J Rehabil Med 2013; 45: 685–693

ORIGINAL REPORT

USEFULNESS OF MULTIPLE DIMENSIONS OF FATIGUE IN FIBROMYALGIA

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Objectives: **To explore in which contexts ratings of multiple dimensions of fatigue are useful in fibromyalgia, and to compare multidimensional fatigue between women with fibromyalgia and healthy women.**
Design: **A cross-sectional study.**
Subjects and methods: **The Multidimensional Fatigue Inventory (MFI-20), comprising 5 subscales of fatigue, was compared with the 1-dimensional subscale of fatigue from the Fibromyalgia Impact Questionnaire (FIQ) in 133 women with fibromyalgia (mean age 46 years; standard deviation 8.6), in association with socio-demographic and health-related aspects and analyses of explanatory variables of severe fatigue. The patients were also compared with 158 healthy women (mean age 45 years; standard deviation 9.1) for scores on MFI-20 and FIQ fatigue.**
Results: **The MFI-20 was associated with employment, physical activity and walking capacity (r_s=–0.27 to –0.36), while FIQ fatigue was not. MFI-20 and FIQ fatigue were equally associated with pain, sleep, depression and anxiety (r_s=0.32–0.63). Regression analyses showed that the MFI-20 increased the explained variance (R^2) for the models of pain intensity, sleep, depression and anxiety, by between 7 and 29 percentage points, compared with if FIQ fatigue alone was included in the models. Women with fibromyalgia rated their fatigue higher than healthy women for all subscales of the MFI-20 and the FIQ fatigue ($p<0.001$).**
Conclusion: **Dimensions of fatigue, assessed by the MFI-20, appear to be valuable in studies of employment, pain intensity, sleep, distress and physical function in women with fibromyalgia. The patients reported higher levels on all fatigue dimensions in comparison with healthy women.**

Key words: fatigue; fibromyalgia; outcome assessment.

J Rehabil Med 2013; 45: 685–693

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Accepted Feb 18, 2013; Epub ahead of print Jun 24, 2013

INTRODUCTION

Fibromyalgia (FM) is characterized by widespread pain, tenderness, fatigue, sleep disturbances, morning stiffness and psychological distress (1, 2). The prevalence of FM in the Western world is estimated to be between 1% and 3% of the population, and it is more prevalent in older ages and among females (2, 3). Environmental factors, such as physical trauma, certain infections, auto-immune disorders, emotional stress and other regional pain conditions, may play a role in triggering the development of FM (4), but there may also be a familial component (5). Aberrations in physiological pain-processing mechanisms, together with psychological and environmental factors, interact in the development and maintenance of widespread pain and tenderness in FM (4, 6). The symptoms can be controlled, to some degree, with pharmacological and non-pharmacological treatments (7).

Besides pain, fatigue appears to be a major limitation for patients with FM (8, 9). Fatigue in FM has been found to be associated with decreased working capacity (10), limited physical performance (11), pain intensity and symptoms of depression (12).

As fatigue is an important domain in FM it has been suggested to be included in all clinical trials involving patients with FM (13). There are many factors that influence fatigue, and assessment of its subjective, fluctuating and multidimensional nature is complicated (14–16).

The traditional way of assessing fatigue has been to use a one-dimensional visual analogue scale (VAS), such as the subscale of fatigue included in the Fibromyalgia Impact Questionnaire (FIQ) (17). Recently, however, instruments have been developed to assess multiple dimensions of fatigue. The Multidimensional Fatigue Inventory (MFI-20) consists of 5 independent subscales of fatigue: General Fatigue, Physical Fatigue, Mental Fatigue, Reduced Motivation and Reduced Activity (15). The MFI-20 has been used in several descriptive and experimental studies of rheumatic diseases, including FM (18–21).

The FIQ is a frequently used instrument in research into FM. We were interested to study in which contexts ratings of multiple fatigue dimensions should be added as a complement to the FIQ fatigue. Both MFI-20 and FIQ fatigue have been recommended for the assessment of fatigue in FM (13).

The primary objective of this study was to explore in which contexts ratings of multiple dimensions of fatigue (MFI-20) are useful in FM, by comparing the MFI-20 and the one-dimensional FIQ fatigue in associations with socio-demographic and health-related aspects. As most patients with FM report some degree of fatigue, the two instruments were also compared in analyses of explanatory factors of severe fatigue.

 doi: 10.2340/16501977-1161

 ISSN 1650-1977

The secondary objective was to compare multiple dimensions of fatigue between women with FM and age-matched healthy women.

MATERIAL AND METHODS

Population

Patient group. Patients were recruited to the cross-sectional study from 3 primary healthcare centres in the west of Sweden. Inclusion criteria were: female patients, 18–60 years of age, with FM according to the American College of Rheumatology criteria for FM: a history of widespread pain for at least 3 months, and pain in 11 of 18 tender points on manual palpation (1). Exclusion criteria were: inability to understand Swedish, pregnancy, and severe psychiatric or somatic disorders. The study was approved by the regional ethics review board in Gothenburg. Written consent was obtained from all patients.

Reference group. A reference group of healthy women was recruited from a mammography screening centre and from employees in the public sector. Inclusion criteria were: women, 18–60 years of age. Exclusion criteria were pregnancy or severe psychiatric or somatic disorders.

Measurements

Multidimensional Fatigue Inventory (4–20). The MFI-20 assesses 5 dimensions of fatigue: General Fatigue, Physical Fatigue, Mental Fatigue, Reduced Motivation and Reduced Activity. It contains 20 statements on a 5-point Likert scale that refer to aspects of fatigue experienced during the most recent days. The sum scores range from 4 to 20 for each subscale. Higher scores indicate a higher degree of fatigue (15, 22). The MFI-20 has shown satisfactory construct and content validity (13) and test-retest reliability in FM (23).

FIQ fatigue (0–100). The VAS for fatigue included in the FIQ (17) was used as a one-dimensional measure of fatigue in this study. The patients estimated how tired they had been during the previous week on a 100-mm scale, where 0 mm was ”No tiredness” and 100 mm was ”Very tired”. The FIQ fatigue has been validated for a Swedish population and has shown satisfactory test-retest reliability (24).

Socio-demographic aspects

Socio-demographic data and information about medication were gathered in a standardized interview.

- *Marital status* was divided into two categories, referring to whether the patient lived with another adult.
- *Employment* was divided into 4 categories, referring to percentage of full-time work, which is defined as 40 h per week.
- *Sick leave and disability pension* were categorized as none, part-time or full-time sick leave/disability pension, based on 40 h work per week.
- *Medication:* use of analgesics/non-steroidal anti-inflammatory drugs (NSAID) and psychotropic drugs (meaning antidepressants and sedatives) was registered as positive when use was regular or as needed.

Health-related aspects

- *Duration* of widespread pain was obtained by a standardized interview.
- *Tender points* (11–18) were examined by manual palpation (1).
- *FIQ pain* (0–100)*,* a subscale of the FIQ measuring pain intensity during the previous week, was used (17, 24).
- *Pain localizations* (0–18). The number of pain localizations was reported in a self-administered pain drawing, with 18 predefined body regions (25).
- *Sleep quantity and quality* (1–4). Two questions about the patients' quantity and quality of sleep (26) was used; "Do you think you get enough sleep?" and "On the whole, how do you think you sleep?" A higher score indicates worse sleep.
- *Anxiety, depression* (0–21). The Hospital Anxiety and Depression Scale (HADS) was used to identify and quantify symptoms of depression and anxiety. The HADS builds two subscales: HADS-A for anxiety and HADS-D for depression (27).
- *Physical activity (h).* The Leisure Time Physical Activity Instrument (LTPAI) assesses the amount of physical activity in leisure time during a typical week, divided into light and moderate exercise (28). The hours spent on moderate exercise were used in the present study.
- *Walking capacity (m).* The 6-minute walk test (6MWT) has been shown to possess satisfactory reliability in a Swedish FM population (29). The patient was instructed to walk for 6 min as quickly as she could without running. The distance covered was measured in metres.

Procedure

The standardized interviews and examinations in the patient group were performed by trained physiotherapists. In the healthy reference group, only socio-demographic data and measures of fatigue (MFI-20 and FIQ fatigue) were collected.

Trial registration. Clinicaltrials.gov identifier NCT00545649.

Statistics

Descriptive statistics are presented as means, standard deviations (SD) and ranges for continuous variables, and as numbers and percentages for categorical variables. The correlations between MFI-20 and FIQ fatigue was calculated using Spearman's correlation coefficient. The MFI-20 and the FIQ fatigue were compared in correlations with socio-demographic and health-related variables in patients with FM, using Spearman's correlation coefficient. If at least one of the MFI-20 subscales was significantly correlated ($p<0.05$) with a specific variable, and the FIQ fatigue was not, the MFI-20 was considered to be preferable to use in relation to that variable. If the FIQ fatigue was significantly correlated ($p<0.05$) with a specific variable, and the MFI-20 was not, the FIQ fatigue was considered to be preferable to use in relation to that variable.

Correlations under 0.25 have been suggested to indicate little or no relationship (30). Therefore, only correlations above 0.25 ($p<0.05$) were taken into account in the analyses described above. The associations between MFI-20/FIQ fatigue variables and socio-demographic and health-related variables in patients with FM were adjusted for possible confounders by using multivariable logistic regression analysis for dichotomous variables and multivariable linear regression analysis for continuous variables. In these analyses, the continuous dependent variables were transformed to normally distributed variables by using Blom's transformation whenever their distribution allowed for it; otherwise the dependent variables were dichotomized at the median value. The main independent variable, i.e. MFI-20 or FIQ fatigue, was the first covariate in the model, and other variables correlating to both the dependent and the main independent variable were considered as possible confounding factors and are included as additional covariates in the model.

If the FIQ fatigue and at least one of the MFI-20 subscales were equally associated ($p<0.05$) with a specific variable, the explained variance (R^2) was calculated in a multiple linear regression analysis for that specific variable. The regression analyses were made with FIQ fatigue as the only included assessment of fatigue, as well as adjusted for the MFI-20 subscales.

The MFI-20 and the FIQ fatigue were also compared in explanatory variables of severe fatigue. Logistic regression was used to analyse which variables were explanatory factors of severe fatigue in the patient group (31). The results were used as a complement to the correlation analyses in conclusions about in which contexts the MFI-20 and the FIQ fatigue are useful. As there is no known cut-off score for any of the 5 continuous MFI-20 subscales or for FIQ fatigue indicating more or less severe fatigue in an FM population, the cut-off value for severe fatigue was defined as the median value of the patients' scorings.

The variables that showed a statistically significant association with MFI-20 and/or FIQ fatigue in the Spearman's correlation analyses were included in the univariable logistic regression.

The statistically significant explanatory factors ($p < 0.05$) of the dichotomized subscales of the MFI-20 and FIQ fatigue in the univariable logistic regression analysis were included in the stepwise multivariable procedure, where a set of independent predictors of explanatory factors were selected for each of the 6 outcome variables. In the stepwise logistic regression a significance level of 0.05 was used for both inclusion and exclusion. Odds ratios (OR) with 95% confidence intervals and *p*-value are presented.

The AUC values (the area under the Receiver Operating Characteristic (ROC) curve) were calculated for description of goodness of explanatory factors (32). Values in the range $0.7 \leq AUC < 0.8$ indicate that the explanatory variables are acceptable, $0.8 \leq AUC < 0.9$ indicates that they are excellent, and $AUC \geq 0.9$ indicates that they are outstanding (33). All tests were 2-sided and conducted at the 5% significance level.

In comparisons of fatigue and socio-demographic variables between the patient group and the healthy reference group, the Mann-Whitney *U* test was used for continuous variables, Fisher's exact test for dichotomous variables, and Mantel-Haenszel χ^2 test for trend in contingency tables for ordinal categorical variables. Logistic regression with group as dependent variable and the fatigue measures and the covariates as independent variables was used to analyse differences in fatigue between the patient group and the reference group adjusted for the covariates.

RESULTS

Patient group

A total of 240 patients were recruited from primary healthcare centres by searching patient records for diagnoses of FM (between 1995 and 2004) and consecutive recruitment (in 2004 and 2005). Of these patients, 32 refrained from participation for various reasons, such as treatment in progress, time restrictions, family reasons, or no interest in participating. Ten patients were excluded due to other severe concomitant disorders, and 65 patients did not meet the inclusion criteria. The final number of patients that participated in the study was 133, of which 81 were recruited from primary healthcare journal archives and 52 consecutively recruited at primary healthcare centres. The socio-demographic data of the patient group is presented in Table I. Descriptive statistics of the health-related aspects for the patient group are given in Table II. All instruments and performance-based tests had a completion rate of between 96.2 and 100%.

Reference group

A total of 189 women between 21 and 60 years of age were recruited from a mammography screening centre ($n = 83$) and from employees in the public sector ($n = 106$). Twenty persons were excluded due to exclusion criteria: pregnancy ($n = 2$), severe psychiatric or somatic disorders ($n = 18$). Eleven persons aged 21–30 years were randomly excluded to achieve adequate age matching with the patient group. The remaining 158 persons constituted the reference group.

The socio-demographic data of the reference group is presented in Table I. There were no significant differences between the patient group and the reference group in age, marital status or smoking. There were significant differences between the

Table I. *Socio-demographic data of the patient group and the age- and sex-matched reference group*

	Patient group ($n = 133$)	Reference group ($n = 158$)	*p*-value
Age, years, mean (SD)	46 (8.6)	45 (9.1)	0.64
Born outside Sweden, *n* (%)	22 (17)	20 (13)	0.40
Marital status, *n* (%)			
Living with adult	103 (77)	107 (68)	0.09
Not living with adult	30 (23)	50 (32)	
Education, *n* (%)			
≤9 years	30 (23)	16 (10)	<0.001*
10–12 years	70 (53)	60 (38)	
>12 years	32 (24)	77 (49)	
Employment, *n* (%)			
0%	83 (62)	8 (5)	<0.001*
1–49%	13 (10)	5 (3)	
50–79%	26 (20)	30 (19)	
80–100%	11 (8)	114 (72)	
Sick leave, *n* (%)			
None	68 (51)	149 (94)	<0.001*
Part-time	25 (19)	7 (4)	
Full-time	40 (30)	2 (1)	
Disability pension, *n* (%)			
None	77 (58)	149 (94)	<0.001*
Part-time	26 (20)	4 (3)	
Full-time	30 (23)	5 (3)	
Medication, *n* (%)			
Analgesic/NSAID	93 (70)	7 (4)	<0.001*
Psychotropics[a]	59 (44)	4 (3)	<0.001*
Current smoker, *n* (%)	35 (26)	36 (23)	0.50

*$p < 0.001$.
Information about smoking and education were collected in 130 and 132 subjects, respectively, in the patient group. Information about education, employment and smoking were collected in 154–157 subjects in the reference group.
[a]Antidepressants, sedatives.
SD: standard deviation; NSAID: non-steroidal anti-inflammatory drugs.

Table II. *Patient group (*n = *133). Means, standard deviations (SD), medians and ranges of the health-related aspects*

	Mean (SD)	Median	Range
Duration, years	10.7 (7.2)	10.0	0.3–45
Tender points, *n*	14.8 (2.4)	15.0	11–18
FIQ pain, mm	71.1 (17.9)	74.0	26–100
Pain localizations, *n*	13.4 (3.3)	14.0	5–18
BMI, kg/m^2	27.3 (5.3)	26.9	18–49
Sleep quantity	3.2 (0.9)	3.0	1–4
Sleep quality	3.0 (0.8)	3.0	1–4
Depression (HADS-D)	7.1 (3.8)	7.0	0–20
Anxiety, (HADS-A)	8.6 (5.2)	8.0	0–16
Physical activity (LTPAI), h/week	2.0 (2.4)	1.0	0–16
Walking capacity (6MWT), m	507.0 (84.0)	515.0	136–686

FIQ pain, sleep quality, depression, anxiety and physical activity were measured in 131–132 patients.
HADS-A: Hospital Anxiety and Depression Scale – Anxiety; HADS-D: Hospital Anxiety and Depression Scale – Depression; LTPAI: Leisure Time Physical Activity Instrument; 6MWT: 6-minute walk test; SD: standard deviation; BMI: body mass index.

Table III. *Spearman's correlation coefficients (rs) between the 5 subscales of the Multidimensional Fatigue Inventory (MFI-20) and FIQ fatigue in the patient group (*n = *132)*

Subscale	FIQ fatigue, rs	*p*-value
General Fatigue	0.57	<0.001
Physical Fatigue	0.32	<0.001
Mental Fatigue	0.38	<0.001
Reduced Motivation	0.31	<0.001
Reduced Activity	0.30	0.001

groups ($p<0.001$) in education, employment, sick leave, disability pension and use of medication (Table I).

Correlation analyses in patients with fibromyalgia

MFI-20 and FIQ fatigue (Table III). All 5 subscales of the MFI-20 showed significant associations with the FIQ fatigue in the patient group.

Socio-demographic aspects (Table IV). Age and education showed no association with fatigue assessed with MFI-20 subscales or FIQ fatigue. Employment showed a fair negative correlation with MFI Physical Fatigue and MFI Reduced Activity, indicating that these two fatigue dimensions were associated with fewer work hours per week. The association between employment and MFI Physical Fatigue and MFI Reduced Activity remained significant also when adjusted for a possible confounder, being FIQ pain. Employment was not associated with FIQ fatigue.

In further analyses of differences in fatigue regarding marital status, no statistically significant differences were found for the MFI-20, but FM patients living with another adult reported less FIQ fatigue than those who did not cohabit ($p=0.01$, mean 78.8, SD 19.8 vs mean 87.3, SD 17.4, data not presented).

In the analyses of differences in fatigue between smoking and non-smoking patients with FM, no statistically significant differences were found for the MFI-20 or FIQ fatigue scores.

Health-related aspects (Table IV). FIQ fatigue and nearly all dimensions of the MFI-20 showed fair to moderate correlations with depression (HADS-D) and anxiety (HADS-A). The association with depression (HASD-D) remained significant for both MFI-20 and FIQ fatigue when adjusted for pain localizations, FIQ pain, sleep quantity and sleep quality. The association with anxiety (HADS-A) remained significant for all fatigue measures except MFI Physical Fatigue, when adjusted for possible confounders, being FIQ pain, sleep quantity and sleep quality.

MFI General Fatigue and FIQ fatigue also showed a fair correlation with sleep quantity and sleep quality. The associations remained significant for sleep quality, but not for sleep quantity, when adjusted for possible confounders, being pain localizations, FIQ pain, anxiety (HADS-A) and depression (HADS-D).

FIQ pain showed a fair correlation with MFI General Fatigue, MFI Physical Fatigue and FIQ fatigue. The association between FIQ pain and MFI General Fatigue remained significant when adjusted for possible confounders, being sleep quantity, sleep quality, depression (HADS-D), anxiety (HADS-A) and walking capacity (6MWT). The association between FIQ pain and MFI Physical Fatigue remained significant when adjusted for possible confounders, being employment, sleep quantity, depression (HADS-D), anxiety (HADS-A) and walking capacity (6MWT).

The association between FIQ pain and FIQ fatigue also remained significant when adjusted for possible confounders, being pain localizations, sleep quantity, sleep quality, depression (HADS-D), anxiety (HADS-A).

Table IV. *Patient group (*n = *133). Spearman's correlation coefficients for the association between fatigue (the 5 dimensions of the Multidimensional Fatigue Inventory (MFI-20) and FIQ fatigue) and socio-demographic and health-related aspects*

	General fatigue	Physical fatigue	Mental fatigue	Reduced motivation	Reduced activity	FIQ fatigue
Socio-demographic aspects						
Age	–0.08	–0.05	–0.13	–0.06	0.06	–0.18*
Education	–0.01	0.02	0.01	–0.11	–0.11	0.11
Employment	–0.17	–0.32***	–0.16	–0.10	–0.27***	–0.11
Health-related aspects						
Duration	–0.20*	–0.22*	–0.05	0.07	–0.11	–0.04
Tender points	0.10	0.09	0.07	–0.06	0.10	–0.00
FIQ pain	0.32***	0.41***	0.15	0.19*	0.23**	0.43***
Pain localizations	0.22**	0.19*	0.20*	0.15	0.19*	0.19*
BMI	0.11	0.06	0.04	0.06	0.11	–0.00
Sleep quantity	0.36***	0.07	0.21*	0.20*	0.14	0.34***
Sleep quality	0.43***	0.19*	0.22**	0.17	0.21*	0.39***
Depression (HADS-D)	0.47***	0.38***	0.55***	0.63***	0.49***	0.44***
Anxiety (HADS-A)	0.34***	0.18*	0.55***	0.42***	0.29**	0.37***
Physical activity (LTPAI)	–0.09	–0.21*	0.02	–0.16	–0.27**	–0.02
Walking capacity (6MWT)	–0.22*	–0.33***	–0.10	–0.11	–0.36***	–0.09

*$p<0.05$; **$p<0.01$; ***$p<0.001$.

FIQ fatigue, education, FIQ pain, sleep quantity, sleep quality and physical activity were measured in 131–132 patients.

HADS-D: Hospital Anxiety and Depression Scale - Depression; HADS-A: Hospital Anxiety and Depression Scale – Anxiety; LTPAI: Leisure Time Physical Activity Instrument; 6MWT: 6-meter walk test.

Number of tender points, pain localizations and body mass index (BMI) were not associated with any of the fatigue measures.

Physical activity (LTPAI) showed a fair negative correlation with MFI Reduced Activity. No possible confounders were identified in the correlation analysis between physical activity (LTPAI) and MFI Reduced Activity.

Walking capacity (6MWT) showed fair negative correlations with MFI Physical Fatigue and MFI Reduced Activity. The associations remained significant when adjusted for possible confounders, being FIQ pain, pain localizations and physical activity (LTPAI).

FIQ fatigue was not associated with physical activity or walking capacity.

Comparisons of the MFI-20 and the FIQ fatigue in relation to pain, sleep and distress

Multiple linear regression calculations were carried out when FIQ fatigue was included as the only measure of fatigue in the model, as well as when FIQ fatigue and the MFI-20 subscales were included in the model. The correlation analyses showed that the FIQ fatigue and the MFI-20 subscales could be equally relevant for use in relation to pain intensity, sleep, depression and anxiety. The explained variance (R^2) was calculated for each model with multiple linear regression respectively for FIQ pain, sleep quantity, sleep quality, depression (HADS-D) and anxiety (HADS-A) as dependent variable.

In the analysis of FIQ pain, the included independent variables were: duration, employment, sleep quantity, sleep quality, depression (HADS-D), anxiety (HADS-A), walking capacity (6MWT) and FIQ fatigue. The R^2 for the model was 0.34 and the adjusted *p*-value for FIQ fatigue was 0.003. When the model was adjusted for the MFI-20 subscales, the R^2 was 0.42 and the fatigue measures with significant adjusted *p*-values were FIQ fatigue ($p<0.001$), MFI General Fatigue ($p=0.044$), MFI Physical Fatigue ($p=0.006$) and MFI Reduced Activity ($p=0.035$).

In the analysis of sleep quantity, the included independent variables were FIQ pain, depression (HADS-D), anxiety (HADS-A) and FIQ fatigue. The R^2 for the model was 0.18 and the adjusted *p*-value for FIQ fatigue was 0.003. When the model was adjusted for the MFI-20 subscales, the R^2 was 0.25 and the fatigue measures with significant adjusted *p*-values were MFI General Fatigue ($p=0.004$) and MFI Physical Fatigue ($p=0.025$). FIQ fatigue was not significant ($p=0.462$).

In the analysis of sleep quality, the included independent variables were pain localizations, tender points, FIQ pain, depression (HADS-D), anxiety (HADS-A) and FIQ fatigue. The R^2 for the model was 0.23 and the adjusted *p*-value for FIQ fatigue was 0.010. When the model was adjusted for the MFI-20 subscales, the R^2 was 0.32 and the fatigue measures with significant adjusted *p*-values were MFI General Fatigue ($p<0.001$) and MFI Physical Fatigue ($p=0.013$). FIQ fatigue was not significant ($p=0.891$).

In the analysis of depression (HADS-D), the included independent variables were employment, pain localizations, FIQ pain, sleep quantity, sleep quality and FIQ fatigue. The R^2 for the model was 0.25 and the adjusted *p*-value for FIQ fatigue was <0.001. When the model was adjusted for the MFI-20 subscales, the R^2 was 0.54 and the fatigue measures with significant adjusted *p*-values were MFI Reduced Motivation ($p<0.001$) and MFI Mental Fatigue ($p=0.007$). FIQ fatigue was not significant ($p=0.591$).

In the analysis of anxiety (HADS-A), the included independent variables were FIQ pain, sleep quantity, sleep quality and FIQ fatigue. The R^2 for the model was 0.17 and the *p*-value for FIQ fatigue was <0.001. When the model was adjusted for the MFI-20 subscales, the R^2 was 0.36 and the only fatigue measure with significant adjusted *p*-value were MFI Mental Fatigue ($p<0.001$). FIQ fatigue was not significant ($p=0.406$).

Explanatory factors of severe fatigue in patients with fibromyalgia (Table V)

Cut-off values. The data were dichotomized by the median value for the scorings, and the following cut-off values were identified: MFI General Fatigue >18 vs ≤ 18, MFI Physical Fatigue >18 vs ≤ 18, MFI Mental Fatigue >15 vs ≤ 15, MFI Reduced Motivation >10 vs ≤ 10, MFI Reduced Activity >16 vs ≤ 16 and FIQ fatigue >85 vs ≤ 85. Independent explanatory factors of MFI-20 and FIQ fatigue from univariable and multivariable analyses are given in Table V.

Applying the cut-off points described above, the proportion of healthy women that experienced severe fatigue was between 3.8 and 6.6% for MFI General Fatigue, Physical Fatigue, Mental Fatigue, Reduced Activity and FIQ fatigue. For MFI Reduced Motivation the proportion was 18.4% among the healthy women.

Univariable and multivariable analyses. Statistically significant explanatory factors ($p<0.05$) of severe fatigue in the univariable analyses (Table V) were included in the stepwise multivariable logistic regression (Table V) searching for the best explanatory model of severe fatigue for the 5 MFI-20 subscales and the FIQ fatigue.

MFI General Fatigue. The multivariable stepwise logistic regression showed that depression (HADS-D) and sleep quality contributed to the strongest model for explanatory factors of severe general fatigue (AUC = 0.77) (Table V).

MFI Physical Fatigue. The multivariable stepwise logistic regression showed that FIQ pain alone contributed to the strongest model for explanatory factors of severe physical fatigue (AUC = 0.70) (Table V). An alternative model could be created with the same AUC value (0.70), in which the variables of employment (OR 0.64, 95% CI: 0.45–0.93, $p=0.02$) and depression (HADS-D) (OR 1.14, 95% CI: 1.03–1.26, $p<0.01$) explained severe physical fatigue.

MFI Mental Fatigue. The multivariable stepwise logistic regression showed that depression (HADS-D) and anxiety (HADS-A) contributed to the strongest model for explanatory factors of severe mental fatigue (AUC = 0.78) (Table V).

Table V. *Patient group (n = 133). Univariable and multivariable logistic regression. Adjusted odds ratios (95% confidence intervals),* p-*values and area under the curve (AUC) values of explanatory factors of severe fatigue for Fibromyalgia Impact Questionnaire (FIQ) fatigue and the 5 subscales of the Multidimensional Fatigue Inventory (MFI-20)*

	Dependent variables											
	General fatigue >18		Physical fatigue >18		Mental fatigue >15		Reduced motivation >10		Reduced activity >16		FIQ fatigue >85	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Univariable models												
Age, years									1.04 (1.00-1.09)	0.05		
Marital status[a] 1–2											0.38 (0.16–0.89)	0.03
Employment[b] 1–4			0.60 (0.42–0.86)	<0.01					0.61 (0.43–0.88)	<0.01		
FIQ pain 0–10 cm	1.34 (1.09–1.65)	0.01	1.54 (1.22–1.94)	<0.001					1.33 (1.07–1.64)	<0.01	1.54 (1.22–1.93)	<0.001
Pain Localizations 0–18			1.12 (1.01–1.25)	0.04					1.15 (1.03–1.29)	0.01	1.12 (1.01–1.25)	0.03
Sleep Quantity 1–4	2.29 (1.48–3.54)	<0.001							1.55 (1.04–2.32)	0.03	1.91 (1.26–2.91)	<0.01
Sleep Quality 1–4	2.72 (1.69–4.36)	<0.001							1.69 (1.10–2.59)	0.02	2.38 (1.49–3.78)	<0.001
Depression (HADS-D) 0–21	1.25 (1.12–1.40)	<0.001	1.16 (1.05–1.28)	<0.01	1.32 (1.18–1.49)	<0.001	1.32 (1.18–1.49)	<0.001	1.32 (1.18–1.49)	<0.001	1.27 (1.14–1.42)	<0.001
Anxiety (HADS-A) 0–21	1.13 (1.05–1.21)	<0.01			1.21 (1.11–1.31)	<0.001	1.21 (1.11–1.31)	<0.001	1.12 (1.04–1.20)	<0.01	1.16 (1.07–1.25)	<0.001
Physical Activity (LTPAI), h	0.90 (0.81–0.99)	0.03							0.88 (0.79–0.97)	0.01		
Multivariable models												
Age, years									1.08 (1.03–1.14)	<0.01		
Employment[b] 1–4									0.62 (0.40–0.95)	0.03		
FIQ pain 0–10 cm			1.54 (1.22–1.94)	<0.001							1.32 (1.03–1.68)	0.03
Sleep Quality 1–4	2.33 (1.42–3.81)	<0.001									1.70 (1.02–2.82)	0.04
Depression (HADS-D) 0–21	1.22 (1.09–1.37)	<0.001			1.21 (1.06–1.38)	<0.01	1.44 (1.26–1.64)	<0.001	1.34 (1.18–1.53)	<0.001	1.20 (1.06–1.35)	<0.01
Anxiety (HADS-A) 0–21					1.12 (1.02–1.23)	0.02						
Physical Activity (LTPAI), h									0.82 (0.72–0.94)	0.001		
AUC	0.77		0.70		0.78		0.80		0.82		0.77	

[a]1 = not living with another adult, 2 = living with another adult.
[b]1 = 0%, 2 = 1–49%, 3 = 50–79%, 4 = 80–100%.
OR: odds ratio; HADS-A: Hospital Anxiety and Depression Scale – Anxiety; HADS-D: Hospital Anxiety and Depression Scale – Depression; AUC: Area under Receiver Operating Characteristic Curve; LTPAI: Leisure Time Physical Activity Instrument.

MFI Reduced Motivation. The multivariable stepwise logistic regression showed that depression (HADS-D) alone contributed to the strongest model for explanatory factors of severely reduced motivation (AUC = 0.80) (Table V).

MFI Reduced Activity. The multivariable stepwise logistic regression showed that age, employment, depression (HADS-D) and physical activity (LTPAI) contributed to the strongest model when predicting severely reduced activity (AUC = 0.82) (Table V).

FIQ fatigue. Multivariable stepwise logistic regression showed that FIQ pain, sleep quality and depression (HADS-D) contributed to the strongest model for explanatory factors of severe FIQ fatigue (AUC = 0.77) (Table V). An alternative model was able to be created with the same AUC value (0.77), in which anxiety (HADS-A) (OR 1.13, 95% CI: 1.04–1.23, $p < 0.01$) together with FIQ pain (OR 1.37, 95% CI: 1.08–1.75, $p = 0.01$) and sleep quality (OR 1.79, 95% 1.08–2.97, $p = 0.02$) explained severe FIQ fatigue.

According to the interpretation of AUC-values (33) the models of independent explanatory factors were acceptable ($0.7 \leq AUC < 0.8$) for 4 of the total of 6 fatigue variables and excellent ($0.8 \leq AUC < 0.9$) for 2 fatigue variables (Table V).

Differences in fatigue between the patient group and the reference group (Table VI)

FIQ fatigue and all 5 dimensions of the MFI-20 differed significantly between the patient and the reference group, also after adjustment for education, employment, sick leave and disability pension ($p < 0.001$ for all comparisons, except for MFI Reduced Motivation, where $p = 0.048$ in the adjusted analysis). The difference between the mean values of the 2 groups was 6.8 for MFI General Fatigue, 7.9 for MFI Physical Fatigue, 5.4 for MFI Mental Fatigue, 2.7 for MFI Reduced Motivation, 6.8 for MFI Reduced Activity, and 36.9 for FIQ fatigue.

DISCUSSION

The MFI-20 and the FIQ fatigue appear to assess different aspects of fatigue and are useful in different contexts. The MFI-20 was associated with employment, physical activity and walking capacity, which the FIQ fatigue was not. The FIQ fatigue and the MFI-20 were equally associated with pain, sleep and symptoms of depression and anxiety. However, multiple linear regression analyses showed that the subscales of the MFI-20 contributed with valuable aspects of fatigue that the FIQ fatigue did not, in relation to pain intensity, sleep, depression and anxiety.

The subscales of the MFI-20 were significantly associated with the one-dimensional FIQ fatigue, with correlation values ranging from 0.30 for MFI Reduced Activity to 0.57 for MFI General Fatigue, implying that the MFI-20 assesses different aspects of fatigue than does the FIQ fatigue. The highest correlation with FIQ fatigue was found for MFI General Fatigue, which was expected since both ratings could be considered to comprehend a more global aspect of fatigue. This result is consistent with findings in patients with primary Sjögren's syndrome (20) and rheumatoid arthritis (21), in which MFI General Fatigue showed the highest correlation with a global VAS for fatigue.

The FIQ is a well-accepted and frequently used instrument for assessing disabilities and symptoms in FM. The FIQ fatigue assesses only one global dimension of fatigue, thus it would be preferable to add the MFI-20 as a complement to obtain a deeper and more variegated picture of the patients' fatigue. However, since the MFI-20 is a more comprehensive and time-consuming instrument, it is of interest to investigate the context in which the examination would benefit from inclusion of the MFI-20 and where the more global assessment FIQ fatigue would be sufficient. There is a lack of similar studies comparing two instruments with regard to field of application. We chose to compare the MFI-20 and the FIQ fatigue by correlating the two instruments with socio-demographic data and health-related variables previously shown to be associated with fatigue, as well as investigating explanatory factors of severe fatigue.

The majority of patients with FM experience work limitations due to their pain, fatigue and cognitive symptoms (10, 34). High scores on MFI Physical Fatigue and MFI Reduced Activity were associated with fewer work hours per week, whereas the 1-dimensional FIQ fatigue was not, which favours the use of multiple dimensions of fatigue in studies of employment.

An intriguing research question in the field of rehabilitation is the low physical activity and reduced physical function in

Table VI. *Scores of the Multidimensional Fatigue Inventory and Fibromyalgia Impact Questionnaire (FIQ) fatigue in the patient group and the age- and sex-matched reference group*

	Patient group $n = 133$			Reference group $n = 158$			
	Mean (SD)	Median	Range	Mean (SD)	Median	Range	p-value
General fatigue	17.5 (2.6)	19.0	9–20	10.7 (4.1)	10.0	4–20	<0.001
Physical fatigue	17.3 (2.8)	18.0	9–20	9.4 (4.1)	9.0	4–20	<0.001
Mental fatigue	14.5 (4.0)	15.0	4–20	9.1 (3.5)	9.0	4–20	<0.001
Reduced motivation	10.5 (3.9)	10.0	4–20	7.8 (3.0)	7.0	4–18	<0.001
Reduced activity	15.7 (3.5)	16.0	7–20	8.9 (3.7)	8.5	4–20	<0.001
FIQ fatigue, mm	80.7 (19.6)	85.0	15–100	43.8 (26.9)	45.0	0–100	<0.001

FIQ fatigue was obtained in 132 subjects in the patient group and 152 subjects in the reference group.
SD: standard deviation.

patients with FM. In the present study, a low amount of physical activity was associated with high scores of MFI Reduced Activity. Furthermore, low walking capacity measured with the 6MWT was associated with high scores of MFI Physical Fatigue and MFI Reduced Activity. The one-dimensional assessment, FIQ fatigue, did not show any associations with LTPAI or 6MWT, indicating the advantage of multiple fatigue dimensions in relation to aspects of physical function. The MFI-20 subscales have also been shown to be sensitive to change in a study of exercise in patients with FM, when FIQ fatigue was not (19), which emphasizes the assumption that the MFI-20 provides useful information in relation to physical activity and exercise.

The FIQ fatigue and some of the subscales of the MFI-20 were equally associated with pain intensity (FIQ pain), sleep quantity, sleep quality and symptoms of depression and anxiety (HADS-D, HADS-A). The explained variance (R^2) was calculated in multiple linear regression models for pain intensity, sleep, depression and anxiety and the results imply that in relation to these variables the MFI-20 contributes with aspects of fatigue that the FIQ fatigue does not. MFI General Fatigue and MFI Physical Fatigue appear to be important dimensions associated with sleep, while MFI Reduced Motivation and MFI Mental Fatigue appear to play a role in relation to distress. FIQ fatigue, MFI General Fatigue, MFI Physical Fatigue and MFI Reduced Activity were important dimensions associated with pain intensity.

As fatigue, to some degree, is almost always prevalent in FM, we were interested in comparing the MFI-20 and the FIQ fatigue, by investigating factors that might explain severe fatigue in FM. There are currently no defined cut-off points for severe fatigue assessed with MFI-20 or FIQ fatigue. We chose to determine the cut-off value for severe fatigue as the median of patients' scorings, and found that symptoms of depression (HADS-D) was the most consistent explanatory factor of severe fatigue overall for all 5 subscales of the MFI-20 as well as FIQ fatigue. Severe FIQ fatigue was explained by high pain intensity, disturbed sleep quality and symptoms of depression, which emphasizes that a one-dimensional rating appears to be sufficient in relation to these aspects. MFI Reduced Activity appeared to be the subscale of the MFI-20 that differed the most from FIQ fatigue in the multivariable analyses, and was found to be explained by higher age, fewer work hours per week, more symptoms of depression and less physical activity.

However, there are limitations with the multiple forward stepwise logistic model. If two predictors are highly correlated, one of the predictors will never enter the model. Thus, there could be other models with nearly as good AUC-values. In the present study, alternative models with the same AUC-values were found and presented for MFI Physical Fatigue and FIQ fatigue.

Measurement error could lead to attenuation of correlation values. The influence of measurement error on the analyses could have been diminished by using the mean values of repeated measures. However, both the FIQ fatigue and the MFI-20 have been found to possess sufficient stability in patients with FM (23, 24), which gives credibly to the results of the present study.

The secondary objective was to compare the levels of multiple dimensions of fatigue between women with FM and age-matched healthy women. The present study showed that women with FM were found to report higher levels of fatigue on all dimensions of the MFI-20 as well as the FIQ fatigue than healthy women, confirming that fatigue is a severe problem for patients with FM. Of the healthy reference group, 4–7% of subjects reported severe fatigue on 4 of the total of 5 MFI-20 subscales and the FIQ fatigue, which could be considered reasonable, since fatigue is also more or less prevalent among healthy individuals (16).

It is notable that 18% of the healthy reference group were found to report severely reduced motivation. As severely reduced motivation in the patient group was found to be associated with psychological distress, the same factors may be related to severely reduced motivation in the reference group. In a Swedish national public health report, 20–30% of the women in the general population report psychological distress (35), which might explain the relatively high proportion of the reference group that reported severely reduced motivation in the present study.

There were significant differences between the patient group and the healthy reference group in terms of sick leave, disability pension and use of medication, which was expected since work disability and pharmacological treatment are common in FM. The patients also had a lower level of education and worked fewer hours per week than the healthy reference group, which is in line with previous studies of pain populations (10, 25). The socio-demographic differences regarding work, education and medication between the two groups, might be regarded as a sampling bias. Therefore the between-group comparisons of fatigue were adjusted for the socio-demographic data that differed significantly between the groups, and the difference between the groups stayed significant for all ratings of fatigue.

Fatigue appears to be related to several aspects of life in patients with FM, and valid and feasible fatigue instruments that adequately assess fatigue are needed in healthcare. The results of the present study indicate that specific questions help the patient to discriminate between different aspects of fatigue, which gives professionals valuable information. Associations between the subscales of MFI-20 and the other health-related aspects showed that it is possible to identify different dimensions of fatigue in FM, supporting previous findings in patients with rheumatoid arthritis (RA) (36).

To conclude, the present study found that the MFI-20 appears to contribute with valuable aspects of fatigue in relation to employment, pain, sleep, distress and physical function. The MFI-20 subscales of physical fatigue and reduced activity were shown to be important dimensions of fatigue associated with employment and physical function, which the FIQ fatigue was not. Furthermore, the MFI-20 subscales of mental fatigue and reduced motivation appear to be valuable dimensions of fatigue associated with depression and anxiety, indicating that the MFI-20 could be recommended for use in relation to distress.

The MFI-20 and the FIQ fatigue also differed in analyses of explanatory variables of severe fatigue in patients with FM, and the results emphasized the recommendation to use the MFI-20 in relation to employment and physical function, which are important aspects in rehabilitation. Women with FM were found to report higher levels of fatigue than healthy women on all dimensions of the MFI-20, as well as the FIQ fatigue.

ACKNOWLEDGEMENTS

The authors would like to thank the GAU Study Group: Mattias Hjelm, Elisabeth Enhörning and Rebecca Kantola in Primary Health Care, Uddevalla; Lena Nordeman, Mona Lind, Eva Melin, Anne Fredriksson, Marianne Hjerpe and Åsa Holmstrand in Primary Health Care, Alingsås; Maudh Arndorw and Ann-Kristine Neuman in Primary Health Care, Göteborg. The authors would also like to thank the Mammography Screening Centre, Kungsgatan, Göteborg, as well as Inga Johansson, Ruth Johansson, Doris Hall, Maria Wistrand, Jenny Sivertsson and Lena Larsson, for contributing to the recruitment of the healthy reference group from the public sector. The statistics adviser was Nils-Gunnar Pehrsson.

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