Early identification of axial psoriatic arthritis among patients with psoriasis: a prospective multicentre study

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ABSTRACT

Objectives To evaluate a dermatologist-centred screening tool followed by a structured rheumatological examination including MRI of sacroiliac joints and spine for the recognition of psoriatic arthritis with axial involvement (axPsA).

Methods This was a prospective multicentre study. Adult patients with a confirmed diagnosis of psoriasis who had chronic back pain (≥3 months), onset <45 years and had not been treated with any biologic or targeted synthetic disease-modifying antirheumatic drug in the 12 weeks before screening were referred to a specialised rheumatology clinic. A rheumatological investigation including clinical, laboratory and genetic assessments as well as imaging with conventional radiography and MRI of sacroiliac joints and spine was performed. The primary outcome of the study was the proportion of patients diagnosed with axPsA among all referred patients with PsO.

Results Rheumatologists examined 100 patients of those who qualified for referral. 14 patients (including 3 with both axial and peripheral involvement) were diagnosed with axPsA and 5 were diagnosed with peripheral PsA solely. All patients diagnosed with axPsA had active inflammatory and/or structural (post) inflammatory changes in the sacroiliac joints and/or spine on imaging. In five patients, MRI changes indicative of axial involvement were found only in the spine. All but one patient with PsA (13/14 with axPsA and 5/5 with pPsA) fulfilled the Classification Criteria for Psoriatic Arthritis criteria for PsA. The Assessment of SpondyloArthritis International Society criteria for axSpA were fulfilled in 9 (64.3%) patients diagnosed with axPsA.

Conclusions Applying a dermatologist-centred screening tool may be useful for the early detection of axPsA in at-risk patients with psoriasis.

INTRODUCTION

Spondyloarthritis (SpA) encompasses a group of overlapping disorders, namely ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis, undifferentiated SpA and non-radiographical axial SpA.7 Psoriatic arthritis (PsA) is a chronic, inflammatory musculoskeletal disease4 that affects up to 30% of patients with psoriasis5,13 and typically manifests as peripheral arthritis, enthesisitis, dactylitis and skin and nail changes.7 Between 20% and 75% of patients with PsA have axial involvement (axPsA) and present with additional symptoms, such as back pain that might have inflammatory characteristics including morning stiffness.14

Back pain in patients with axPsA is caused by inflammation in sacroiliac joints and/or spine that over time might result into development of structural damage including radiographical sacroiliitis, syndesmophytes and ankylosis. AxPsA is associated with more severe disease and patients with axial involvement often experience worse pain, significantly impaired physical function and overall activity and reduced quality of life compared with patients without axial involvement.2,9

Because a delayed diagnosis of PsA (and axPsA in particular) may lead to irreversible joint and spinal

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Early diagnosis of psoriatic arthritis (PsA) (and psoriatic arthritis with axial involvement (axPsA) in particular) is essential and dermatologists are in a strategic position to screen at-risk patients with psoriasis before advanced structural damage of the joints and spine appears.

⇒ While different validated screening/referral tools focusing on peripheral manifestations of PsA exist, validated referral algorithms for axPsA are missing.

WHAT THIS STUDY ADDS

⇒ Our study revealed that application of a dermatologist-centred screening tool focusing on identifying signs of axial involvement among patients with psoriasis may be useful for the detection of PsA (and specifically axPsA) in these patients.

⇒ MRI of the spine in addition to MRI of sacroiliac joints is required to recognise patients presenting with spinal involvement only.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings provide insights into the possibility of diagnosing axPsA early with the ultimate goal of improving the care and quality of life of patients living with this disease.
damage and poor long-term outcomes, early diagnosis and treatment of patients with PsA is essential. However, PsA is a heterogeneous disease with a very variable clinical manifestation, which makes early identification very challenging.

In the absence of reliable serological and/or imaging biomarkers for early PsA and an existing diagnostic delay, there is a need for screening tools for detection of early PsA. Skin lesions associated with psoriasis typically precede symptoms of PsA, which places dermatologists in a strategic position to screen at-risk patients before advanced structural damage of the joints and spine appears. However, despite awareness of the disease, prevalence of undiagnosed PsA among patients with psoriasis at risk remains high with up to one-third of patients with psoriasis who regularly attend dermatology clinics being undiagnosed for PsA.

Moreover, while different validated screening/referral tools focusing on peripheral manifestations of PsA exist, validated referral algorithms for PsA with axial involvement (axPsA) are missing. To address this gap, we conducted a prospective, multicentre study in which we applied a dermatologist-centred, easy and not time-consuming screening tool followed by a structured rheumatological examination including MRI of sacroiliac joints and spine to identify patients with axPsA among patients with psoriasis attending dermatology clinics.

METHODS
Study design and patient eligibility
This prospective, multicentre study was conducted in coordination with the Charité—Universitätsmedizin Berlin specialised rheumatology clinic and 14 dermatology sites in the area of Berlin, Germany between October 2019 and January 2020. Consecutive patients with psoriasis who consented to participating in the study were screened by their treating dermatologist for eligibility for referral to Charité specialised rheumatology clinic. Patients eligible for referral were adults (18 years or older) with a confirmed diagnosis of psoriasis who reported having chronic back (defined as back pain lasting ≥3 months) with onset prior to 45 years of age and who had not been treated with any biologic or targeted synthetic disease-modifying anti-rheumatic drug (DMARD) within 12 weeks prior to screening (online supplemental Annex 1).

Patients who qualified for referral were contacted to schedule an appointment at the rheumatology clinic, where they confirmed their interest participating in the study and signed a second informed consent form. For all patients who attended the rheumatology clinic, a complete rheumatological investigation, including MRI of sacroiliac joints and spine to identify patients with axPsA among patients with psoriasis attending dermatology clinics.

Patient and public involvement
Patients and/or public were not involved in any steps of the design, conduct, analysis and results dissemination of this study.

Outcomes
The primary outcome of the study was the proportion of patients diagnosed with axPsA with or without peripheral involvement, among all referred psoriasis patients seen at the rheumatology clinic. Secondary outcomes included the proportion of patients diagnosed with peripheral PsA (pPsA) without axial involvement and the proportion of patients fulfilling the Assessment of SpondyloArthritis International Society (ASAS) classification criteria for axial spondyloarthritis (axSpA) and/or the Classification Criteria for Psoriatic Arthritis (CASPAR) for PsA criteria.

Statistical analysis
The proportion of patients with psoriasis diagnosed with axPsA or pPsA was calculated out of the total number of psoriasis patients referred and seen at the rheumatology clinic. The same approach was applied for the calculation of the proportion of patients fulfilling the ASAS classification criteria for axSpA and the CASPAR classification criteria for PsA.

Patient demographic, clinical, laboratory and imaging characteristics were tabulated and summarised by means, medians, SD, IQR (Q3–Q1), minimum and maximum for continuous variables and by number and percentages for categorical variables. All patients with psoriasis seen at the rheumatology clinic had fully completed screening questionnaires and underwent a complete rheumatological investigation. As only patients with PsO with fully completed screening questionnaires and complete data of the rheumatological assessment including imaging were included into this analysis, there were no missing data in the dataset.

Statistically significant differences between the psoriasis patients diagnosed with axPsA and patients with psoriasis diagnosed with neither axPsA nor pPsA were determined by using Mann-Whitney U test for continuous variables and χ² test for categorical variables. Significance tests were conducted at significance level α=0.05. All statistical analyses were conducted in SAS Studio V9.4 (SAS Institute).

RESULTS
Patient disposition and diagnosis of axPsA and pPsA
In total, 355 patients were screened at 14 dermatology sites, of whom 151 (42.5%) qualified for referral to Charité specialised rheumatology clinic. Rheumatologists ultimately examined 100 (28.2%) consecutively referred patients to reduce the risk of bias. The diagnosis of axPsA was made in 14 patients (14%), and 3 of these patients presented with both axial and peripheral involvement. The diagnosis of pPsA without axial involvement was made in five patients (5%). Finally, 81 (81%) patients were diagnosed with neither axPsA nor pPsA (figure 1).

The ASAS classification criteria for axSpA were fulfilled in nine (64.3%) of the patients diagnosed with axPsA. All but one patient diagnosed with PsA (13/14 with axPsA and 5/5 with pPsA) fulfilled the CASPAR for PsA as illustrated in figure 1.

Demographic and clinical characteristics
Demographic and clinical characteristics of all patients are presented in table 1. The mean (SD) age was similar among patients diagnosed with axPsA (46.2 (13.6) years) and patients diagnosed with neither axPsA nor pPsA (45.7 (13.3) years), while patients diagnosed with pPsA were slightly younger (42.8 (9.0) years). Fifty-six per cent of all patients were female; the
The proportion of females was higher among patients diagnosed with axPsA (64.3%) and lower among patients diagnosed with pPsA (40.0%).

Patients with axPsA had a lower mean (SD) psoriasis duration with 13.6 (9.2) years than those patients not diagnosed with PsA (20.3 (16.7) years); nevertheless, this difference did not reach statistical significance. Mean (SD) duration of back pain was lower as well among patient with axPsA (12.2 (15.2) years) compared with patients not diagnosed with PsA (18.6 (14.8) years). A larger proportion of patients with axPsA experienced inflammatory back pain compared with patients not diagnosed with PsA (57.1% vs 44.4%).

Compared with patients not diagnosed with PsA, patients with axPsA presented with a significantly higher disease activity as assessed by the Ankylosing Spondylitis Disease Activity (ASDAS) score; the mean (SD) ASDAS score was 2.9 (0.8) for patients with axPsA and 2.3 (0.7) for patients not diagnosed with PsA (p=0.017). Patients with axPsA also presented with higher disease activity as assessed by the Disease Activity in Psoriatic Arthritis (DAPSA) score; the mean (SD) DAPSA score was 17.5 (14.3) for patients with axPsA and 11.2 (7.4) for patients not diagnosed with PsA.

Laboratory and imaging characteristics

Laboratory and imaging characteristics of all patients are presented in table 2. A higher proportion of patients with axPsA had HLA-B27 positive compared with patients not diagnosed with PsA (28.6% vs 14.8%). Significant differences were noted on CRP (mg/L) levels among patients with axPsA and patients not diagnosed with PsA. The mean (SD) CRP level was 8.0 (10.8) in patients with axPsA and 2.3 (0.7) for patients not diagnosed with PsA.

All patients diagnosed with axPsA had active inflammatory and/or structural (post)inflammatory changes in the sacroiliac joints and/or spine on imaging (table 2). In five (35.7%) patients, MRI changes indicative of axial involvement were found only in the spine (figure 2). Five (35.7%) patients with axPsA presented with radiographic sacroilitis ≥2 unilaterally and four (26.6%) patients in this group presented with radiographic sacroilitis fulfilling the mNY criteria.

None of the patients diagnosed with pPsA or not diagnosed with PsA had active inflammatory and/or structural (post)inflammatory changes in the sacroiliac joints and/or spine on imaging. Among patients not diagnosed with PsA, four (4.9%) presented with radiographic sacroilitis ≥2 unilaterally; one of them (1.9%) had radiographic sacroilitis fulfilling the mNY criteria. After MRI assessment, axPsA in these four patients could be excluded: three cases showed typical imaging patterns of osteitis condensans ili (OCI) and one did not present any active inflammatory or structural changes in the SIJ.
Spondyloarthritis

Previous and current treatments

A substantial proportion of patients with psoriasis seen at rheumatology were using non-steroidal anti-inflammatory drugs (NSAIDs) at screening (42%), although no significant differences were noted in NSAIDs use between patients diagnosed with axPsA and patients not diagnosed with PsA (57.1% vs 38.3%; χ² = 10.3, p = 0.001). Among all patients seen, a minority reported previous use of non-opioid and opioid analgesics (10% and 5%, respectively) (Table 3).

The most common systemic psoriasis therapy was methotrexate, used by 11% of patients in total. Common topical psoriasis therapies included steroids and vitamin D analogues, used by 78% and 52% of the patients, respectively (Table 3).

**Table 2** Laboratory and imaging characteristics of patients diagnosed with psoriasis with pPsA, axPsA and patients not diagnosed with PsA

| Patient characteristic | HLA-B27 positive—n (%) | CRP (mg/L)—mean (SD) | Elevated CRP (>5 mg/L)—n (%) | Peripheral arthritis, current (last 7 days)—n (%) | Radiographic sacroiliitis as per mNY criteria—n (%) | Active inflammation, sacroiliac joint (MRI)—n (%) | Structural (post) inflammatory changes, sacroiliac joint (MRI)—n (%) | Active inflammation, spine (MRI)—n (%) | Structural (post) inflammatory changes, spine (MRI)—n (%) |
|------------------------|------------------------|----------------------|-------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| All patients seen at rheumatology (N=100) | 16 (16.0) | 3.5 (6.1) | 17 (17.0) | 11 (11.0) | 5 (5.0) | 8 (8.0) | 8 (8.0) | 13 (13.0) | 8 (8.0) |
| pPsA (N=5) | 0 | 8.0 (15.4) | 1 (20.0) | 5 (100.0) | 0 | 0 | 0 | 0 | 0 |
| axPsA (N=14) | 4 (28.6) | 8.0 (10.8) | 5 (35.7) | 3 (21.4) | 4 (28.6) | 8 (57.1) | 8 (57.1) | 13 (92.9) | 8 (57.1) |
| No PsA (N=81) | 12 (14.8) | 2.5 (3.1) | 11 (13.6) | 3 (3.7) | 1 (1.2) | 0 | 0 | 0 | 0 |
| p value* | 0.204 | 0.039 | 0.041 | 0.012 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

*Statistically significant differences between the axPsA and noPsA groups of patients were determined by using Mann–Whitney U test for continuous data and χ² test for categorical data.

1n those four patients not diagnosed with axPsA suspicious findings by conventional radiography were observed (one of the even fulfilling the mNYc), but those were then judged as not compatible with axPsA after MRI evaluation.

axPsA, axial psoriatic arthritis; CRP, C reactive protein; HLA-B27, human leucocyte antigen B27; mNY, modified New York; N, number; pPsA, peripheral psoriatic arthritis.

Significant differences were noted in the proportion of patients that had radiographic sacroiliitis in this group compared with the axPsA group (Table 2).

**DISCUSSION**

This prospective, multicentre study is, to our knowledge, one of the first studies that applied a dermatologist-centred screening/referral tool focusing on detecting axial involvement in patients with psoriasis. Furthermore, the current algorithm was useful for the detection of PsA in patients with psoriasis by applying a straightforward and simple criterion such as age (18 years of age or older), confirmed diagnosis of psoriasis, chronic back pain, defined as back pain lasting ≥3 months, having back pain onset prior to 45 years of age and not treated with biologics or targeted synthetic DMARD within the last 12 weeks.

In addition, in order to capture inflammatory/structural postinflammatory changes in the axial skeleton objectively, our study included MRI of sacroiliac joints and spine as a part of the rheumatological diagnostic approach for all patients. Our data provide further support for previous reports on the prevalence of PsA with and without axial involvement among patients with psoriasis and highlights the demographic and clinical characteristics of these patients with a special focus on imaging data.

We have found that 19% of patients seen by a rheumatologist in our study were diagnosed with PsA (5/100 with pPsA and 14/100 with axPsA), whereas 73.7% (14/19) of patients with PsA had axial involvement that is clearly related to the screening methodology focusing on axial symptoms. A study published in 2019 reported an overall prevalence of PsA among patients with psoriasis of 19.7%, whereas previous studies suggest that 25%–70% of patients diagnosed with PsA have axial involvement.

One study investigated presence of axial involvement in patients with PsA as defined by radiographic sacroiliitis ≥grade 2 unilaterally. In this study, 45% of patients presented with radiographic sacroiliitis ≥grade 2 unilaterally and 35% of patients fulfilled the mNY criteria for radiographic sacroiliitis. In our study, we have found that 28.6% and 35.7% of patients with axPsA presented with sacroiliitis ≥grade 2 unilaterally and as per the mNY criteria, respectively. However, we also investigated the overlap between radiographic and MRI findings and found that, while all four patients who fulfilled the mNY criteria for radiographic sacroiliitis also presented with active and/or structural (post)inflammatory changes in the sacroiliac joints on MRI, in five other patients, evidences of involvement of sacroiliac joints were only detected on MRI (figure 2). These findings highlight the importance of MRI in detecting axial involvement in patients with PsA in the absence of definite radiographic changes in the sacroiliac joints. Furthermore, even MRI of sacroiliac joints would have resulted in missing of patients with isolated spinal involvement, which represent a substantial proportion of patients with axial involvement in PsA. Additionally, also in the group not diagnosed with axPsA, suspicious findings by conventional radiography were observed in four patients, which were then judged as not compatible with axPsA but rather due to other causes such as OCI after MRI evaluation. This stresses again the rather low specificity of borderline abnormalities seen in conventional radiographs of the SI joints and highlights the importance of MRI assessments in patients with suspected inflammatory axial involvement.

Previous data reported suggest that males and females are, in general, equally affected by PsA. Among patients with axPsA, whereas Carvalho et al reported that males more commonly present with axial involvement, Nas et al have found a larger...
With regard to laboratory findings, a larger proportion of patients with axPsA in our study were HLA-B27 positive compared with patients not diagnosed with PsA (28.6% vs 14.8%) although the difference was not statistically significant.16 17 19 Interestingly, none of the patients diagnosed with PsA without axial involvement in our study were HLA-B27 positive.

In addition, elevated C reactive protein (CRP) level has been considered strongly associated with incidence of PsA according to a recently published systematic literature review.20 While only one patient with pPsA in our study presented with elevated CRP (>5 mg/L), we have found that 35.7% of patients with axPsA had elevated CRP, and a significant difference was noted when compared with the group of patients not diagnosed with PsA. This finding is consistent with data reported by one study that demonstrated an association between elevated CRP and axial involvement in patients with PsA.21

A major strength of this study is its prospective design that allowed collection of high quality data since there were no missing data from records of patients who underwent a complete clinical and imaging investigation and included in this analysis. Furthermore, we collected data from patients attending 14 different dermatology sites in the Berlin area, which increased the representativeness of this population.

Our study has limitations. First, patients with PsO not fulfilling the referral strategy have not been evaluated; thus, the specificity of the strategy and the negative predictive value could not be evaluated. Furthermore, no validated and established PsA screening tool was part of this project and therefore no comparisons of the performances between our screening tool and already existing screening tools for PsA in general could be applied. In

Figure 2 Imaging features of axial involvement in patients with psoriasis diagnosed with axPsA. This Venn diagram represents imaging overlapping and non-overlapping imaging features in patients diagnosed with axPsA. There are five features spread across the image: radiographic sacroiliitis as per mNY criteria at the upper left corner, active inflammation on MRI of SIJ at the top, structural (post)inflammatory changes on MRI of SIJ at the upper right corner, active inflammation on MRI of spine at the bottom and structural (post)inflammatory changes on MRI of spine at the bottom left. For each, we see the number of patients who presented with a feature defined by a coloured lining and the patients that have overlapping features. The number of overlapping features in patients is also represented in colour. For example, we see that out of 13 patients with active inflammation in spine (MRI), 4 also had structural post inflammatory changes in spine (MRI) as coloured in red. Following, out of eight patients with structural changes SIJ (MRI), three had structural post inflammatory changes in spine (MRI) and three radiographic sacroiliitis (mNY criteria) as represented in light red. mNY, modified New York; SIJ, sacroiliac joint.
addition to that, our screening approached specifically focused on patients with chronic back pain that started before the age of 45 years and therefore patients with a later onset of their axial disease or those with isolated peripheral involvement of their PsA would have been missed. Further, imaging—representing at the same time one the major strengths of the study—had a relatively high impact on the final judgement on the presence or absence of axial involvement. Finally, a relatively small number of patients diagnosed with axPsA introduces some uncertainty in the estimation of the effects in the given populations.

To conclude, our study revealed that application of a dermatologist-centred screening tool may be useful for the detection of PsA (and specifically axPsA) in patients with psoriasis. The tool is easy to apply and not time-consuming, which makes its application feasible in daily practice ideally in combination with a screening for peripheral disease. In addition, the study provided evidence for the important role of imaging (and specifically MRI) in diagnosing axPsA. These results provide valuable real-world insights into the possibility of diagnosing axPsA early with the ultimate goal of improving the care and quality of life of patients living with the disease.

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Table 3  Previous and current treatments of patients diagnosed with psoriasis with pPsA, axPsA and patients not diagnosed with PsA

| Patient group | All patients seen at rheumatology (N=100) | pPsA (N=5) | axPsA (N=14) | No PsA (N=81) | P value* |
|---------------|------------------------------------------|------------|-------------|---------------|---------|
| NSAIDs use | 42 (42.0) | 3 (60.0) | 8 (57.1) | 31 (38.3) | 0.185 |
| Analgesics (non-opioid) | 10 (10.0) | 0 | 2 (14.3) | 8 (9.9) | 0.620 |
| Analgesics (opioid) | 5 (5.0) | 0 | 2 (14.3) | 3 (3.7) | 0.102 |
| Systemic psoriasis therapy—n (%) | 1 (1.0) | 0 | 1 (7.1) | 0 | 0.016 |
| Methotrexate | 11 (11.0) | 0 | 2 (14.3) | 9 (11.1) | 0.722 |
| Systemic retinoids | 2 (2.0) | 0 | 1 (7.1) | 1 (1.2) | 0.155 |
| Phosphodiesterase inhibitor | 1 (1.0) | 0 | 1 (7.1) | 0 | 0.016 |
| Systemic glucocorticoids | 1 (1.0) | 0 | 1 (7.1) | 0 | 0.016 |
| Other therapies | 3 (3.0) | 1 (20.0) | 0 | 2 (2.5) | 0.552 |
| Topical psoriasis therapy—n (%) | | | | | |
| Topical steroids | 78 (78.0) | 5 | 12 (85.7) | 61 (75.3) | 0.394 |
| Vitamin D analogues | 52 (52.0) | 1 (20.0) | 4 (28.6) | 47 (58.0) | 0.041 |
| Topical retinoids | 1 (1.0) | 0 | 0 | 1 (1.2) | 0.676 |
| Topical calcineurin inhibitors | 1 (1.0) | 0 | 0 | 1 (1.2) | 0.676 |
| UVB therapy | 1 (1.0) | 0 | 0 | 1 (1.2) | 0.676 |

*Statistically significant differences between the axPsA and noPsA groups of patients were determined by using Mann–Whitney U test for continuous data and χ² test for categorical data.
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