Clinical and Psychological Assessment of Patients With Rheumatoid Arthritis and Fibromyalgia

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Abstract

Objective

This study aimed to assess the clinical features as well as the functional and psychological status of patients with rheumatoid arthritis and fibromyalgia in a real-world setting in China.

Methods

A total of 202 inpatients with rheumatoid arthritis from the Department of Rheumatology and Immunology at Peking University People's Hospital were enrolled between December 2018 and April 2019. These inpatients were assessed for the presence of fibromyalgia using the 1990 American College of Rheumatology's classification criteria for fibromyalgia. Disease activity and functional and psychological status were assessed using the Disease Activity Score in 28 Joints (DAS-28), Short Form-36 health survey questionnaire (SF-36), Health Assessment Questionnaire (HAQ), Hospital Anxiety and Depression Scale, and Visual Analog Scale.

Results

Of 202 patients with rheumatoid arthritis, 42 (20.8%) had concurrent fibromyalgia. Compared to patients without fibromyalgia, those with rheumatoid arthritis and fibromyalgia had higher DAS-28 scores (6.0 vs. 4.4, $P=0.011$) and notably higher tender joint counts (16.5 vs. 4.5, $P<0.001$). Patients with rheumatoid arthritis and fibromyalgia had worse HAQ scores (1.24 vs. 0.66, $P<0.001$) and lower SF-36 scores (28.6 vs. 58.2, $P<0.001$). Additionally, patients with rheumatoid arthritis and fibromyalgia experienced more fatigue (88.1% vs. 50.6%, $P<0.001$) and had higher anxiety (10 vs. 4, $P<0.001$) and depression scores (12 vs. 6, $P<0.001$). No significant differences in erythrocyte sedimentation rate, C-reactive protein concentration, morning stiffness period, or swollen joint counts were identified between the groups.

Conclusions

Patients with rheumatoid arthritis and fibromyalgia had higher disease activity, worse functional and psychological status, and poorer quality of life. DAS-28 scores may have been overestimated in these patients. When patients with rheumatoid arthritis do not achieve remission, the possibility of fibromyalgia should be considered.

Background

Rheumatoid arthritis (RA) is a chronic, typically progressive autoimmune disease that causes joint damage and functional impairment. Fibromyalgia (FM)—a chronic disorder characterized by diffuse musculoskeletal pain, fatigue, stiffness, and the presence of multiple tender points [1]—occurs in 2–8% of the general population [2] and has a prevalence of 12–48% in patients with RA [3–8]. Most studies concerning patients with RA have reported a relationship between FM and non-inflammatory pain. Chronic unexplained pain may lead to fatigue, sleep disturbances, mental and psychological disorders,

and impaired sleep quality [9]. The reduction in overall health in patients with RA with comorbid FM illustrates that FM remains a significant burden in RA [10]. However, the lack of reliable and objective evidence leads to difficulties in accurately diagnosing this disorder. The first diagnostic classification criteria for FM were published in 1990 through the evaluation of 18 anatomical sites. The American College of Rheumatology (ACR) criteria emphasized “pain” as a core symptom, although it did not include the evaluation of other clinical characteristics such as fatigue, sleep disorders, and psychosocial symptoms. A simplified standard for fibromyalgic RA, defined as ≥ 7 tender minus swollen joint counts, was proposed by Pollard et al. [11]. To date, neither the ACR classification criteria or Pollard’s standard for FM has been entirely or widely used in China. Hence, the present study aimed to assess the utility of Pollard’s standard and compare the clinical characteristics as well as the functional and psychological status of patients with RA and FM in a real-world population in China.

Methods

Patients

The present study was conducted at the Department of Rheumatology and Immunology of Peking University People’s Hospital. A total of 202 patients who met the ACR classification criteria for RA were enrolled in this study, which was conducted over 6 months between December 2018 and June 2019. All patients were evaluated for the presence of FM using the 1990 ACR classification criteria for FM [12]. Patients with other rheumatic illnesses, severe somatic or psychiatric diseases, or disabling medical problems were excluded from this study. This study was approved by the Institutional Medical Ethics Review Board of Peking University People’s Hospital and was conducted in compliance with the Declaration of Helsinki. Patients were classified into two groups: those with FM and those without FM.

Data collection

All participants were questioned about their demographics, including their age, sex, ethnicity, disease duration, educational level, working status, total family income, and direct medical costs. The clinical assessments performed were as follows: a) The Disease Activity Score in 28 Joints (DAS-28), which includes the examination of 28 joints, was used to evaluate the disease activity of patients with RA; for this purpose, the tender joint count (TJC), swollen joint count (SJC), erythrocyte sedimentation rate (ESR), and global assessment score were calculated. A DAS-28 score >5.1 indicates high disease activity, while a score <3.2 indicates low disease activity. Besides, data on an inflammatory marker, such as C-reactive protein (CRP), was also collected. b) Functional status was assessed using the Visual Analog Scale (VAS) for pain severity, where a score of 0 indicates that “there is no pain” while a score of 10 indicates that “there is very severe pain”; furthermore, the Short Form-36 health survey questionnaire (SF-36) and Health Assessment Questionnaire (HAQ) were used to assess health-related quality of life. The SF-36 comprises 36 questions in 8 categories: bodily pain, physical functioning, general health perceptions, social functioning, vitality, general mental health, and role limitations due to either physical or social problems. The HAQ score covers 20 questions in 8 dimensions: dressing, grooming, rising, eating, walking, reaching,

gripping, and outdoor activities. Each response is scored based on ability, with scores ranging from 0 to 3: no difficulty, some difficulty, much difficulty, and unable to do. c) Psychological status was assessed using the Hospital Anxiety and Depression Scale. This scale was developed to measure both anxiety and depression among patients in non-psychiatric hospital clinics. Each subscale comprises 7 items which are rated by the patient on a 4-point (0–3) scale, based on the previous week. A score of 0 to 7 represents the reference range, 8 to 10 indicates the presence of a possible case of anxiety or depression, and 11 or higher suggests the probable case of anxiety or depression. d) Fatigue was assessed using the Fatigue Assessment Instrument (FAI). The FAI was formulated in 1993 by the American Institute of Psychological and Behavioral Sciences and the Laboratory of Neurology. It is a 4-factor model containing 29 entries that reflect different aspects of fatigue: severity (Factor I), sensitivity (Factor II), psychological consequences (Factor III), and response to rest or sleep. Each question is scored on a 7-point (1–7) scale. According to the score of Factor I, the severity of fatigue is divided into four levels: no fatigue (<4), mild fatigue (=4), moderate fatigue (=5), and severe fatigue (≥ 6). Fatigue was also measured using a 10-mm VAS.

Statistical analysis

Normally distributed numeric data are presented as means and standard deviations or as median (interquartile range [IQR]). The Shapiro–Wilk test was used to analyze the normal distribution assumption of quantitative outcomes. Student's t-test and the Mann–Whitney test were used for numeric variables, whereas the chi-square test was employed for the comparison of categorical variables among groups. P-values <0.05 were considered statistically significant. Direct medical costs and total family income were missing for 0.48% of all included individuals. Those with missing data were excluded from the analyses. All analyses were performed using IBM SPSS Statistics for Windows version 24.0 (IBM Corp., Armonk, NY).

Results

Sociodemographic characteristics

Of 243 individuals enrolled in this study, 38 were excluded due to the presence of other autoimmune diseases—36 cases of Sjogren's syndrome, 1 case of inflammatory myositis, and 1 case of systemic lupus erythematosus. Another three individuals were excluded because of serious deafness. Among the 202 included participants, 42 (20.8%) met the requirements for FM. The major demographic data of the participants are presented in Table 1. Those with FM were 1.5 years younger and had RA for 2.5 years longer than those without FM. Participants with FM were slightly more likely to be of Han nationality (2.6%), and all of them were married. There were fewer participants with FM who had completed college and were employed. Overall, a comparison of sociodemographic factors revealed that participants with FM had a socioeconomic disadvantage compared to those who did not have FM, with the most significant disadvantages being in educational level and occupational status. Those participants with FM had a slightly higher level of poverty according to total household income than those without FM. The analysis of total household income showed that 59.5% of participants with FM had an income exceeding

50 thousand renminbi (RMB) per year, as compared to 67.5% of participants without FM over the same interval. As for direct medical costs, participants with and without FM with medical costs exceeding 20 thousand RMB per year constituted 26.9% and 31.0%, respectively. Those with higher medical costs used more types of non-steroidal anti-inflammatory drugs. There were no significant differences in demographic features between the two study groups ($P<0.05$).

Clinical measures

The clinical characteristics of the two study groups are compared in Table 2. In comparison to participants with RA without FM, those with FM had a higher DAS-28 score (6.0 vs. 4.4, $P=0.011$) and a markedly higher TJC (16.5 vs. 4.5, $P<0.001$). The trend for differences in the duration of morning stiffness and the SJC was not significant. CRP concentration was 27.9 mg/dL and 14.9 mg/dL, and the ESR 50.5 mm/h and 43.5 mm/h, for the participants with and without FM, respectively. However, no differences in inflammatory index values were found.

Functional status

A significant difference was found between the HAQ and SF-36 scores of the two different groups (Table 3). The median HAQ score was 0.66 (IQR: 0.2 to 0.9) and 1.24 (IQR: 0.26 to 1.5) in participants without and with FM, respectively. The median VAS score for pain was 5.0 for participants with FM compared to 3.0 for participants without FM. The SF-36 scores revealed that the quality of life of participants with RA and FM was unsatisfactory, with median values of 58.22 (IQR: 47.26 to 73.17) and 28.63 (IQR: 19.80 to 39.97) in those without and those with FM, respectively.

Psychological status

Participants with FM reported considerably greater anxiety and depression ratings, and a higher level of fatigue, than those without FM (Table 4). They also had higher scores with respect to the severity (Factor I), sensitivity (Factor II), and psychological consequences (Factor III) of fatigue. As for the response to rest or sleep, there were no significant differences between the two groups. According to the VAS-fatigue data, participants with FM reported a higher level of fatigue compared to participants without FM.

Discussion

Our findings verified the utility of Pollard's standard in the Chinese population and suggested that physicians should be vigilant regarding possible FM complications with RA, especially when no laboratory or imaging evidence exists, which is consistent with previous studies [13, 14]. Those patients tended to have excessive examination and treatment for their disease, and their disease activities might also have been overestimated. Physicians must avoid overestimation and enable patients to receive appropriate interventions that they really need.

It is challenging to distinguish FM from RA given that both present as joint pain. Therefore, Pollard's standard uses ≥ 11 tender points as a key diagnostic criterion to differentiate FM from RA based on the

ACR criteria. Pollard et al. proposed that tender minus swollen joint counts of ≥ 7 predicted the identification of fibromyalgic RA with 83% sensitivity and 80% specificity. This standard increases the sensitivity and specificity for identifying RA-FM because it eliminates the effects of active synovitis by subtracting the number of swollen joints, which is applicable clinically and can be considered as a screening criterion for RA combined with FM [9]. In our study, the diagnostic sensitivity of Pollard's criteria was 95.2% and the specificity was 52.6%. Previous literature shows that the prevalence of FM in patients with RA is approximately 20% [4, 5]. In our study, 20.8% (42/202) of patients with RA met the 1990 ACR classification criteria for FM, and 37.6% (76/202) met Pollard's standard for FM. The probability of "fibromyalgic RA" was higher than we had predicted.

Our study shows that patients with RA and FM had a poor functional condition with higher SF-36 and HAQ scores, which is consistent with the results of previous studies [7, 15]. Literature shows that the concomitant presence of FM and severity of FM symptoms are independent predictors of physical deterioration in patients with RA [16]. We should be cautious that patients with RA may have concomitant FM if their disease activity ratings are rather high while their objective inflammatory markers, such as CRP and ESR, are not elevated, especially when complaining of tender joints that are not related to synovitis, fatigue, or quality of life disability due to high HAQ scores.

Meanwhile, we emphasized the significance of a nurse-assisted strategy for specialty care for RA patients. Nurses usually spend longer time with the patients and have more opportunities to perceive mental or psychological abnormality. Therefore, the role of the rheumatological specialist nurse should not be neglected. Instead, regular and effective training for nurses should aim to improve their specialty assessment skills, aid doctors in accelerating early and accurate diagnosis, and offer appropriate interventions to patients with RA and FM.

Consideration should be given to non-drug intervention, such as exercise and psychotherapy, in the management of patients with RA. In 2016, the European League Against Rheumatism suggested that aerobic exercise and strength training should be strongly recommended in FM management [17]. If adding new disease-modifying antirheumatic drugs or adjusting to biological therapies still do not improve the disease condition of patients with RA, we should consider the possibility of concurrent FM. However, further research is required to assess whether these activities could enhance the physical and mental health of patients with RA.

Our study has some limitations. First, the sample size was relatively small and selection bias exists. This is a single-center study that is unable to represent the whole picture of "fibromyalgic RA" in China. Second, the FAI is a self-reported measure of fatigue that, according to some research, does not correspond with objective assessments. Conversely, the four-variables evaluation approach can evaluate different components of fatigue.

Conclusions

If patients with RA do not experience relief of their symptoms for an extended period, physicians should consider the possibility of the concurrent presence of FM. In this study, patients with RA and FM had a worse functional and psychological status, while their DAS-28 score may have been overestimated. It is of vital importance that physicians avoid overtreatment in this sub-phenotype and enable these patients to receive the treatment that they need, including non-drug interventions.

Abbreviations

ACR: American College of Rheumatology

CRP: C-reactive protein

DAS-28: Disease Activity Score in 28 Joints

ESR: Erythrocyte sedimentation rate

FAI: Fatigue Assessment Instrument

FM: Fibromyalgia

HAQ: Health Assessment Questionnaire

IQR: Interquartile range

RA: Rheumatoid arthritis

RMB: Renminbi

SF-36: Short Form-36 health survey questionnaire

SJC: Swollen joint count

TJC: Tender joint count

VAS: Visual Analog Scale

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Medical Ethics Review Board of Peking University People's Hospital, Beijing. Patients' written informed consent was obtained.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

CG conducted most of the experiments. LC and TL conceived and designed the study. HZ drafted the manuscript and participated in data analysis. LW, HY, XH, and YJ helped in collecting the data. TL and CL participated in the interpretation of results and reviewed the manuscript. All authors approved the final version of the manuscript submitted for publication.

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Tables

Table 1 Demographic characteristics of patients with RA and FM vs. those with only RA

Feature	RA (n=160)	RA-FM (n=42)	P-value
Age, years	64 (56, 71)	63 (56, 72)	0.779
Disease duration, years	9 (4, 18)	12 (2, 21)	0.617
Sex			0.567
Male, n (%)	33 (20.6%)	7 (16.7%)	
Female, n (%)	127 (79.4%)	35 (83.3%)	
Smoking, n (%)	144/160 (90.0%)	37/42 (88.1%)	0.939
Education			0.584
Literate, n (%)	26 (16.3%)	9 (21.4%)	
Primary, n (%)	47 (29.4%)	11 (26.2%)	
Secondary, n (%)	41 (25.6%)	14 (33.3%)	
College, n (%)	46 (28.8%)	8 (19.0%)	
Race			0.755
Han, n (%)	152 (95.0%)	41 (97.6%)	
Others, n (%)	8 (5.0%)	1 (2.4%)	
Marital status			0.536
Married, n (%)	155 (84.9%)	42 (100.0%)	
Unmarried, n (%)	5 (3.1%)	0 (0.0%)	
Occupation			0.792
Employed, n (%)	16 (10.0%)	2 (4.8%)	
Retired, n (%)	113 (70.7%)	30 (71.4%)	
Others, n (%)	31 (19.4%)	10 (23.8%)	
Direct medical costs ($\times 10^3$)			0.871
<5, n (%)	24 (15.0%)	6 (14.3%)	
5–20, n (%)	93 (58.1%)	23 (54.8%)	
>20, n (%)	43 (26.9%)	13 (31.0%)	
Total family income ($\times 10^3$)			0.624
<50, n (%)	52 (32.5%)	17 (40.5%)	
50–100, n (%)	87 (54.4%)	20 (47.6%)	

>100, n (%)	21 (13.1%)	5 (11.9%)
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RA rheumatoid arthritis, *FM* fibromyalgia

Table 2 Clinical and immunological characteristics of patients with RA and FM vs. those with only RA

Feature	RA (n=160)	RA-FM (n=42)	P-value
DAS-28	4.4+1.4	6.0+1.2	0.011
TJC	4.5 (1, 8)	16.5 (10, 24)	<0.001
SJC	1 (0, 4)	2 (1, 4)	0.470
Morning stiffness, min	15 (0, 60)	25 (4, 99)	0.062
CRP, mg/dL	14.9 (4.1, 36.1)	27.9 (3.0, 54.7)	0.152
ESR, mm/h	43.5 (17.0, 70.8)	50.5 (16.8, 76.5)	0.518

RA rheumatoid arthritis, *FM* fibromyalgia, *DAS-28* Disease Activity Score in 28 Joints, *TJC* tender joint count, *SJC* swollen joint count, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate

Table 3 Quality of life and functional status of patients with RA and FM vs. those with only RA

Feature	RA (n=160)	RA-FM (n=42)	P-value
HAQ	0.66 (0.2, 0.9)	1.24 (0.26, 1.5)	<0.001
VAS, cm	3 (2, 5)	5 (3, 7)	0.010
SF-36	58.22 (47.26, 3.17)	28.63 (19.8, 39.97)	<0.001

RA rheumatoid arthritis, *FM* fibromyalgia, *HAQ* Health Assessment Questionnaire, *VAS* Visual Analog Scale, *SF-36* Short Form-36 health survey questionnaire

Table 4 Psychological and fatigue characteristics of patients with RA and FM vs. those with only RA

Feature	RA (n=160)	RA-FM (n=42)	P-value
Anxiety	4 (1, 7)	10 (7.75, 12.25)	<0.001
Depression	6 (3, 8)	12 (9.75, 15)	<0.001
Fatigue, n%	68, 42.5%	38, 90.5%	<0.001
FAI			
Factor I	3.21±1.64	5.13±0.09	<0.001
Factor II	3.05±1.17	4.62±0.33	<0.001
Factor III	3.34±2.17	6.15±0.83	<0.001
Factor IV	3.95±0.25	4.18±0.51	0.779
Fatigue VAS (0–10)	3.55 (1.00, 4.73)	5.55 (4.61, 5.91)	<0.001

RA rheumatoid arthritis, FM fibromyalgia, FAI/Fatigue Assessment Instrument, VAS Visual Analog Scale