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Original article

Flare in spondyloarthritis: Thresholds of disease activity variations



Marie Godfrin-Valnet^a, Marc Puyraveau^b, Clément Prati^a, Daniel Wendling^{a,*},^c

^a Service de rhumatologie, CHRU de Besançon, boulevard Fleming, 25030 Besançon, France

^b Methodologie clinique, CIC, CHRU de Besançon, 25030 Besançon, France

^c EA 4266, université de Franche-Comté, 25030 Besançon, France

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ABSTRACT

There is no definition of flare in spondyloarthritis (SpA). The aim of this study was to evaluate thresholds of disease activity variations using validated composite indexes.

Methods: SpA patients (ASAS criteria) prospectively followed with at least two visits, were evaluated. Patients and physician answered at each visit the question: “do you consider your SpA/patient in a state of flare?”. Variations of BASDAI and ASDAS between visits were assessed and associated to the change of perception of a flare (yes/no). ROC curves were built to assess thresholds of variation in BASDAI and ASDAS associated with the change flare between visits.

Results: The patients were issued from a prospective series of 250 SpA. Ninety-nine cases with at least 2 visits were analysed. They were: 67% men, mean age 45 ± 12 years; disease duration: 16 ± 10 years; 84% HLA-B27 positive; purely axial SpA: 81%; PASS at baseline: 56%; mean CRP: 8.6 ± 13.5 mg/l. Mean BASDAI and ASDAS-CRP at baseline were 4.3 ± 2.2 and 2.5 ± 1.1 , respectively. The kappa coefficient of agreement between patient and physician for considering a flare was 0.68. The main results of the ROC curves are: a variation ≥ 2.1 units in BASDAI (sensitivity 59%, specificity 83%), 0.8 units in ASDAS-ESR (sen 56%, spe 91%) or 1.3 units in ASDAS-CRP (sen 47%, spe 100%) is associated to a flare.

Conclusion: We propose thresholds of variations of BASDAI, ASDAS-ESR, and ASDAS-CRP associated to (and that may define) a flare, as considered by the patient and the physician.

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Spondyloarthritis (SpA) is a chronic inflammatory disease with various patterns/profiles of evolution. This disease is most often characterized by episodes of flare (of variable duration), followed by more or less complete remission period. Recognition of flare (as well as remission) is important in the management of the patients [1,2]. There is no clear current definition of a flare of disease in SpA.

Disease activity vary with time and treatment. A more precise definition of the notion of flare may help to the management of the disease. Some studies focused on flare in this condition. Brophy et al. [3], described two types of flare from a series of 214 patients: one localized, and one generalized associated with systemic signs. From the patient perspective, pain, stiffness and fatigue were the most important in the definition of a flare. Stone et al. [4], using graphic illustration, analysed the flare condition in 113 patients; 93% of them reported flares, but 83% reported also persisting symptoms between “flares”. Cooksey et al., [5], reported a flare frequency of about 70% in 134 patients, with variations of BASDAI and BASFI scores according to minor or major flares. However,

none of these studies was able to provide thresholds of variation in disease activity associated to or defining a flare of the disease.

The aim of this study was to determine thresholds of variations in BASDAI and ASDAS scores associated with a flare perceived by the patient and/or the physician, without notion of severity.

1. Methods

A retrospective analysis of prospectively collected information on the active file, monocentric hospital-based, of patients with SpA fulfilling ASAS criteria [6,7] at time of inclusion, was conducted from March 2012 to September 2013. Patients were followed either on scheduled intervals, or on demand (in event of problem). Patients with at least 2 consecutive evaluations were included. At each visit, patient and physician (2 experienced rheumatologists) independently were asked to answer the question: “do you consider your SpA/your patient in state of flare?”. Scores of BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), ASDAS (Ankylosing Spondylitis Disease Activity Score), ASDAS-CRP and ASDAS-ESR, were recorded and correlated to the changes of state (no flare to flare and flare to no flare) evaluated by patient and physician (not aware of the results of the activity scores). ROC

* Corresponding author.

E-mail address: dwendling@chu-besancon.fr (D. Wendling).

Table 1
Thresholds of variation of the scores of activity associated with the perception of flare.

Variation of the activity score	Flare considered by patient and physician	Flare considered by physician	Flare considered by patient
BASDAI	2.1	2.1	2.1
AUC	0.715	0.671	0.694
CI	0.591–0.818	0.568–0.763	0.578–0.794
Specificity %	83	82	83
Sensitivity %	59	53	55
ASDAS-CRP	1.3	0.7	1.3
AUC	0.740	0.698	0.682
CI	0.548–0.881	0.543–0.825	0.501–0.830
Specificity %	100	72	100
Sensitivity %	47	59	40
ASDAS-ESR	0.8	0.8	0.8
AUC	0.779	0.779	0.759
CI	0.583–0.912	0.583–0.912	0.572–0.893
Specificity %	91	91	92
Sensitivity %	56	56	50

AUC: area under the curve; CI: 95% confidence interval.

curves were built to determine the thresholds of variation of the different activity scores according to perception of a flare, with a preference for specificity to have more efficient cut-offs.

2. Results

From the 250 patients followed prospectively, 99 cases with at least 2 consecutive visits with evaluable data were analysed. The main characteristics of this population at the first visit were: 75% men, mean age 45 ± 12 years, with a disease duration of 16 ± 10 years; 93% were HLA-B27 positive. Presentation was purely axial in 82%, peripheral in 13% and mixed in 5% of the cases, according to the ASAS classification. Patients considered themselves in PASS (patient acceptable symptomatic state) in 58.4% of the cases. Disease activity VAS (visual analog scale) by the patient was 4.1 ± 2.8, mean BASDAI was 4.3 ± 2.2, ASDAS-CRP 2.5 ± 1.1 and ASDAS-ESR 2.4 ± 1.1. Mean CRP was 9.9 ± 16.5 mg/l, and ESR 18.3 ± 19 mm. The average number of visits was 3.1 ± 1.3, with an average spacing between 2 visits of 69 ± 43 days.

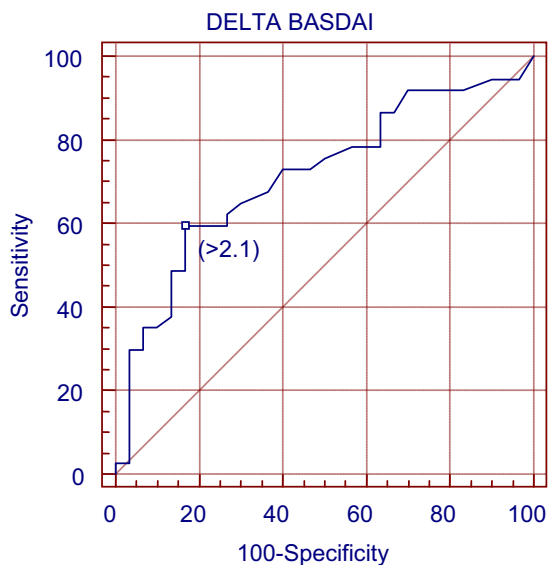


Fig. 1. ROC curve for the threshold of variation of BASDAI between two visits associated with state of flare.

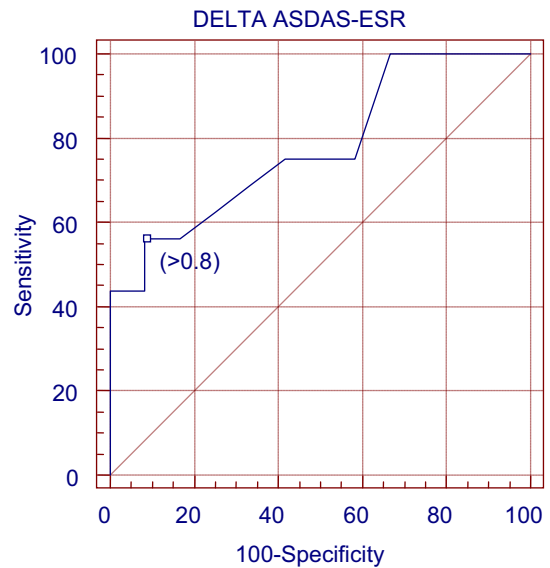


Fig. 2. ROC curve for the threshold of variation of ASDAS-ESR between two visits associated with state of flare.

The perception of a state of flare was reported by 45.4% of the patients, and only 28.9% of the physicians at the same time. Cohen's Kappa score for concordance of flare perception between patient and physician was 0.68. Using ROC curves, a threshold of the variation of the BASDAI associated with a flare was calculated as 2.1, with a sensitivity of 59.5% and a specificity of 83.3% (Table 1, Fig. 1), flare considered by the patient alone, the physician alone or both. For ASDAS-CRP, a variation of at least 1.3 (sensitivity 41%, specificity 100%) and a variation of at least 0.8 for ASDAS-ESR (sensitivity 56.3%, specificity 91.7%) (Table 1, Fig. 2) are associated to a change in perception of state associated to and defining a flare of SpA for the patient and/or the physician. When favoring sensitivity the results are somewhat different: for a sensitivity of 78% the threshold of BASDAI variation is 0.9 (with a specificity of 43%) (Table 2); for a sensitivity of 82%, the threshold of ASDAS-CRP variation is 0.5, with a specificity of 46% (Table 3).

3. Discussion

In this study of patients with SpA, followed prospectively, with at least two evaluations of disease activity and assessment of a flare perceived by the patient and the physician, we were able to propose thresholds of the variation in disease activity (in BASDAI, ASDAS-CRP, ASDAS-ESR) associated with change of status no flare to flare or vice-versa, with a range of thresholds according to sensitivity and specificity. The thresholds proposed had much better specificity than sensitivity, this was chosen in view to select values more specific for a flare, but other thresholds are available in Tables 2 and 3. The best area under the curve was obtained with ASDAS-ESR (Table 1, Table 4). These thresholds are coherent and concordant, whatever flare is recognized by the patient, the physician or both. However, the kappa coefficient for the perception of a flare by the patient and by the physician is not high (0.68); this difference in perception of disease activity between patients and doctors has already been reported [8]. To date, no clear definition of a flare is available and no study evaluated the variations of several activity scores associated to a change from no flare to flare. Using the different ASDAS scores, levels of activity were proposed [9], with some differences between the values of the validation study, and current practice use [10]. In a previous study [10], we reported that a condition of flare was associated with absolute values of BASDAI over 5.2 and ASDAS-CRP over 2.3. Variations in ASDAS-CRP

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