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## Frequency of concomitant fibromyalgia in rheumatic diseases: Monocentric study of 691 patients<sup>☆</sup>

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## ABSTRACT

**Objective:** Fibromyalgia (FM) is a confounding factor for diagnosing and assessing rheumatic disease activity. This study sought to assess the extent of this syndrome in rheumatism patients at a French rheumatology department.

**Method:** This monocentric epidemiological study enrolled all patients consulting due to rheumatoid arthritis (RA), spondyloarthritis (SpA), or connective tissue disease (CTD). FM diagnosis was confirmed or excluded according to the rheumatologist opinion and the 1990 American College of Rheumatology (ACR) criteria.

**Results:** We enrolled 691 patients, including 451 women (65.3%), with a mean age of 55.8 years (18–93). Of the enrolled patients, 325 presented with RA, 298 SpA [59 psoriatic arthritis (PsA), 137 ankylosing spondylitis (AS), 64 non-radiographic SpA (nr-SpA), and 38 peripheral SpA], and 71 CTD. The rheumatologist established FM diagnosis in 97 patients (14%), while 55 (8%) fulfilled the 1990 ACR criteria. The frequency of FM was lower in RA patients (4.9% by 1990 ACR criteria; 7.7% by expert opinion) compared to SpA (11.1% by 1990 ACR,  $p < 0.05$ ; 17.5% by expert opinion,  $p < 0.003$ ) and CTD (11.3% by 1990 ACR, non-significant; 28.2% by expert opinion,  $p < 0.001$ ). In the SpA subgroups, FM was more common in the nr-SpA than in PsA or AS (23.9%, 9.6%, and 6.4%, by 1990 ACR,  $p = 0.001$ ; 37.3%, 13.5%, and 7.2%, by expert opinion,  $p < 0.001$ ).

**Conclusion:** FM-like symptoms are commonly associated with rheumatic diseases. The frequency of FM is particularly high in non-radiographic axial SpA, thus raising questions about the specificity of the Assessment of SpondyloArthritis International Society (ASAS) classification criteria.

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### Introduction

Fibromyalgia (FM) is a syndrome combining cognitive disturbance, sleep disorders, fatigue, and associated chronic widespread pain. Its prevalence is 2% in the general population, higher in rheumatic disease cases, and considerably varying depending on the diagnostic criteria used [1,2]. FM is diagnosed in 6.6–22.4% of patients with rheumatoid arthritis (RA) [3–5], with an incidence of 7%, maximal in the first year following RA diagnosis [6]. It has also been reported in association with ankylosing spondylitis (AS) (4–15% of patients) [7,8], systemic

lupus erythematosus (SLE) (6.2–24% of patients) [5,9–11], and Sjögren's syndrome (SS) (12–30%) [12,13].

In clinical practice, FM is a confounding factor in rheumatic disease cases in terms of both diagnosis and disease activity assessment. Firstly, distinguishing FM from rheumatic disease can be challenging, particularly in non-radiographic axial spondyloarthritis (nr-axial SpA), due to the widespread, primarily axial pain, fatigue, and sleep disorders that are common clinical features of both conditions, as well as the enthesitis sites potentially overlapping with FM tender points. Secondly, concomitant FM disrupts disease activity and functional impairment assessment of RA and spondyloarthritis (SpA). It leads to overestimations in the 28-joint Disease Activity Score, as well as the BASFI and BASDAI indices, and causes non-justified therapeutic intensification [4–6,14] with more frequent use of biological therapy [15].

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Our study sought to compare frequency of concomitant FM in rheumatic diseases in a rheumatology department in routine practice.

## Methods

The study was approved by the local ethics committee (*Comité de Protection des Personnes Sud Est VI*) (IRB: 00008526), and written consent was obtained from all patients who agreed to participate in the study, in accordance with the Declaration of Helsinki.

### Patients and diagnoses

All patients who consulted a rheumatologist in the Rheumatology Department of Clermont-Ferrand University Hospital for RA, SpA, or CTD were invited to participate in the study. The following criteria were used to classify patients: the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for RA, New York criteria for AS, axial Assessment of SpondyloArthritis International Society (ASAS) criteria for non-radiographic SpA, peripheral ASAS criteria for peripheral SpA, Classification Criteria for Psoriatic Arthritis (CASPAR) for psoriatic arthritis (PsA), Systemic Lupus International Collaborating Clinic (SLICC)/ACR criteria for SLE, American-European Consensus Group (AECG) criteria for SS, ACR/EULAR 2013 criteria for scleroderma (Scl), and Troyanov et al. [16] criteria for myositis. The FM diagnosis was partly based on the 1990 ACR criteria and the rheumatologist's expert opinion.

### Study description

Clinical and demographic data including age, gender, type of rheumatic disease, and year of diagnosis were collected. The rheumatologist determined the patient's FM status using his professional judgment and assessed tender points to classify FM according to the 1990 ACR criteria [17].

### Statistical analysis

Statistical analysis was performed using Stata 13 software (StataCorp. LP, College Station, TX). The tests were two-sided, with type I error set at  $\alpha = 0.05$ . Continuous data were presented as means  $\pm$  standard deviation or medians (interquartile range), depending on the statistical distribution (assumption of normality checked using normal probability plots and the Shapiro–Wilk test). Comparisons between independent groups were analyzed using Student's *t*-test, or the Mann–Whitney test when conditions for the *t*-test were not met (normality and homoscedasticity verified using the Fisher–Snedecor test) for quantitative variables. Comparisons concerning categorical data were performed using the chi-squared test or Fisher's exact test.

## Results

### Patient characteristics

In total, 691 patients with a rheumatic disease were enrolled between September 2014 and April 2015. The total population consisted of 451 women (65.3%) and 240 men (35.7%), with a mean age of  $55.8 \pm 15.5$  years (Table 1). The population included 325 RA cases, 298 SpA cases (categorized as 59 PsA, 137 AS, 64 nr-axial SpA, and 38 peripheral SpA), and 71 CTD cases (28 SLE, 27 SS, 14 Scl, and 6 myositis).

**Table 1**  
Demographic and clinical characteristics of the population.

Age, years $\pm$ standard deviation (min–max)	55.8 $\pm$ 15.5 (18–93)
Gender	
Female, N (%)	451 (65.3)
Duration of disease, years	
Median (IQR) (min–max)	11 (5–20) (0–58)
Rheumatoid arthritis, N	325
Gender	
Female, N (%)	236 (72.8)
Rheumatoid factor, N (%)	216 (66.7)
Anti-CCP, N (%)	222 (68.5)
Spondyloarthritis, N	298
Gender	
Female, N (%)	152 (51.0)
Psoriatic arthritis, N (%)	59 (19.8)
AS (New York criteria), N (%)	137 (45.9)
SpA, non-radiographic (axial ASAS), N (%)	64 (21.5)
MRI arm	35 (54.7)
Clinical arm	29 (45.3)
SpA, peripheral (peripheral ASAS), N (%)	38 (12.8)
Connective tissue disease (CTD), N	71 <sup>a</sup>
Gender	
Female, N (%)	65 (91.6)
Systemic lupus erythematosus (SLE)	28 (39.4)
Sjögren's syndrome (SS)	27 (38.0)
Scleroderma (Scl)	14 (19.7)
Myositis	6 (8.45)

ASAS, Assessment of SpondyloArthritis International Society; AS, ankylosing spondylitis; CTD, connective tissue disease; SLE, systemic lupus erythematosus; SS, Sjögren's syndrome; Scl, scleroderma; SpA, spondyloarthritis; MRI, magnetic resonance imaging.

<sup>a</sup> Four patients had two CTD associated (2 SLE + SS, 1 SS + Scl, 1 SLE + myositis).

### Frequency of concomitant fibromyalgia in the three inflammatory rheumatic disease groups

The frequency of concomitant FM varied according to the criteria used and the rheumatic disease group (Table 2). The 1990 ACR criteria detected fewer FM cases than expert opinion did: 55/691 (8%) vs. 97/691 (14%).

The frequency of FM was lower in RA (4.9% by 1990 ACR criteria; 7.7% by expert opinion) than in SpA (11.1% by 1990 ACR,  $p < 0.05$ ; 17.5% by expert opinion,  $p < 0.003$ ) and CTD (11.3% by 1990 ACR, non-significant; 28.2% by expert opinion,  $p < 0.001$ ).

**Table 2**  
Frequency of fibromyalgia according to 1990 ACR criteria and physician opinion.

	ACR 1990 criteria	Physician's diagnosis
Rheumatoid arthritis (%)	4.9 <sup>a</sup>	7.7 <sup>b</sup>
Spondyloarthritis (%)	11.1	17.5
Nr-axial SpA	23.9	37.3
Psoriatic arthritis	9.6	13.5
Ankylosing spondylitis	6.4	7.2
Peripheral SpA	5.3	28.9
Connective tissue diseases (%)	11.3	28.2
All rheumatic diseases (%) (95% CI)	8.0 (6.1–10.2)	14.0 (11.5–16.8)

ACR, American College of Rheumatology; CI, confidence interval; SpA, spondyloarthritis.

<sup>a</sup> RA vs. SpA ( $p = 0.05$ ).

<sup>b</sup> RA vs. SpA ( $p = 0.003$ ), RA vs. CTD ( $p = 0.001$ ).

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