Fibromyalgia in patients with rheumatoid arthritis: driven by depression or joint damage?

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ABSTRACT

Objectives. *Studies have shown an increased incidence of fibromyalgia (FMS) in RA patients. The aims of this study were to explore the effect of mood and disease damage on the prevalence of FMS.*

Methods. *RA patients underwent a standardised clinical assessment, including disease activity (DAS-28), disease damage (mechanical joint score, MJS), fibromyalgia tender point assessment and the Hospital Anxiety and Depression Scale (HADS) and Health Assessment Questionnaire (HAQ). Patients were classified with FMS using two criteria a) tender-swollen joint count was ≥7 or b) tender point score of ≥11/18.*

Results. *44/285 (15%) patients were classified as having FMS using the joint count difference of ≥7, compared to 18/285 (6%) using the tender point score of >11. Using the joint count difference to classify patients as having FMS, those with FMS had higher HAQ scores than those without FMS (2.12 vs. 1.5, p<0.0001). Although the DAS-28 was higher in this group (5.4 vs. 3.82, p<0.0001), the MJS was similar (8 vs. 7, p=0.19), suggesting similar levels of joint damage. Those classified as having FMS were more likely to have HAD-D scores of >11 (25% vs. 6%, p=0.0001).*

Conclusions. *Coexistent FMS was common in our cohort, although using the tender point count to define FMS classified fewer patients with FMS. Within this group those with FMS had higher levels of depression but similar scores for joint damage indicating that in this cohort FMS and poorer physical functioning is mediated by low mood rather than joint damage.*

Background

The co-existence of fibromyalgia (FMS) and rheumatoid arthritis (RA), is increasingly recognised with studies suggesting between 14–19% of RA patients could be classified as having FMS (1-3) compared with an estimated prevalence of FMS in the normal population of 2% (4). It has been shown that FMS is related to worse scores on the DAS28, HAQ and SF-36 in patients with RA (5).

Until recently, diagnosis of fibromyalgia required pain on deep palpation of 11 out of 18 predefined tender points (6). In 2010 complementary new American College of Rheumatology (ACR) criteria for FMS were published which removed the need for a tender point examination and emphasise the importance of widespread pain and symptom severity (7). Given the problems of using a tender point count to classify RA patients as having FMS or not, a recent study by Pollard *et al.* (8) examining fibromyalgic RA took an alternative approach and used a difference in the tender minus swollen joint count of ≥7 as an indicator of FMS, with a sensitivity and specificity of >80%, compared with using the tender point count. Clearly tender joints in RA may be caused by either active synovitis or joint damage, or the joint tenderness may be a feature of underlying FMS.

Anxiety and depression are common in RA and can influence perception of well-being and severity of symptoms (9-16). Major depression affects between 13–17% of RA patients and is between two and three times more common in patients with RA than the general population. It is associated with other RA related factors, including pain, physical disability, disease activity and duration of disease. If RA patients have co-existing fibromyalgia, compared to RA patients without fibromyalgia, depression occurs more commonly and they receive treatment for depression more frequently (17).

Less is known about the effects of joint damage on FMS, therefore the central aim of this study was to determine whether the increased incidence

of FMS (as measured using higher tender-swollen joint counts) in RA is secondary to an alteration in mood or increased levels of joint damage.

Patients and methods

Subjects

We studied 285 patients recruited randomly from routine RA follow up clinics at a UK secondary care rheumatology department (Staffordshire Rheumatology Centre), who were participating in an RA outcome study. All patients fulfilled ARA criteria for RA (18). Demographic data including age, gender and disease duration were collected. Patients underwent a standardised clinical assessment including tender and swollen joint counts, disease activity using DAS-28 (19) and measurement of fibromyalgia tender points using a standard approach of palpation at fibromyalgic trigger points with the pulp of the thumb at a pressure of 4kg, determined by examiners using a similar effort to required for a dolorimeter to reach the 4kg mark (6). Joint damage was measured using the mechanical joint score (20) a composite score incorporating joint appearance at 18 joint sets (including those used within the DAS-28) on a scale of 0–3, with 0 representing no abnormality and 3 severe damage or surgery. Patients were also asked to complete the HAQ (21). Patients were assessed for depression using the Hospital Anxiety and Depression Scale (HADS) (22) and classified as depressed if they had a HADS-D of ≥11. Patient written consent was obtained according to the declaration of Helsinki and the study was approved by the North Staffordshire local research ethics committee.

Statistical Analysis

Patients were classified as having fibromyalgia by two methods, firstly using the method of Pollard *et al*. (8) if the difference between the tender and swollen joint count was ≥7 and secondly if they had a tender point count of ≥11/18. Differences in the clinical variables between patients classified as having fibromyalgia and those with no fibromyalgia were investigated using the Wilcoxon Mann-Whitney test for continuous variables, as the data were not normally distributed. Data are presented as median (interquartile range) unless otherwise stated. Logistic regression was used to model predictors of being classified as having FMS. Univariate logistic regression was used first to examine whether each variable predicted being classified with FMS. Variables which were statistically significant on univariate analysis were then entered into a multivariate stepwise logistic regression model to determine which combination of variables best predicted being classified with FMS. The discriminatory power of the resulting models was examined using the area under the curve-receiver operating curve (AUC-ROC) with confidence intervals. All analyses were performed using STATA 9.

Results

Patient characteristics and prevalence of FMS in RA

We studied 285 patients, all of whom fulfilled ARA criteria for RA, 202 (71%) were female, with a mean (SD) age of 59.5 (10.2) years. Patients had a mean (SD) disease duration of 10.9 (9.3) years.

Using the difference between TJC and SJC of ≥7, 44/285 (15%) patients were classified as having FMS. Using the 1990 classification criteria for FMS (6) of ≥11 tender points, 18/285 (6%) patients were classified as having FMS.

Effect of disease activity, damage and mood on FMS

Patients classified as having FMS using the difference between the tender and swollen joint count of ≥7 had higher ESR, higher DAS-28 and higher HAQ scores than those not classified as having FMS (Table I). They were more likely to have a HAD-D score of >11, indicating a likely diagnosis of depression. No difference was seen in the mechanical joint score between the two groups. Using the ≥11 tender points as the cut off for FMS, those classified as having FMS had higher ESR, higher TJC, higher DAS-28 and higher HAQ than those not classified as having FMS. Irrespective of how FMS was classified, patients with FMS were also more likely to be considered to have active disease with DAS-28 scores of >5.1. By contrast, in the group defined as having FMS on the tender point criteria there was no difference in the proportion of people classified as depressed (11% *vs*. 9%, p=0.07), although the numbers were small. In addition, using the tender point criteria those classified as having FMS had a higher mechanical joint score than those without (median (IQR) MJS 12 (6-26) *vs*. 7 (3-14), p=0.04). Table 1 illustrates effect of being classified as having FMS on clinical variables.

Predicting FMS in this cohort

Using the difference between TJC and SJC of ≥7 to define FMS, on univariate logistic regression, ESR, HAQ, patient global score and HAD-D >11 were all associated with FMS (data not shown). The final multivariate model retained HAQ, patient global VAS and HAD-D >11 and was moderately predictive of FMS, AUC-ROC 0.76 (95% CI 0.68–0.84). However, similar results were obtained using HAQ score alone, OR 3.75 (95% CI 2.09–6.72, p=0.0001), AUC-ROC 0.73 (95% CI 0.65–0.82), suggesting that the addition of HAD-D or patient global VAS did not significantly improve the discriminatory power of the model. These results are summarised in Table II. Mechanical joint score was not predictive of FMS in this cohort. Logistic regression was not performed using the tender point criteria for RA, as only 18 patients were classified as having FMS using these criteria.

Discussion

Our findings confirm previous reports that coexistent FMS is common in patients with RA. Previous studies highlight the difficulties with assessing FMS (24) using the tender point examination, especially when FMS co-exists with other disorders, leading to development of alternative classifications for FMS such as a difference between SJC and TJC (8) and the development of the 2010 ACR FMS diagnostic criteria (7) which do not depend on tender point examination. Our data support the difficulty of using the tender point examination in RA patients, which may significantly underestimate FMS when compared to

Table I. Effect of being classified as having FMS on Disease Activity, Damage and Depression Scores.

	Difference JC <7 (n=241)	Difference JC >7 (n=44)	*p*-value	Tender point <11 (n=267)	Tender point >11 (n=18)	*p*-value
*Age (yrs)	59.2 (10.15)	60.9 (10.6)	0.33	60 (53–67)	62.5 (59–64)	0.26
Female gender n. (%)	168 (70)	34 (77)	0.31	186 (70)	16 (89)	0.08
*Disease duration (yrs)	11.1 (9.5)	9.98 (8.7)	0.46	8 (3–16)	13.5 (8–23)	0.07
ESR (mm/hr)	16 (10–30)	34 (16–46)	0.0001	18 (10–32)	23 (15–54)	0.08
MJS	7 (3–14)	8 (5–16)	0.19	7 (3–14)	12 (6–26)	0.04
Pt global VAS	39 (20–55)	55 (34–75)	0.0001	40 (21–59)	47 (33–56)	0.22
TJC	3 (1–6)	14 (11–18)	0.00001	4 (1–8)	8 (6–13)	0.001
SJC	3 (1–6)	3 (1–7)	0.75	3 (1–6)	4 (1–6)	0.63
Difference TJC ≥7				36 (13)	8 (44)	0.0001
DAS28	3.82 (3.04–4.8)	5.4 (4.8–6.47)	0.0001	4.11 (3.16–5.14)	4.76 (4.11–5.34)	0.02
DAS28 ≥5.1 n. (%)	44 (18)	29 (66)	0.0001	68 (25)	5 (28)	0.82
HAQ	1.5 (0.875–1.875)	2.12 (1.69–2.4)	0.00001	1.625 (1–2)	2.25 (1.75–2.5)	0.0007
HAD-D	4 (2–6)	6 (3–11)	0.035	5 (2–7)	6 (3–8)	0.22
HAD-D ≥11	14 (6)	11 (25)	0.0001	23 (8.6)	2 (11)	0.7

Table II. Multivariate Logistic Regression model using difference in joint counts to classify patients with FMS.

Variables included	OR (95% CI)	*p*-value	AUC-ROC (95% CI)
HAQ	2.46 (1.32–4.58)	0.004	
HAD-D ≥11	3.04 (1.17–7.86)	0.022	0.76 (0.68–0.84)
Pt global VAS	1.02 (1.00–1.04)	0.033	

using the joint count difference, since using a tender point examination only 18/285 (6%) patients were classified as having FMS, compared to 44/285 (15%) patients using the joint count difference to classify patients as having FMS.

Previous studies have shown that high DAS-28 scores are common in patients with FMS and RA (5, 23) and evidence suggests that there is a subgroup of RA patients who have pain and disability which is not directly related to synovial inflammation. Whether high pain scores in this subgroup are related to disability secondary to joint damage or low mood had not previously been explored. Within this cohort we have shown that the high pain levels are related to both higher HAQ and higher depression scores but not related to levels of mechanical damage as measured by the mechanical joint score. These data support those of Salaffi *et al*. (25) who examined health related quality of life in FMS and RA patients and found that although pain scores were similar physical functioning was worse in the RA group.

DAS-28 is routinely used to define active RA and is used in clinical practice to define eligibility to start or continue on treatments such as anti-TNF therapy. We have shown that a high DAS-28 in patients with RA and concomitant FMS may overestimate inflammatory disease activity. This may lead to both the over treatment of RA in these patients with concomitant FMS and a failure to recognise or address the symptoms of FMS. Treating patients with both FMS and RA can be challenging, but we have shown that FMS related elevated pain levels in RA patients are related to depression rather than joint damage. For these patients to feel symptomatically better treatments need to be aimed at treating depression as well as synovial inflammation.

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