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Fibromyalgia Predicts Two-Year Changes in Functional Status in Rheumatoid Arthritis Patients

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Abstract

Background/Purpose—Previous cross sectional studies have shown that rheumatoid arthritis (RA) patients with fibromyalgia (FM) have higher disease activity, greater medical costs and worse quality of life compared to RA patients without FM. We determined the impact of FM on 2-year changes in functional status of RA patients in a prospective study.

Methods—Subjects included participants in the Brigham Rheumatoid Arthritis Sequential Study enrolled in a substudy of the effects of pain in RA. Subjects completed questionnaires, including the Multi-Dimensional Health Assessment Questionnaire (MDHAQ) and Polysymptomatic Distress (PSD) Scale, semi-annually and underwent physical examination and laboratory tests yearly.

Results—Of the 156 included RA subjects, 16.7% had FM, while 83.3% did not. In a multivariable linear regression model adjusted for age, gender, race, baseline MDHAQ score, disease duration, rheumatoid factor (RF)/cyclic citrullinated peptide antibody (CCP) seropositivity, disease activity and psychological distress, RA patients with FM had a 0.14 greater 2-year increase in MDHAQ score than RA patients without FM ($P = 0.021$). In secondary analyses examining the association between continuous PSD Scale score and change in MDHAQ, higher PSD Scale scores were significantly associated with greater 2-year increases in MDHAQ score (β -coefficient 0.013; $P = 0.011$).

Conclusion—Both the presence of FM and increasing number of FM symptoms predicted worsening of functional status among individuals with RA. Among individuals with RA and FM, the magnitude of the difference in changes in MDHAQ was 4 to 7-fold higher than typical changes in MDHAQ score among individuals with established RA.

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Introduction

Pain is the primary reason rheumatoid arthritis (RA) patients seek medical attention, and it is also their highest priority for improvement^{1,2}. Although pain in RA is often considered to have an inflammatory origin, previous studies demonstrated ongoing pain even after treatment of RA with anti-tumor necrosis factor (TNF) agents and during disease remission^{3,4}. Also, studies assessing pain sensitivity found that pain thresholds were lower in RA patients compared to healthy controls, both at joint and non-joint sites^{5,6}. These observations suggest that non-inflammatory, central nervous system (CNS) pain regulatory mechanisms may contribute to RA pain. This type of pain is often found in patients with chronic widespread pain conditions, such as fibromyalgia (FM).

FM, a debilitating syndrome characterized by widespread, non-articular pain, is more common in RA patients, with a prevalence of approximately 20%, compared to 2.5% in the general population⁷⁻⁹. In several cross sectional studies in RA, FM has been associated with substantially higher self-reported disease activity^{10,11} and worse functional status⁷. Wolfe, et al. found RA patients with FM had lower quality of life scores, assessed by the Health Assessment Questionnaire (HAQ), Short Form-36 (SF-36) and the EuroQol, than patients without chronic widespread pain and fatigue⁷. Naranjo et al.'s study also showed that RA patients with FM had significantly higher HAQ scores than RA patients without FM¹².

Assessment of quality of life or functional status using validated self-report measures, such as the HAQ or MDHAQ, is one of the most significant predictors of future outcomes in RA patients, and thus an important focus in RA research¹³⁻¹⁸. To our knowledge, there has not been a longitudinal study to determine whether FM or FM characteristics predicts change in functional status in RA. In this study, we prospectively followed 209 RA patients over 2 years and demonstrate that RA patients with widespread non-joint pain have greater decrements in functionality than those who do not have FM.

Patients and Methods

Study population

The study population was derived from a subgroup of the Brigham and Women's Hospital Rheumatoid Arthritis Sequential Study (BRASS). BRASS is a prospective cohort of over 1,400 patients over the age of 18 years with a diagnosis of RA, confirmed by a board-certified rheumatologist^{4,19}. From this cohort, 209 patients participated in a substudy examining characteristics of FM. A convenience sample of individuals with a BRASS study visit between September 2009 and December 2011 was recruited. Written informed consent was obtained from all participants for the BRASS study and for this substudy. The Partners Institutional Review Board approved both studies.

Longitudinal assessment

Subjects completed questionnaires every 6 months to assess measures listed below. They also underwent physical examination, including examination of 28 joints and laboratory tests yearly.

Measures

FM symptoms and status—FM symptoms and status were assessed using the Polysymptomatic Distress (PSD) scale²⁰, a combination of the Widespread Pain Index (WPI) and the Symptom Severity (SS) Scale⁸. The WPI is a validated, 19-item survey that measures the extent of body pain, focusing on non-articular sites. Higher WPI scores indicate more widespread pain. The SS scale measures severity of fatigue, unrefreshed sleeping, and cognitive symptoms on a scale of 0 to 12, with 12 being the most severe symptoms²¹. FM was defined as a PSD scale score ≥ 13 . In a previous study, this threshold correctly identified individuals with FM, with a sensitivity of 96.6% and a specificity of 91.8%⁸.

Functional status—Functional status was measured by the Multi-Dimensional Health Assessment Questionnaire (MDHAQ), a validated questionnaire used commonly in rheumatology practice. The MDHAQ includes questions about physical function, pain and global status and yields a combined score between 0 and 3, with higher scores indicating worse functional status²².

RA disease activity—RA disease activity was measured by the Disease Activity Score in 28 joints, using the CRP (DAS28-CRP). Board-certified rheumatologists performed 28-joint counts to assess tenderness and swelling of joints. Global assessments of disease activity (on a range of 0 to 100) were obtained from the patient. Laboratory tests were obtained to measure the CRP level. The DAS28-CRP score was calculated according to the published formula^{23,24}.

Psychological Distress—Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS), a 14-item questionnaire validated in physically ill patients²⁵. The HADS total score ranges from 0-42, with higher scores indicating higher levels of psychological distress.

Medication Use—Subjects self-reported medication use at baseline. Disease-modifying antirheumatic drugs (DMARDs), corticosteroids, narcotic and non-narcotic pain medications were included in the analyses.

Primary predictors and outcomes

The primary outcome was change in MDHAQ score from baseline to 2 years. The primary predictor was FM status, a dichotomous variable derived from the PSD scale. In secondary analyses, we examined the association between the baseline PSD scale score, as a continuous variable, and change in MDHAQ score over 2 years. Potential confounders included in the analyses were age, gender, race, disease duration, seropositivity, baseline MDHAQ score, disease activity and psychosocial distress. Corticosteroid use and pain medication use at the first visit were also included in an additional analysis because the baseline prevalence of individuals taking these medications differed significantly between the two groups.

Conversion from MDHAQ to HAQ (Health Assessment Questionnaire)

In the literature, functional status is more frequently reported in terms of HAQ than MDHAQ scores. Therefore, to compare functional status change in our data to that reported in literature, we converted MDHAQ to HAQ, using a validated conversion formula²⁶.

Statistical analysis

Participants with missing data in either baseline PSD scale score or baseline functional status were excluded from the statistical analyses. To determine if these data were missing at random, baseline characteristics of excluded participants were compared to baseline characteristics of participants included in the analysis using t-tests. For participants with missing information on functional status at the 2-year follow-up, the last observation carry forward method was used to fill in missing data.

Univariate distributions of variables were inspected to assess normality and identify outliers. Multicollinearity between covariates was assessed with the variance inflation factor.

Univariate analyses were performed using simple linear regression to identify associations between FM status, PSD scale score and change in MDHAQ score from baseline to 2 years, as well as to assess relationships between change in MDHAQ score and potential confounders. Multivariable linear regression models, adjusted for age, gender, race, disease duration, seropositivity, baseline MDHAQ score, disease activity, and psychosocial distress were used to examine the association between: 1) the diagnosis of FM and change in functional status, and 2) PSD scale score and change in functional status.

Results

Participant characteristics

Among the 209 participants enrolled in this study, 11 participants were excluded due to missing data on baseline functional status. Forty-two (20%) participants were excluded because they were lost to follow-up before completing at least 18 months of follow-up. Eight of 53 excluded patients had FM (15.1%), while 26 of 156 included participants had FM (16.7%). There was no significant difference in the proportion of FM between the excluded and included groups ($P = 1.0$). The mean baseline MDHAQ of included participants was 0.48 (SD 0.41) and 0.67 (SD 0.59) in excluded participants ($P = 0.015$). Excluded patients did not differ from those who completed follow-up in age, disease duration, seropositivity, disease activity or psychosocial distress. Data were imputed for 40 participants with at least 18 months of follow up but missing MDHAQ score at 24 months, using the method of last observation carry forward (LOCF). No statistically significant difference was noted when comparing the MDHAQ change among 116 participants with complete data versus the MDHAQ change among 40 participants whose data were imputed using LOCF ($P = 0.985$).

Of the 156 RA patients included in this study, 134 (85.9%) were female, and 145 (93.6%) were Caucasian. The mean age was 58.5 ± 11.0 years. 111 (72.1%) out of 154 participants were seropositive for either rheumatoid factor (RF) or anti-cyclic citrullinated peptide (CCP). Mean RA disease duration was 15.4 ± 9.2 years, and mean baseline DAS28-CRP

was 3.0 ± 1.3 . Mean PSD scale score at baseline was 8.1 ± 4.8 , and psychosocial distress, measured by the total HADS score, was 9.1 ± 6.2 .

Twenty-six RA patients (16.7%) had FM, while 130 patients (83.3%) did not (Table 1). Compared to RA patients without FM, RA patients with FM had significantly higher baseline MDHAQ scores (RA with FM: 0.7 ± 0.4 , RA alone: 0.4 ± 0.4 ; $P < 0.001$), HADS scores (RA with FM: 13.7 ± 6.7 , RA alone: 8.2 ± 5.8 ; $P < 0.001$), pain intensity (RA with FM: 56.3 ± 22.8 , RA alone: 25.9 ± 24.2 ; $P < 0.001$), corticosteroid use (RA with FM: 0.3 ± 0.5 , RA alone: 0.1 ± 0.3 $P = 0.003$), and DAS28-CRP scores (RA with FM: 3.9 ± 1.3 , RA alone: 2.8 ± 1.3 $P < 0.001$). In additional analyses comparing subcomponents of the DAS28-CRP at baseline, there was no difference in CRP between the two groups, but painful joint count (RA with FM: 8.0 ± 6.7 , RA alone: 4.0 ± 5.2 $P = 0.007$), swollen joint count (RA with FM: 4.8 ± 4.8 , RA alone: 2.3 ± 3.6 $P = 0.018$) and patient global assessment score (RA with FM: 51.7 ± 20.0 , RA alone: 22.6 ± 21.9 $P < 0.001$) were higher in the RA with FM group.

Longitudinal changes in disease activity, polysymptomatic distress, pain intensity and psychosocial distress

Over 2 years, mean disease activity, measured by DAS28-CRP, decreased by 1.2 points in individuals with RA and FM (95% CI -1.6, -0.7) and 0.3 points in individuals with RA alone (95% CI -0.5, -0.1). The mean PSD scale score decreased by 1.8 in individuals with RA and FM (95% CI -3.9, 0.3) and increased by 0.2 in individuals with RA alone (95% CI -0.5, 0.8) over 2 years. Pain intensity, measured on a scale of 0 to 100, decreased by 6.5 in individuals with RA and FM (95% CI -18.3, 5.3) and 2.2 (95% CI -6.5, 2.1) in individuals with RA alone. On a scale of 0 to 42, the mean HADS score increased by 1.0 in the group with RA and FM (95% CI -1.7, 3.7) and 2.0 in the group with RA alone (95% CI 1.2, 2.8).

Primary analysis FM status associated with worsening in functional status

In the initial multivariable regression model adjusting for demographics (age, gender, ethnicity) and baseline functional status, FM was associated with a 0.14 greater increase in MDHAQ score over 2 years ($P = 0.010$), compared to RA patients without FM (Table 2). When we constructed a model further adjusting for RA measures (disease duration, seropositivity and baseline disease activity), the magnitude of association increased to 0.15 ($P = 0.009$). In the final model, further adjusting for psychosocial distress (HADS total score), baseline FM remained predictive of a 0.14 greater increase in MDHAQ score over 2 years, compared to RA patients without FM ($P = 0.021$). In an additional regression model, further adjusting for the difference in steroid use between the two groups, the effect measure and p-value did not change significantly ($\beta = 0.13$, $P = 0.032$).

To compare our results with changes in HAQ scores reported in the literature, we used a validated conversion formula to convert MDHAQ scores into HAQ scores²⁶. The absolute HAQ score in RA patients with FM increased by 0.14 over 2 years, while the absolute HAQ score in RA patients without FM decreased 0.017, after adjusting for the same covariates in the final regression models.

Secondary analysis High FM symptoms associated with worsening in functional status

Although FM is commonly viewed as a diagnosis that is either present or not present, the concept of FM as a part of a continuous spectrum recently has emerged^{27,28}. As secondary analyses, we performed multivariable linear regressions with the PSD scale score as a continuous variable to determine if higher baseline PSD scale score was an independent predictor of worsening functional status over 2 years in RA patients.

In the baseline model, adjusting for demographic factors and baseline functional status, the β -coefficient for the PSD scale score was 0.014 ($P = 0.001$) (Table 3). In other words, for every one-point increase in baseline PSD scale score, there was, on average, a 0.014 point greater increase in MDHAQ over two years. The magnitude and significance of this association did not change with adjustment for RA-related measures, psychosocial distress and medication use differences ($\beta = 0.014$, $P = 0.004$ / $\beta = 0.013$, $P = 0.011$ / $\beta = 0.012$, $P = 0.018$ respectively).

Discussion

In this subset of the BRASS cohort, we demonstrated that FM status and higher number/severity of FM symptoms, assessed by the PSD scale, were independent predictors of 2-year worsening of functional status in RA patients. In the primary analysis, adjusting for demographics, baseline functional status, RA measures (disease duration, seropositivity and baseline disease activity) and psychosocial distress (HADS total score), FM status was predictive of a 0.14 increase in MDHAQ score over 2 years ($P = 0.021$). In the secondary analysis, every one-point increase in baseline PSD scale score was predictive of a 0.013 greater increase in MDHAQ over 2 years, after adjusting for the same factors as in the primary analysis ($P = 0.011$). To our knowledge, this is the first longitudinal study to show that both diagnosis of FM and higher PSD scale score predict declines in functional status in RA.

To put our results in clinical context, we searched the literature for studies examining changes in functional status over time in RA. Recent studies suggest that HAQ rises immediately after RA onset, followed by a slow increase of 0.010-0.016 points per year (0.02-0.032 every two years)^{29,30}. To compare our results with these observations, we used a validated conversion formula to convert MDHAQ scores into HAQ scores²⁶. The absolute increase in HAQ score was 0.14 over 2 years in RA patients with FM, while RA patients without FM experienced a decrease of 0.017 in HAQ score over 2 years, likely as a result of treatment with DMARDs. The 0.14 increase in HAQ score over 2 years in RA patients with FM reflects an approximate 4 to 7 fold greater increase in HAQ than would be expected based on data from other studies of established RA patients.

To further aid in the interpretation of these findings, we considered previously reported values for the minimum clinically important difference (MCID) for the HAQ. Previous studies have reported a wide range of values, between 0.01 to 0.495 for deterioration in the HAQ and 0.04 to 0.71 for improvement in the HAQ^{31,32}. The heterogeneity in these reports may be due to differences in the method of calculating the MCID, as well as differences in study populations. In particular, some researchers have suggested that the MCID may be

smaller in observational studies than in clinical trials³³. In an observational study of 225 RA patients in a large clinical practice, the HAQ change score for individuals who reported “somewhat improved” overall status was -0.09, and the HAQ change score for individuals who reported “somewhat worsened” overall status was 0.15. The latter value is comparable to the increase in HAQ of 0.14 among the group of patients with RA and FM in our study. Ultimately, however, the heterogeneity in reported MCIDs makes it difficult to interpret the clinical relevance of the changes observed in this study. Additional studies are needed to further define the MCID for the HAQ and other patient-reported outcomes in individuals with RA.

Evaluations of changes in functional status also need to consider related factors, such as changes in disease activity and pain^{34,35}. In our study, RA patients without FM experienced a decrease in disease activity, measured by the DAS28-CRP, whereas PSD, MDHAQ and pain intensity scores remained relatively stable. These observations may reflect our study population, which consists of subjects with long-standing disease. Many of these subjects may have structural changes that are unlikely to change, even with optimal treatment of inflammatory disease activity. Conversely, functional status worsened in RA patients with FM despite improvements in disease activity. Pain intensity also decreased during this time, but the changes were small, statistically insignificant, and unlikely to be clinically meaningful. These observations suggest that factors, beyond changes in disease activity and pain, are associated with changes in functional status.

In consideration of the possible impact of psychosocial factors on changes in HAQ, we adjusted for baseline psychosocial distress, measured by the HADS, when calculating the absolute change in HAQ. In addition, we examined the trend in HADS score over the 2-year study period. Only the RA without FM group experienced statistically significant increases in HADS scores during this time, and, in both groups, the increase in HADS score was small and unlikely to be clinically meaningful. These observations suggest that the worsening of functional status observed in the RA with FM group cannot be fully explained by worsening psychosocial distress.

These results build on previous cross-sectional studies showing associations between FM and poor physical function^{7,10-12}. In a study of 120 RA patients, Abbasi et al. demonstrated that 31 RA patients with concomitant FM had worse functional capacity compared to 89 RA patients without FM. All RA with FM patients were classified as functional class 3 (range 1-4 with higher class signifying worse functional capacity). In comparison, only 20% of RA patients without FM were in functional class 3 or 4 ($P < 0.001$)¹⁰. In a cross-sectional study of 270 RA patients, Ranzolin et al. also observed that RA patients with FM had significantly worse functional status than RA patients without FM ($P = 0.009$). RA patients with FM had a median HAQ of 2.00 (IQR 1.37-2.44), while RA patients without FM had a median HAQ of 1.12 (IQR 0.62-2.00) ($P < 0.001$)¹¹. Lastly, in a large cohort of 11,866 RA patients, of which 2078 (17.5%) had FM, the mean HAQ score was 1.8 in RA patients with FM compared to 1.0 for RA patients without FM⁷.

Similar to these previous studies, our study also revealed that RA patients with FM had higher baseline MDHAQ scores than RA patients without FM. As a result, we adjusted for

baseline MDHAQ score in our models. In addition, baseline corticosteroid use was higher in RA with FM compared to RA without FM. One explanation for the difference in corticosteroids use may be that individuals with RA and FM had higher baseline inflammatory load, as individuals with RA and FM had higher baseline DAS28-CRP scores and higher swollen joint counts than individuals with RA alone. We think it is more likely that the higher corticosteroid use among RA patients with FM reflects higher pain levels in the RA and FM group, which was reflected by the large differences in baseline pain intensity between the two groups. It is not clear whether this difference in pain reflects differences in inflammation. This area is in need of further investigation.

A strength of our study lies in the use of the PSD scale score to reflect a continuous spectrum of FM symptom severity. Although FM is commonly viewed as a distinct dichotomous entity in clinical practice, recent data suggest that FM may be more appropriately viewed as a continuous spectrum. This concept has been given many terms, including fibromyalgias and polysymptomatic distress^{27,28,36}. In addition to providing a broad picture of symptoms that spans the FM dichotomy, the PSD scale can also be used to represent severity of FM symptoms⁸. Therefore, the use of the PSD scale score as a continuous measure may provide valuable information that cannot be extracted from a simple dichotomous variable of yes/no FM.

The role of the continuous FM symptom scale score as a predictor of poor outcomes has been investigated in other disease entities, including osteoarthritis. In studies of osteoarthritis patients undergoing total knee or hip arthroplasty, Brummett et al. reported that the FM symptom scale predicted post-operative opioid use and long-term analgesic outcomes^{37,38}. A similar study in women undergoing hysterectomy also illustrated that a higher preoperative FM symptom scale score was associated with greater post-operative analgesic consumption³⁹. Our study builds upon these results, showing that both FM diagnosis and PSD scale score were significantly associated with 2-year worsening of functional status in RA, a systemic inflammatory condition.

Our study has potential limitations. First, we defined FM according to the 2011 modified ACR preliminary diagnostic criteria for FM. These criteria have not been formally endorsed by the ACR, and the ACR does not plan to fund or endorse diagnostic criteria going forward. Second, our cohort was derived from an established single center RA registry with a mean RA disease duration of over 15 years. Since the first year after diagnosis of inflammatory arthritis is the period of highest risk for the development of FM, the prevalence of FM and the distribution of PSD scale scores in our cohort likely differ from the prevalence and distribution of PSD scale scores in early RA⁴⁰. In addition, MDHAQ scores typically rise immediately after the diagnosis of RA and stabilize after the initiation of DMARD treatment^{29,30}. Thus, a study with an early RA cohort is necessary to elucidate the impact of FM status and PSD scale score on changes in functional status during the initial stages of the disease. Lastly, MDHAQ is a self-reported measure of functional status, and some studies suggest that it may not correlate with objective measure of functionality, but rather be associated with disease activity, psychosocial risks, and pain level. Although we recognize that this is a potential limitation of using MDHAQ as a measure of functional status, we

explored the evolution of disease activity, HADS score, and widespread pain level to account for possible effects from these variables.

Our results have many potential clinical implications. Among individuals with RA, a formal assessment of FM characteristics, using the PSD scale, may identify a subgroup of individuals who are more likely to experience clinically important declines in functional status. These individuals may benefit from treatment programs, such as physical and occupational therapy, targeted towards maintaining and/or improving physical function. In addition, FM symptoms (e.g., widespread, non-articular pain) are thought to reflect dysregulation of central nervous system mechanisms of pain modulation. Some of these mechanisms are likely to be a result of non-inflammatory CNS factors, whereas others may be a result of peripheral inflammatory drive. Rheumatologists may want to consider using pharmacologic (e.g., tricyclic antidepressants, serotonin norepinephrine reuptake inhibitors, anti-convulsants) and/or non-pharmacologic (e.g., tai chi, aerobic exercise, cognitive behavioral therapy) modalities to treat non-articular, widespread pain in RA. Further research is needed to evaluate whether treatment of FM can improve, or at least attenuate the decline of, functional status in RA.

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Innovation

- To our knowledge, this manuscript is the first to show that fibromyalgia is associated with greater functional decline in a prospective cohort of rheumatoid arthritis patients followed for two years.
- We demonstrated that a larger number of fibromyalgia symptoms predict worse functional status in rheumatoid arthritis. This observation is consistent with the recent view of fibromyalgia as a spectrum disorder, with a continuous range of severity, rather than a dichotomous entity.

Significance

- Formal assessment of fibromyalgia symptoms, using the Polysymptomatic Distress (PSD) Scale, in rheumatoid arthritis patients may identify subgroup of individuals who are more likely to experience clinically important decline in functional status.
- These individuals may benefit from early treatment programs for fibromyalgia symptoms.

Table 1
Clinical Characteristics of RA patients with FM vs. those without FM

Covariate		RA with FM (n=26)	RA without FM (n=130)	P-value
Demographic				
Age	Years, mean. (SD)	61.8 (8.7)	57.8 (11.3)	0.05
Sex	Female, no. (%)	23 (88.5)	111 (85.4)	1.00
Race	White, no. (%)	25 (96.2)	120 (93.0)	1.00
Disease characteristics				
Disease duration	Years, mean. (SD)	14.7 (9.8)	15.5 (9.1)	0.69
Seropositivity (RF or CCP)	Positive, no. (%)	15 (60.0)	96 (74.4)	0.15
Baseline disease activity (DAS28-CRP)	Mean. (SD)	3.9 (1.3)	2.8 (1.3)	<0.001
Baseline Polysymptomatic Distress Scale Score	Mean. (SD)	16.4 (3.2)	6.5 (3.1)	<0.001
Baseline functional status (MDHAQ)	Mean. (SD)	0.7 (0.4)	0.4 (0.4)	<0.001
Baseline pain intensity (0-100 NRS)	Mean. (SD)	56.3 (22.8)	25.9 (24.2)	<0.001
Anxiety and Depression (HADS)	Mean. (SD)	13.7 (6.7)	8.2 (5.8)	<0.001
Flare number at Baseline [*]	Mean. (SD)	1.2 (1.0)	1.0 (1.2)	0.48
Baseline Medication use				
Any DMARDs ⁺	No. (%)	22 (84.6)	118 (90.8)	0.31
Corticosteroids	% (SD)	0.3 (0.5)	0.1 (0.3)	0.003
Narcotic medications [§]	No. (%)	3 (11.5)	4 (3.1)	0.09
Non-narcotic pain medications [°]	No. (%)	15 (57.7)	73 (56.2)	0.89

RA = rheumatoid arthritis; FM = fibromyalgia; RF = rheumatoid factor; CCP = cyclic citrullinated peptide; DAS28-CRP = Disease Activity Score in 28 joints using the C-reactive protein level; MDHAQ = Multi-Dimensional Health Assessment Questionnaire; HADS = Hospital Anxiety and Depression Scale; DMARDs = disease-modifying antirheumatic drugs;

^{*} Number of flares within the 6 months prior to the visit, grouped as a categorical variable: 1=1 flare, 2=2-3 flares, 3= 4-5 flares and 4=more than 5 flares;

⁺ DMARDs included methotrexate, leflunomide, cyclosporine, azathioprine, penicillamine, cyclophosphamide, hydroxychloroquine, sulfasalazine, aurothiomalate, auranofin, etanercept, infliximab, anakinra, adalimumab, rituximab, abatacept, certolizumab and tocilizumab;

[§] Narcotic medications included oxycodone/acetaminophen, oxycodone, butalbital/acetaminophen/caffeine, butalbital, oxycodone/aspirin, propoxyphene/acetaminophen, propoxyphene, morphine, hydrocodone/acetaminophen and tramadol;

[°] Non-narcotic pain medications included acetaminophen and nonsteroidal anti-inflammatory drugs.

Table 2
Multivariable linear regression models for the association between FM (PSD scale score 13 indicating FM) status and change in functional status (MDHAQ score) over 2 years

Covariates included in the model	FM β coefficient	P-value
1. Baseline model (baseline FM diagnosis + demographics + baseline functional status)	0.14	0.010
2. Baseline model + RA measures (disease duration + seropositivity + baseline disease activity)	0.15	0.009
3. *Baseline model + RA measures + psychosocial distress (total HADS score)	0.14	0.021

* Final model; FM = fibromyalgia; PSD = Polysymptomatic Distress; MDHAQ = Multi-Dimensional Health Assessment Questionnaire; RA = rheumatoid arthritis; HADS = Hospital Anxiety and Depression Scale

Table 3
Multivariable linear regression models for the association between PSD scale score and change in functional status (MDHAQ score) over 2 years

Covariates included in the model	FM survey score β coefficient	P-value
1. Baseline model (baseline PSD scale score + demographics + baseline functional status)	0.014	0.001
2. Baseline model + RA measures (disease duration + seropositivity + baseline disease activity)	0.014	0.004
3. *Baseline model + RA measures + psychosocial distress (total HADS score)	0.013	0.011

* Final model; FM = fibromyalgia; PSD = Polysymptomatic Distress; MDHAQ = Multi-Dimensional Health Assessment Questionnaire; RA = rheumatoid arthritis; HADS = Hospital Anxiety and Depression Scale