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VALIDATION STUDIES

The subjective components of the Disease Activity Score 28-joints (DAS28) in rheumatoid arthritis patients and coexisting fibromyalgia

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Abstract

To determine the contribution of fibromyalgia (FM) to the subjective components of the Disease Activity Score 28-joints (DAS28) in patients with rheumatoid arthritis (RA), and to analyse the discriminatory performance of the derived DAS28 patient-reported components (DAS28-P) to identify patients with fibromyalgic RA. Consecutive RA patients underwent clinical and clinimetric assessment. The DAS28-P index was derived from the components of the DAS28 scores by rearranging the DAS28-ESR formula. Patients were distinguished by the presence of FM. Student parametric t tests or Mann–Whitney non-parametric *U* tests were used to determine any between-group differences. Receiver operating characteristic (ROC) curve analysis was used to test the ability of the DAS28-P index to distinguish patients with RA and those with fibromyalgic RA. The study involved 292 RA patients (80.5% females, mean age 63 years) with a mean disease duration of 11.6 ± 8.5 years. Forty-three patients (14.7%) had concomitant FM, and significantly higher tender joint count ($p < 0.001$), pain numerical rating scale, global health status ($p = 0.007$), and DAS28 scores ($p = 0.006$) than those without FM. The DAS28-P values were also significantly higher in the patients with FM (0.68 ± 0.09 vs 0.58 ± 0.06; $p < 0.001$). The discriminatory power of the DAS28-P was very good (area under the ROC of 0.858, optimal cut-off value of 0.631). The presence of FM strongly influences the DAS28 results. The assessment of patient-reported components to the DAS28 through the DAS28-P can be a useful way to identify patients with fibromyalgic RA.

Keywords Rheumatoid arthritis · Fibromyalgia · Disease Activity Score 28-joints

Introduction

One of the distinct clinical phenotypes of rheumatoid arthritis (RA), a chronic autoimmune disease characterised by systemic inflammation, joint destruction, impaired physical function, and a compromised health-related quality of life (HRQoL) [1, 2], is the coexistence of fibromyalgia (FM). This condition is called "fibromyalgic RA" [3]. Fibromyalgia may be a comorbidity or a continuous phenotypic spectrum associated with variations in central pain processing [4], and it has been estimated that from 10 to 20% of RA patients have a fibromyalgic RA [1, 5, 6]. Fibromyalgic RA is generally characterised by greater pain, higher disease activity scores, and poorer mental health [7, 8]. It has been recently demonstrated that, in comparison with patients with simple RA, those with fibromyalgic RA have worse mental component summary scores on the self-administered Short Form (SF)-36 questionnaire (SF-36 MCS), worse sleep measured by the visual analogue scale (VAS), higher self-counts of tender joints, and higher painDETECT questionnaire (PDQ)

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[9]; none of these patients achieved the remission [10]. Data from the ESPOIR cohort have confirmed these findings in patients with early RA [11].

The Disease Activity Score 28-joints (DAS28), combining swollen joint count (SJC), tender joint count (TJC), a marker of acute-phase response (erythrocyte sedimentation rate [ESR] or C-reactive protein [CRP]), and general health status (GH) into an overall score, is a composite measure of disease activity in RA [12]. GH and TJC are patient-reported measures, while the SJC and acute-phase reactants are objective parameters.

Greater pain contributes to higher DAS28 scores [13, 14]. The TJC can be influenced by the features of FM, and subjects with an elevated TJC may be erroneously considered in a higher disease activity state [15, 16]. Moreover, a greater sensitivity to pain is usually associated with psychological distress, with a consequent worsening of GH [17].

McWilliams et al. demonstrated that, among patients with early RA, less pain improvement is associated with female sex, and a higher proportion of the baseline DAS28 is attributable to its patient-reported components (the DAS28-P index) [18]. The DAS28-P is a derived instrument that allows a quantitative assessment of the non-inflammatory contributors to pain in RA. DAS28-P may be higher in RA patients with coexisting FM. It is currently used in research, but has not yet been validated as a measure of increased pain in patients with long-standing fibromyalgic RA.

The aim of this study was to determine the contribution of FM to the subjective components of the DAS28 and analyse the discriminatory performance of DAS28-P in identifying patient populations.

Materials and methods

Patients

Between June 2015 and September 2017, consecutive RA patients in treatment with conventional disease-modifying anti-rheumatic drugs (cDMARDs: methotrexate, leflunomide, sulfasalazine or hydroxychloroquine) or biological DMARDs (bDMARDs) were recruited at the outpatient clinic of an Italian tertiary rheumatology centre (Rheumatological Clinic, Ospedale "Carlo Urbani", Università Politecnica delle Marche, Jesi, Ancona).

The inclusion criteria were an age > 18 years, the fulfilment of the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for RA [19], and a moderate or high disease activity status (defined by a DAS28-ESR ≥ 3.2).

The presence of FM was identified on the basis of the 2010 ACR criteria, which include the Widespread Pain Index (WPI) and a Symptom Severity (SS) scale, the sum of which is used as a measure of FM [20, 21].

The exclusion criteria were: haemoglobin level < 90 g/L, hematocrit < 30%, leukocyte count $< 3.0 \times 10^9$ cells/L, neutrophil count $< 1.2 \times 10^9$ cells/L, platelet count $< 100 \times 10^9$ cells/L, estimated glomerular filtration rate ≤ 40 mL/min/1.73 m^2 (Cockcroft-Gault), aspartate aminotransferase or alanine aminotransferase levels of > 1.5 times the upper limit of normal, and evidence of active infection, including inadequately treated latent or active *Mycobacterium tuberculosis*.

Assessment

After the collection of the sociodemographic data and of the laboratory parameters (ESR in mm/h, CRP in mg/dL, IgM rheumatoid factor [RF] with a positive cut-off value of > 40 IU/mL as measured by means of nephelometry, and anti-citrullinated protein antibodies [ACPA] with a positive cut-off value of > 10 IU/mL as measured by means of an immunofluorometric assay), the participants underwent a clinic and clinimetric evaluation.

For the purposes of this study, DAS28 was calculated on the classical way using the four variables (considering the ESR) and considering three variables (DAS28v3).

The DAS28-ESR includes 28-SJC and 28-TJC in addition to GH and ESR values. The DAS28v3 is calculated based on 28-SJC, 28-TJC and ESR values. Both DAS28-ESR and DAS28v3 were computed using the Web-site calculator (http://www.das-score.nl/das28).

In the present study, only subjects with moderate (3.2 ≤ DAS28-ESR < 5.1) or high disease activity (DAS28-ESR ≥ 5.1) have been enrolled.

The DAS28-P was calculated by rearranging the components of the DAS28-ESR into the following formula: $(0.56 \times \sqrt{\text{TJC}} + 0.014 \times \text{GH})/\text{DAS28}$.

The patients also completed a questionnaire package including two patient-reported outcomes (PROs): the Recent-Onset Arthritis Disability (ROAD) questionnaire [22], and the Rheumatoid Arthritis Disease Activity Index (RADAI) [23].

The RADAI is a patient-assessed measure of disease activity made of five-items exploring: (a) global disease activity in the previous 6 months; (b) disease activity in terms of current swollen and tender joints; (c) arthritic pain; (d) the duration of morning stiffness, and (e) the rating of tender joints "today" using a mannequin list consisting of 16 joints or joint groups (shoulders, elbows, wrists, fingers, hips, knees, ankles, and toes). The first three items are rated on 0–10 numerical rating scale (NRS), with higher scores indicating greater disease activity. The scores for the last two items, respectively, range from 0 to 6 and from 0 to 48, are transformed to the same 0–10 scale. If all of the items are

answered, the scores are added and divided by the number of items to give a single index of patient-assessed disease activity that ranges from 0 to 10.

The ROAD questionnaire evaluates the physical function [22, 24, 25]. Patients are requested to reply 12 items, each made of a 5-point scale (from 0 = not at all difficult to do, to 4 = impossible to do), to describe the difficulties they found to carry out movements and activities during the previous week. The total score ranges from 0 to 48. However, to express it in a more clinically meaningful way, the score is mathematically normalised to a 0–10 scale (with higher scores representing a poorer status) [22].

Statistical analysis

We calculated both parametric and non-parametric statistics for all variables and questionnaires because not all data met the requirements of being normally distributed and/or continuous. Descriptive statistics were used to describe the sample, and are given as mean values ± standard deviation and median values and interquartile range depending on the distribution (skewness) of the continuous data. The normal distribution was confirmed by Kolmogorov–Smirnov test. Student parametric t tests or Mann–Whitney non-parametric U tests were used to determine between-group differences in DAS28-P. Spearman's correlation coefficient was used to test convergent validity. Correlation values of 0.40 or above were considered satisfactory (rho = 0.81–1.0 as excellent, 0.61–0.80 very good, 0.41–0.60 good, 0.21–0.40 fair, and 0–0.20 poor) [26].

To test the ability of DAS28-P to distinguish patients with simple RA from those with fibromyalgic RA, we used the receiver operating characteristic (ROC) curves created by plotting the proportions of true-positives (sensitivity) and false-positives (100–specificity) for multiple cut-off points. The area under the ROC curves (AUC) was calculated using Wilcoxon's non-parametric signed ranks test to quantify their discriminatory accuracy and compute the optimal cut-off value corresponding to the maximum sum of sensitivity and specificity. AUCs between 0.50 and 0.70 indicate poor accuracy, those between 0.70 and 0.90 are "useful for some purposes", and higher values indicate a high degree of accuracy [27].

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

Results

The cross-sectional study was completed by 292 RA patients (80.5% females), with a mean age of 63 years (range 18–76), a mean disease duration of 11.6 ± 8.5 years, and a mean BMI 26.3 ± 4.3. Two-hundred and five (70.2%) subjects were positive for RF and 181 (61.9%) for ACPA.

The majority of patients were treated with a DMARD (85.3%) and/or a biological agent (37.7%). Of the 110 patients receiving a biologic agent, 32 (29.1%) were receiving etanercept, 29 (26.4%) adalimumab, 18 (16.4%) infliximab, 12 (10.9%) golimumab, 10 (9.1%) abatacept, and 9 (8.2%) tocilizumab. Fifty-eight patients (20.2%) were taking oral corticosteroids at a mean prednisone or equivalent dose of 6.1 mg/day (range 2.5–25), and 101 (34.5%) were prescribed non-steroidal anti-inflammatory drugs (NSAIDs) on demand.

Disease activity was moderate (DAS28 > 3.2) in 198 (67.8%), and high (DAS28 > 5.1) in 94 (32.2%).

Table 1 shows the demographic and disease-related characteristics of the whole cohort, and the results of the comprehensive evaluation.

Forty-three patients (14.7%) had concomitant FM. The fibromyalgic RA patients showed a significant higher TJC ($p < 0.001$), NRS pain (the third item of RADAI) ($p = 0.007$), GH ($p = 0.007$), RADAI ($p = 0.027$), and DAS28 (four variables) ($p = 0.006$), compared to the patients with simple RA (Table 2).

The DAS28-P values were also significantly higher in the patients with fibromyalgic RA (0.68 ± 0.09 vs

Table 1 Demographic and disease-related characteristics of the 292 patients, and the results of the comprehensive baseline clinimetric evaluation

	Median	25th–75th percentile
Age (years)	64.00	53.50–72.50
Disease duration (years)	8.00	4.35–15.50
Education (years)	8.00	8.00–13.00
BMI	25.39	23.01–28.81
ACPA titre (IU/mL)	122.00	10.00–339.25
RF titre (IU/mL)	61.00	10.00–159.80
ESR (mm/h)	31.00	20.00–44.00
TJC (0–28)	6.00	4.00–9.00
SJC (0–28)	4.00	2.00–6.00
Pain NRS (0–10)	7.00	5.00–8.00
GH (0-100)	70.00	60.00–80.00
DAS28	3.81	3.36–4.49
DAS28v3	4.75	4.12–5.39
DAS28-P	0.60	0.56–0.63
RADAI (0–10)	5.79	4.23–7.25
ROAD (0–10)	5.21	3.54–6.46

BMI body mass index, *ACPA* anti-citrullinated protein antibodies, *RF* rheumatoid factor, *ESR* erythrocyte sedimentation rate, *TJC* tender joint count, *SJC* swollen joint count, *NRS* numerical rating scale, *VAS-GH* general health visual analogue scale, *DAS28* 28-joint Disease Activity Score, *RADAI* self-administered Rheumatoid Arthritis Disease Activity Index, *ROAD* Recent-Onset Arthritis Disability Questionnaire

Table 2 Demographic and disease-related characteristics of the patients with simple RA and those with fibromyalgic RA, and the results of the comprehensive baseline clinimetric evaluation

	Rheumatoid arthritis ($n=249$)		Fibromyalgic Rheumatoid Arthritis ($n=43$)		P
	Median	25th–75th percentile	Median	25th–75th percentile	
Age (years)	64.00	53.00–73.00	67.00	56.00–72.00	NS
Disease duration (years)	8.00	5.00–15.000	7.00	4.00–19.00	NS
Education (years)	8.00	8.00–13.00	13.00	7.25–13.00	NS
BMI	25.06	23.27–28.64	25.71	22.89–31.14	NS
ACPA titre (IU/mL)	122.00	10.00–339.50	169.00	4.00–316.75	NS
RF titre (IU/mL)	70.40	19.15–163.20	25.00	10.00–140.25	NS
ESR (mm/h)	32.00	22.00–44.00	24.00	11.25–34.00	NS
TJC (0–28)	6.00	3.00–8.00	12.00	7.25–14.00	<0.001
SJC (0–28)	4.00	2.00–6.00	3.00	1.00–5.75	NS
Pain NRS (0–10)	7.00	5.00–8.00	7.00	6.00–8.00	0.007
GH (0–100)	70.00	60.00–80.00	80.00	62.50–90.00	0.007
DAS28	3.77	3.31–4.31	4.51	3.64–4.73	0.006
DAS28v3	4.73	4.15–5.31	4.93	3.69–5.71	NS
DAS28-P	0.59	0.55–0.62	0.68	0.63–0.72	<0.001
RADAI (0–10)	5.57	4.11–7.05	6.83	4.72–7.76	0.027
ROAD (0–10)	4.79	3.32–6.51	5.83	4.38–6.51	NS

BMI body mass index, *ACPA* anti-citrullinated protein antibodies, *RF* rheumatoid factor, *ESR* erythrocyte sedimentation rate, *TJC* tender joint count, *SJC* swollen joint count, *NRS* numerical rating scale, *VAS-GH* general health visual analogue scale, *DAS28* 28-joint Disease Activity Score, *RADAI* self-administered Rheumatoid Arthritis Disease Activity Index, *ROAD* Recent-Onset Arthritis Disability Questionnaire

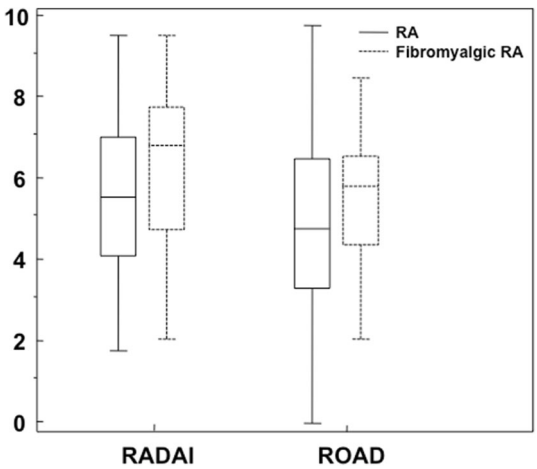

Fig. 1 Box-and-whisker plots comparing the RADAI and ROAD values in RA and fibromyalgic RA patients

0.58 ± 0.06; $p < 0.001$). Similarly, RADAI and ROAD scores were also higher in the patients with fibromyalgic RA (5.62 ± 1.77 vs 6.43 ± 1.89; $p < 0.041$ and 4.95 ± 2.11 vs 5.38 ± 2.02; $p < 0.033$, respectively) (Fig. 1).

There was a very high degree of correlation between the DAS28-P with respect to composite disease activity indices (DAS28, DAS28v3 and RADAI) (all at a p level < 0.0001). The highest correlations were seen between DAS28-P and DAS28 (rho = 0.851). In addition, DAS28-P showed similar correlations with the ROAD (rho = 0.369).

The ability of the DAS28-P to distinguish patients with simple RA from those with fibromyalgic RA was very good, with a ROC AUC of 0.858 (standard error = 0.037; 95% confidence intervals 0.786–0.931). The optimal DAS28-P cut-off value with the highest diagnostic accuracy was 0.631 (sensitivity 81.4%, specificity 80.3%, positive likelihood ratio 4.14) (Fig. 2; Table 3).

Discussion

In this paper, we described how and to what extent FM influences the subjective components of DAS28 in RA patients.

Pain is still the most important problem for patients with inflammatory arthritis, and the area of their health that they would most like to see improved [28, 29]. Active inflammatory disease contributes to pain, but the pain due to non-inflammatory mechanisms can confound disease activity assessment which is central to establish disease severity.

The DAS28 is a composite score calculated on the basis of physician assessment (SJC), blood markers of inflammation, and patient-reported measures (GH and TJC) [30, 31]. The ACR recommendations on the use of disease activity measures for RA do not distinguish between DAS28-CRP and DAS28-ESR, implying that both measurements use the same cut-offs for remission and low disease activity [32].

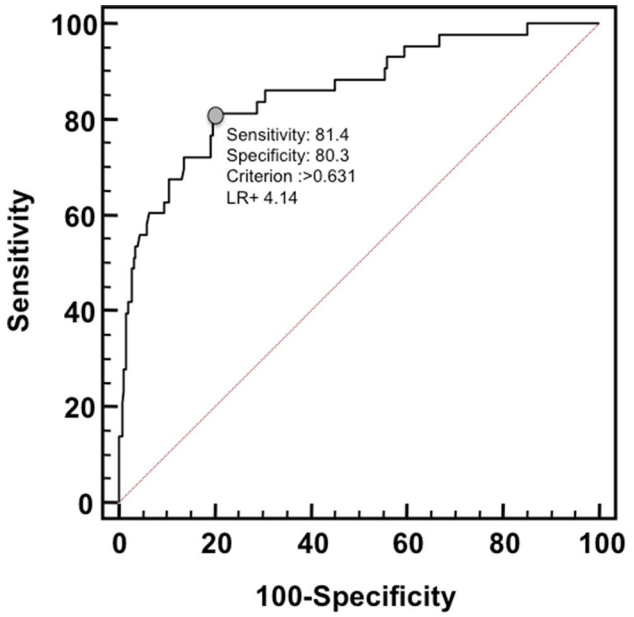

Fig. 2 Receiver operating characteristic curve for the discriminatory DAS28-P power to distinguish patients with RA and fibromyalgic RA. The circle on the curve shows optimal cut-off point, corresponding with the maximum sum of sensitivity and specificity

The 2015 ACR treatment guideline for RA provides cut-offs for DAS28-ESR but does not mention DAS28-CRP [33]. The EULAR and Asia Pacific League of Associations for Rheumatology (APLAR) recommendations for managing RA refer to remission and low disease activity (LDA) calculating DAS28, without specifying whether ESR or CRP should be used [34, 35]. For this study we used DAS28-ESR.

The relationship between FM and RA has been widely investigated. In 1983, Wolfe and Cathey for the first time focused the attention on this association [36], while Lee and colleagues revealed that the FM prevalence is higher in RA patients compared to the general population [37]. Approximately, the 10% of the RA patients in one large U.S. longitudinal cohort study satisfied the criteria for FM at a given time point, and nearly the 20% satisfied the criteria at different times [38]. More recently, Joharatnam *et al*. demonstrated that 48% of their patients with established RA satisfied the same criteria for FM [39].

A number of studies have reported that there is not a close association between pain and objective measures of inflammation [40]. TJC and patient global assessments may both be influenced by generalised hyperalgesia, and chronic inflammation alters the processing of neuropeptides leading to long-term functional/structural changes in innervation, altered neurovascular regulation, and changes in immune function [41]. The pathogenesis of hyperalgesia and allodynia may result from long-lasting nociceptive inputs from inflamed joints, generating peripheral and central sensitisation, and increasing sympathetic nervous system activity [42, 43]. Chronic pain and central sensitisation can lead to disconnections between TJC and SJC that may affect disease evaluation and treatment [40, 44].

Bliddal and Danneskiold-Samsøe underlined the importance of chronic widespread pain in RA patients, and pointed out that not all patients meet the accepted tender point criteria for diagnosing FM [45].

According to Pollard et al., a high ΔTSJ (tender minus swollen joint count) may identify patients with fibromyalgic RA in whom an evaluation of disease activity by means of DAS28 alone may lead to misclassification [14]. A more recent study of a Swedish RA cohort has found that the swollen-to-tender joint count ratio predicts an ACR50 response to TNF inhibitors [46].

DAS28-P assesses the contribution of the patient-reported components to DAS28 scores.

In the present study, patients in low disease activity or remission (DAS28 ≤ 3.2) have been excluded not to inflate the results of DAS28-P itself (a small denominator reduces the variation of the calculation).

DAS28-P may quantitatively evaluate the effect of non-inflammatory factors on the pain experienced by patients with early RA [18]. Joharatnam *et al*. have also found that there is an association between DAS28-P and pain in patients with longer-lasting RA [39]. This suggests that the DAS28 may itself mainly reflect increased pain processing in RA patients with well-controlled inflammatory disease, and should, therefore, be cautiously used when assessing inflammatory disease activity.

The findings of our study confirmed previous reports that 14.7% of the RA patients attending specialist units have co-existing FM [10, 38]. The ability of DAS28-P to distinguish patients with simple RA from those with fibromyalgic RA was good.

Of course, DAS28-P calculation does not exempt the clinician to screen for FM in RA patients. This index should be regarded somewhat as a measure of pain sensitisation. In this sense, DAS28-P is more informative than DAS28v3, which includes TJC, and TJC was higher in fibromyalgic RA.

As expected, disability (measured by ROAD) and disease activity based on a fully PRO like RADAI, showed higher values in fibromyalgic RA patients. How a coexisting FM impacts the results of PROs is a cross-cutting problem in inflammatory arthritis [47].

This study has some limitations that should be taken into account when interpreting the findings. First of all, as it was carried out in a tertiary referral setting, thus patients with more severe RA may be over-represented and it may not be possible to generalise the results to all RA patients in the community. This was due to the need to recruit only patients with a high (DAS28 > 5.1) or moderate level of disease activity (DAS28 > 3.2). According to McWilliams

Table 3 Criterion values and coordinates of the receiver operating characteristic curve

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	95% CI	−LR	95% CI
> 0.5354	97.67	87.7–99.9	14.86	10.7–19.9	1.15	0.8–1.5	0.16	0.02–1.1
> 0.5411	97.67	87.7–99.9	18.07	13.5–23.4	1.19	0.9–1.6	0.13	0.02–0.9
> 0.5501	97.67	87.7–99.9	22.09	17.1–27.8	1.25	1.0–1.6	0.11	0.02–0.7
> 0.5566	97.67	87.7–99.9	25.70	20.4–31.6	1.31	1.1–1.6	0.090	0.01–0.6
> 0.5721	95.35	84.2–99.4	36.55	30.6–42.9	1.50	1.3–1.8	0.13	0.03–0.5
> 0.5801	95.35	84.2–99.4	40.56	34.4–46.9	1.60	1.4–1.9	0.11	0.03–0.4
> 0.5911	88.37	74.9–96.1	48.19	41.8–54.6	1.71	1.4–2.0	0.24	0.1–0.6
> 0.6007	88.37	74.9–96.1	52.21	45.8–58.6	1.85	1.6–2.2	0.22	0.10–0.5
> 0.6101	86.05	72.1–94.7	61.85	55.5–67.9	2.26	1.9–2.6	0.23	0.1–0.5
> 0.6212	81.40	66.6–91.6	71.49	65.4–77.0	2.85	2.4–3.4	0.26	0.1–0.5
> 0.6295	81.40	66.6–91.6	77.91	72.2–82.9	3.68	3.1–4.3	0.24	0.1–0.5
> 0.6296	81.40	66.6–91.6	78.31	72.7–83.3	3.75	3.2–4.4	0.24	0.1–0.5
> 0.6312*	81.40	66.6–91.6	80.32	74.8–85.1	4.14	3.5–4.8	0.23	0.1–0.5
> 0.6353	72.09	56.3–84.7	83.53	78.3–87.9	4.38	3.6–5.3	0.33	0.2–0.6
> 0.6415	72.09	56.3–84.7	86.35	81.4–90.4	5.28	4.4–6.4	0.32	0.2–0.6
> 0.6503	67.44	51.5–80.9	88.76	84.2–92.4	6.00	4.9–7.4	0.37	0.2–0.6
> 0.6602	60.47	44.4–75.0	91.57	87.4–94.7	7.17	5.6–9.2	0.43	0.2–0.7
> 0.6642	60.47	44.4–75.0	91.97	87.9–95.0	7.53	5.9–9.6	0.43	0.2–0.8
> 0.6743	55.81	39.9–70.9	94.78	91.2–97.2	10.69	8.2–14.0	0.47	0.2–0.9
> 0.6785	53.49	37.7–68.8	96.39	93.2–98.3	14.80	11.2–19.6	0.48	0.2–1.0
> 0.6846	41.86	27.0–57.9	97.19	94.3–98.9	14.89	10.5–21.2	0.60	0.3–1.3
> 0.6958	41.86	27.0–57.9	97.99	95.4–99.3	20.85	14.7–29.7	0.59	0.2–1.5
> 0.7005	39.53	25.0–55.6	98.39	95.9–99.6	24.61	17.0–35.6	0.61	0.2–1.7
> 0.7106	30.23	17.2–46.1	98.39	95.9–99.6	18.82	11.9–29.6	0.71	0.3–1.9
> 0.7293	23.26	11.8–38.6	98.80	96.5–99.8	19.30	11.2–33.2	0.78	0.2–2.4
> 0.7374	20.93	10.0–36.0	99.20	97.1–99.9	26.06	14.6–46.6	0.80	0.2–3.2
> 0.7433	16.28	6.8–30.7	99.20	97.1–99.9	20.27	10.3–39.9	0.84	0.2–3.4

LR likelihood ratio, *95% CI* 95% confidence intervals

* Cut-off point with the best combination of sensitivity and specificity

et al. [18], the effects of inactive disease markedly change the output of the DAS28-P formula as small denominators may contribute to high variation in DAS28-P values. Second, the prevalence of FM among our patients may be overestimated because of the overlapping features of FM and RA, such as fatigue and somatic symptoms. However, it may also reflect common underlying mechanisms, or indicate that a subgroup of patients with established RA is susceptible to experience increased pain.

In conclusion, RA patients frequently have associated FM and, therefore, report persisting pain even when inflammation is well controlled. DAS28 of patients whose assessments are discordant with those of their physicians may not accurately reflect disease activity. The DAS28-P may be a convenient and useful means of identifying patients with fibromyalgic RA and selecting patients for specific treatments. Further prospective research is warranted to explore the use of the DAS28-P in larger and more generalisable populations.

Author contributions FS and MDC contributed to the study design, data collection, data analysis, the interpretation of the results, and the preparation of the manuscript. MC contributed to the revision of the manuscript. PSP contributed to the revision of the manuscript and the design of the study. All of the authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest All the authors declare that they have not received any financial support or other benefits from commercial sources for the work described in this paper. They also declare that they have no other financial interests that could create a potential conflict of interest or the appearance of a conflict of interest with regard to this work.

Ethical approval All the procedures in this work were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent Informed consent was obtained from all individual participants included in the study.

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