From pain catastrophising to multidimensional psychological distress: unravelling the complexity of difficult-to-treat psoriatic arthritis

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Abstract

Objective

Pain catastrophising (PC), a maladaptive cognitive response to pain, has been implicated in poor outcomes in inflammatory arthritis, but its relationship with psoriatic arthritis difficult-to-treat (D2T) remains underexplored. This study aimed to investigate how the D2T phenotype impacts pain catastrophising (PC) and its domains (helplessness, rumination, magnification), along with other psychosocial and functional dimensions in PsA patients.

Methods

A cross-sectional study was conducted in a cohort of 182 PsA patients. Clinical and psychosocial data were collected, including Disease Activity for Psoriatic Arthritis (DAPSA), Minimal Disease Activity (MDA), Pain Catastrophising Scale (PCS), HADS anxiety and HADS depression. Univariable and multivariable regressions were used to evaluate psychometric variables associated with D2T.

Results

Univariable analysis showed a significant association between high PCS scores and D2T status. Multivariable models, adjusted for age, sex, disease duration, BMI, fibromyalgia, and disease activity, confirmed this relationship (b=7.637, 95% CI 3.261–12.014, p=0.001), specifically with PCS' dimensions helplessness and rumination, but not magnification. Additionally, D2T predicted higher HADS anxiety scores, while its association with HADS depression was not statistically significant.

Conclusion

Our results indicate that D2T status remains a significant predictor of PC, even when controlling for relevant clinical characteristics, including fibromyalgia and disease activity, highlighting the intricate relationship between D2T PsA and psychological dimensions, which may exacerbate disease burden and hinder treatment targets.

Key words

psoriatic arthritis, difficult to treat, pain catastrophising, anxiety, depression

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Introduction

Psoriatic arthritis (PsA), a multifaceted inflammatory disease affecting up to 30% of psoriasis patients, is characterised by heterogeneous clinical manifestations, including arthritis, enthesitis, dactylitis, and axial involvement, which can vary independently of the severity of skin or nail psoriasis. The pathogenesis involves genetic predispositions, environmental factors, and dysregulated immune responses, particularly in the IL-17/IL-23 axis. Recent progress in targeted treatments, including biologics and small-molecule inhibitors, has greatly improved outcomes by treating both joint and skin symptoms. However, early diagnosis, clinical variability, and the impact of the disease on quality of life remain key challenges (1).

Pain in inflammatory arthritides, including PsA, arises from joint inflammation but is also significantly influenced by psychosocial factors. Anxiety and depression are well-known factors that can negatively affect the subjective (patient-reported) components of the clinimetric indices used to assess disease remission and/or low disease activity. (2, 3). Moreover, a growing body of literature highlights the pivotal role of pain catastrophising (PC) (4, 5), defined as an exaggerated negative cognitive and emotional response to actual or anticipated pain. It describes a maladaptive cognitive style often observed in individuals with anxiety and depression (5-9). The Pain Catastrophising Scale (PCS) evaluates PC across three dimensions: Rumination, persistent and intrusive thoughts about pain; Magnification, overestimation of the severity and threat posed by pain; Helplessness, the perception of being unable to cope with pain effectively (10, 11). Previous research demonstrated that higher levels of PC negatively affect the likelihood of achieving remission or low disease activity in inflammatory arthritides (4, 12, 13), and were significantly associated with an increased risk of therapy discontinuation (14).

Since PC is generally conceptualised as a relatively stable trait, previous research has primarily focused on its predictive role in various patient-reported outcomes. However, PCS captures both state and trait components (15, 16), with evidence suggesting that PC is malleable depending on patients' clinical status. For instance, medical treatments significantly improved PC over time in patients with RA (17) and with lumbar spinal stenosis (18). Accordingly, PC may not only be considered a maladaptive trait predicting worse clinical outcomes, but also a psychological reaction to unresolved musculoskeletal conditions. Similarly, symptoms of anxiety and depression may increase as a consequence high disease activity (19).

The treatment of inflammatory rheumatic diseases, including PsA, has greatly progressed with the use of biological and targeted synthetic therapies (21, 22). These approaches, guided by treat-to-target strategies, aim for disease remission. However, some PsA patients remain difficult-to-treat (D2T), showing ongoing disease activity despite multiple treatments (23, 24). Although D2T criteria exist for rheumatoid arthritis (RA), there is no standardised definition for D2T PsA (25). Still, researchers are working to establish criteria for D2T PsA by considering factors such as disease activity, treatment response, comorbidities, and quality of life (26-30).

Research investigating clinical factors that explain PC in PsA is still limited. Wilk *et al*. found that biological subjective parameters (*e.g*. 28-tender joint count) were more influential on PC than biological objective, psychological, and social parameters across RA, PsA, and AxSpA diagnoses (5). Specifically, factors independently associated with PC in PsA were higher tender joint count, pain, and lower functional status.

Against this background, the objective of the present study was to examine the role of D2T status and other disease-related and clinical factors on PC (and its dimensions), anxiety, and depression. Specifically, we explored if D2T status was associated with these outcomes when controlling for other relevant clinical characteristics.

Materials and methods

Participants and procedure

A cross-sectional observational study was conducted involving PsA patients

enrolled at the Arthritis Center, Rheumatology Clinic of Fondazione Policlinico Campus Bio-Medico in Rome. Consecutive outpatients were recruited between November 2023 and June 2024. Inclusion criteria encompassed individuals of both genders, aged over 18 years old, who fulfilled the Classification Criteria for Psoriatic Arthritis (CASPAR) (31). Exclusion criteria included a history of or current psychiatric disorders as per DSM 5 with the exception of anxiety and depressive disorders, a history of malignancy, a current pregnancy, age exceeding 85, or an inability to provide informed consent for participation in the study. Psychiatric exclusions were applied based on the inspection of each patient's electronic health record, which includes comorbid conditions diagnosed by a psychiatrist and/or self-reported by the patient at the time of their first hospital visit. The study received approval from the Ethics Committee of the University Campus Bio-Medico of Rome and was carried out in accordance with the Declaration of Helsinki and its subsequent amendments (approval no. 78.20 OSS).

Measures

Pain catastrophising was measured with the PCS (10), which consists of 13 items rated on a 5-point Likert scale ranging from 0 (not at all) to 4 (all the time). It provides a total score and three subscales, namely rumination (sample item: 'I keep thinking about how much it hurts'), helplessness (sample item: 'It's awful and I feel that it overwhelms me'), and magnification (sample item: "I become afraid that the pain may get worse"). Higher scores indicate higher levels of catastrophising. Depressive-anxious symptoms were measured with the Hospital Anxiety and Depression Scale (HADS) (32). It comprises two subscales (*i.e.* HADS-A, HADS-D) to measure anxiety and depression, respectively. Each subscale is composed of 7 items which are rated on a 4-point Likert scale, ranging from 0 to 3. Higher scores indicate greater anxiety and depression. A cut-off score of 8 on each scale discriminates between cases without (<8) and those with a possible anxiety/depressive disorder. D2T PsA patients were identified according to the D2T criteria proposed by Perrotta *et al*. (27, 29). All three criteria must be present to define a PsA patient as *D2T*: i. Treatment according to European League Against Rheumatism recommendation and/or GRAPPA recommendations and failure of ≥2 biologic/targeted synthetic DMARDs (b/tsDMARDs, with different mechanisms of action) after failing conventional synthetic disease-modifying anti-rheumatic drugs (csDMARD) therapy (unless contraindicated); ii. Signs and/or symptoms suggestive of active/progressive disease, defined as ≥1 of: a. At least moderate disease activity (according to validated composite measures including joint counts, for example, DAPSA ≥14 or not achieving the Minimal Disease Activity criteria (MDA); b. Signs (including acute phase reactants and imaging) and/or symptoms suggestive of active disease (joint related or other); c. Rapid radiographic progression (with or without signs of active disease); d. Well-controlled disease according to above standards but still having PsA symptoms that are causing a reduction in quality of life; iii. The management of signs and/or symptoms perceived as problematic by the rheumatologist and/or the patient. Moreover, the following data were collected: age, sex, body mass index (BMI), Disease Activity for Psoriatic Arthritis (DAPSA), Minimal Disease Activity (MDA), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) – applied only to the population with axial involvement – Psoriasis Area Severity Index (PASI), Leeds Enthesitis Index (LEI), presence of uveitis and inflammatory bowel disease (IBD), treatments, disability and physical function via the Health Assessment Questionnaire (HAQ) (33), the presence of metabolic syndrome (MetS) according to NCEP-ACT III criteria. Patients fulfilling the 2016 American College of Rheumatology revised criteria for fibromyalgia were further identified in our cohort (34).

Data analyses

Continuous variables are described as median (25–75th percentile), whilst categorical variables are described as percentages (%). The Shapiro-Wilk test was used to evaluate the normality of data. Chi square test was used for the analysis of contingency tables, while Mann-Whitney test and Kruskal-Wallis with Holm's pairwise comparison corrections were used to compare ranks.

Table I. Main demographic, anthropometric and clinical characteristics of the study sample.

	PsA (n=182)
Age	58.5 (53-65)
Female	119 (65.4%)
D2T	47 (25.8%)
Disease duration, months	72 (25-132)
BMI	27 (24.5-30.2)
MetS	73 (42.9%)
Fibromyalgia	66 (37.1%)
Smoking	67 (36.8%)
Periferal joint involvement:	
Oligoarticular	137 (77.4%)
Polyarticular	26 (14.7%)
Axial involvement	87 (50.9%)
Enthesitis	72 (39.6%)
Dactylitis	23 (13.1%)
Psoriasis	113 (63.1%)
Onychopsoriasis	34 (19.1%)
Uveitis	4 (2.2%)
IBD	10 (5.6 %)
cDMARDs	78 (42.9%)
b/tsDMARDs	130 (71.4%)
CCs	29 (15.9%)
NSAIDs	53 (29.3%)
TJ	1 (0-5)
SJ	0 (0-1)
PP	5 (3-8)
PtGA	5 (2-7)
Phyga	0 (0-2)
LEI	0 (0-0)
Dactylitis	0 (0-0)
CRP	0.26 (0.1-0.48)
ESR	15 (7-23)
HAQ	1 (0.13-1.63)
PASI	0 (0-0.4)
DAPSA	12.3 (4.23-22)
BASDAI	5.15 (2.6-7.15)
MDA	64 (36.2%)

D2T: difficult-to-treat; BMI: Body Mass Index; MetS: metabolic syndrome; IBD: inflammatory bowel disease; csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs: biologic disease-modifying anti-rheumatic drugs; HCQ: hydroxychloroquine; CCS: corticosteroids; NSAIDs: non-steroidal anti-inflammatory drugs; TJ: tender joints; SJ: swollen joints; PP: patient pain; PtGA: patient global assessment; PhGA: Physician global assessment; LEI: Leeds Enthesitis Index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; PASI: Psoriasis Area Severity Index; DAPSA: Disease Activity in PSoriatic Arthritis; CCs: corticosteroids; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; MDA: minimal disease activity.

To evaluate the associations between demographic, clinical variables, including D2T (independent variables), with PC, anxiety, and depression (dependent variables), univariable and multivariable regressions were performed. For the latter, we omitted several variables that were significant in the univariate analysis, as different variables resulted in high multicollinearity when considered at the same time in the multivariable analysis. Additionally, we created two separate multivariable models: one using DAPSA as the disease activity index and another applying a stricter criterion, such as MDA, to assess disease control. The statistical analyses were performed using Stata v.14 and *p*-values <0.05 have been considered as significant.

Results

Sample characteristics

The analysed cohort was composed of 182 patients affected by PsA with a median age of 58.5 (53–65) years and a larger percentage of females (65.4%) (Table I). Of note, 47 participants (25.8%) showed a D2T phenotype. The median disease duration (namely, time since diagnosis) was 72 (25–132) months. CsDMARDs were used by 78 patients (42.9%), and bDMARDs or the phosphodiesterase-4 (PDE-4) inhibitor, were used by 130 patients (71.4%).

Our patients showed a median DAPSA value of 12.3 (4.23–22), and a median BASDAI score of 5.15 (2.6–7.15); 64 participants (36.2%) achieved MDA criteria. Of interest in PsA, concomitant fibromyalgia was present in 66 patients (37.1%). Furthermore, we observed a BMI median value of 27 (24.5–30.2) and 73 patients (42.9%) were classified as affected by MetS.

Considering the psychometric scales, PCS median value in our sample was 18 (6–32). Regarding its dimensions, the median value for Helplessness was 7 (2–14), for Rumination was 7 (2–13.5), and for Magnification was 3 (1–5). Moreover, the median value forHADS anxiety was 6 (3–10), and for HADS depression was 5 (2–8).

The influence of D2T status on pain catastrophising

Considering PCS as the dependent variable, univariable analysis revealed a significant relationship between high PCS scores and D2T status in our patients (b=14.5, 95%CI 10.1 to 18.9, *p*<0.0001). Moreover, elevated PCS levels were associated with female sex, concomitant fibromyalgia and comorbid MetS. PCS was also significantly associated with all composite scores, specifically with high disease activity as measured by DAPSA and BASDAI, as well as with not being in MDA (Table II).

In multivariable analyses (Table III), D2T was an independent predictor of PCS (b=7.6, 95%CI 3.2 to 12.01, *p*=0.001), after adjusting for age, sex, disease duration, BMI, concomitant fibromyalgia, and MDA (Model 1). In Model 2, which adjusted for the same variables except MDA and included DAPSA as an additional covariate, D2T remained independently associated with PCS. Fibromyalgia (b=4.4, 95%CI 0.2 to 8.5, *p*=0.039) and MDA (b= -11.296, 95%CI -15.7 to -6.8, *p*<0.0001) were also significantly associated with higher PCS scores. Furthermore, disease duration showed a modest but significant negative association with PCS (b= -0.022, 95%CI -0.042 to -0.001, *p*=0.04).

Table II. Univariable analysis of factors associated with pain catastrophising as the dependent variable.

	B	95%CI	*p*
Age	0.048	-0.140-0.236	0.6
Sex	8.859	4.543-13.170	**<0.0001**
Disease duration (months)	-0.033	-0.056-0.009	**0.007**
D2T	14.529	10.136-18.922	**<0.0001**
BMI	0.544	0.081-1.006	**0.02**
MetS	13.718	9.678- 17.758	**<0.0001**
Fibromyalgia	12.454	8.353-16.556	**<0.0001**
Smoking	2.311	-1.105-5.728	0.2
Peripheric involvement	4.30	-0.477-9.096	0.08
Axial involvement	-1.445	-5.833-2.942	0.5
Entesitis	-1.471	-5.856- 2.914	0.5
Dactylitis	3.108	-3.233-9.449	0.3
Psoriasis	-2.070	-6.526-2.387	0.4
Nail involvement	1.800	-3.683-7.282	0.5
Uveitis	-3.484	-17.838- 10.870	0.6
IBD	1.819	-7.440-11.077	0.7
csDMARDs	-1.241	-5.607-3.125	0.6
csDMARDs line	0.081	-2.141-2.303	0.9
bDMARDs	4.452	-0.373- 9.276	0.07
bDMARDs line	3.214	1.564- 4.864	**<0.0001**
HCQ	-2.821	-31.418-25.776	0.8
CCs	-2.025	-6.048-1.998	0.3
NSAIDs	3.272	-1.452- 7.996	0.2
TJ	1.101	-0.602- 1.601	**<0.0001**
SJ	2.105	0.698-3.512	0.004
PP	2.788	2.197-3.379	**<0.0001**
PtGA	2.628	2.015-3.240	**<0.0001**
PhyGA	3.085	1.315-4.855	**0.001**
LEI	2.063	-2.260-6.386	0.3
CRP	0.519	-1.023- 2.062	0.5
ESR	0.124	-0.017-0.265	0.08
HAQ	10.545	8.417-12.673	**<0.0001**
PASI	-0.442	-2.266- 1.383	0.6
DAPSA	0.739	0.548-0.930	**<0.0001**
BASDAI	3.240	2.571- 3.908	**<0.0001**
MDA	-17.222	-20.898- -13.546	**<0.0001**

D2T: difficult-to-treat; BMI: Body Mass Index; MetS: metabolic syndrome; IBD: inflammatory bowel disease; csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs: biologic disease-modifying anti-rheumatic drugs; HCQ: hydroxychloroquine; CCs: corticosteroids; NSAIDs: non-steroidal anti-inflammatory drugs; TJ: tender joints; SJ: swollen joints; PP: patient pain; PtGA: patient global assessment; PhGA: physician global assessment; LEI: Leeds Enthesitis Index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; PASI: Psoriasis Area Severity Index; DAPSA: Disease Activity in PSoriatic Arthritis; CCS: corticosteroids; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; MDA: minimal disease activity.

Multivariable analyses for PCS dimensions (helplessness, rumination, and magnification) are shown in Table IV. Overall, D2T was an independent predictor of higher helplessness and rumination, but not magnification. This pattern of associations remained consistent across Model 1 – adjusting for relevant characteristics including MDA – and Model 2, which included DAPSA.

Specifically, Model 1 showed that helplessness was strongly influenced by D2T status (b=4.08, 95%CI: 2.1 to 6.02, $p<0.0001$), fibromyalgia (b=2.4, 95%CI 0.5 to 4.2, $p=0.01$), disease duration (b= -0.01, 95%CI -0.01 to -0.01, $p=0.02$), and MDA (b=-4.3, 95%CI -6.3 to -2.3, $p<0.0001$). This analysis also revealed an association between high rumination scores and D2T (b=2.9, 95%CI 1.04 to 4.7, $p=0.002$), and with not being in MDA (b= - 6.05, 95%CI -7.9 to -4.1, $p<0.0001$). Interestingly, none of the variables emerged as independent predictors of magnification.

Table III. Multivariable analyses of factors associated with pain catastrophising as the dependent variable.

	B	95%CI	*p*
Model 1			
Age	-0.028	-0.193-0.137	0.7
Sex	1.330	-2.796-5.460	0.5
Disease duration (months)	-0.022	-0.042- -0.001	**0.04**
BMI	0.096	-0.308-0.500	0.6
Fibromyalgia	4.400	0.229-8.570	**0.04**
MDA	-11.296	-15.766- -6.826	**<0.0001**
D2T	7.637	3.261-12.014	**0.001**
Model 2			
Age	0.275	-0.144-0.1988	0.7
Sex	0.430	-3.883-4.742	0.8
Disease duration (months)	-0.291	-0.050- -0.008	**0.007**
BMI	0.060	-0.378-0.498	0.8
Fibromyalgia	4.925	0.352-9.499	**0.03**
DAPSA	0.118	0.186-0.655	**0.001**
D2T	8.099	3.272-12.925	**0.001**

D2T: difficult-to-treat; BMI: Body Mass Index; DAPSA: Disease Activity in PSoriatic Arthritis; MDA: minimal disease activity.

The influence of D2T status on anxiety and depression

Taking into account HADS anxiety and HADS depression as dependent variables, both showed significant associations with D2T in univariable analyses. Anxiety had a strong positive relationship (b=3.7, 95%CI 2.2 to 5.2, $p<0.0001$), as did Depression (b=2.8, 95%CI 1.5 to 4.2, $p<0.0001$) (Supplementary Table S1).

Of note, multivariable models with HADS anxiety and depression as dependent variables, adjusted for key covariates (age, sex, disease duration, BMI, D2T, fibromyalgia and MDA), confirmed D2T as a predictor of elevated levels of anxiety (b=2.05, 95%CI 0.3 to 3.7, $p=0.01$). Conversely, the association between HADS depression and D2T did not reach statistical significance. Notably, MDA achievement was inversely associated with both anxiety (b= -3.04, 95%CI -4.7 to -1.3, $p=0.001$) and depression (b= -2.2, 95%CI -3.7 to -0.8, $p=0.002$) (Suppl. Table S2).

Discussion

This study evaluated a cohort of 182 PsA patients, revealing significant insights into the interplay between D2T status and relevant psychological characteristics, including PC, anxiety, and depression.

The key finding of the present study is that D2T status emerged as a robust independent predictor of high levels of PC and anxiety, but not depression. We also explored which specific dimensions of PC were most sensitive to D2T status, finding that helplessness and rumination about pain, but not magnification, were key psychological characteristics related to D2T.

Our results indicate that D2T status remains a significant predictor of PC, even when controlling for relevant clinical characteristics, including fibromyalgia, DAPSA, and MDA. Fibromyalgia, a prototype of central sensitisation syndromes, is highly prevalent in D2T patients and has been linked to PC (29, 35, 36). In our sample, while fibromyalgia was associated with higher PC levels, potentially reflecting central sensitisation mechanisms (37), D2T status showed a stronger independent association. This suggests that D2T may exacerbate catastrophising responses to pain, independently of fibromyalgia. Notably, the D2T-catastrophising association also appeared to be independent of DAPSA and MDA, both of which were also significantly associated with PC. The latter finding is in line with previous studies showing higher levels of PC in PsA patients with a DAPSA score greater than 14 (4). Overall, our data suggest that multidimensional disease control and management (*i.e.* targeting fibromyalgia, disease activity, refractoriness) may reduce patients' catastrophising responses. Specifically, the independent D2T-catastrophising association suggests that D2T patients experience catastrophising responses to pain, even when disease is under control (*i.e.* low disease activity and being in MDA). As a possible explanation, D2T status may reflect specific aspects explaining PC, not captured by DAPSA and MDA. For instance, treatment failure, a hallmark of D2T, may affect not only clinical signs and symptoms but also patients' perceptions of the possibility to control the disease and alleviate pain-related suffering, potentially leading them to feel helpless and to ruminate on pain (38). Alternatively, the D2T-catastrophising association may reflect unaddressed central sensitisation independent of fibromyalgia.

Further analysis of PCS dimensions revealed distinct patterns of associations. Helplessness was independently associated with D2T status, absence of MDA, presence of fibromyalgia, and shorter disease duration. Similarly, rumination was independently predicted by D2T status and absence of MDA. However, magnification did not exhibit significant associations, suggesting its

Table IV. Multivariable analyses of factors associated with the dimensions of pain catastrophising as dependent variables.

	Helplessness			Rumination			Magnification		
	B	95%CI	*p*	B	95%CI	*p*	B	95%CI	*p*
Model 1									
Age	-0.020	-0.093-0.053	0.6	-0.026	-0.096-0.450	0.5	0.017	-0.02-0.055	0.4
Sex	0.390	-1.430-2.220	0.7	0.213	-1.555-1.976	0.8	0.603	-0.35-1.55	0.2
Disease duration (months)	-0.010	-0.019 - -0.011	**0. 02**	-0.008	-0.016- -0.001	0. 09	-0.004	-0.010- -0.001	0.1
BMI	0.056	-0.123- 0.235	0.5	0.009	-0.163- 0.182	0.9	0.035	-0.058- 0.127	0.5
Fibromyalgia	2.407	0.559-4.255	**0.01**	1.137	-0.646-2.921	0.2	0.922	-0.038-1.882	0.06
MDA	-4.376	-6.357- -2.396	**<0.0001**	-6.051	-7.962- -4.140	**<0.0001**	-0.824	-1.853-0.205	0.1
D2T	4.0	2.143- 6.022	**<0.0001**	2.920	1.048-4.791	**0.002**	0.766	-0.241- 1.773	0.1
Model 2									
Age	0.006	-0.675-0.901	0.9	-0.001	-0.770-0.749	0.9	0.022	-0.017-0.060	0.3
Sex	-0.119	-1.977-1.738	0.9	0.085	-1.827-1.997	0.9	0.345	-0.623-1.31	0.5
Disease duration (months)	-0.013	-0.022 - -0.004	**0. 005**	-0.011	-0.020- -0.001	**0. 02**	-0.005	-0.01 - -0.001	**0.02**
BMI	-0.003	-0.192- 0.185	0.9	0.076	-0.117- 0.270	0.4	-0.007	-0.105- 0.091	0.9
Fibromyalgia	2.621	0.652-4.590	**0.009**	1.179	-0.849-3.206	0.2	1.218	0.192-2.447	**0.02**
DAPSA	0.187	0.862-0.288	**<0.0001**	0.190	0.086-0.294	**<0.0001**	0.038	-0.015-0.091	0.1
D2T	3.843	1.764-5.921	**<0.0001**	3.814	1.679- 5.954	**0.001**	0.618	-0.465- 1.701	0.3

D2T: difficult-to-treat; BMI: Body Mass Index; DAPSA: Disease Activity in Psoriatic Arthritis; MDA: minimal disease activity.

limited relationship with D2T status and MDA in PsA patients. Interestingly, in a previous study by our group, magnification was the only PCS dimension that did not correlate with drug retention rates in PsA patients (14). These results suggest that rumination and helplessness may have more importance than magnification in PsA patients with no history of psychiatric disorders. Indeed, patients with a documented history of psychiatric disorders, as outlined in DSM 5, were excluded from our sample, potentially leading to an attenuation of the effects of clinical variables on magnification. Accordingly, it has been reported that magnification is associated with psychopathological conditions, such as suicide risk in rheumatic conditions (39).

Univariable analyses showed that both anxiety and depression were significantly associated with D2T status. However, in multivariable models, D2T was an independent predictor of high anxiety levels, but not of depression. These results are consistent with previous findings by Alp *et al*., showing higher levels of anxiety, but not depression, in D2T rheumatoid arthritis patients compared to non-D2T patients (40). This suggests that the psychological burden of D2T may be primarily driven by anxiety-related mechanisms, such as uncertainty, fear of disease progression, and treatment dissatisfaction, rather than depressive symptoms. Alternatively, the association between D2T and depression may be mediated by factors such as fibromyalgia, BMI or disease activity, which were accounted for in the model (4, 41, 42). Unlike D2T, absence of MDA was an independent predictor of both anxiety and depression, mirroring previous findings that linked failure to achieve MDA with increased anxiety and depression (19).

The present study investigated multiple dimensions of PsA, including psychological, functional, and disease-related characteristics, by emphasising the potential role of D2T. This comprehensive approach aimed to elucidate the impact of these factors on the patients' burden, conceptualised as pain catastrophising, anxiety, and depression. We specifically investigated the influence of D2T on patients' psychosocial burden, rather than the reverse, recognising that disease-related factors such as persistent inflammation, chronic pain, and treatment refractoriness are primary drivers of mental health outcomes in PsA. This approach reflects the understanding that improving disease control is essential to mitigating psychosocial burden, rather than attributing poor disease outcomes solely to pre-existing psychological conditions.

The results of the present study should be interpreted in light of several limitations. First, the cross-sectional design precludes causal inferences. Second, the lack of universally accepted D2T criteria for PsA, which may affect comparisons with other studies. However, we adopted recently proposed potential D2T criteria, providing initial evidence on the associated psychosocial burden. Third, our data were collected from a single center, which may limit generalisability of findings to more diverse populations or different healthcare settings. Fourth, although fibromyalgia was statistically controlled for in the analyses, its high prevalence in our cohort may still influence the interpretation of results, as it could independently affect both psychological measures and D2T status. Furthermore, our study did not explicitly control for the multiplicity of statistical tests, which could increase the risk of Type I errors (false positives). Additionally, we encountered some issues with multicollinearity among the independent variables, which were addressed through VIF analysis and the exclusion of highly correlated variables from the multivariate analyses.

Despite these limitations, the findings of this study offer practical implications for clinical practice. Rheumatologists can incorporate these psychosocial metrics, such as pain catastrophising and related psychological dimensions, into their daily clinical assessments. This can help provide a more comprehensive

picture of the patient's overall well-being, beyond traditional disease activity indices. For instance, recognising high levels of pain catastrophising could encourage the inclusion of psychological interventions or more targeted therapies to better manage both the musculoskeletal and psychosocial aspects of PsA.

Conclusion

The findings of this study highlight the critical role of D2T status in shaping the psychological and functional landscape of PsA patients. Elevated PC and anxiety levels, closely associated with D2T status, emphasise the profound influence of persistent disease activity on patients' mental well-being. These results point to the necessity of adopting a more integrative approach to PsA management to improve patient quality of life. By identifying D2T status as a key determinant of psychological distress and pain catastrophising, this study underscores the need for tailored therapeutic strategies that target and prioritise both musculoskeletal symptoms and mental health support. Future research should aim to refine D2T definitions in PsA and explore multidisciplinary interventions to improve outcomes for these challenging patients.

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