression in axPsA [3, 5], the lack of HLA-B27 limits the identification of different subsets. Despite these limitations, this registry reflects the real-life experience, and for including 32 centers across the country, the data represent the routine practice in rheumatology.

In summary, PsA patients with more severe peripheral disease, such as more tender/swollen joints, had higher risk of being underdiagnosed for the axPsA, which was more common in women. Underdiagnosed patients were less frequently treated with biologic treatments. Axial disease needs to be ruled out using imaging modalities, even if back pain does not clinically suggest of an inflammatory pattern.

Compliance with ethical standards

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