Consistency between the 2016 ACR criteria and a previous diagnosis or hypothesis of fibromyalgia in a specialised referral clinic

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Abstract

Objective

Fibromyalgia (FM) is a complex syndrome whose hallmark features are chronic widespread pain, sleep disturbances, fatigue and cognitive dysfunctions. However, it is still difficult to apply validated diagnostic criteria. The aim of this study is to examine the accuracy of a previous diagnosis/diagnostic hypothesis of FM according to the 2016 ACR diagnostic criteria.

Methods

All of the patients newly referred to a private rheumatological clinic with the specific request for a consultation because if FM over an 18-month period were evaluated by means of a standardised protocol in order to determine whether they fulfilled the 2016 ACR diagnostic criteria for FM. They were initially divided into three groups: those with a previous diagnosis of FM (group 1), those with a physician's diagnostic hypothesis of FM (group 2) and those who personally hypothesised FM (group 3). They were subsequently classified as having FM, IFM (borderline scores) or not having FM (non-FM) on the basis of the 2016 ACR diagnostic criteria.

Results

The study involved 216 patients (25 males and 191 females): 112 in group 1, 49 in group 2, and 55 in group 3. Only 89 patients (41.2%) fulfilled the ACR criteria; 42 (19.44%) met the study protocol-defined scores for IFM; and 85 (39.35%) were diagnosed as not having FM. Only 50% of the patients with a previous diagnosis of FM fulfilled the ACR criteria, and just under 25% did not have FM. Almost 50% of the patients with a physician's diagnostic hypotheses of FM did not have FM, whereas 20% of the patients who personally hypothesised FM fulfilled the ACR criteria. GP scores and TPCs were significantly different (FM > IFM, FM > non-FM, and IFM > non-FM) as were WPI, SSS and PSD scores for FM > IFM group. Rheumatologists made the previous diagnosis in 92.85% of patients, 53.84% of whom met the ACR criteria and about 20% did not have FM; and as many as 37.5% of the patients with a previous diagnosis made by a non-rheumatologist did not have FM. The non-FM patients were given 84 alternative diagnoses, 78.5% of which referred to rheumatic diseases. One hundred and thirty-one patients had 86 closely pain-related co-morbidities, 94.1% of which were rheumatic diseases.

Conclusion

Our findings confirm the inaccuracy of FM diagnoses and highlights the possibility that in everyday clinical practice, they are not always made with reference to very specific criteria and that there is a high risk of classifying non-FM patients as having FM. They also underline the importance of an accurate differential diagnosis. Separately classifying as IFM those patients who do not meet the ACR criteria, but have clinical findings indicating FM, may help to prevent their exclusion from specific treatment(s).

Key words

fibromyalgia, diagnosis, criteria, incomplete fibromyalgia, comorbidity, misdiagnosis, differential diagnosis

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Introduction

Fibromyalgia (FM) is a complex syndrome characterised by a wide range of different symptoms. Its hallmark feature is chronic widespread pain (CWP), and the other cardinal symptoms are sleep disturbances and fatigue. However, over the last 20 years, it has become increasingly widely accepted that a complete evaluation should also include an assessment of cognitive dysfunctions and many other functional symptoms. This has further complicated the diagnosis, although in the recent years the diagnostic procedure has become clearer (1).

The 1990 American College of Rheumatism (ACR) classification criteria established CWP and tenderness as the foundations for new research (2), although Yunus had previously stressed the importance of other historical features in his preliminary criteria of 1989 (3). Subsequently, the unreliability of CWP and tender point counts (TPCs), which were to be denounced by Wolfe in his historical editorial of 2003 (4), indicated that other symptoms also needed to be considered. The WHO-ICF (International Classifications of Function) core sets for CWP were validated in FM patients in 2009, but did not include a number of categories that are very significant for defining FM (5, 6). In 2010 and 2011, the ACR proposed new preliminary diagnostic criteria in an attempt to improve (but not replace) its much criticised 1990 criteria (7), and these had the merit of finally recognising the importance of non-painful symptoms such as fatigue, thought or memory disturbances, and unrefreshing sleep, as well as many other somatic symptoms. However, they simultaneously undermined the concept of widespread pain, which had always been recognised as essential by almost everyone because they made it possible to diagnose FM even in patients with only three pain sites, thus giving rise to the risk of inflated estimates of prevalence (8).

In 2016, the ACR extended its criteria by introducing the concept of generalised pain almost as if it were an entry diagnostic criterion; the three cardinal symptoms of fatigue, sleep disturbances and cognitive dysfunction were confirmed; and the list of somatic symptoms was greatly simplified to include only depression, headache and abdominal pain. Furthermore, the previous recommendations concerning diagnostic exclusions were eliminated and so a diagnosis of FM did not exclude the presence of other clinically important illnesses (9).

However, despite these changes and as they have been doing for many years (10), physicians continue to complain about the way in which FM was diagnosed, because a significant proportion of patients who actually have the disease do not fulfil the diagnostic criteria (11, 12), and clusters of patients are over-diagnosed or (much worse) misdiagnosed (13, 14).

The clinical picture of FM is hardly ever clear, immediate or logical and, in many cases, its diagnosis is only a result of the exclusion of other similar diseases or the absence of any other plausible diagnosis. Furthermore, the majority of health professionals do not use currently validated diagnostic criteria in their everyday practice, but rely on their clinical skills and experience (14).

Although Wolfe pointed out the unreliability of digital palpation and TPCs (4), physicians probably still use it while referring to the older ACR classification criteria. However, it is only fair to note that, though approximate, evaluating tender points is the only practical and reliable means of testing the pain threshold, which is the manifestation of the central sensitisation that is the essence of FM (15, 16). Furthermore, FM is often associated with rheumatic diseases such as osteoarthritis, rheumatoid arthritis or spondyloarthritis, or connective tissue diseases such as Sjögren's syndrome (17-19), and the simple count of painful points for the widespread pain index of the 2016 ACR 2016 criteria may be insufficient, unsatisfactory, or even dangerous in the absence of a careful evaluation of the features and sites of pain.

The difficult of ensuring that all patients satisfy the ACR diagnostic criteria could be overcome by adopting the old and new concept of "incom-

plete FM" to describe the patients who do not meet the positive FM criterion at a first evaluation, but have its main features in a milder form with fewer symptoms (15, 20, 21). It must also be remembered that CWP itself can be a diagnosis, especially in the absence or minimal presence of the typical non-painful symptoms of FM (21-25). Finally, it is frequent to come across patients who have been given an often questionable, inconclusive diagnostic hypothesis of FM that leads them on a continuous pilgrimage in the search for diagnostic confirmation. Worse, a diagnostic hypothesis often becomes a diagnosis in itself. Furthermore, the advent of the Internet and social media has led many patients with multi-faceted symptoms to self-suspect an FM diagnosis (26).

The aim of this study was to investigate whether patients attending a consultation after receiving a definite diagnosis or a diagnostic hypothesis of FM meet the current ACR diagnostic criteria, determine the type of physician making the diagnosis or hypothesis, and establish the presence of other alternative or associated diseases.

Methods

Population

Two hundred and sixteen consecutive patients, referred to a private rheumatological clinic with a specific request for a consultation concerning FM, were evaluated by means of a standardised protocol in order to determine whether they fulfilled the 2016 ACR diagnostic criteria. The clinic is a referral centre for the diagnosis and treatment of FM in the vast Italian area of the Triveneto (Veneto, Friuli Venezia Giulia, and Trentino Alto-Adige).

The study

This interventionless observational study was carried out between June 2018 and November 2020, and involved 2-3 first medical examinations a week. At the time of booking an appointment by telephone, the patients were asked whether they had received a diagnosis or hypothesis of FM, and then classified as undergoing a "first examination for FM".

Table I. Sub-division of the cases.

FM	GP 4 or 5	Case A Case B	WPI ≥7 WPI 4-6	SSS ≥5 SSS ≥9	2016 ACR criteria
IFM	GP 4-5 GP 4-5 GP 3		PSD 9-11 PSD 12-14 non-A non-B PSD ≥9		Patients with borderline ACR scores
Non-FM	GP 3-5		PSD <9		Patients without FM
pCWP	GP 4-5		WPI ≥7	SSS <3	Primary CWP scoring hypothesis

FM: fibromyalgia; IFM: incomplete fibromyalgia; non-FM: not fibromyalgia; pCWP primary chronic widespread pain.

The evaluations began with three preliminary questions: "Have you already received a diagnosis of FM? If not, is it just your personal hypothesis or that of another doctor? What kind of doctor diagnosed or suspected FM?" The patients were then divided into three groups: those with a previous diagnosis of FM (group 1); those with a physician's hypothesis of FM (group 2); and those with a personal hypothesis of FM (group 3). The previous diagnoses had to be certified by a medical report.

The protocol

The protocol of the one-hour examinations included a complete medical history and a physical examination, with joint evaluation and a TPC, after which the 2016 ACR diagnostic criteria were verified. The other data collected were the age and sex of the patients, and disease duration from the initial onset of painful symptoms and (only for group 1 patients) from the time of the diagnosis.

Endpoints and score collection

The primary study endpoint was the accordance between the previous diagnosis/hypothesis of FM and the new ACR diagnostic criteria. Generalised pain (GP), the widespread pain index (WPI), the symptom severity scale (SSS), and poly-symptomatic distress (PSD) were assessed. The WPI, SSS, and PSD were only calculated in the case of patients with a GP score of >2; the other patients were not diagnosed as having FM. The patients with a GP score of 4–5, a WPI of ≥7 and a SSS score of ≥5 (case A) or a WPI of 4–6 and a SSS score of 9 (case B) were diagnosed as having FM according to the 2016 ACR criteria.

In the case of clinical correspondence, the definition of incomplete FM (IFM) was used for the patients with a previous diagnosis/hypothesis of FM (as proposed by Yunus) (15), but in the presence of borderline ACR scores. Borderline scores not fulfilling the ACR criteria were defined as follows: a GP score of 4–5 and a PSD score of 9–11, a GP score of 4–5 and a PSD 12–14 (not corresponding to case A or B), or a GP score of 3 and a PSD score of ≥9. A PSD score of 9 is the result of the sum of the minimum WPI and SSS scores required by the ACR criteria.

The patients with a GP score of 3-5 but a PSD score of <9 were not diagnosed as having FM or IFM (non-FM). An attempt to define a diagnosis of primary CWP was made in the case of patients with a GP score of 4–5, a WPI score of ≥7 and an SSS score of <3 who did not qualify for a diagnosis of FM, IFM, or any other disease that could explain the pain. Table I shows the practical subdivision of cases.

The patients diagnosed as having FM or IFM were asked to return for a follow-up consultation after two months; those without a diagnosis of FM or IFM could choose whether to return for a check-up of their diagnosed disease or further investigations.

The secondary endpoint was the type of doctor making the diagnosis/hypothesis of FM. Any rheumatological comorbidities in the FM and IFM patients were highlighted, and an alternative, closely pain-related diagnosis based on the examination findings, available test results, and the findings of any further investigations, was proposed for the non-FM patients.

Table II. Data at the time of the first examination by group and sex.

Group	no. pts	M	F	Age (years)	Pain duration (years)	Time since diagnosis (years)	GP	WPI in FM-IFM pts	SSS in FM-IFM pts	PSD in FM-IFM pts	TPC
Total	216	25 (11.57%)	191 (88.43%)	48,47±12.71	9.11±8.67	4.08±4.5	3.77±1.4	7.64±2.41 (131)	6.48±1.68	13.99 ± 3.27	12.22 ± 5.94
1	112 (51.85%)	12 (10.71%)	100 (89.29%)	50.27±11.85	10.38±9.04	4.08±4.5	4.13±1.21	7.52±2.13 (85)	6.51±3.2	13.82±3.2	14.19±4.48
2	49 (22.69%)	6 (12.24%)	43 (87.76%)	47.38±13.69	7.84±7.77	-	3.57±1.51	8.23±2.84 (26)	6.38±1.55	14.61±3.45	10.346.85±
3	55 (25.46%)	7 (12.73%)	48 (87.27%)	45.78±13.25	7.65±8.48	-	3.21±1.49	7.35±2.96 (20)	6.55±1.56	13.9±3.5	9.87±6.43
M	25	-	-	40.6±15.74	7.18±6.65	-	3.51±1.61	8±1.8 (12)	6.66±1.82	14.66±2.74	7.64±6.92
F	191	-	-	49.5±11.96	9.36±8.9	-	3.8±1.38	7.6±2.48 (119)	6.47±1.68	13.92±3.34	12.82±5.56

Statistical analysis

Age	Pain duration	GP	TPC
Group 1 *vs.* 2 p=0.177	Group 1 *vs.* 2 p=0.0835	Group 1 *vs.* 2 $p < 0.013$	Group 1 *vs.* 2 p<0.0001
Group 1 *vs.* 3 p< 0.0282	Group 1 *vs.* 3 p=0.0602	Group 1 *vs.* 3 $p < 0.0001$	Group 1 *vs.* 3 p<0.0001
Group 2 *vs.* 3 p=0.54	Group 2 *vs.* 3 p=0.452	Group 2 *vs.* 3 p=0.23	Group 2 *vs.* 3 p=0.716
M *vs.* F p<0.0009	M *vs.* F p=0.2702	M *vs.* F p=0.1705	M *vs.* F p<0.0001

Group 1: patients with a previous diagnosis of FM; group 2: patients with a physician's suspicion of FM; group 3: patients with a personal suspicion of FM. pts: patients; M: males; F: females; FM: fibromyalgia; IFM: incomplete fibromyalgia; GP: generalised pain; WPI: widespread pain index; SSS: symptom severity scale; PDS: polysymptomatic distress; TPC tender point count.

Statistical analysis

GraphPad statistical programme by Dotmatics was used to analyse the result, measuring differences between exactly the means of different group using the simple unpaired t-test (Student's t-test) for age, pain duration, GP, WPI, SSS, PSD and TPC.

Results

Twenty-five (11.57%) of the 216 patients were males, and 191 (88.43%) were females. The mean age of the patients as a whole was 48.47 years (range 13–79), but the males were significantly younger than the females (males 40.6, females 49.5) (p<0.0009). The mean duration of pain was 9.11 years, and the mean time from diagnosis among those who had received a diagnosis of FM was 3.96 years (group 1). The mean GP and PSD scores were 3.77 and 13.99, and the mean TPC was 12.22.

As shown in Table II, 112 patients (12 males and 100 females; 51.85%) had previously been diagnosed as having FM (group 1); 49 (6 males and 43 females; 22.69%) had received a diagnosis of suspected FM (group 2); and 55 (7 males and 48 females; 25.46%) had self-hypothesised FM (group 3). The previous medical diagnosis of the group 1 patients was usually generic: although it was sometimes possible to retrieve a generic reference to tender points, very few reports recorded a TPC, and none of the diagnoses was based on the 2016 ACR criteria.

The patients in group 1 were older than those in group 2 or 3, but the difference was significant only between groups 1 and 3 (p<0.02).

Pain duration was longer in group 1 than in group 2 or 3, and longer in the females than the males, but these differences were not significant.

The WPI, SSS and PSD values were quite homogeneous, without any significant between-group differences. The GP score was significantly higher in group 1 than in group 2 (p<0.013), and even more significantly higher than in group 3 (p<0.0001), but there was no significant difference between groups 2 and 3, or between males and females.

TPCs were significantly higher in group 1 than in group 2 or 3, and significantly higher in the females than the males (p<0.0001 in all cases). There was no significant difference between groups 2 and 3.

Table III shows the data concerning the final diagnoses. Only 89 (41.2%) of the 216 patients fulfilled the ACR diagnostic criteria. Forty-two (19.44%) had the study protocol-defined scores for IFM; and as many as 85 (39.35%) were not diagnosed as having FM or IFM (non-FM), including eight with scores defining CWP as defined above, five of whom had diseases that could explain the pain: only the remaining three could be classified as having primary CWP.

In groups 1, 2 and 3, respectively, 60 (53.57%), 18 (36.73%) and 11 patients (20%) fulfilled the ACR criteria; respectively 25 (22.32%), 8 (16.33%) and 9 (16.36%) patients met the study protocol-defined scores for IFM; and respectively 27 (24.11%), 23 (46.94%) and 35 (63.64%) patients were categorised as non-FM. This means that, although just over 50% of the previous diagnoses met the 2016 ACR criteria, just under 25% did not; almost 50% of the medical hypotheses of FM were not FM. However, and very interestingly, 20% of the patients with self-hypothesised FM actually satisfied the ACR criteria.

The mean age and mean time since diagnosis (in group 1) were similar in the FM, IFM, and non-FM groups. Mean pain duration was longer in the FM group (10.75 years) than in IFM (8.36 years) or non-FM group (7.67), but only the difference between the FM and non-FM groups was statistically significant (p<0.03).

However, the mean GP score and TPC were very different in the three diag-

Table III. Data according to the final diagnoses (FM, IFM, non-FM).

Group	no. pts	M	F	Age (years)	Pain duration (years)	Time since diagnosis (years)	GP	WPI	SSS	PSD	TPC
FM	89 (41.2%)	9 (11.25%)	80 (88.75%)	48.33±13.35	10.75±9.46	-	4.84±0.36	8.55±2.28	6.91±1.45	15.41±2.77	15.75±3.29
1	60	6 (10%)	54 (90%)	49.5±13.19	12.15±10.09	4.53±4.99	4.85±0.36	8.33±1.89	6.95±1.44	15.21±2.42	16.1±2.35
2	18	2 (11.11%)	16 (88.89%)	49.44±11.87	9.19±8.45	-	4.89±0.82	8.83±3.14	6.89±1.41	15.72±3.54	15.38±4.35
3	11	1 (9.09%)	10 (90.91%)	39.81±14.53	5.68±4.59	-	4.72±0.46	9.27±2.61	6.72±1.67	16±3.28	14.45±5.24
IFM	42 (19.44%)	3 (7.14%)	39 (92.86%)	48.88±10.75	8.36±6.23	-	3.97±0.86	5.71±1.36	5.61±1.83	10.97±2.04	14.14±3.61
1	25	3 (12%)	22 (88%)	52.36±10.41	8.68±5.41	3.5±3.57	4±0.84	5.6±1.29	5.48±2.12	10.48±2.25	13.88±3.65
2	8	0	8 (100%)	43.5±4.7	7.18±8.31	-	4±0.92	6.87±1.35	5.25±1.28	12,12±1.35	13±4.69
3	9	0	9 (100%)	44±12.4	8.55±7	-	3.88±1.05	5±1	6.33±1.22	11.33±1.5	15.88±1.69
Non-FM	85 (39.35%)	13 (15.29%)	72 (84.71%)	48.4±13.12	7.67±8.69	-	2.55±1.35	-	-	-	7.57±6.01
1	27	3 (11.11%)	24 (88.89%)	49.92±9.99	8.05±8.68	3.64±4.13	2.66±1.38	-	-	-	10.25±6.02
2	23	4 (17.39%)	19 (82.61%)	47.13±16.84	7.02±7.22	-	2.39±1.3	-	-	-	5.47±5.71
3	35	6 (17.14%)	29 (82.86%)	48.11±12.74	8.04±9.74	-	2.57±1.39	-	-	-	6.88±5.6

Statistical analysis

Pain duration		GP		WPI / SSS / PSD		TPC		TPC in non-FM group	
FM *vs*. IFM	p=0.139	FM *vs*. IFM	p<0.0001	FM *vs*. IFM	p<0.0001	FM *vs*. IFM	p<0.0126	1 *vs*. 2	p<0.006
FM *vs*. non-FM	p<0.0321	FM *vs*. non-FM	p<0.0001	FM *vs*. IFM	p<0.0001	FM *vs*. non-FM	p<0.0001	1 *vs*. 3	p<0.026
IFM *vs*. non-FM	p=0.69	IFM *vs*. non-FM	p<0.0001	FM *vs*. IFM	p<0.0001	IFM *vs*. non-FM	p<0.0001	2 *vs*. 3	p=0.35

Group 1: patients with a previous diagnosis of FM; group 2: patients with a physician's suspicion of FM; group 3: patients with a personal suspicion of FM; pts: patients; M: males; F: females; FM: fibromyalgia; IFM: incomplete fibromyalgia; Non-FM: not fibromyalgia; GP: generalised pain; WPI: widespread pain index; SSS: symptom severity scale; PDS: polysymptomatic distress; TPC tender point count.

nostic groups. The GP scores were 4.84 in the FM group, 3.97 in the IFM group, and 2.55 in the non-FM group, with the differences being highly significant between the FM and the IFM and non-FM groups, and between the IFM and non-FM groups (p<0.0001). The mean WPI and PSD scores were different between the FM and IFM group (respectively 8.55 *vs*. 5.71, and 15.41 *vs*. 10.97) and, although less marked, the same was true of the SSS scores (6.91 *vs*. 5.61). All of these differences were highly significant (p<0.0001). The TPCs were 15.75 in the FM group, 14.14 in the IFM group, and 7.57 in the non-FM group: the difference between the FM and non-FM group and that between the IFM and non-FM group was highly significant (p<0.0001), and the difference between the FM and IFM group was statistically significant (p<0.01).

The GP, WPI, SSS and PSD scores and TPCs were similar within the three diagnostic groups except in the case of the non-FM group in which the TPC was significantly higher in group 1 than in group 2 (10.25 *vs*. 5.47; p<0.006) and group 3 patients (10.25 *vs*. 6.88; p<0.026).

Table IV shows the data concerning the physicians who made the previous diagnosis/hypothesis of FM (it is necessary to remember that these were sometimes more than one in the same patient, which is why the sums of the percentages may not be 100). A rheumatologist made the diagnosis in 104 of the patients in group 1 (92.85%): only 53.84% of these cases met the ACR diagnostic criteria, 21.15% fell within the study protocol-defined scores for IFM, but as many as approximately 20% were not cases of FM (five patients had previously unrecognised inflammatory arthritis). In group 2, the hypothesis of FM was mainly suggested by non-rheumatologist physicians (87.75%), while rheumatologists suggested it only in just under 30% of cases, but just over 40% of these were not cases of FM.

Of the 21.42% of diagnoses made by non-rheumatologists (group 1), as many as 37.5% were not FM, and the same was true of 45% of the hypothesised diagnoses (group 2).

As shown in Table V, the 84 alternative, closely pain-related diagnoses proposed (possibly also in comorbidity) for the non-FM patients (78.5% of which were rheumatic diseases) included inflammatory arthritis (19), soft-tissue rheumatism (31), degenerative arthritis (15), chronic pain (8), neuropathy (3), and connective tissue disease (1). Fifty-seven of these were previously unknown. Among previously unknown diagnosis are notable the number of inflammatory arthritis and myofascial pain syndrome. A diagnosis was not possible in 17 cases.

Table VI shows the data concerning 86 closely pain-related co-morbidities in FM and IFM patients, 81 of which were rheumatic diseases. Forty-nine patients in the FM group had a total of 56 co-morbidities: inflammatory arthritis (28), degenerative arthritis (15), soft-tissue rheumatism (9), osteoporosis (2), and connective tissue disease (2). Twenty-three patients in the IFM

Table IV. Data concerning the physicians who made the diagnosis of FM or hypothesised FM.

Group	no. pts	RHEUM % on pts	NON-RHEUM % on pts	PHYS	NEURO	PAIN THER	ORTHO	FAM DOC	INTERN	OTHER	UNKN
1	112	104 (92.85%)	24 (21.42%)	8	6	4	1	1	2	1	1
2	49	14 (28.57%)	43 (87.75%)	5	6	4	6	10	1	10	1
		% of 104 rheum	% of 24 non-rheum								
1 FM	60	56 (53.84%)	10 (41.6%)	3	2	2	1	1	1		
1 IFM	25	22 (21.15%)	5 (20.83%)	3	1				1		
1 Non-FM	27	22 (21.15%)	9 (37.5%)	2	3	2				1	1
		% of 14	% of 43								
2 FM	18	7 (50%)	17 (39.53%)	4	4	1		5		3	
2 IFM	8	1 (7.1%)	7 (16.28%)	1	1	1	1	1	1	1	
2 Non-FM	23	6 (42.85%)	19 (44.18%)		1	2	5	4		6	1

Note: the percentages in groups 1 and 2 do not add up to 100 because the diagnosis/hypothesis of FM in some patients was formulated by more than one physician.
Group 1: patients with a previous diagnosis of FM; group 2: patients with a physician's suspicion of FM; FM: fibromyalgia; IFM: incomplete fibromyalgia; Non-FM: not fibromyalgia; pts: patients; RHEUM: rheumatologist; NON-RHEUM: non rheumatologist: PHYS: physiatrist; NEURO: neurologist; PAIN THER: pain therapist; ORTHO; orthopaedic; FAM DOC; familial doctor; INTERN: internist; UNKN: unknown.

Table V. Alternative diagnoses in patients without FM.

Group	no. pts	IA	OA	MPS	CWP	RCWP	NEUR	HEDS	TEND	SS	GAD	Total	UNDET
1	27	9	7	5	2	2					2	27	6
2	23	3	6	9	2		3	2	1	1	1	28	1
3	35	7	2	13		2		1			4	29	10
Total	85	19	15	27	4	4	3	3	1	1	7	84	17
Prev Unkn		13	2	26	3	3	2	3			5	57	

Prev Unkn: previously unknown diagnoses; pts: patients; IA: inflammatory arthritis; OA: osteoarthritis; MPS: myofascial pain syndrome; CWP: chronic widespread pain; RCWP: regional CWP; NEUR: neuropathy; HEDS: hypermobile Ehlers-Danlos syndrome; TEND: tendonitis; SS: Sjögren's syndrome; GAD generalised anxiety disorder; UNDET: undetermined.

Table VI. Co-morbidities in the FM and IFM groups.

Diagnoses	no. pts	Pts with comorbid	IA	OA	MPS	CWP	RCWP	OP	HEDS	CTD	PMR	GAD	Total
FM													
1	60	36	16	14	4			2	2	2	1		41
2	18	9	7	1	3								11
3	11	4	4										5
Total	89	49	27	15	7			2	2	2	1		56
UNK			19	2	6			2	2				31
IFM													
1	26	16	7	4	6	1		1		1		1	21
2	8	1	1										1
3	9	6	3	2	2		1						8
Total	42	23	11	6	8	1	1	1		1		1	30
UNK			7	1	10	1							19

IFM: incomplete fibromyalgia; Pts: patients; comorb: comorbidities; UNK: previously unknown comorbidities; IA: inflammatory arthritis; OA: osteoarthritis; MPS: myofascial pain syndrome; CWP: chronic widespread pain; RCWP: regional CWP; OP: osteoporosis; HEDS: hypermobile Ehlers-Danlos syndrome; CTD: connective tissue disease; PMR: polymyalgia rheumatica; GAD generalised anxiety disorder.

Table VII. Proposed differential diagnoses in patients with CWP syndromes (30).

A) Functional

Fibromyalgia
Chronic fatigue syndrome

Related to/associated with
- PTSD
- GAD
- Depression
- RLS and sleep disturbances

B) Organic

Related to/associated with cerebral disease
- Chronic cerebral vasculopathy
- Parkinson's disease
- Senile dementia

Related to/associated with chronic inflammatory disease or connective tissue disease
- Sjögren's syndrome
- Systemic lupus erythematosus
- Chronic primary arthritis
- Systemic sclerosis
- Polymyalgia rheumatica
- Polymyositis

Infectious or post-infectious diseases

Chronic fatigue syndrome

Related to/associated with viral infection
- Active chronic hepatitis C
- Post-Lyme syndrome
- HTLV-1
- HIV
- Hepatitis B carriers
- Parvovirus B19

Related to/associated with cancer
- Metastatic bone cancer
- Myeloma bone disease
- Leukemia/lymphoma

Related to/associated with endocrine or metabolic diseases
- Hypovitaminosis D
- Hypocalcemia or magnesium deficiency
- Endometriosis
- Hypothyroidism

Causative drugs
- Statins
- Fibrates
- Reserpine

Other conditions
- Myofascial pain syndromes
- Hypermobile Ehlers-Danlos syndrome

CWP: chronic widespread pain.

group had a total of 30 co-morbidities: inflammatory arthritis (11), soft-tissue rheumatism (8), degenerative arthritis (6), chronic pain (2), osteoporosis (1), connective tissue disease (1), and generalised anxiety disorder (1). Fifty of these co-morbidities were previously unknown, including 16 cases of inflammatory arthritis in patients previously examined by a rheumatologist.

Ninety-nine of the 216 patients (45.83%) did not return for the scheduled follow-up after two months: 33/89 in the FM group, 14/42 in the IFM group, and 52/85 in the non-FM group.

Discussion

FM is a pathological entity that is being increasingly recognised by physicians and lay people alike. The outdated belief that it does not exist, or is only somatisation, depression or "in your head" has now fortunately almost disappeared (27). Nevertheless, the procedures that allow physicians to make a correct diagnosis in everyday practice are anything but homogeneous or appropriately carried out.

The findings of a number of recent studies suggest that FM is inaccurately diagnosed in the community, and that about 75% of the people reporting a physician's diagnosis would not satisfy validated criteria (11, 12, 21). So how do most physicians diagnose FM? Are the new criteria actually followed? What is the main parameter used: clinical experience, TPCs, CWP, symptom severity, or the "incomprehensible" nature of the pain? Unfortunately, it is still common to hear claims such as: "You are not sick, you look fine!", or such as: "You have already done a lot of tests… then you have fibromyalgia!"

The new criteria have defined the importance of some parameters that are essential for a diagnosis: CWP and the presence of at least four painful points in four different body regions are mandatory, and SSS scores are decisive in making a final decision. However, it is likely that not all cases of FM fully meet the diagnostic criteria, and it is probably useful to distinguish such borderline cases by re-introducing the concept of IFM as a means of defining the disease in patients who do not satisfy the 2016 ACR diagnostic criteria (15, 20).

The issue of CWP has long been debated, as is shown by an old article that pointed out that only 20% of patients with CWP could be diagnosed as having FM according to the 1990 ACR criteria (28). The differential diagnosis of CWP is very intricate as it requires due consideration of all of the possible causes of pain, such as systemic inflammatory rheumatic disease, non-rheumatic musculoskeletal or medical conditions, neuropathy, spinal myelopathy, and myopathy/myositis (29), as suggested too by an Italian Expert Group in 2011 (Table VII) (30). It is also necessary to consider infections and vaccinations as possible causes of CWP, particularly post-Lyme syndrome (31) or the emerging problem of post-COVID syndrome (32). In rheumatological practice, both early and atypical arthritis require attention as co-morbidities and in terms of pain distribution (17), and pain patterns are particularly insidious in patients

with Hypermobile Ehlers-Danlos syndrome, which is much more prevalent than previously thought (33). Finally, it is necessary to calculate the WPI carefully, and decide whether it should be also eligible all painful joint sites, for example like those affected by arthritis or enthesitis.

The findings of our study confirm what many other authors have previously stated: a high percentage of FM diagnoses are inaccurate.

Only 41.2% of all patients undergoing a first examination for FM were found to have FM, and 39.35% were diagnosed as not having the disease. Only 53.5% of the patients with previously diagnosed FM had their diagnoses confirmed on the basis of the 2016 ACR criteria, and 24% were diagnosed as not having FM. The situation was even worse in the case of FM hypothesised by a physician or a patient. When the hypothesis was raised by a physician, the corresponding figures were 36.7% and 46.9%.

In comparison with the confirmed diagnosed FM group, the percentage of males was higher in the non-FM group.

On the other hand, 22.3% of the patients previously diagnosed as having FM, and 16.3% of those with a physician's hypothesis of FM were classified as having IFM, and it is worth noting that about 36% of the patients with self-hypothesised FM actually had FM or IFM. However, regardless of whether FM was confirmed or not, the patients with a previous diagnosis of FM had significantly higher generalised pain scores and TPCs, and were therefore suffering more from pain and tenderness than the patients in the other groups.

Regarding the diagnostic groups, pain duration was significantly longer among the FM patients than among the non-FM patients. All of the ACR parameter scores (GP, WPI, SSS and PSD) were significantly higher in the FM than in the IFM group, and the GP score was also higher in the IFM group than in the non-FM group. Symptoms were therefore generally more severe or more frequent in the FM group. The trend of TPCs was the same in the different groups, thus confirming the close correlation between TPCs and FM.

Most of the previous diagnoses (92.8%) were made by rheumatologists, which confirms their special interest in FM even if 20% of the diagnoses were misdiagnoses. However, diagnostic error was more frequent among the other physicians (37.5%).

The alternative diagnoses of the non-FM patients were rheumatic diseases in 78.5% of cases, which means that physicians (including rheumatologists) overlooked common rheumatological conditions, which were incorrectly diagnosed/hypothesised to be FM in 51.1% of cases.

Finally, 54.6% of the FM and IFM patients had at least one co-morbidity, and 50% of these were previously unknown, of which 32% were cases of inflammatory arthritis.

Our findings highlight the fact that FM diagnoses are not always unambiguous, positive, or based on very specific criteria, and the high risk of misdiagnosing FM is potentially dangerous for the patients. It is likely that some patients with clinically apparent FM simply do not meet the current classification criteria, and there is evidence that patients with milder symptoms may not qualify for a formal diagnosis of FM (15). Given the now universal acceptance that FM represents a continuum of symptoms, it may be time to consider IFM patients as having "mild FM" as it is now the case for other diseases and, in particular, rheumatic diseases. The idea of graduating the severity of FM syndrome has also recently been espoused by other authors (34). This would allow the diagnosis of wider range of cases (35).

Our findings also underline the importance of making a precise differential diagnosis. Physicians need to be more rigorous when evaluating chronic pain, suspected or disputable FM, and rheumatic conditions that may mimic FM syndrome, and should also take into account the fact that a diagnosis of FM does not exclude a concomitant co-morbidity (35). On the basis of our data, rheumatologists seem to be the most suitable specialists for diagnosing FM, particularly given their experience in making differential diagnoses. However, it is interesting to note that many of our more educated and scientifically prepared patients were intuitively capable of making a self-diagnosis.

This study has some limitations. The fact that all of the patients were assessed at a single rheumatology referral clinic may represent a selection bias towards more diagnostically challenging patients. Furthermore, a large percentage of the patients (45.8%) did not return for the expected follow-up examination, and so we were unable to check the diagnosis of FM or IFM, co-morbidities, and alternative diagnoses. It is likely that many of the patients attended the first consultation more for counselling or confirmation of the diagnosis than for treatment. Finally, it is difficult to know whether the patients with a previous diagnosis of FM did not meet the 2016 ACR criteria at the time of our evaluation because FM generally has fluctuating symptoms or because their treatment(s) had fortunately improved their condition.

In conclusion, and in almost complete agreement with Fitcharles *et al*. (10), we believe it is essential to be cautious when evaluating patients with widespread musculoskeletal symptoms. Despite the introduction of new diagnostic criteria, the persistence of such a high rate of diagnostic inaccuracy should alert physicians to the need to consider a wider range of possibilities when evaluating a patient's pain. A thorough anamnestic evaluation, the use of validated criteria, a careful physical examination (including a TPC), and the exclusion of other diseases is the best way of guaranteeing that patients receive a correct diagnosis.

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