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ORIGINAL ARTICLE

Fibromyalgia subgroups: profiling distinct subgroups using the Fibromyalgia Impact Questionnaire. A preliminary study

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Abstract The main goal of this project was to identify the presence of fibromyalgia (FM) subgroups using a simple and frequently used clinical tool, the Fibromyalgia Impact Questionnaire (FIQ). A total of 61 women diagnosed with FM participated in this study. FM subgroups were created by applying a hierarchical cluster analysis on selected items of the FIQ (pain, fatigue, morning tiredness, stiffness, anxiety and depressive symptoms). We also tested for group differences on experimental pain, psychosocial functioning and demographic characteristics. Two cluster profiles best fit our data. FM-Type I was characterized by the lowest levels of anxiety, depressive and morning tiredness symptoms, while FM-Type II was characterized by elevated levels of pain, fatigue, morning tiredness, stiffness, anxiety and depressive symptoms. Both FM subgroups showed hyperalgesic responses to experimental pain. These results suggest that pain and stiffness are universal symptoms of the disorder but that psychological distress is a feature present only in some patients.

Keywords Fibromyalgia · Subgroups · Cluster analyses · Heterogeneity · Fibromyalgia Impact Questionnaire

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Introduction

Fibromyalgia (FM) is a chronic pain syndrome predominantly affecting adult women. It is characterized by widespread pain experienced for at least 3 months combined with tenderness at palpation to 11 or more of 18 specific tender points [1]. Symptoms, such as sleep disturbance, fatigue, stiffness, anxiety and depressive symptoms are frequently associated with the disorder [2]. The complex clinical profile observed among FM patients indicates that FM is not a homogeneous disorder. Variability in the intensity of FM-related symptoms, including differences in psychological functioning [3–5], altered cardiovascular reactivity [6], and disturbed pain perception [5, 7, 8] clearly demonstrates this heterogeneity. Moreover, the relatively small percentage of patients who are helped when one or two treatments are used, bolsters the idea that FM is complex [9–11]. A recent study even showed that individual differences in expected symptom relief differentiates the functional profile of FM patients [11–13]. This finding is particularly interesting because it shows that psychological factors play a critical role in predicting FM subgroups.

More recently, Giesecke et al. [5] found that the combination of psychological and pain-sensitivity indices best distinguished subgroups of FM patients. Unfortunately, the Giesecke's group did not use clinical pain scores to construct their clusters, which restricts their results. Their profiles were also constructed using a total of six different instruments. A single, comprehensive questionnaire which, assesses the most prevalent symptoms reported by FM patients, would have provided a more parsimonious way of identifying subgroups. The advantage of such an approach is that it would facilitate the task of assigning individual patients to distinct FM clusters. This approach was used in the present study.

We used the Fibromyalgia Impact Questionnaire (FIQ) to identify subsets of FM patients. The FIQ is an ideal questionnaire to use for cluster formation because it is quickly administered and easily assesses a large number of different FM-related clinical characteristics. Importantly, the FIQ assesses both psychological and physical symptoms allowing for a broad measurement of the different indicators of FM. We also studied how the different FM subgroups differed in response to experimental pain (pressure and cold pain). Finally, we tested for demographic and psychosocial differences. Therefore, with this preliminary study we aim to describe the factors that might be operative in predicting symptom differences in FM.

Methods

Subjects

A total of 61 women between 29 and 65 years of age (mean age = 49.54 ± 7.34) participated in this study. They were recruited through newspaper ads, FM associations and doctors' referrals. All patients were diagnosed with FM and all were suffering from FM for more than 6 months. Women who were pregnant or breastfeeding, who had diabetes, lupus, rheumatoid arthritis or suffering from a cardiac pathology were excluded from the study. The Human Ethics Committees of Université du Québec en Abitibi-Témiscamingue and Université de Sherbrooke approved our research protocol, and all women gave their written, informed consent.

Design

Testing was carried out on two different days, separated by 2 weeks, to reduce carryover effects with respect to pain. The study was carried out as follows:

Day 1: Consisted of a 1-h interview. The goal was to obtain demographic information, identify FM characteristics (i.e., symptom-related information), record principal complaints, measure clinical pain and evaluate the sensitivity of each of the 18 tender points. A comprehensive evaluation of their pharmacological profile was also recorded.

Day 2: Patients returned to the lab so that we could measure their sensitivity to cold pain and so that they could fill out various questionnaires (described below).

Questionnaires and assessments

Fibromyalgia Impact Questionnaire

This is a self-administered questionnaire that measures the components of health most affected by FM over the past week [2]. This 10-item questionnaire is composed of three questions rated on Likert-type scale and seven questions rated on a visual analogue scale (VAS). All VAS ranged from 0 to 10 where high scores indicated a higher negative impact and/or a greater severity of symptoms. FM patients typically report average VAS scores of 6.4 (0.25) and 7.9 (0.18) [14]. The French version of the FIQ was administered. This version is widely used by researchers and clinicians and has acceptable internal consistency, test–retest reliability and construct validity [15].

Multidimensional pain inventory

The multidimensional pain inventory (MPI) is a self-administered questionnaire assessing multiple aspects of psychosocial functioning in chronic pain patients [16]. In the present study, we administered only the first five subscales of the questionnaire because these subscales specifically assess pain-related variables. The five subscales measure pain severity (extent of perceived pain severity), interference (perceptions about how pain interferes with daily living), support (how supportive significant others are regarding pain), life control (perceptions about control over pain and life events) and affective distress (mood, irritability and tension). Items for each of these five subscales were rated using Likert-type scale ranging from 0 to 6, where higher scores indicate higher pain severity, higher interference, higher support, higher life control and higher affective distress. Chronic pain patients usually report mean values of 4.37(±1.05), 4.71(±0.93), 4.33(±1.63), 3.12(±1.32) and 3.55(±1.26), respectively [17]. The French version of the MPI was used [17].

Medical outcome study short-form health survey

This instrument is a 36 item, self-administered questionnaire used to assess general health status. Structural analyses confirm the presence of two principal components, corresponding to mental and physical health [18]. The French version of the short-form health survey (SF-36) was used in this study. It possesses excellent psychometric properties [19].

Pain Catastrophizing Scale

The Pain Catastrophizing Scale (PCS) is a self-administered questionnaire consisting of 13 items used to assess pain catastrophizing (i.e., psychological distress and dysfunctional adjustment to pain) [20]. The PCS uses a 5-point scale to measure the frequency with which individuals experience different pain-related thoughts and feelings. The (zero) endpoint represents the lowest frequency and the (four) endpoint represents the highest frequency. Scores for

the PCS represent the sum of the 13 items. The French version of the PCS was administered [21]. Healthy women obtain mean values of 20, 13 (±9.51) [21].

Pressure pain thresholds at tender points

Pressure pain thresholds at tender points were assessed by a trained investigator, using a digital force gauge with a 1 cm^2 tip (Shimpo, FGE-100). Pressure was applied at a rate of 1 kg/s on each one of 18 specified tender points. Subjects were instructed to verbally report when their sensations changed from pressure to pain. A mean tender point threshold (kg) was calculated from all points. Healthy women usually start to perceive pain when 4 kg of pressure (or more) is given [1].

Cold pain

Patients were asked to immerse their whole arm in a bath of noxious cold water (12 ± 0.2°C) for 2 min and to rate the intensity of pain perceived every 15 s. Pain intensity was evaluated using a numeric rating scale, ranging from zero (no pain) to 100 (the most intense pain), as used in our previous study [22, 23].

Data analyses

A hierarchical cluster analysis was used to identify FM subgroups. Clusters were created using the scores obtained on six of the seven VAS of the FIQ. These scales included clinical pain, overall fatigue, morning fatigue, joint stiffness, anxiety and depressive symptoms. The seventh scale, job difficulty, was not included in the cluster analysis because a large number of patients were not currently working (54%). FM subgroups were formed using squared Euclidean distances in the proximities matrix [24]. This measure was chosen because it is sensitive to subtle changes in inter-subject profile shape [24]. Participants were assigned to their respective clusters using the Ward's clustering method. The Ward's cluster analytic method was chosen because it minimizes within-cluster variance and creates smaller, more distinct cluster solutions [24]. The maximum percentage change in the agglomeration coefficient recorded between successive cluster profiles was used as a stopping rule to reveal our final cluster structure. In addition to this stopping rule, the Calinski and Harabasz index as well as the step-size criterion (both valid external measures used to determine the adequacy of clusters) were used to validate our cluster solution [25]. The final number of clusters in our data set was determined by analyzing progressive changes in the agglomeration coefficient [25]. Following cluster formation, a discriminant function analysis was conducted to explore the relative weight of each predictive variable in discriminating between our groups. In the loading matrix of the discriminate function analysis, only correlations (saturation loadings) in excess of 0.33 were considered as good predictors of the discriminant function.

Finally, a series of MANOVAs were conducted to explore the preliminary nature of the difference between groups. These MANOVAs were conducted across demographic variables (age, years since symptom onset, years with FM diagnosis, work status, and presence or absence of an identifiable trigger event), experimental pain scores (pressure pain threshold at tender points, and pain intensity scores recorded during the immersion procedure) and psychosocial descriptors (mean catastrophizing on the PCS, pain-related interference on daily living, perception of life control, support from significant others, the mental component summary and the physical component summary on the SF-36). It is important to point out that, for this MANOVA, we only included three of our five MPI subscale scores (i.e., interference, life control and support). The other subscale scores (i.e., pain severity and affective distress) were not included in the MANOVA because they measured patient characteristics that were similar to those already assessed by the FIQ (i.e., pain and depressive symptoms). For each of our MANOVAs, the Wilks' λ criterion was used to determine if the combined set of dependant variables was affected by our FM subgroups. If the multivariate analysis was significant, a series of univariate ANOVAs were conducted on each dependant variable.

Results

Patient characteristics

All screened participants ($N = 61$) completed the study protocol. Sixteen subjects failed to complete the PCS and so the average value for the PCS was calculated on 45 scores. All subjects successfully completed all other measures. Demographic data and the average score for each of our instruments are shown in Table 1. For the FIQ, only the scores of the six subscales used for clustering are shown. The average number of years with FM-like symptoms and the average number of years with a FM diagnosis are also shown in Table 1. On average, patients waited six years before a diagnosis was given, suggesting that, in clinical practice, obtaining a diagnosis of FM continues to be a difficult and lengthy process.

Cluster analysis and discriminant function analysis

Two cluster profiles best fit our data (Fig. 1). The average scores and standard deviations for each of the variables

Table 1 Participant characteristics

Demographic data and questionnaire scores	Mean (SD)
Age (year)	49.7 (7.3)
Years with symptoms of chronic pain	12.4 (8.7)
Years with Fibromyalgia diagnosis	6.6 (5.3)
Proportion of subjects working (either full or part-time)	46%
Proportion of subjects living with a partner	58%
Proportion of subjects with a university degree	31%
Proportion of subjects with idiopathic FM	34%
Average pressure pain threshold at tender points (kg)	0.59 (0.41)
FIQ	
Pain	7.2 (1.8)
Fatigue	7.5 (1.5)
Morning tiredness	7.5 (1.8)
Stiffness	7.6 (1.9)
Anxiety	6.2 (2.6)
Depression	5.0 (3.0)
PCS[a]	26.38 (12.55)
Mental component summary (SF-36)	38.6 (11.9)
Physical component summary (SF-36)	30.5 (5.8)

FIQ Fibromyalgia Impact Questionnaire, *PCS* Pain Catastrophyzing Scale, *SF-36* short-form health survey

[a] The sample size was 45 patients for PCS. For all other variables it was 61

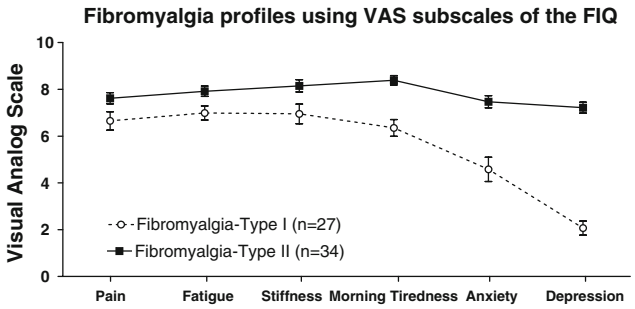

Fig. 1 Clusters created using the visual analogue subscales of the FIQ

included in the cluster analysis are shown in Table 2. Cluster 1 (FM-Type I) included 27 patients who had considerable pain, fatigue and stiffness but had the lowest levels of anxiety, depressive and morning tiredness symptoms. Cluster 2 (FM-Type II) was comprised of 34 FM patients who were characterized by elevated levels of pain, fatigue, morning tiredness, stiffness, anxiety and depressive symptoms. Our clusters profiles suggest that morning tiredness, anxiety and depressive symptoms are particularly important in distinguish FM subtypes.

Results from the discriminant function analysis (Table 2) confirmed that morning tiredness, anxiety and depressive symptoms were important in separating our FM subgroups, whereas pain, fatigue and stiffness were not. Classification function coefficients are shown in Table 2 and can be used to classify patients into their respective FM subgroups. Individual patients can be assigned to their respective clusters by multiplying the classification coefficient (Table 2) with the actual score reported by the patient for each variable. The products are then added to the constant to give a final value. This is repeated twice, once for each of the two clusters. The highest value determines the cluster to which the patient must be assigned [5].

Demographic variables

Results from our first MANOVA revealed that the values recorded for the combined set of demographic variables were comparable across both FM clusters ($F_{multivariate}$ = 1.11; $P = 0.36$) and that the linear combination of dependent variables explained only 9.5% of the difference between groups. Results from our univariate analyses (Table 3) further confirmed that our clusters did not differ across demographic variables.

Psychosocial descriptors

Results from our second MANOVA revealed that the scores for the combined set of psychosocial descriptors were significantly affected by group membership ($F_{multivariate} = 4.418$; $P = .003$). The linear combination of dependent variables explained 48.6% of the difference between groups. Univariate analyses conducted to investigate the impact of group membership on the dependent variables confirmed that pain catastrophizing (PCS), pain-related interference on daily living, perception of life control and Mental Component Summary scores significantly distinguished our FM subgroups (Table 4). These results showed that, compared to patients from FM-Type I, patients from FM-Type II presented with higher levels of pain catastrophizing (PCS), greater pain-related interference, less life control and smaller values on their SF-36 mental summary scores.

Experimental pain scores

Results from our last MANOVA revealed that the values recorded for the combined set of experimental pain variables were comparable across both FM clusters ($F_{multivariate} = 0.372$; $P = 0.69$) and that the linear combination of dependent variables explained only 1.4% of the difference between groups. Table 5 shows the results from our univariate analyses and confirms that the clusters do not differ across experimental pain scores.

Table 2 Cluster characteristics

FIQ subscales	FM-Type I mean (SD) (n = 27)	FM-Type II Mean (SD) (n = 34)	Saturation loadings	Classification function coefficients	
				FM-Type I	FM-Type II
Pain	6.65 (2.01)	7.62 (1.41)	0.144	1.837	1.975
Fatigue	6.99 (1.58)	7.92 (1.26)	0.167	2.230	1.452
Stiffness	6.95 (2.20)	8.15 (1.53)	0.164	0.522	0.097
Morning tiredness	**6.35 (1.89)**	**8.39 (1.14)**	**0.341**	1.782	2.998
Anxiety	**4.58 (2.72)**	**7.47 (1.49)**	**0.345**	0.050	0.035
Depression	**2.07 (1.53)**	**7.22 (1.37)**	**0.904**	−0.459	2.312
Constant				−21.827	−35.315

Print in boldface indicates the variables that most distinguish the clusters (with the highest saturation loadings)

Discriminant function was significant ($\chi^2 = 89.99$; $P < 0.0001$)

Table 3 Multivariate analysis of demographic data

Variables	FM-Type I mean (SD) (n = 27)	FM-Type II mean (SD) (n = 34)	$F_{univariate}$; P value
Age (year)	51.3 (7.2)	48.1 (7.3)	$F = 2.64$; $P = 0.11$
Years with symptoms of chronic pain	12.2 (7.7)	12.5 (9.4)	$F = 0.009$; $P = 0.92$
Years with fibromyalgia diagnosis	6.6 (4.4)	6.4 (6.0)	$F = 0.002$; $P = 0.97$
At work (full or part-time)	24%	20%	$F = 1.090$; $P = 0.30$
Idiopathic FM	15%	23%	$F = 2.448$; $P = 0.12$

Table 4 Multivariate analysis of psychosocial data

Questionnaires	FM-Type I mean (SD) (n = 20)	FM-Type II mean (SD) (n = 25)	$F_{univariate}$; P value	Effect size (power%)
PCS	**21.665 (10.42)**	**30.16 (13.01)**	***F* = 5.820; *P* = 0.02**	**0.72 (65%)**
Interference (MPI subscale)	**4.18 (0.80)**	**5.06 (0.60)**	***F* = 13.640; *P* < 0.01**	**1.26 (98%)**
Life control (MPI subscale)	**3.68 (0.91)**	**2.96 (1.20)**	***F* = 4.893; *P* = 0.03**	**0.68 (60%)**
Support from significant others (MPI subscale)	3.73 (1.30)	3.77 (1.82)	$F = 0.006$; ***P*** = 0.94	NS
Mental component summary from SF-36	**45.42 (9.46)**	**33.21 (11.0)**	***F* = 24.202; *P* < 0.01**	**1.19 (97%)**
Physical component summary from SF-36	30.14 (6.10)	30.84 (5.68)	$F = 1.925$; $P = 0.18$	NS

Values in boldface indicate that the variable differs significantly between clusters. Univariate effect sizes were only provided in Table 4 because, here, the multivariate analysis was significant and required univariate tests at follow-up

PCS Pain Catastrophyzing Scale, *SF-36* short-form health survey

Table 5 Multivariate analysis of experimental pain

Variables	FM-Type I mean (SD) (n = 27)	FM-Type II Mean (SD) (n = 34)	$F_{univariate}$; P value
Pressure pain threshold (kg) (allodynia)	0.66 (0.46)	0.58 (0.40)	$F = 0.739$; $P = 0.39$
Cold pain (hyperalgesia)	77.1 (16.3)	76.0 (17.6)	$F = 0.001$; $P = 0.98$

Discussion

The present findings support the presence of distinct subgroups among FM women. Subgroups were identified by conducting a cluster analysis on selected items of the FIQ. Based on this analysis, we propose that FM can be divided in two groups: FM-Type I and FM-Type II. Forty-four percent of patients in our sample belonged to FM-Type I. Patients in this cluster reported high levels of pain, fatigue and stiffness, but low levels of morning tiredness, anxiety and depressive symptoms. Patients in FM-Type II reported high levels of pain, fatigue, stiffness, morning tiredness, anxiety and depressive symptoms. Differences between the two FM subgroups were driven, therefore, by differences in psychological distress (including anxiety and depressive symptoms) and morning fatigue. Even if the levels of

depressive and anxiety symptoms of patients from FM-Type I were low, and comparable to those typically found among healthy women [14], it is important to keep in mind that patients in FM-Type I continued to meet the diagnostic criteria for FM.

In the current study, confirmation that neurophysiological changes underlie the development of FM is provided by evidence that all FM patients show the presence of hyperalgesia (elevated intensity ratings to cold pain) and allodynia (low tender point thresholds). Consistent with a previous study, FM patients with or without depression reported significantly lower pain threshold when compared to healthy subjects.

When compared to the scores typically obtained among healthy subjects, tender point thresholds [26] were much lower and cold pain ratings [27] were much higher for both FM subtypes. As shown here, even changes in profile shape did not affect cold hyperalgesia and the mechanical allodynia observed among FM patients.

Overall, our study found that the heterogeneity that characterizes FM patients is largely due to differences in depressive and anxiety symptoms. We interpret these differences as evidence of comorbid depressive and anxiety symptoms for FM-Type II patients but not for FM-Type I patients. Psychological distress is a common comorbid symptom for a large number of different organic diseases, including pulmonary hypertension [28], coronary heart disease [29] and diabetes [30]. Whereas the manifestation of depression as a comorbid symptom is well accepted for these diseases, it is unfortunate to see that for FM, some practitioners continue to question the organicity of the disorder and prefer to see it as a masked form of depression. As shown here, this hypothesis is unlikely since feelings of depression were not present in all of our patients, yet elevated levels of pain, fatigue and stiffness were always present.

Most importantly, our results suggest that tailored treatments may help. For example, it may be necessary to address the depression of FM-Type II patients, whereas this is not necessary for FM-Type I patients. Given the common set of physical symptoms reported by all our FM patients, some aspects of treatment should be universal [9, 10]. For example, treatment programs should deal with the hyperalgesia, stiffness and fatigue presented by all FM patients.

One potential limit of the study is the relatively small number of subjects per group. Although a small sample size limits the generalizability of our findings, and potentially increases the risk of empirical overfitting, we are confident that our results reflect true inter-group differences. This is in part motivated by the very large effect sizes reported in Table 4 and the consistency of our multivariate effects. Nevertheless, future studies should be conducted to confirm our cluster profiles.

In conclusion, there is little doubt that different FM profiles exist. Since we used the VAS subscales of the FIQ to identify our profiles, clinicians now have access to a single, comprehensive instrument, which can help them to assign individual patients to one of two clusters (see "results" for a description of the assignment procedure).

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