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Evaluation and stability of the Patient Acceptable Symptom State (PASS) over time in patients with ankylosing spondylitis

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ABSTRACT

Objectives. *The Patient Acceptable Symptom State (PASS) is the value beyond which patients consider themselves well. Our aim was to determine the PASS estimate for patients with AS by assessing pain, disease activity and functional impairment and evaluate whether the PASS is stable over time.*

Methods. *A 4-week prospective study of patients with AS was carried-out. The PASS was estimated at week 2 and 4 for the following patient reported outcomes: global and nocturnal pain measured on a visual analogue scale, disease activity (BASDAI), and functional impairment (BASFI). We used an anchoring method based on patients answering yes or no to, "is your current condition satisfactory, when you take your general functioning and your current pain into consideration?" The PASS was defined as the 75th percentile of the score for patients who considered their state satisfactory. Pearson's chi square and binary logistic regression were used to analyse the data.*

Results. *A total of 200 patients were recruited of whom 110 (55%) were in PASS. The PASS estimates were 60 mm for global pain, 40 mm for night pain, 4.0 for BASDAI and 4.3 for BASFI. These PASS values were stable over time for all criteria except for pain. Significant contributors to PASS were low functional impairment ([BASFI]; p<0.001), low pain intensity (p=0.02), intensive physical activity (p=0.004) and high educational level (p=0.01).*

Conclusion. *A high percentage of Moroccan patients with AS (55%) reported being in PASS. PASS threshold for pain was unexpectedly high, possibly suggesting a high level of patients' tolerance to pain.*

Introduction

There is increasing interest in reporting health status in concepts that are relevant to the individual patient and clearly understood by clinicians. In clinical trials, at the group level, results are usually reported as continuous variables. Translating these continuous criteria (*e.g.* BASDAI score) to more clinically meaningful information would be helpful in better understanding the results of trials and the cut-off chosen for the dichotomisation must be relevant.

Many studies have recently dealt with new concepts such as the minimal clinically important difference (MCID) (1-3), or the minimal clinically important improvement (MCII) (4) that could help in interpreting changes in scores in individual patients by expressing the results as a proportion of improved patients. Another two complementary concepts have been proposed in rheumatology to define absolute health status, namely, Low Disease Activity State (LDAS) or minimal disease activity and the Patient Acceptable Symptom State (PASS) (4, 5) defined as the value beyond which patients consider themselves well. The MCID deals with the concept of improvement (feeling better) and the PASS the concept of well-being or remission of symptoms (feeling good). Thus, the PASS is undoubtedly a clinically relevant outcome for the patient. Moreover, at the end of a trial, it was possible to classify each patient as having a therapeutic success or not based on whether or not the patient achieved the PASS. The results could be expressed as the proportion of patients in a satisfactory state.

The aim of this prospective study was to determine the PASS estimates for the main outcome criteria used to assess patients with AS, evaluate whether the PASS is stable over time and identify contributors to PASS.

Patients and methods

Study design and study population

We conducted a 4-week prospective study involving 200 patients who had a diagnosis of AS according to the modified New York criteria for AS (6). To be included in the study, the patients had to be between 18 and 75 years of age and had to have received daily treatment with a non-steroidal anti-inflammatory drug (NSAID) during the previous month before the enrolment in the study. All patients initially visited the rheumatologist in charge of the patient. The physician could switch from one NSAID to another, during the study period, if the NSAID was not efficient. A second and a final visit to the same

Table I. Demographic and disease baseline characteristics of patients with AS.

Characteristics	Patients with AS (n=200)
Age, mean ± SD years	38.9 ± 12.2
Male sex, n° (%)	160 (72)
Body mass index, mean ± SD (kg/m²)	28.13 ± 5.8
Completed high school, n° (%)	103 (51.5)
Disease duration, mean ± SD years	10.6 ± 7.9
Intensive physical activity, n° (%)	66 (33)
Nocturnal pain (VAS, 0–100 mm)	39 ± 29
Global pain (VAS, 0–100 mm)	46 ± 23
BASDAI (0–10 scale)	4.08 ± 2.23
BASFI (0–10 scale)	4.7 ± 2.9

AS: ankylosing spondylitis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index.

Table II. Patient Acceptable Symptom State (PASS) estimates over time for the outcome criteria in patients with ankylosing spondylitis*.

Parameter	Week 2 (n=200)	Week 4 (n=200)
Global pain (VAS, 0-100 mm)	52	60
Nocturnal pain (VAS, 0-100 mm)	50	40
BASDAI (0-10 scale)	4.2	4.0
BASFI (0-10 scale)	4.4	4.3

*Values are the PASS estimate. The PASS is defined as the 75th percentile of the final score among patients who considered their state to be satisfactory. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index.

rheumatologist were scheduled 2 and 4 weeks later, respectively.

Measurements

At the baseline visit, demographic and disease data consisted of age, gender, body mass index (BMI; kg/m²), level of education (illiteracy, primary school, high school, university), physical activity categorised into low, moderate and high physical activity using the International Physical Activity Questionnaire (IPAQ) which is a validated questionnaire on physical activity (Arabic version) (7, 8), disease duration, global and nocturnal pain measured on a visual analog scale (VAS; 0–100mm), disease activity (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)), and functional impairment (Bath Ankylosing Spondylitis Functional Index (BASFI)).

Patients assessed their status at week 2 and week 4. As previously described (9, 10), we used an anchoring method based on patients' satisfaction with their current status to determine the PASS. The external anchor was patients' answer "yes" or "no" to "taking into account all the activities you have during your daily life, your level of pain and also your functional impairment, do you consider that your current status is satisfactory?" The PASS was estimated at each of the 2 following visits (after 2 and 4 weeks of treatment) for the following patient reported outcomes: global and nocturnal pain intensity as measured on a 0–100 VAS, disease activity as measured on the BASDAI (0–10) and functional impairment as measured on the BASFI (0–10).

Statistical analyses

Descriptive statistics were used to describe the study sample. At each visit the PASS was defined as the 75th percentile of the score for patients who consider their state to be satisfactory (8) (this level of symptoms or a lower level was achieved by 75% of patients with a satisfactory state). We further compared patients in a PASS condition *versus* those who reported not being in a PASS condition for demographic and disease characteristics by descriptive statistics (mean ± SD, median) and using 2-tailed *t*-test. Stepwise logistic regression was used to determine predictors of PASS. Statistical analysis was performed with SPSS 10.0 statistical software package.

Results

A total of 220 patients with AS were enrolled in the study. The mean (SD) age was 38.9 (12.2) years and 168 (76,3%) were male. A total of 200 patients completed the final visit. Among the completers, 110 (55%) indicated that they considered their state, at the final visit, as satisfactory. Baseline characteristics of the patients are shown in Table I.

The PASS thresholds for the patient reported outcomes criteria are listed in Table II. Patients with AS considered their state to be satisfactory if their global pain was <60 mm on the 0–100 VAS. At week 4, the estimates of PASS were 60 mm for global pain, 40 mm for nocturnal pain, 4.0 for the BASDAI (0–10) and 4.3 for the BASFI (0–10). The BASDAI cutoff was 4.0. Patients with BASDAI <4 (PASS positive) were compared with those who reported having BASDAI ≥4 (PASS negative). Univariate analysis demonstrated that all patients reported being in PASS had less global and nocturnal pain, lower BASDAI score and better function (BASFI)) (p<0.001 for all comparisons with PASS negative patients). Patients in PASS had also significantly higher educational level (p=0.01) and intensive physical activity (p=0.01) (Table III). In stepwise logistic regression analysis, being in PASS was significantly and independently associated with lower patient global and nocturnal pain, better function, higher educational level and intensive physical activity (Table IV).

Discussion

In this prospective study, we determined the PASS estimates for the main outcome criteria in patients suffering from AS comprising global and nocturnal pain, the BASDAI and the BASFI. 55% of patients with AS consider themselves to be in an acceptable state.

It should be realised that the concept of PASS is new in rheumatology and it can represents a clinically relevant treatment target. This concept add useful information in daily practice by describing the number of patients achieving and maintaining a good health status for a specified period.

The PASS addresses the concept of well-being which is complementary to other follow-up parameters and has been shown to be important to patients (11). The PASS thresholds in this study were similar and stable over time whatever the outcome criteria except for pain which PASS threshold was unexpectedly high. This stability of the PASS over time for the BASDAI and the BASFI in patients with AS is an interesting finding that confirmed the role of this concept to determine the number of patients in a satisfactory status for a period of time. However, this finding should be validated in further studies with a longer follow-up period. Another interesting result of this study is that the PASS threshold of the BASDAI was found to be 4. Patients with BASDAI <4 reported being in a PASS condition. Clinical studies of treatment for patients with AS have used a BASDAI cutoff of 4 as the major inclusion criteria for entry to the study (12, 13). In addition, the ASAS working group recommended that a BASDAI >4 be used as the primary inclusion criterion for institution of TNF blockers therapy after standard therapies have failed (14). When analysing demographic, social and disease parameters to determine contributors to a PASS condition, patients who were PASS positive had a high level of education, intensive physical activity, lower level of pain and lower BASDAI and BASFI. Multivariate analysis by binary logistic regression confirmed the independence and significance of the association between being in PASS and all contributors' factors to a PASS condition already cited. It is likely that other factors such as psychological and environmental factors unrelated to disease can influence the patients' perception of acceptability of a health status (15-17). Adaptation or high tolerance to pain might explain high PASS threshold of global pain. Moreover, patient expectation might also explain the unexpected high threshold of PASS for global and nocturnal pain. For example, patients with AS treated by anti-TNF therapy might have a positive perception of beneficial effects of this treatment when comparing with NSAIDs and exercise therapy. Then, perception of beneficial effects of treatment will influence patient's conception of PASS. Many previous studies have dealt with the concept of PASS in patients with a rheumatic disease. The first one evaluated the PASS in patients with knee and hip osteoarthritis (9). In this study, PASS thresholds of pain scores were less than those noted in our study. This might be due to other factors like the involvement of weight-bearing joints. The second study was a cross-sectional survey of patients with AS that estimated the

Table III. Univariate analysis of PASS contributors according to the BASDAI score in patients with AS.

Parameter	PASS + (BASDAI <4) (n=110)	PASS – (BASDAI ≥4) (n=90)	*p*-value
Age, mean ± SD years	39.6±13	38.4 ±12.2	0.4
Male sex, n. (%)	88 (57.5)	65 (42.5)	0.1
Body mass index (kg/m²)	28.13±5.57	28.34 ±6.06	0.8
Educational level, n. (%)			
Illiteracy	18 (38.3)	29 (61.7)	
Primary school	35 (70)	15 (30)	0.01
High school	30 (53.6)	26 (46.4)	
University	27 (57.4)	20 (42.6)	
Physical activity, n. (%)			
Low	20 (39.5)	46 (60.5)	
Moderate	40 (58.8)	28 (41.2)	0.01
High	50 (75.8)	16 (24.2)	
Disease duration, mean ± SD years	11.6±8.7	10.9 ±7.3	0.5
Global pain, (VAS, 0–100 mm)	35.8±20.6	60.1 ±19.7	<0.001
Nocturnal pain, (VAS, 0–100 mm)	25±22	58.5 ±25.7	<0.001
BASFI (0–10 scale)	3.7±1.4	7.0 ±2.1	<0.001

AS: ankylosing spondylitis; PASS: Patient Acceptable Symptom State; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index.

Table IV. Multivariate analysis of PASS contributors according to the BASDAI score in patients with AS by a logistic regression analysis.

Odds ratio		95% confidence interval		*p*-value
		Lower	Upper	
Male sex	0.92	0.22	3.85	0.91
Educational level				
Illiteracy	1			
Primary school	0.12	0.02	0.67	0.8
High school	0.74	0.15	3.51	0.7
University	0.85	0.13	5.62	0.01
Physical activity				
Low	1			
Moderate	0.35	0.08	1.44	0.1
High	0.13	0.03	0.51	0.004
Global pain	1.04	0.99	1.07	0.05
Nocturnal pain	1.04	1.00	1.06	0.02
BASFI	1.4	1.17	1.66	<0.001

AS: ankylosing spondylitis; PASS: Patient Acceptable Symptom State; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index.

BASDAI cut-off for acceptable pain and morning stiffness (18). However, the question posed to determine the PASS in this survey differed from the wording used in our study emphasising the importance of standardisation of wording if the concept of PASS is to be developed in the future. Another cross-sectional cohort (10) using the same question to assess PASS thresholds of self reported outcomes in patients with AS validated the concept of the PASS using many approaches, and identified as significant contributors to PASS age, patient global disease activity, and function (BASFI).

In conclusion, our study of patients with AS is added to previous and few studies of rheumatic diseases dealing with a concept of emerging use. The PASS is an interesting tool to evaluate and interpret results obtained in clinical trials or in daily practice in patients with AS. Estimates of PASS according to thresholds for the individual AS self-reported measures must be confirmed and validated in further studies with different data sets, countries, clinical settings, methods of analysis and languages.

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