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# Good clinimetric alignment between remission and a low impact of disease in patients with axial psoriatic arthritis

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## ABSTRACT

**Objective.** *The concept of axial disease in psoriatic arthritis (PsA) is not well established. It is also unclear how this disease domain should be evaluated. We aimed to test whether the remission is aligned with a low impact state of the disease in patients with axial PsA.*

**Methods.** *Post hoc analysis of a multicentre study conducted in 223 patients with PsA under treatment with systemic biological and non-biological therapies. To define axial disease, ASAS criteria were used. Remission corresponded to a BASDAI less than or equal to 2. The impact of the disease was evaluated according to the PsAID. The Cohen's kappa agreement between remission and patient-acceptable symptoms state (PASS) was analysed.*

**Results.** *Thirty-seven of the 223 patients (16.6%) met ASAS criteria for axial disease. Fifteen of the 122 (12.3%) patients in PASS situation had axial disease compared to 22 of 101 (21.8%) who did not reach this state, p<0.05. All items, as well as the total score of the BASDAI (4.48±2.03 vs. 1.14±1.02) were significantly higher in the patients who did not achieve a PASS, p<0.001. The kappa agreement between BASDAI remission and PASS was high [κ: 0.73 (95%CI: 0.64–0.83) p<0.0001].*

**Conclusion.** *BASDAI remission and a low impact of the disease show good clinimetric alignment. Both measures could be useful for a more comprehensive assessment of axial disease in PsA.*

## Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis that may affect up to one-third of patients with psoriasis and that characteristically displays a wide range of manifestations, both joint and extra-articular (1). PsA may result in a variety of manifestations, such as axial and peripheral arthritis, enthesitis, dactylitis, and skin and nail disease. These manifestations usually overlap and change over time (1).

The clinical picture, the imaging distinctive features, as well as the form of the evaluation of the activity, are well-characterised aspects of the peripheral arthritis, dactylitis, and enthesitis that accompany PsA (2). However, the axial or spondylitic involvement of PsA has been less studied, and, most importantly, it has not been characterised as well as the other aforementioned manifestations (3). In fact, the concept of axial disease itself is not fully established in PsA; resultantly, for some authors, the spondylitis of PsA is no more than a classic ankylosing spondylitis (AS) that is associated with psoriasis, while others maintain that this axial involvement exhibits clinical, imaging, and even genetic distinctive features (3, 4).

The most appropriate way to evaluate axial PsA is not yet defined. However, some studies show that the BASDAI and the ASDAS display similar behaviour in axial PsA, specifically regarding the assessment of inflammatory activity and response following drug interventions (5).

Although we currently have different composite indices to evaluate PsA, one of the main issues with using composite indices is that, to a lesser or greater extent, they lose or do not capture all the relevant information that patients can provide (6).

Emphasis has recently been placed on the importance of several patient-reported measures (7). These measures result in a more accurate reflection of how the disease affects several aspects of the patient's life. One of these instruments is the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire, a tool promoted by EULAR to reflect the impact of PsA on various areas of a patient's life (8). Some recent studies show that patients with PsA who achieve their therapeutic goals also achieve an acceptable symptomatic state, according to the PsAID (9). However, there is currently little information on the performance of this tool in patients with axial PsA.

We aimed to analyse the degree of agreement between a patient-acceptable symptoms state (PASS), according to the PsAID, and axial remission, according to the BASDAI, in PsA patients undergoing systemic therapy.

## Patients and methods

Post hoc analysis of the MAAPS study (a Spanish acronym for minimal activity in PsA) was made. The MAAPS

study is a multicentre study that was carried out in 25 outpatient clinics in order to analyse the prevalence of the Minimal Disease Activity (MDA) response, as well as the disease factors associated with it. The main results, as well as the methodological details of the MAAPS study, have been published elsewhere (10).

All patients provided their informed written consent. The study was approved by the Clinical Research Ethics Committee of La Fe Hospital [(ref. number: FPNT-07-14-EO (C)] and was conducted in accordance with the Declaration of Helsinki for human studies. Data was collected between May of 2014 and February of 2015.

The impact of the disease was evaluated according to the PsAID questionnaire. The PsAID questionnaire reflects the impact of PsA from the patient's perspective. It is comprised of 12 physical and psychological domains. Each domain is rated from 0 to 10, with each having a different weight. The total score is divided by 20. The final score has a range from 0 (best status) to 10 (worst status), with a cut-off of 4. A PsAID value of less than four is defined as PASS status (8).

Patients with axial disease were classified according to the Assessment of SpondyloArthritis international Society (ASAS) criteria for axial spondyloarthritis (11). The BASDAI score was used to define axial disease activity. A BASDAI score ≤ 2 was the criterion for axial remission (12). Sacroiliac joint x-rays were assessed following the New York criteria (13).

*Statistical methodology*

A descriptive statistical analysis of all the variables was performed, including central tendency and dispersion measures for continuous variables, as well as absolute and relative frequencies for categorical variables. Student's t-test, the Mann-Whitney U-test, and the Kruskall-Wallis H-test were used to compare quantitative variables, and Pearson's chi-square test or Fisher's exact tests were used for qualitative variables. Concordance was assessed using Cohen's kappa (κ) and was considered as follows: <0.20 = poor, 0.21–0.40 = fair, 0.41–0.60 = moderate, 0.61–0.80 = good, and 0.81–1.00 = very good. The tests were two-tailed with a significance level of 5%. The data was analysed using SPSS v. 19.0 statistical software.

## Results

Out of the 223 patients included in this analysis, 122 (54.7%) were in PASS status. Table 1 shows the clinical characteristics of patients in the PASS state. Fifteen of the 122 (12.3%) patients in the PASS state had axial disease, compared to 22 out of 101 (21.8%) patients who did not reach this state ($p$<0.05). There were no statistically significant differences between patients who achieved PASS status in comparison to those who did not, specifically regarding the use of systemic drugs. The percentage of use of systemic therapies was similar between both PASS and non-PASS patients with axial involvement.

In 85 out of 122 (69.7%) PASS patients, complete radiological study of the axial skeleton was available (pelvic, lumbar, dorsal, and cervical radiographs), while 73 out of 101 (72.3%) non-PASS patients also possessed such studies. The prevalence of radiographic sacroiliitis was 30.6% in PASS patients, *versus* 31.5% in non-PASS patients. On the other hand, the prevalence of syndesmophyte formation was 9.4% in PASS patients, compared to 19.2% in non-PASS patients ($p$=0.07). Most syndesmophytes were formed in the lumbar spine in both groups, but there was no evidence of significant differences between them.

All the items, as well as the total score of the BASDAI (4.48±2.03 *vs.* 1.14±1.02) were significantly higher in the patients who did not achieve PASS status ($p$<0.001). Twenty-five of the 37 patients with axial disease were in BASDAI remission. Seventy-two percent of patients in BASDAI remission were also in PASS status, compared to 16.6% who were in BASDAI remission and were non-PASS ($p$<0.001). The degree of agreement, according to the kappa index, between PASS and BASDAI remission was substantial (κ: 0.73 [95% CI: 0.64–0.83] $p$<0.0001).

**Table I.** Demographic and clinical characteristics of PsA patients with a PsAID score <4.

| | Total n. (122) |
|---|---|
| Male, n (%) | 70 (57.4) |
| Age, mean (SD), yrs. | 54.5 (12.7) |
| BMI, mean (SD) (kg/m$^2$) | 27.1 (3.9) |
| CRP (mg/L), mean (SD) | 2.8 (3.3) |
| Comorbidities, n (%) | |
| Dyslipidaemia | 40 (32.8) |
| HBP | 33 (27.0) |
| Obesity | 30 (24.6) |
| DM | 12 (9.8) |
| PsA clinical patterns, n (%) | |
| Axial | 3 (2.5) |
| Peripheral | 107 (87.7) |
| Mixed | 12 (9.8) |
| DIP disease | 45 (36.9) |
| Familial history, n (%) | |
| Psoriasis | 60 (49.2) |
| PsA | 11 (9.0) |
| Ankylosing spondylitis | 2 (1.6) |
| PsA duration, mean (SD), yrs. | 9.6 (7.9) |
| Skin symptoms duration, mean (SD), yrs. | 21.6 (14.5) |
| Articular symptoms duration, mean (SD), yrs. | 11.9 (8.7) |
| Radiologic findings | |
| Erosions in hands, n (%) | 40 (32.8) |
| Erosions in feet, n (%) | 33 (27.0) |
| PASI, mean (SD) | 1.2 (3.8) |
| HAQ, mean (SD) | 0.2 (0.3) |
| HAQ ≤0.5, n (%) | 104 (85.2) |
| MDA, n (%) | 76 (62.3) |
| Kappa [$CI_{95\%}$] HAQ ≤0.5 *vs.* PsAID <4 | 0.53 [0.42–0.64] |
| Kappa [$CI_{95\%}$] MDA *vs.* PsAID <4 | 0.36 [0.24–0.48] |

MDA: minimal disease activity; SD: standard deviation; BMI: Body Mass Index; CRP: C-reactive protein; HBP: high blood pressure; DIP: distal interphalangeal joint disease; DM: diabetes mellitus; PASI: Psoriasis Area and Severity Index; HAQ: Health Assessment Questionnaire; PsAID: Psoriatic Arthritis Impact of Disease; CI: confidence intervals.

## Discussion

In this post hoc analysis, we found a good alignment between the results of the BASDAI and the PsAID data in patients with axial PsA. In fact, the concordance between BASDAI remission and PASS was quite apparent (κ >0.6). On the other hand, all the components of the BASDAI, as well as the total value thereof, were significantly lower in patients who achieved PASS status.

Slightly more than 16% of the 223 patients analysed in the MAAPS study presented axial disease in accordance with ASAS criteria (11). However,

there were more patients with axial involvement in the group that did not reach PASS status. This perhaps reflects a plus of disease severity in this axial subpopulation, with respect to patients who only displayed peripheral involvement.

Despite the fact that 16% of this series met ASAS criteria for axial involvement, by analysing the axial radiographs of PASS and non-PASS patients, we discovered that around one-third of them (both those with and without PASS status) presented radiographic sacroiliitis. These findings imply that it may be necessary to develop and validate proper criteria to define axial disease in PsA patients, and, on the other hand, that some patients with radiographic involvement probably have few symptoms that may go unnoticed if they do not perform radiological ad hoc studies (14).

We have not collected the axial activity in terms of the ASDAS, which is currently a more in vogue instrument to evaluate the activity of axial spondyloarthritis. However, in patients with axial PsA, both ASDAS and BASDAI scores, show similar good-to-moderate discriminative ability and correlations with different constructs of disease activity (5).

Outcome measures such as BASDAI may overestimate the activity of the disease when patients also have associated fibromyalgia. However, in recent studies it has been shown that although the extreme values of BASDAI could identify a subpopulation with spondyloarthritis and associated depression, the ability of this tool to identify ASAS responders remained intact. On the other hand, the higher or extreme values of BASDAI are good predictors of the discontinuation of anti-TNF-α therapy in patients with spondyloarthritis. All these data reinforce the essential role that the BASDAI still has in the assessment of spondyloarthritis (15, 16).

There are very few instruments that capture the impact of spondyloarthritis on patients' lives. The ASAS Health Index has been developed to assess health in patients with all forms of spondyloarthritis. This self-report questionnaire measures function and health across 17 aspects of health and 9 environmental factors in patients with spondyloarthritis (17). However, the PsAID is a tool that is specifically designed to assess the impact of PsA from a variety of perspectives (8). Our study is one of the first to compare the remission of axial PsA with a low impact of the disease according to the PsAID, demonstrating that both instruments are well aligned.

In this study, we have only analysed the degree of agreement between two continuous measures, but only as regards remission and the symptomatic status acceptable to patients. Therefore, it has not been analysed which part of the variability of one instrument could explain that of the other and viceversa. Moreover, it has been recently shown that no single score threshold but rather an absolute change ≥2 or relative change ≥30% could be better to explain symptomatic deterioration for most BASDAI components (18). Therefore this aspect is an important handicap of our study.

In summary, we have been able to prove that patients with axial PsA in BASDAI remission also have a low impact of the disease according to the PsAID, demonstrating a good clinimetric alignment between both instruments. The information obtained from both sources should lay the foundation for clinical and therapeutic decision making in everyday practice.

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