
A proposal on how to assess the weight of the subjective components of the DAPSA in patients with psoriatic arthritis and comorbid fibromyalgia syndrome

M. Di Carlo, M. Tardella, A. Di Matteo, G. Beci, R. De Angelis, F. Salaffi

Rheumatology Clinic, Dipartimento di Scienze Cliniche e Molecolari, Università Politecnica delle Marche, Jesi, Ancona, Italy.

Marco Di Carlo, MD
Marika Tardella, MD
Andrea Di Matteo, MD
Giacomo Beci, MD

Rossella De Angelis, MD, PhD
Fausto Salaffi, MD, PhD

Please address correspondence to:
Marco Di Carlo,
Clinica di Reumatologia,
Università Politecnica delle Marche,
Ospedale Carlo Urbani,
Via Aldo Moro 25,
60035 Jesi (AN), Italy.
E-mail: dica.marco@yahoo.it

Received on November 3, 2019; accepted in revised form on February 3, 2020.

Clin Exp Rheumatol 2020; 38 (Suppl. 123): S60-S64.

© Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2020.

Key words: psoriatic arthritis, fibromyalgia, DAPSA, DAPSA-P, comorbidity

ABSTRACT

Objective. To establish the weight of the subjective components of the Disease Activity index for Psoriatic Arthritis (DAPSA) in psoriatic arthritis (PsA) patients and comorbid fibromyalgia syndrome (FM).

Methods. In PsA patients not fulfilling the DAPSA remission, it has been calculated the DAPSA-patient (DAPSA-P), an index represented by the ratio between the sum of the subjective components (tender joint count+patient global assessment of disease activity+visual analogue scale pain) and DAPSA in its entirety (swollen joint count+tender joint count+patient global assessment of disease activity+visual analogue scale pain+C-reactive protein [in mg/dl]). The DAPSA-P ranges from 0 to 1, and values closer to 1 suggest a major weight of the subjective components, while values closer to 0 indicate a greater contribution of the swollen joint count and C-reactive protein, the two factors more closely related to inflammation. It was also defined as the presence of a comorbid FM, and it was established the DAPSA-P cut-off point distinguishing for the presence of a comorbid FM through the receiver operating characteristic (ROC) curve analysis.

Results. DAPSA-P was higher in all PsA+FM patients. Analysing the receiver operating characteristic curve, the DAPSA-P cut-off distinguishing a comorbid FM was 0.775.

Conclusion. DAPSA-P can help to measure how comorbid FM inflates DAPSA.

Introduction

The protean clinical picture of psoriatic arthritis (PsA) is frequently complicated by the presence of comorbid fibromyalgia syndrome (FM). FM shows a higher prevalence in patients suffering

from inflammatory rheumatic diseases compared to general population and involves approximately the 16-22% of PsA patients (1). It has been demonstrated that FM inflates the measures of disease activity, including patient-reported outcomes, in patients suffering from seronegative spondyloarthritis (2). The role of FM in PsA disease activity indices has been investigated by Brikman and coworkers in an interesting cross-sectional study: subjects with PsA+FM never fulfilled the minimal disease activity criteria, and the composite indices were significantly higher in this kind of patients (3).

On the other hand, to measure disease activity using validated instruments has become the mainstay to manage chronic inflammatory diseases, being a fundamental aspect of the treat-to-target strategy (T2T) (4). While the composite disease activity indices for rheumatoid arthritis (RA) are clearly and largely accepted, such as the 28-joint Disease Activity Score (DAS28) or the Composite Disease Activity Index (CDAI) (5), how to measure disease activity in a multifaceted disease like PsA is still an unresolved issue (6). During the last years, the Disease Activity index for Psoriatic Arthritis (DAPSA) has become the reference tool for monitoring peripheral joint involvement in PsA. DAPSA is easily computed being the algebraic sum of swollen joint count (SJC, 0-66 joints)+tender joint count (TJC, 0-68 joints)+patient global assessment of disease activity (PGA, 0-10 visual analogue scale [VAS])+VAS pain (0-10)+C-reactive protein (CRP, in mg/dl). This index distinguishes among disease activity states with appropriate cut-off values: ≤ 4 for remission (REM), > 4 and ≤ 14 for low disease activity (LDA), > 14 and ≤ 28 for moderate disease activity (MDA), and > 28 for high disease activ-

Competing interests: none declared.

Table I. Differences between age, duration of disease, DAPSA, DAPSA-P and other parameters of disease activity in patients with psoriatic arthritis (PsA) and in patients with psoriatic arthritis and comorbid fibromyalgia syndrome (PsA+FM).

	PsA (126 patients)						PsA+FM (31 patients)					
	Min	Max	Mean	Median	SD	25 - 75 P	Min	Max	Mean	Median	SD	25 - 75 P
Age (years)	26	74	52.65	53.50	11.88	45.00- 61.00	28	80	53.92	56.00	14.18	42.00-62.00
Disease duration (years)	0.5	40.0	10.18	6.00	8.52	4.00- 16.00	1.5	22.0	10.04	9.50	6.38	4.50-16.00
DAPSA	4.08	31.90	13.74	11.53	7.54	8.10- 18.30	7.10	28.10	15.99	16.06	5.60	12.10-18.06
DAPSA-P	0.57	0.991	0.85	0.863	0.10	0.80-0.94	0.73	0.999	0.929	0.96	0.08	0.89- 0.99
VAS pain	0	10	4.69	4.50	2.38	3.00-7.00	1.0	10	6.61	7.00	1.96	5.00-8.00
PGA	1.0	10	4.71	4.50	2.27	3.00-6.00	3.0	10	6.65	6.50	1.92	5.00-8.00
CRP (mg/dl)	0.08	4.40	0.73	0.40	0.82	0.20-1.00	0.02	2.80	0.62	0.29	0.84	0.10-0.60
SJC (0-66 joints)	0	9	1.35	1.00	1.61	0.00-2.00	0	3	0.69	0.00	1.05	0.00-1.00
TJC (0-68 joints)	0	10	2.16	1.00	2.36	1.00-3.00	0	6	1.50	1.00	1.68	0.00- 2.00
LEI	0	6	0.28	0.00	0.68	0.00-0.00	0	6	1.19	0.00	1.67	0.00-3.00

SD: standard deviation; P: percentile; DAPSA: Disease Activity index for Psoriatic Arthritis; DAPSA-P: Disease Activity index for Psoriatic Arthritis-patient; VAS: visual analogue scale; PGA: patient global assessment of disease activity; CRP: C-reactive protein; SJC: swollen joint count; TJC: tender joint count.

ity (HDA) (7). Two of the five DAPSA domains are closely patient-reported measures (PGA and VAS pain), and also TJC can be largely influenced by a central sensitisation of pain. These can be considered subjective parameters. Taking these aspects into account, the objective of this study was to establish the weight of the subjective components of the DAPSA in measuring disease activity in patients suffering from PsA and comorbid FM.

Materials and methods

Patients

This study involved subjects from the outpatient clinic of an Italian tertiary rheumatology centre.

The inclusion criteria were: age >18 years, diagnosis of PsA fulfilling the Classification criteria for Psoriatic Arthritis (CASPAR) (8), and for the purposes of this study were included patients with predominant peripheral joint involvement not in DAPSA REM. Patients with exclusive axial (psoriatic spondylitis or sacroiliitis) or exclusive enthesal inflammatory involvement, or with coexisting inflammatory joint conditions (such as gout or calcium pyrophosphate deposition disease) were excluded.

Assessment

The clinimetric assessment was comprehensive of SJC (0-66 joints), TJC (0-68 joints), PGA (0-10 VAS), and

VAS pain (0-10), carried out by a single assessor (MDC). CRP was collected in mg/dl. With these parameters available, the DAPSA has been calculated and patients have been categorised according to disease activity status (respectively LDA, MDA, and HDA). The presence of a comorbid FM was established by a second assessor (MT or ADM) through the 2016 American College of Rheumatology revised criteria (9).

To calculate the weight of subjective components of DAPSA, in this study we proposed the introduction of a new composite disease activity index, called DAPSA-patient (DAPSA-P). DAPSA-P has been calculated using the following formula: (TJC+PGA+VAS pain)/DAPSA, where the numerator is the sum of the subjective components, while the denominator is represented by the DAPSA in its entirety. The DAPSA-P score is 0 to 1. The closer the DAPSA-P is to 1, the greater the weight of the numerator, and thus the subjective components of the DAPSA. Conversely, DAPSA-P values closer to 0 indicate a greater contribution of the SJC and CRP, the two factors more closely related to inflammation.

Statistical analysis

The Mann-Whitney U-test was used to determine the DAPSA-P differences between the two groups (respectively PsA, and PsA+FM), while to test the DAPSA-P properties in distinguishing

between PsA and PsA+FM patients, we analysed the receiver operating characteristic (ROC) curve, applying the presence of FM as external criterion. As optimal cut-off DAPSA-P value (better discriminatory accuracy, given by the maximum sum of sensitivity and specificity) was chosen the closest point to (0.1).

The statistical analyses were made using the MedCalc 7.1.02 statistical software package for Windows XP (MedCalc Software, Ostend, Belgium).

Results

Cohort features

The cross-sectional study was completed by 157 patients (86 men, 54.7%; and 71 women, 45.3%), with a mean age (\pm SD) of 52.9 \pm 12.4 years (range 26-80 years) and a mean disease duration (\pm SD) of 10.1 \pm 7.9 years (range 0.5-40.0 years). The majority of the patients were treated with methotrexate (105, 66.8%) and 27 (17.2%) with sulphasalazine. Eighty-nine subjects (56.7%) were taking a biologic drug, respectively 22 (14.0%) adalimumab, 18 (11.5%) etanercept, 16 (10.2%) golimumab, 12 (7.6%) certolizumab pegol, 11 (7.0%) secukinumab, and 10 (6.4%) ustekinumab.

In 31 patients (19.7%) was diagnosed a comorbid FM. The main differences between the disease characteristics in the two subgroups of patients are summarised in Table I.

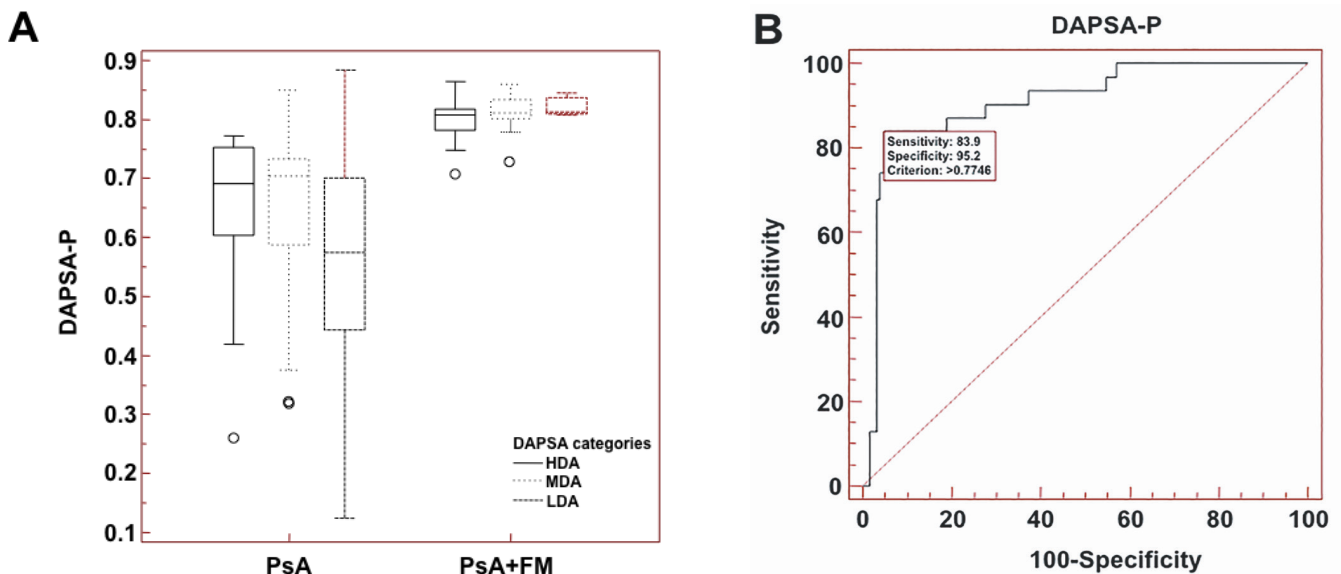


Fig. 1. A: Box-and-Whisker plots of the DAPSA-P scores according to each disease activity status, respectively high disease activity (HDA, solid line), moderate disease activity (MDA, thin dotted line), and low disease activity (LDA, thick dotted line) in patients with psoriatic arthritis (PsA) and in patients with psoriatic arthritis and comorbid fibromyalgia (PsA+FM). Boxes represent the values from the 25th to the 75th percentiles, while middle lines inside boxes represent medians.

B: Receiver operating characteristic curve for the discriminatory ability of DAPSA-P applying the presence of comorbid fibromyalgia as external criterion.

DAPSA-P properties

In patients with comorbid FM, DAPSA-P values were significantly higher in all PsA disease activity states, respectively LDA, MDA, and HDA (Mann-Whitney U test, $p < 0.001$) (Fig. 1A). In addition, DAPSA-P showed good properties in distinguishing the presence of comorbid FM. In particular, when analysing the ROC curve, the optimal cut-off point value was 0.775 (sensitivity 83.87%, specificity 95.24%, positive likelihood ratio 17.61) (Fig. 1B; Table II).

Treatment with biological drugs did not result in significant differences in DAPSA-P (ANOVA, $p = 0.433$).

Discussion

To the best of our knowledge, no other research before had tried to establish the weight of the subjective components of the DAPSA in the context of the index itself. The definition of DAPSA-P, *i.e.* the ratio between the subjective components (numerator) and the clinical index in its entirety (denominator), has been borrowed from a similar approach already taken for the DAS28 (10, 11). With the current investigation, we have revealed how DAPSA-P is significantly higher for all disease activity states in PsA patients with

comorbid FM. Through this kind of index, in particular with the definition of its cut-off point on the ROC curve, we have tried to provide the clinician with a key (fairly easy to apply in daily clinical practice) to understanding FM inflation on the DAPSA.

The problem of defining disease activity in patients with chronic arthritis with comorbid FM remains difficult to solve. On the other hand, it is fundamental to keep in mind how the PsA can manifest with characteristics very similar to those of FM, especially in forms with a predominantly enthesitic involvement (12). In a study by Marchesoni *et al.* in 2012, aimed at establishing the main clinical features capable of distinguishing between FM and PsA, it was found that the presence of at least six somatic symptoms and at least eight tender points is highly suggestive for the presence of FM (13). Generally, imaging techniques (expensive and time-consuming) are needed to support clinical judgment for differential diagnosis. The non-recognition of a comorbid FM in patients with chronic arthritis can lead to misinterpretation of the state of disease activity, which in turn can result in excessive and unnecessary (if not potentially harmful) use of disease-modifying drugs (14).

The impact of comorbid FM on patients with PsA is a recent topic of interest. In 2016, the study by Brikman *et al.* for the first time documented the effect of a comorbid FM on common composite indices of disease activity in patients with PsA. Patients with PsA+FM are not only less likely to achieve MDA, but the common activity indices, including DAPSA, have also been significantly higher (3). A previous investigation of our group demonstrated how a comorbid FM also inflates the measurement of a fully patient-reported index such as the PsA Impact of Disease 12 items (PsAID-12) (15). In the context of the T2T strategy, it is important to carry out FM screening in all patients with PsA, given the high prevalence of this comorbidity. Confirming a prevalence of about 20% of a comorbid FM in PsA, in about one patient out of five the evaluation of disease activity can not fully rely on composite indexes. As recently demonstrated by Iannone *et al.*, the presence of comorbid FM in patients with PsA is one of the major predictors of discontinuation of therapy with biological drugs. The probability of reaching a state of REM or LDA is extremely low in these patients (16). The main limitations of this study are three. In the first instance, a single

Table II. Receiver operating characteristic curve analysis of the optimal DAPSA-P cut-off point applying the presence of a comorbid fibromyalgia syndrome as external criterion.

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	95% CI	-LR	95% CI
>0.625	96.77	83.3 - 99.9	44.44	35.6 - 53.6	1.74	1.4 - 2.1	0.073	0.01 - 0.5
>0.652	93.55	78.6 - 99.2	48.41	39.4 - 57.5	1.81	1.5 - 2.2	0.13	0.03 - 0.5
>0.658	93.55	78.6 - 99.2	49.21	40.2 - 58.3	1.84	1.5 - 2.2	0.13	0.03 - 0.5
>0.661	93.55	78.6 - 99.2	50.00	41.0 - 59.0	1.87	1.5 - 2.3	0.13	0.03 - 0.5
>0.666	93.55	78.6 - 99.2	52.38	43.3 - 61.3	1.96	1.6 - 2.4	0.12	0.03 - 0.5
>0.680	93.55	78.6 - 99.2	56.35	47.2 - 65.2	2.14	1.8 - 2.6	0.11	0.03 - 0.4
>0.684	93.55	78.6 - 99.2	57.14	48.0 - 65.9	2.18	1.8 - 2.6	0.11	0.03 - 0.4
>0.691	93.55	78.6 - 99.2	59.52	50.4 - 68.2	2.31	1.9 - 2.7	0.11	0.03 - 0.4
>0.705	93.55	78.6 - 99.2	62.70	53.6 - 71.1	2.51	2.1 - 3.0	0.10	0.03 - 0.4
>0.710	90.32	74.2 - 98.0	65.08	56.1 - 73.4	2.59	2.2 - 3.1	0.15	0.05 - 0.4
>0.722	90.32	74.2 - 98.0	69.05	60.2 - 77.0	2.92	2.5 - 3.4	0.14	0.05 - 0.4
>0.725	90.32	74.2 - 98.0	71.43	62.7 - 79.1	3.16	2.7 - 3.7	0.14	0.04 - 0.4
>0.733	87.10	70.2 - 96.4	75.40	66.9 - 82.6	3.54	3.0 - 4.2	0.17	0.07 - 0.4
>0.740	87.10	70.2 - 96.4	78.57	70.4 - 85.4	4.06	3.5 - 4.8	0.16	0.06 - 0.4
>0.751	83.87	66.3 - 94.5	82.54	74.8 - 88.7	4.80	4.0 - 5.7	0.20	0.08 - 0.5
>0.762	83.87	66.3 - 94.5	89.68	83.0 - 94.4	8.13	6.9 - 9.6	0.18	0.07 - 0.5
>0.775 *	83.87	66.3 - 94.5	95.24	89.9 - 98.2	17.61	15.0 - 20.7	0.17	0.06 - 0.5
>0.781	77.42	58.9 - 90.4	95.24	89.9 - 98.2	16.26	13.4 - 19.7	0.24	0.09 - 0.7
>0.803	67.74	48.6 - 83.3	96.03	91.0 - 98.7	17.07	13.4 - 21.8	0.34	0.1 - 0.9
>0.807	64.52	45.4 - 80.8	96.83	92.1 - 99.1	20.32	15.6 - 26.4	0.37	0.1 - 1.1
>0.807	61.29	42.2 - 78.2	96.83	92.1 - 99.1	19.31	14.6 - 25.6	0.40	0.1 - 1.2
>0.808	58.06	39.1 - 75.5	96.83	92.1 - 99.1	18.29	13.5 - 24.7	0.43	0.2 - 1.2
>0.809	51.61	33.1 - 69.8	96.83	92.1 - 99.1	16.26	11.5 - 22.9	0.50	0.2 - 1.4
>0.810	45.16	27.3 - 64.0	96.83	92.1 - 99.1	14.23	9.6 - 21.0	0.57	0.2 - 1.6
>0.818	29.03	14.2 - 48.0	96.83	92.1 - 99.1	9.15	5.3 - 15.9	0.73	0.3 - 2.0
>0.825	22.58	9.6 - 41.1	96.83	92.1 - 99.1	7.11	3.7 - 13.7	0.80	0.3 - 2.1
>0.832	19.35	7.5 - 37.5	96.83	92.1 - 99.1	6.10	3.0 - 12.5	0.83	0.3 - 2.2
>0.841	16.13	5.5 - 33.7	96.83	92.1 - 99.1	5.08	2.3 - 11.3	0.87	0.3 - 2.3
>0.845	12.90	3.6 - 29.8	96.83	92.1 - 99.1	4.06	1.6 - 10.1	0.90	0.3 - 2.4
>0.852	12.90	3.6 - 29.8	98.41	94.4 - 99.8	8.13	3.3 - 20.3	0.89	0.2 - 3.5
>0.859	3.23	0.08 - 16.7	98.41	94.4 - 99.8	2.03	0.3 - 14.0	0.98	0.2 - 3.9

DAPSA-P: Disease Activity index for Psoriatic Arthritis-patient; CI: confidence intervals; +LR: positive likelihood ratio; -LR: negative likelihood ratio. *optimal cut-off point.

evaluation was made, without a prospective verification of the new index. Secondly, no instrumental data (e.g. ultrasound) was available, and in a validation study it will be important to consider this aspect of disease activity. Thirdly, an additional limit may be the single centre recruitment.

In this study we propose a new index to interpret the subjective components of DAPSA in patients with PsA and comorbid FM, helping for a quick and practical recognition of painful non-inflammatory symptoms. This paper is certainly not proposed as a work of validation of DAPSA-P, but as an innovative proposal from which to start to lead prospective and multicentre studies.

Ethical approval

All procedures performed were in accordance with the ethical standards of the institutional and/or national re-

search committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from all individual participants included in the study.

References

1. MEASE PJ: Fibromyalgia, a missed comorbidity in spondyloarthritis: prevalence and impact on assessment and treatment. *Curr Opin Rheumatol* 2017; 29: 304-10.
2. SALAFFI F, DE ANGELIS R, CAROTTI M, GUTIERREZ M, SARZI-PUTTINI P, ATZENI F: Fibromyalgia in patients with axial spondyloarthritis: epidemiological profile and effect on measures of disease activity. *Rheumatol Int* 2014; 34: 1103-10.
3. BRIKMAN S, FURER V, WOLLMAN J *et al.*: The effect of the presence of fibromyalgia on common clinical disease activity indices in patients with psoriatic arthritis: a cross-sectional study. *J Rheumatol* 2016; 43: 1749-54.
4. SMOLEN JS: Treat-to-target: rationale and strategies. *Clin Exp Rheumatol* 2012; 30 (Suppl. 73): S2-6.
5. SMOLEN JS, ALETAHA D: Scores for all sea-

sons: SDAI and CDAI. *Clin Exp Rheumatol* 2014; 32 (Suppl. 85): S75-9.

6. LAPADULA G, MARCHESONI A, SALAFFI F *et al.*: Evidence-based algorithm for diagnosis and assessment in psoriatic arthritis: results by Italian DELphi in psoriatic Arthritis (IDEA). *Reumatismo* 2016; 68: 126-36.
7. SMOLEN JS, SCHOELS M, ALETAHA D: Disease activity and response assessment in psoriatic arthritis using the Disease Activity index for Psoriatic Arthritis (DAPSA). A brief review. *Clin Exp Rheumatol* 2015; 33 (Suppl. 93): S48-50.
8. TAYLOR W, GLADMAN D, HELIWELL P, MARCHESONI P, MEASE P, MIELANTS H: Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum* 2006; 54: 2665-73.
9. WOLFE F, CLAUW DJ, FITZCHARLES MA *et al.*: 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Semin Arthritis Rheum* 2016; 46: 319-29.
10. MCWILLIAMS DF, ZHANG W, MANSELL JS, KIELY PD, YOUNG A, WALSH DA: Predictors of change in bodily pain in early rheumatoid arthritis: an inception cohort study. *Arthritis Care Res (Hoboken)* 2012; 64: 1505-13.
11. SALAFFI F, DI CARLO M, CAROTTI M, SARZI-

- PUTTINI P: The subjective components of the Disease Activity Score 28-joints (DAS28) in rheumatoid arthritis patients and coexisting fibromyalgia. *Rheumatol Int* 2018; 38: 1911-8.
12. MARCHESONI A, DE MARCO G, MERASHLI M *et al.*: The problem in differentiation between psoriatic-related polyarthralgia and fibromyalgia. *Rheumatology (Oxford)* 2018; 57: 32-40.
13. MARCHESONI A, ATZENI F, SPADARO A *et al.*: Identification of the clinical features distinguishing psoriatic arthritis and fibromyalgia. *J Rheumatol* 2012; 39: 849-55.
14. ATZENI F, MASALA IF, SALAFFI F, DI FRANCO M, CASALE R, SARZI-PUTTINI P: Pain in systemic inflammatory rheumatic diseases. *Best Pract Res Clin Rheumatol* 2015; 29: 42-52.
15. DI CARLO M, BECCIOLINI A, LATO V, CROTTI C, FAVALLI EG, SALAFFI F: The 12-item Psoriatic Arthritis Impact of Disease Questionnaire: Construct Validity, Reliability, and Interpretability in a Clinical Setting. *J Rheumatol* 2017; 44: 279-85.
16. IANNONE F, NIVUORI M, FORNARO M, VENERITO V, CACCIAPAGLIA F, LOPALCO G: Comorbid fibromyalgia impairs the effectiveness of biologic drugs in patients with psoriatic arthritis. *Rheumatology (Oxford)* 2019 Oct 25 [Epub ahead of print].