Fibromyalgia severity according to age categories: results of a cross-sectional study from a large national database

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Abstract

Objective

The role of age in influencing the severity of fibromyalgia (FM) is still controversial. The aim of this study is to define the contribution of age in the severity of FM from data from a large national database.

Methods

This cross-sectional study included adult patients with FM diagnosed according to the 2010/2011 American College of Rheumatology criteria. Disease severity was assessed with the revised Fibromyalgia Impact Questionnaire (FIQR) and the modified Fibromyalgia Assessment Status (FAS 2019mod). Patients were grouped into five age categories (between 18-40 years, between 41-50 years, between 51-60 years, between 61-70 years, and ≥71 years). Differences in disease severity between groups were assessed by one-way analysis of variance (ANOVA).

Results

The study included 2889 patients (199 males and 2690 females), mean age of 52.58 (±11.82) years, with a mean FIQR score of 59.22 (±22.98) and a mean FAS 2019mod of 25.50 (±8.66). Comparing the mean values of the various indices between age categories, there were no statistically significant differences between the groups for FIQR total score and FAS 2019mod. However, the 60–70 years category showed the lowest scores for both scales. The main difference emerged for the FIQR physical function subscale, where the ≥71 years category showed significantly higher scores ($p<0.05$) compared the 18–40 years category.

Conclusion

The severity of FM has a significant level of stationarity according to age categories. Patients between 60–70 years have a lower disease burden. Physical function is the health domain with the most significant difference between the groups.

Key words

fibromyalgia, disease severity, age, FIQR, FAS 2019mod

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Introduction

Fibromyalgia (FM) is a syndrome characterised by a wide range of symptoms, the most prominent of which are chronic widespread pain, fatigue, and unrefreshing sleep (1). The prevalence of FM is variable depending on the set of diagnostic/classification criteria used (2). In Italy, it is estimated that FM affects 2.22% of the general population (3).

The pathophysiological mechanisms of FM are still not fully understood and, to date, there are no imaging or laboratory markers that can be used for diagnostic purposes in daily clinical practice. The diagnosis of FM is purely clinical. The presence of symptoms and their severity are therefore the diagnostic cornerstones of FM. This aspect is emphasised in the American College of Rheumatology (ACR) criteria based on the concept of the polysymptomatic distress scale (PDS) from 2010 onwards (4, 5): the diagnosis of FM is a dichotomous choice on a symptom continuum defined as "fibromyalgianess" (6).

There are several recognised factors that may favour the onset of FM, such as a previous physical or psychological trauma (7), or that may be associated with an increased severity of symptomatic distress, such as the clear predilection of FM for the female sex (8) or the greater severity of FM in overweight or obese subjects (9). With regard to age, FM is commonly diagnosed in adulthood between the ages of 20 and 55 years, although juvenile FM, with onset during childhood and adolescence, is increasingly recognised. In most juvenile patients, symptoms persist into adulthood (10).

Several researches have considered age as one of the potential variables associated with symptom severity in FM patients. However, from the data available in the literature, there is no unified view on this issue.

In a study conducted in 2008 on 30 patients suffering from FM, aged between 24 and 56 years, a negative correlation with age was documented in relation to different domains of the Short Form (SF)-36, with reference to physical functioning (r= -0.54), bodily pain (r= -0.50), emotional role (r= -0.48), social functioning (r= -0.42) and physical role (r= -0.38) (11). Another study, conducted on 214 FM patients (mean age 46.9±9.5) and using a dedicated disease severity index, *i.e.* the Fibromyalgia Impact Questionnaire (FIQ), showed that age is a variable linked to greater disease severity (p=0.02) (12).

In contrast to what has already been described, a work carried out on a more robust sample size (978 patients), categorising the patients into young (age ≤39 years), middle-aged (age 40-59 years) and older (age ≥60 years), showed a significantly higher severity of symptoms (p<0.001) in the young and middle-aged patients compared to the older group, with mean FIQ scores of 64.96±15.07, 64.43±16.75 and 56.45±17.45, respectively (13).

Concerning the relationship between symptom severity and age, the data are controversial, and the literature offers no consistent conclusions. Starting from these assumptions and using data from a large national database, the goal of this study is to investigate the role of age in defining the severity of FM.

Materials and methods

Setting and patients

Adult patients with FM, diagnosed according to the ACR 2010/2011 criteria (4), were included in this cross-sectional study. Patients were enrolled from November 2018 to January 2021 in 19 Italian rheumatology centres belonging to the Italian Fibromyalgia Registry (IFR), with experience in the diagnosis and treatment of FM. In each centre, the diagnosis of FM was made by an experienced rheumatologist (with at least 10 years of clinical practice). Each patient underwent an objective examination and laboratory evaluation as indicated in the EUropean League Against Rheumatism (EULAR) recommendations for the management of FM (14). The study did not involve any therapeutic intervention, but was based exclusively on a clinical and clinimetric evaluation of FM patients. Therefore, patients were included regardless of current therapy, and regardless of disease severity. Patients with conditions that would interfere with the clinimetric assessment of FM were excluded, such

as patients with chronic inflammatory joint diseases or connective tissue diseases, psychosis or severe depression, uncontrolled endocrinopathies, and current malignancies. All patients gave written informed consent for participation in the study and for anonymous data collection on the IFR web platform. The study protocol and the procedures performed were approved by the ethics committee of the Università Politecnica delle Marche (Comitato Etico Unico Regionale - ASUR Marche, number 1970/AV2) and by the ethics committees of all the centres belonging to the IFR.

Assessment

Patients completed a paper package with demographic variables (age, sex, schooling, marital status) and two clinimetric indices as disease severity assessment, specifically the revised FIQ (FIQR) (15) and the modified Fibromyalgia Assessment Status (FAS 2019mod) (16). Data from the IFR allowed, in a previous analysis, to define interpretative disease severity cut-offs for both FIQR and FAS 2019mod, introducing the possibility of defining remission, mild disease, moderate disease, severe disease, and very severe disease for FM (17).

FIQR

FIQR investigates the severity of FM through 21 items represented by 11-point numerical rating scales (NRS, 0-10 scales), referring to the last seven days. Three health domains are covered, with the first nine items dealing with physical function, followed by two items covering overall general health status and the last domain focusing on 10 items referring to symptoms. The total FIQR score ranges from 0 to 100, with higher scores indicating greater disease severity. The overall score is the algebraic sum of the individual domains, where the score of the physical function domain has to be divided by three, the two items of the overall impact are considered as they are, while the score of the symptom domain has to be divided by two (15).

FAS 2019mod

FAS 2019mod is a revised and simplified version of the Fibromyalgia Assessment Status (FAS). FAS 2019mod is made by two sections recalling symptoms over the last seven days: the first one is represented by two 11-points NRS scales investigating fatigue and unrefreshing sleep; the second is a front-back mannequin with 19 body areas, realised to analyse widespread pain, where patients are asked to rate the presence/absence of pain in each area (the presence of pain on each area is scored 1). The final score, ranging from 0 to 39, is the sum of the two NRS scales and the painful areas of the mannequin (17).

Table I. Data regarding age, FIQR, its subscales and individual items, and distribution of case series.

	Mean	SD	Median	IQR	normal distribution*
Age	52.68	11.82	53.00	46.00 - 60.00	<0.0001
FIQR total	59.23	22.98	63.00	43.00 - 78.00	<0.0001
FAS 2019mod	25.50	8.66	27.00	20.00 - 32.00	<0.0001
FIQR physical function	16.42	7.65	18.00	11.00 - 23.00	<0.0001
FIQR symptoms	31.60	11.13	34.00	24.00 - 40.00	<0.0001
FIQR overall impact	11.26	5.99	12.00	6.00 - 16.00	<0.0001
FIQR items					
FIQR-1 (physical function)	3.56	3.23	3.00	0.00 - 6.00	<0.0001
FIQR-2 (physical function)	5.41	3.33	6.00	2.00 - 8.00	<0.0001
FIQR-3 (physical function)	4.24	3.09	5.00	1.00 - 7.00	<0.0001
FIQR-4 (physical function)	6.28	3.02	7.00	4.00 - 9.00	<0.0001
FIQR-5 (physical function)	6.99	3.40	8.00	5.00 - 9.25	<0.0001
FIQR-6 (physical function)	5.43	3.17	6.00	2.00 - 8.00	<0.0001
FIQR-7 (physical function)	5.79	3.36	6.00	3.00 - 8.00	<0.0001
FIQR-8 (physical function)	6.06	3.18	7.00	4.00 - 9.00	<0.0001
FIQR-9 (physical function)	5.53	3.30	6.00	2.00 - 8.00	<0.0001
FIQR-10 (overall impact)	5.66	3.08	6.00	3.00 - 8.00	<0.0001
FIQR-11 (overall impact)	5.61	3.23	6.00	3.00 - 8.00	<0.0001
FIQR-12 (symptoms)	6.83	2.58	8.00	5.00 - 9.00	<0.0001
FIQR-13 (symptoms)	7.32	2.69	8.00	6.00 - 10.00	<0.0001
FIQR-14 (symptoms)	6.81	2.73	8.00	5.00 - 9.00	<0.0001
FIQR-15 (symptoms)	6.99	2.87	8.00	5.00 - 9.00	<0.0001
FIQR-16 (symptoms)	4.94	3.23	5.00	2.00 - 8.00	<0.0001
FIQR-17 (symptoms)	5.54	3.06	6.00	3.00 - 8.00	<0.0001
FIQR-18 (symptoms)	5.74	3.07	6.00	3.00 - 8.00	<0.0001
FIQR-19 (symptoms)	6.81	2.74	8.00	5.00 - 9.00	<0.0001
FIQR-20 (symptoms)	5.26	3.16	6.00	3.00 - 8.00	<0.0001
FIQR-21 (symptoms)	6.47	2.98	7.00	5.00 - 9.00	<0.0001

FIQR: revised Fibromyalgia Impact Questionnaire; SD: standard deviation; IQR: interquartile range. Shapiro-Wilk test.

Statistical analysis

The data collected from the different centres of the IFR were exported centrally and were analysed using MedCalc®, v. 19.0.1.0 (MedCalc Software, Mariakerke, Belgium).

For the purposes of this study, patients were divided into five age categories, respectively between 18–40 years, between 41–50 years, between 51–60 years, between 61–70 years, and ≥71 years.

The variables studied are presented as mean values and standard deviations (SD) and as median values and interquartile ranges (IQR), where appropriate. The normal distribution was tested with the Shapiro-Wilk test. Since the distribution was normal for the FIQR and FAS 2019mod total scores and subscales, one-way analysis of variance (ANOVA) was used to compare differences in disease severity between age categories. Scheffé's test was used to compare the individual categories, one to the other. The *p*-values were considered significant if <0.05.

Results

The final analysis was conducted on 2889 patients referred to the IFR, 199 males and 2690 females respectively. The mean age was 52.68 (±11.82, range 18–87) years, with a mean FIQR score

Table II. Mean values of FIQR, its subscales, and FAS 2019mod distributed across age categories.

Age categories	FIQR total Mean (SD)	FIQR physical function Mean (SD)	FIQR symptoms Mean (SD)	FIQR overall impact Mean (SD)	FAS 2019mod Mean (SD)
18–40 years	57.90 (21.76)	15.51 (7.56)	31.32 (10.49)	11.19 (5.86)	25.48 (8.34)
41–50 years	59.26 (23.31)	16.44 (7.78)	31.57 (11.32)	11.25 (5.99)	25.28 (8.65)
51–60 years	60.32 (22.89)	16.77 (7.51)	32.10 (11.02)	11.50 (5.94)	25.80 (8.62)
61–70 years	57.13 (23.59)	15.97 (7.83)	30.68 (11.48)	10.58 (6.11)	24.89 (9.03)
≥71 years	62.14 (22.45)	17.69 (7.27)	32.24 (11.34)	12.21 (5.97)	26.59 (8.44)

FIQR: revised Fibromyalgia Impact Questionnaire; FAS 2019mod: revised Fibromyalgia Assessment Status; SD: standard deviation.

Table III. One-way analysis of variance (ANOVA) data for FIQR, its subscales, and FAS 2019mod.

	Source of variation	Sum of squares	Mean square	df	F-ratio	*p*
FIQR total	Between groups	5671.23	1417.80	4	2.691	0.030
	Within groups	1519304.35	526.80	2884		
	Total	1524975.58		2888		
FIQR physical function	Between groups	838.19	209.54	4	3.597	0.006*
	Within groups	167917.35	58.26	2882		
	Total	168755.54		2886		
FIQR symptoms	Between groups	808.24	202.06	4	1.631	0.164
	Within groups	357123.01	123.87	2883		
	Total	357931.25		2887		
FIQR overall impact	Between groups	457.12	114.28	4	3.199	0.012
	Within groups	103023.51	35.72	2884		
	Total	103480.64		2888		
FAS 2019mod	Between groups	523.91	130.97	4	1.748	0.137
	Within groups	216076.07	74.94	2883		
	Total	216599.99		2887		

FIQR: revised Fibromyalgia Impact Questionnaire; FAS 2019mod: revised Fibromyalgia Assessment Status; df: degree of freedom.
*significant difference ($p<0.05$) between the 18–40 years and ≥71 years categories (Scheffé test).

of 59.23 (±22.98) and a mean FAS 2019mod score of 25.50 (±8.66) in the entire case series. The patients on average therefore showed moderately severe disease, as defined by FIQR, and very severe disease, as defined by FAS 2019mod. Table I summarises the mean and median scores of the FIQR and FAS 2019mod total scores, of the individual FIQR items, and the verification of normal distribution ($p<0.0001$ for each variable). The worst scores, indicative of a greater burden of FM, were found for FIQR-13, which explores fatigue, and FIQR-15, which explores sleep quality. Conversely, the lowest scores with the lowest impact on the final FIQR score were found for FIQR-1 (brush hair) and for FIQR-3 (prepare meals), two items belonging to the physical function domain.

Of the 2889 patients included, 403 pertained to the 18–40 years category, 756 to the 41–50 years category, 1035 to the 51–60 years category, 528 to the 61–70 years category, and 167 to the ≥71 years category.

Table II includes the mean scores (and SD) of the FIQR, its three subscales, and the FAS 2019 mod. According to the results obtained, for each scale the highest mean scores were found in the category ≥71 years, followed by the category between 51–60 years. In the 61–70 years category, between the two above, lower mean disease severity scores were documented and, for the FIQR total, FIQR symptoms, FIQR overall impact and FAS 2019mod scores, it was the age category with the lowest disease severity. For the FIQR physical function the age category with the lowest score was 18–40 years.

ANOVA documented significant between-categories differences for both FIQR total score ($p=0.030$), FIQR overall impact ($p=0.012$), and, most importantly, for FIQR physical function ($p=0.006$) (Table III). However, when comparing one category versus the other through the Scheffé test, the only statistically significant difference ($p<0.05$) (Fig. 2) emerged for FIQR physical function between the categories 18–40 years and ≥71 years.

Discussion

In this study, a substantial steady-state disease severity was demonstrated in accordance with different age categories in FM patients. However, although the scores of the total FIQR do not undergo significant changes with age, there are fluctuations that do not reflect a linear trend. Disease severity seems to show a bimodal pattern, being higher in patients over 70 and 50–60 years old. At the same time, an attenuation of disease severity was revealed in patients aged 60–70 years. This decade of patients is the one that appears to have the less severe disease. The main changes related to age categories are related to the physical function domain. To the best of our knowledge, no study before this one had revealed this kind of trend in disease severity in FM patients.

The variables that can potentially influence the burden of FM are several. To date, age remains one of the most debated and controversial. The available studies, although showing contradictory results, have revealed a linear relationship between FM severity and age, both in one direction, worsening of disease severity with increasing age, and in the other, improvement of disease severity with increasing age.

Chronic widespread pain caused by musculoskeletal disorders is a major

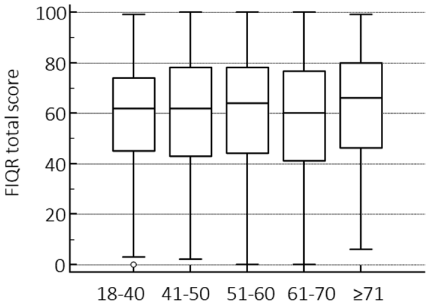

Fig. 1. Box-and-whisker plot for the revised Fibromyalgia Impact Questionnaire total score according to age categories differences (one-way analysis of variance).
Boxes represent the interquartile range. The middle line within the plot represents the mean. X-axis age categories expressed in years.

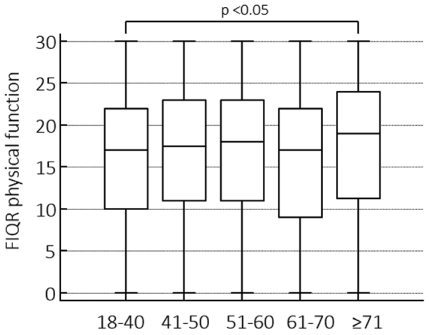

Fig. 2. Box-and-whisker plot for the revised Fibromyalgia Impact Questionnaire subscale physical function according to age categories differences (one-way analysis of variance).
Boxes represent the interquartile range. The middle line within the plot represents the mean. X-axis age categories expressed in years. Significative difference between the first (18–40 years) and the last (≥71 years) category.

social burden since it affects up to 24% of the general population in some studies, and age seems to be a risk factor (18). The relationship between pain and age is complex. Ageing does not seem to have a relevant effect on pain tolerance, but only to reduce the sensitivity to low intensity painful stimuli (19). Chronic pain tends to show a higher prevalence in older patients than in younger patients (20). There is a strand of literature that indicates for FM, as for other chronic pain conditions, this kind of age-related trend.

Tander *et al*., in a comparative study of quality of life (QoL) and depression in patients with FM and rheumatoid arthritis (RA), documented a correlation mainly between age and worsening of physical functioning and bodily pain. Conversely, in RA patients, no associations emerged between the subscales of the SF-36 and age (11). Similarly, a 2008 study investigating variables associated with QoL in patients with FM documented that older age was associated with greater disease severity (12).

There are studies showing an opposite attitude of FM severity with respect to age. Jiao and colleagues revealed how, when distinguishing patients into three categories, the burden of FM is more severe in the two age categories below 39 years and between 40–59 years. Young and middle-aged patients would have a worse QoL than older patients (above 60 years), and also higher FIQ scores. In the subscale analysis of the SF-36, this study also found that physical component summary (PCS) scores were lower (indicative of worse physical health-related QoL) in young FM patients than in middle-aged or older patients. This same study also revealed that mental component summary scores are indicative of reduced QoL in middle-aged patients (13). The findings regarding the PCS are in contrast to those of the general population, however, they are not the only ones. Campos and Vazquez, while showing stability in the absence of significant differences between age categories, documented that scores on health domains related to physical function were better in older patients (21). Cronan *et al*., in turn, have documented that as age and disease duration increase, symptoms related to FM severity are reduced (22). These last three studies cited were all based on the distinction of three age groups (≤39 years, between 40 and 59 years, and ≥60 years). Arguably, the distinction into five categories instead of three allowed for a more detailed analysis of trends in FM severity in relation to age. This categorisation revealed that the population with the lowest overall FM severity (considering the total FIQR and FAS 2019mod scores) is that between 60–70 years of age. This finding, although not statistically significant, may be of some interest, as it has not been documented by any other study before.

The explanation for the deflection in FM severity in the decade 60–70 years could be provided mainly by the fact that this age category coincides with retirement from employment in Italy and generally in Western countries. Being retired seems to have a positive influence on several health domains. An Australian study conducted on women showed that retirement is beneficial on several key health aspects in patients with FM, namely physical functioning, role physical and bodily pain (23). The positive health effects of retirement are thought to be related to increased physical activity, among other factors. The fundamental role of exercise in the management of FM patients is well known (24), and is one of the main therapeutic indications suggested by the recommendations for the management of FM (14). However, this explanation remains a matter of hypothesis and will need to be evaluated in further population studies.

The most significative finding of the present study is the difference in FIQR physical function between the older and younger categories, with a greater burden in the older subjects. Although, as already discussed, the evidence in the literature is contradictory, this result was somewhat expected. Conditions characterised by chronic pain tend to become more prevalent with aging. A meta-analysis on the prevalence of chronic pain conducted in the United Kingdom showed that the prevalence of chronic pain increases with age, ranging from a prevalence of 14.3% between the ages of 18–25 years to a prevalence of 62% over the age of 75 years (25). FM generally is a condition that is associated with other comorbidities that negatively impact functional capacity, primarily osteoarthritis (OA) (26). The association between OA and advanced age is well known, and it is also known that OA is a predisposing condition for frailty (27). A portion of FIQR physical function is likely influenced by comorbidities. An elegant study by Dutta and colleagues demonstrated that genetic predisposition predominantly affects individuals with FM diagnosed at a younger age, *i.e*. those with a primary FM condition. In older subjects, the genetic predisposition to FM would wane, so they would be more prone to develop FM concom-

itant with other nociceptive pain conditions (28).

Conversely, the peak in severity between the ages of 50–60 years could also be attributable to the effects of menopause. The relationship between hormonal changes at certain times in the life of the female population with exacerbation of musculoskeletal pain symptoms is well known (29). Patients with FM in the post-menopausal period report increased pain compared with the pre-menopausal period. The post-menopausal period also exacerbates FM symptoms in at least one-quarter of patients (30).

The major strength of the study is the large sample size, obtained from a national registry that includes adult patients with a wide range of FM severity. The case series is therefore a reliable representation of the real life of patients with FM from different social and cultural backgrounds. The large sample size also allowed the distinction between five categories of disease severity, with adequate representation for each category. The study with the largest sample size had previously identified only three age categories (14). The five categories enabled a more detailed analysis of the severity of the disease in accordance with age.

The limitations of the study include the cross-sectional evaluation that does not allow the analysis of causal relationships, and the different sample size in the age categories, which led to a relatively lower representation of patients over 70 years. A third limitation may be the absence of data regarding comorbidities that could potentially cause nociceptive pain and affect functional capacity.

In conclusion, this study demonstrated that clinimetric indices measuring the severity of FM show substantial stationarity by distinguishing patients in five age categories. However, patients between 60–70 years of age have a lower burden of disease. Significant differences emerge only in the FIQR physical function, where the category of older patients has worse scores than younger subjects. Future studies should investigate the role of comorbidities and retirement on the severity of FM.

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