REVIEW ARTICLE

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Clinical relevance of resistance training in women with fibromyalgia: A systematic review and meta-analysis

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Abstract

Background and Objective: There has been an increase in the number of papers assessing the effects of resistance training (RT) in patients with fibromyalgia. Therefore, the objective of our study was to evaluate the clinical relevance and effectiveness of RT for pain intensity, functionality and severity of the disease specifically in women with fibromyalgia through a systematic review with meta-analysis.

Databases and Data Treatment: Seven databases were searched. Randomized controlled trials conducted in women over 18 years of age with fibromyalgia were included. Fifteen trials were included in the systematic review and 14 of these studies were included in the three meta-analyses performed. Study quality assessment was performed using the PEDro scale. In addition, the GRADE recommendations were used.

Results: The global meta-analysis revealed statistically significant differences in the RT group versus the control group on pain intensity (SMD$=-0.49$; 95% CI $[-0.74, -0.24]$, $p=0.0001$), functionality (SMD$=-0.23$; 95% CI $[0.01, 0.45]$, $p=0.04$) and on severity of the disease (SMD$=-0.58$; 95% CI $[-0.90, -0.26]$, $p=0.0005$). Clinically relevant improvements in the overall outcome of the three variables studied in favour of RT were obtained.

Conclusions: RT is effective to improve pain intensity, functionality and severity of the disease in women with fibromyalgia. These improvements are clinically relevant. More clinical trials of RT are needed in women with fibromyalgia to support our results due to the low strength of evidence.

Significance: This systematic review with meta-analysis provides evidence that RT produces clinically relevant improvements in women with fibromyalgia. The absence of immediate benefit is often a major barrier to adherence to treatment. Our findings will help clinicians to empower patients that if they continue treatment, they will achieve improvement in their disease.

1 | INTRODUCTION

Fibromyalgia is a syndrome that causes widespread musculoskeletal pain, fatigue, sleep disturbances and physical disability (Andrade et al., 2020; Macfarlane et al., 2017; Marques et al., 2017; Russell et al., 2018; Sarzi-Puttini et al., 2020). It is also related to autonomic alterations, cognitive dysfunction, hypersensitivity to external stimuli, somatic symptoms and psychiatric disorders (Arendt-Nielsen & Graven-Nielsen, 2003; Sarzi-Puttini et al., 2020) and to other diseases, such as chronic fatigue syndrome and irritable bowel syndrome (Silverwood et al., 2017; Yunus, 2008). The prevalence of fibromyalgia is currently estimated to be 2%–4% of the world's population (Cabo-Meseguer et al., 2017; Elizagaray-Garcia et al., 2016; Galvez-Sánchez et al., 2019; Macfarlane et al., 2017; Marques et al., 2017; Sarzi-Puttini et al., 2020), making it the leading cause of chronic widespread pain and the third most common musculoskeletal condition (Elizagaray-Garcia et al., 2016; Sarzi-Puttini et al., 2020). At present, it is estimated that at least 80%–90% of people with fibromyalgia are women, so the disease mainly affects subjects of this sex (Wolfe et al., 2018). However, its aetiopathological mechanisms are still unclear (Silverwood et al., 2017). Over the last 20 years, neurobiological characteristics have been identified that correlate nociplastic pain with fibromyalgia (Sarzi-Puttini et al., 2020); this has provided a new outlook on the diagnosis of these patients, characterized by a process of central sensitization (Cagnie et al., 2014; Desmeules et al., 2003; Meeus & Nijs, 2007; Nijs & Van Houdenhove, 2009; Sarzi-Puttini et al., 2020; Yunus, 2008). Central sensitization is defined as 'amplification of neural signalling within the central nervous system resulting in hypersensitivity to pain' (Woolf, 2011) and was first linked to fibromyalgia in 1994 (Gibson et al., 1994). Clinically, fibromyalgia has many features of central sensitization: hyperalgesia, allodynia, temporal summation and hypersensitivity to external stimuli such as sounds or lights (Sarzi-Puttini et al., 2020). Therefore, it appears that central sensitization plays an important role in these patients, but this process remains a descriptive label for the possible pathophysiological mechanism (Van den Broeke et al., 2018), and further research is required to clarify its involvement in fibromyalgia, as well as to determine its aetiopathological mechanisms.

The latest EULAR (European League Against Rheumatism) recommendations on the management of fibromyalgia emphasize the importance of not resorting to medication as the first intervention measure. The only 'strong' evidence recommendation favours physical exercise (Macfarlane et al., 2017; Sarzi-Puttini et al., 2020).

The indication for physical exercise as a treatment modality in fibromyalgia is to prevent the inactivity and deconditioning that is often associated with pain and fatigue. This deconditioning, resulting from inactivity, can worsen the symptoms associated with fibromyalgia. Patients who engage in consistent physical exercise have been found to report fewer symptoms, better physical function and greater overall well-being (Fink & Lewis, 2017). However, there is controversy around which exercise modality is most beneficial and the optimal dosage parameters (Andrade et al., 2018).

After aerobic exercise, resistance training (RT) is the most researched exercise modality. This modality is also often called 'strength training' (ST). However, there are some differences. Resistance exercise is considered any exercise that causes the skeletal muscles to contract against external resistance to increase skeletal muscle strength, tone, mass or endurance. Strength exercises are specifically resistance exercises with the objective specifically to increase skeletal muscle strength (Hansen et al., 2019).

People with fibromyalgia have decreased muscle strength, which contributes to the loss of functionality observed in these patients (DeSantana & Araújo, 2019). This exercise modality appears to improve pain, tenderness, fatigue, sleep, depression and muscle strength in patients with fibromyalgia (Andrade et al., 2018, 2020). However, aspects related to the duration, frequency and intensity required to improve symptoms remain unknown, as protocols differ between studies, and a consensus is lacking.

Classically, it was believed that training sore muscles was counterproductive (Jones, 2015). However, more than 20 years ago, a growing body of evidence began to emerge that challenged the assumption that RT worsened muscle pain in people with fibromyalgia; and, conversely, that when training was customized to the individual patient's needs, it improved the severity of the disease symptoms (Albuquerque et al., 2022; Vilarino et al., 2022). Patients with chronic pain present severe structural and functional alterations in the central nervous system (Kuner & Flor, 2016; Smallwood et al., 2013). Physical exercise can acutely alter brain processing and cortical inhibition, regulating the inflammatory and immune response (Sluka et al., 2018), but the practice of RT on a regular basis promotes central neuroplastic changes that are supposed to favour pain processing (Pearcey et al., 2021); while regional musculoskeletal adaptations can reduce pain by improving function and capacity of the structure (Sluka et al., 2018). However, having fibromyalgia poses a high hurdle to overcome before reaping the rewards of RT, as these patients are less physically active and have high levels of physical deconditioning. Deconditioned muscles can be a powerful pain generator due to delayed onset muscle soreness (DOMS) as a result of a natural, physiological inflammatory response that contributes to the process of muscle repair and adaptation (Jones, 2015).

In recent years, there has been an increase in the number of publications assessing the effects of RT in patients with fibromyalgia. However, we have not found any meta-analysis that examined the efficacy and clinical relevance of this intervention specifically in women with fibromyalgia, as it is the most affected population. The reviews and meta-analyses mentioned above were conducted in both men and women, this heterogeneity of the study sample may imply a limitation in the results, since the effectiveness of any intervention is affected by several variables and sex is one of these variables.

Therefore, the objective of our study was to evaluate the clinical relevance and effectiveness of RT for pain intensity, functionality and severity of the disease in women with fibromyalgia through a systematic review with meta-analysis.

2 | METHODS

2.1 | Protocol and registration

A systematic review with meta-analysis of randomized control trials was carried out in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses; Page et al., 2021).

This systematic review with meta-analysis is registered in PROSPERO (International Prospective Register of Systematic Reviews; Booth et al., 2012) with code CRD42022312777.

2.2 | Data sources and searches

The literature search was carried out between 24 February and 20 April 2022. With regard to the information search, the databases selected were Web of Science, PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Scopus, Cochrane, Physiotherapy Evidence Database (PEDro) and Dialnet. The search strategies and keywords used are shown in Table S1.

To minimize publication bias, we searched ClinicalTrials.gov. Additional records were also sought by hand searching references from relevant literature reviews to supplement the database findings.

2.3 | Study selection

The outcome measures considered in our study were pain intensity, functionality and severity of the disease. The criteria the studies had to meet to be included were the following:

1. Randomized controlled clinical trials published up to 20 April 2022.
2. Study conducted in women over 18 years of age with fibromyalgia according to the American College of Rheumatology (ACR) diagnostic criteria (1990/2010/2016; Wolfe et al., 1990, 2011, 2016)
3. Including RT or ST as the only intervention in any of the groups. As a comparison group, any intervention to be performed in front of the RT or ST was accepted.
4. Evaluating pain intensity, functionality and severity of the disease.
5. Published in English, Spanish, French, Italian or Portuguese.

We excluded studies that combined ST or RT with another intervention (combined treatment).

2.4 | Data extraction

Two authors independently carried out the selection of studies conducted and data extraction. A third author was consulted in case of disagreement. Reviewers were not blinded to information about the authors, journal of origin or results of each article reviewed. A standardized form was used for data extraction, covering participants, type of intervention, study variables and tools used, follow-up time and results obtained (Table 1).

2.5 | Quality assessment

Methodological quality was assessed using the PEDro (Maher et al., 2003). Quality review of the studies was performed by two independent assessors, with a third consulted in the event of disagreement. The included studies were classified according to scores of 9 or 10, 6 to 8 and ≤5 on the PEDro scale, which were interpreted as excellent, good and fair quality respectively (Ghai et al., 2018).

2.6 | Data synthesis and analysis

Cohen's Kappa coefficient was used to quantify the degree of agreement between the two reviewers in the article selection process. This analysis was carried out with Epidat 4.2 software.

Data were analysed using a qualitative synthesis and, wherever possible, a quantitative synthesis (meta-analysis). Only one study was not included in the quantitative synthesis, as it did not provide sufficient data to do so. When studies used different tools for the assessment of the same outcome measure, we calculated the

TABLE 1 Characteristics of the included studies.

Study	Sample	PEDro score	Intervention
Häkkinen et al. (2001)	21 women with FM Mean age: 38 years Exp: 11–11 Ctrl: 10–10	7/11	**Exp**: RT included squat exercise, knee and trunk extension/flexion exercises and bench press. Initially, 1 set of 15–20 reps (40%–60% 1RM), and then 15–20 (70%–80% 1RM). Each session included warm up (bicycle ergometer and stretching) **Ctrl**: no intervention **Duration**: Twice a week for 21 weeks
Jones et al. (2002)	68 women with FM Mean age: 48 years Exp: 34–28 Ctrl: 34–28	7/11	**Exp**: The main muscle groups were worked, but exercises were not specified. Initially, 1 set of 4–5, and then to 12. Each session concluded with 10 min cooldown and stretching **Ctrl**: Supervised stretching program Stretches targeted the same 12 major muscle groups as the strengthening group **Duration**: Twice a week for 12 weeks
Valkeinen et al. (2004)	26 women with FM Mean age: 59 years Exp: 13–13 Ctrl: 13–13	6/11	**Exp**: The main muscle groups were worked, but exercises were not specified. Initially, 3 sets of 15–20, and then to 4 sets of 8–12 and 5 sets of 5–10 **Ctrl**: no intervention **Duration**: Twice a week for 21 weeks
Kingsley et al. (2005)	29 women with FM Mean age: 46 years Exp: 15–8 Ctrl: 14–12	9/11	**Exp**: RT included chest press, leg extension, standing leg curl, shoulder press, lumbar extension, abdominal Crunch, low-pulley biceps curl, high-pulley triceps extension, mid-pulley standing row, standing calf raises and body weight swiss ball squats. 1 set of 8–12 (60%–80% 1RM) **Ctrl**: No intervention (wait-listed for exercise) **Duration**: Twice a week for 12 weeks
Bircan et al. (2008)	30 women with FM Mean age: 47 years Exp: 15–13 Ctrl: 15–13	7/11	**Exp**: RT were not specified; however, free weights were used and the patient's body weight. Initially, 1 set of 4, and then to 12 reps. Each session started and concluded with 5 min of stretching **Ctrl**: AE comprised walking on treadmill, initially for 20 min and then 30 min as the patient tolerated. Intensity was adjusted to 60%–70% of age-adjusted maximum heart rates **Duration**: Twice a week for 8 weeks
Panton et al. (2009)	27 women with FM Mean age: 48 years Exp: 15–10 Ctrl: 12–11	7/11	**Exp**: RT included chest press, leg extension, leg curl, leg press, arm curl, seated dip, overhead press, seated row, abdominal crunch and low back extension. Initially, 1 set of 12 (50% 1RM), and then 1RM (100%) **Ctrl**: the same RT program combined with chiropractic treatment **Duration**: twice a week for 16 weeks
Kayo et al. (2011)	90 women with FM Mean age: 46 years Exp: 30–22 Ctrl 1: 30–23 Ctrl 2: 30–23	6/11	**Exp**: RT included 11 free active exercises using free and body weight. 3 set of 10 reps, and them 3 set of 15 reps **Ctrl 1**: aerobic exercise (walking). Initially, 25–30 min (40%–50% HHR), and them 50 min (60%–70%) **Ctrl 2**: no intervention **Duration**: three times a week for 16 weeks
Gavi et al. (2014)	80 women with FM Mean age: 46 years Exp: 40–35 Ctrl: 40–31	7/11	**Exp**: RT included leg press, leg extension, hip flexion, fly, triceps extension, shoulder flexion, abduction and extension, leg curl, calf, pulldown, biceps flexion. Three sets of 12 (45% 1RM) **Ctrl**: A flexibility exercise program of the major muscles, but exercises were not specified **Duration**: Twice a week for 16 weeks
Larsson et al. (2015)	130 women with FM Mean age: 51 years Exp: 67–48 Ctrl: 63–43	6/11	**Exp**: The main muscle groups were worked, but exercises were not specified. Intensity increased progressively **Ctrl**: Relaxation therapy approximately 25 min **Duration**: Twice a week for 15 weeks

Outcome measure and follow-up	Reported results
(1) Pain intensity—VAS (0–100) (2) Functionality—HAQ Follow-up at 0 and 21 weeks	Pain intensity and functionality were significantly improved in RT
(1) Pain intensity—FIQ pain, VAS (0–10) (2) Severity of the disease—FIQ (0–100) Follow-up at 0 and 12 weeks	Pain intensity and severity of the disease improved significantly in RT
(1) Functionality—(HAQ) Follow-up at 0 and 21 weeks	Functionality improved in RT
(1) Functionality—CS-PFP (2) Severity of the disease—FIQ (0–100) Follow-up at 0 and 12 weeks	• Functionality improved significantly in RT • Severity of the disease did not change
(1) Pain intensity—VAS (0–100) (2) Functionality—SF-36 (physical component summary) Follow-up at 0 and 8 weeks	Pain intensity and functionality were improved in RT
(1) Functionality—CS-PFP (2) Severity of the disease—FIQ (0–100) Follow-up at 0 and 16 weeks	There were similar improvements in severity of the disease and functionality in both groups
(1) Pain intensity—VAS (0–10) and SF-26 (bodily pain) (2) Functionality—FIQ (0–100) and SF-36 (physical function) (3) Severity of the disease—FIQ (0–100) Follow-up at 0, 8, 16 and 28 weeks (7 months)	All variables improved in both intervention group.
(1) Pain intensity—VAS (0–10) (2) Functionality—SF36 (physical component summary) (3) Severity of the disease—FIQ (0–100) Follow-up at 0 and 16 weeks	Both groups showed improvements in the pain intensity, functionality and severity of the disease, and there was no significant difference observed between the groups
(1) Pain intensity—VAS (0–100) (2) Functionality—SF-36 (physical component summary) (3) Severity of the disease—FIQ (0–100) Follow-up at 0 and 15 weeks, and 13 and 18 months	Pain intensity, functionality and severity of the disease improved significantly in RT

(Continues)

Study	Sample	PEDro score	Intervention
Assumpção et al. (2018)	37 women with FM Mean age: 52 years Exp: 19–16 Ctrl 1: 18–14 Ctrl 2: 16–14	6/11	**Exp**: RT included exercise for triceps surae, quadriceps, hip adductors and abductors, hip flexors, elbow flexors and extensors, pectoralis major and rhomboids. 1 set of 8 reps **Ctrl 1**: stretching program-based postural re-education method included triceps surae, gluteus, ischiotibial, paravertebral, latissimus dorsi, hip adductor and pectoralis muscles. The position was held for 30 seconds **Ctrl 2**: No intervention **Duration**: Twice a week for 12 weeks
Glasgow et al. (2017)	26 women with FM Mean age: 52 years Exp: 14–13 Ctrl: 12–12	5/11	**Exp**: RT included chest press, leg extension, leg curl and seated row. Three sets of 8–12 (50%–60% 1RM) **Ctrl**: No intervention **Duration**: Twice a week for 8 weeks
Ernberg et al. (2018)	125 women with FM Mean age: 49 years Ctrl: 67–49 Exp: 58–43	6/11	**Exp**: RT were not specified but focusing on the lower body. Each session included warm up (10 min bicycling) **Ctrl**: Relaxation therapy **Duration**: Twice a week for 15 weeks
Silva et al. (2019)	60 women with FM Mean age: 47 years Exp: 30–28 Ctrl: 30–27	8/11	**Exp**: RT included exercises for biceps brachial, triceps, pectoralis, trapezius, knee extensors and flexors, and hip abductors. Three sets of 12%–60% 1RM, and then 70%–80% **Ctrl**: Relaxation therapy (sophrology technique). The patients remained lying on comfortable mats with relaxing music playing in the background in a room with pleasant temperature. Each session lasted 40 min **Duration**: Twice a week for 12 weeks
Jablochkova et al. (2019)	75 women with FM Mean age: 49 years Exp: 41–41 Ctrl: 34–34	7/11	**Exp**: RT were not specified but focusing on the lower body. Each session included warm up (10 min) **Ctrl**: Relaxation therapy contained mental exercises (25 min). All sessions ended with stretching **Duration**: Twice a week for 15 weeks
Arakaki et al. (2021)	60 women with FM Mean age: 47 years Exp: 30–28 Ctrl: 30–26	9/11	**Exp**: RT using a swiss ball (65 cm) and dumbbells. Three sets of 12 to 60% 1RM with 1–2 min rest between exercises **Ctrl**: flexibility exercise was realized. The same muscles trained. Three sets of 30 s stretching **Duration**: Three times a week for 12 weeks

Abbreviations: 1RM, repetition maximum; AE, aerobic exercise; CS-PFP, Continuous-Scale Physical Functional Performance; Ctrl, control group; Exp, experimental group; FIQ, Fibromyalgia Impact Questionnaire; FM, Fibromyalgia; HAQ, Stanford Health Assessment Questionnaire; MPI, Multidimensional Pain Inventory; SF-36, short-form health survey; ST, strength training; VAS, visual analogue scale.

standardized mean difference and its standard error (Higgins & Green, 2006). The quantitative synthesis of the results was performed by one of the other authors. In each meta-analysis, a subgroup division was made considering the different comparison groups. In this way, the studies were grouped by different intervention modalities compared to the experimental group. Where studies provided several post-intervention measurements, we selected the measurement closest to 3 months (12 weeks). This criterion was established because most studies performed this intervention period. According to Cochrane, 'thresholds for the interpretation of the I^2 statistic can be misleading since the importance of inconsistency depends on several factors. A rough guide to interpretation in the context of meta-analyses of randomized trials is as follows: 0% to 40%: might not be important; 30% to 60%: may represent moderate heterogeneity; 50% to 90%: may represent substantial heterogeneity; 75% to 100%: considerable heterogeneity' (Deeks et al., 2022). In all cases, the appropriate forest plot is depicted. Review Manager version 5.4.1 software was used for the statistical analysis.

Where possible, publication bias was estimated using the Begg and Egger test and the funnel plot. Moreover, a sensitivity analysis was carried out (where possible) to estimate the degree of influence of each article included in each meta-analysis on the results of that meta-analysis. The 'Epidat 3.1.' program was used to analyse publication bias and sensitivity analysis.

Where it was not possible to combine the study results in the meta-analysis, narrative and descriptive summaries

Outcome measure and follow-up	Reported results
(1) Pain intensity (2) Functionality—FIQ (physical function) and SF-36 (physical function) Severity of the disease—FIQ (0–100) Follow-up at 0 and 12 weeks	• Pain intensity and functionality improved in both intervention group, but stretching group was higher than RT group • Severity of the disease decreased in RT
(1) Severity of the disease—FIQ (0–100) Follow-up at 0 and 8 weeks	Severity of the disease was significantly reduced in the RT
(1) Pain intensity—VAS (0–100) (2) Severity of the disease—FIQ (0–100) Follow-up at 0 and 15 weeks	Pain intensity and severity of the disease was improved in RT
(1) Pain intensity—VAS (0–10) (2) Functionality—SF-36 (functional capacity) (3) Severity of disease—FIQ Follow-up at 0, 4, 8 and 12 weeks	• Pain intensity showed no improvement at 4 and 8 weeks, but showed significant improvement at 12 weeks in RT • Functionality and severity of disease improved significantly in RT
(1) Pain intensity—VAS (0–100) (2) Functionality—SF-36 (physical component summary) (3) Severity of the disease—FIQ (0–100) Follow-up at 0 and 15 weeks	• Pain intensity was significantly decreased in RT • Functionality and severity of the disease improved in RT
(1) Pain intensity—VAS (0–100) and SF-36 (bodily pain) (2) Functionality—SF-36 (functional capacity) (3) Severity of the disease—FIQ (0–100) Follow-up at 0, 6 and 12 weeks	All variables improved significantly in both groups, but in RT group was higher than control group

were completed, and a qualitative synthesis of these was carried out. The strength of evidence was assessed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) using the GRADE Pro/Guideline Development Tool. This tool covers risk of bias, inconsistency, indirectness, imprecision and publication bias (Balshem et al., 2011).

2.7 | Clinical relevance

Clinical relevance was determined by the minimal clinically important difference (MCID), defined as the minimal difference in scores of an outcome measure that is perceived by patients as beneficial or harmful (King, 2014).

The Philadelphia Panel developed the standard of 15% relative benefit based on extensive input by rheumatology and biostatistics experts (Albright et al., 2001). This is consistent with Bennett 2009, who indicated that a MCID in the FIQ total score (severity of disease) was at least a 14% reduction (Bennett et al., 2009). We evaluated the clinical relevance of the effects in the main outcomes by calculating the relative difference in change from a pooled baseline in the intervention group as compared with the change from a pooled baseline in the control or comparison group. This method was used by Cochrane 2013 to calculate the percentage change in people with fibromyalgia (Busch et al., 2013). To obtain the mean difference, independent pairwise meta-analyses were performed for each tool per variable.
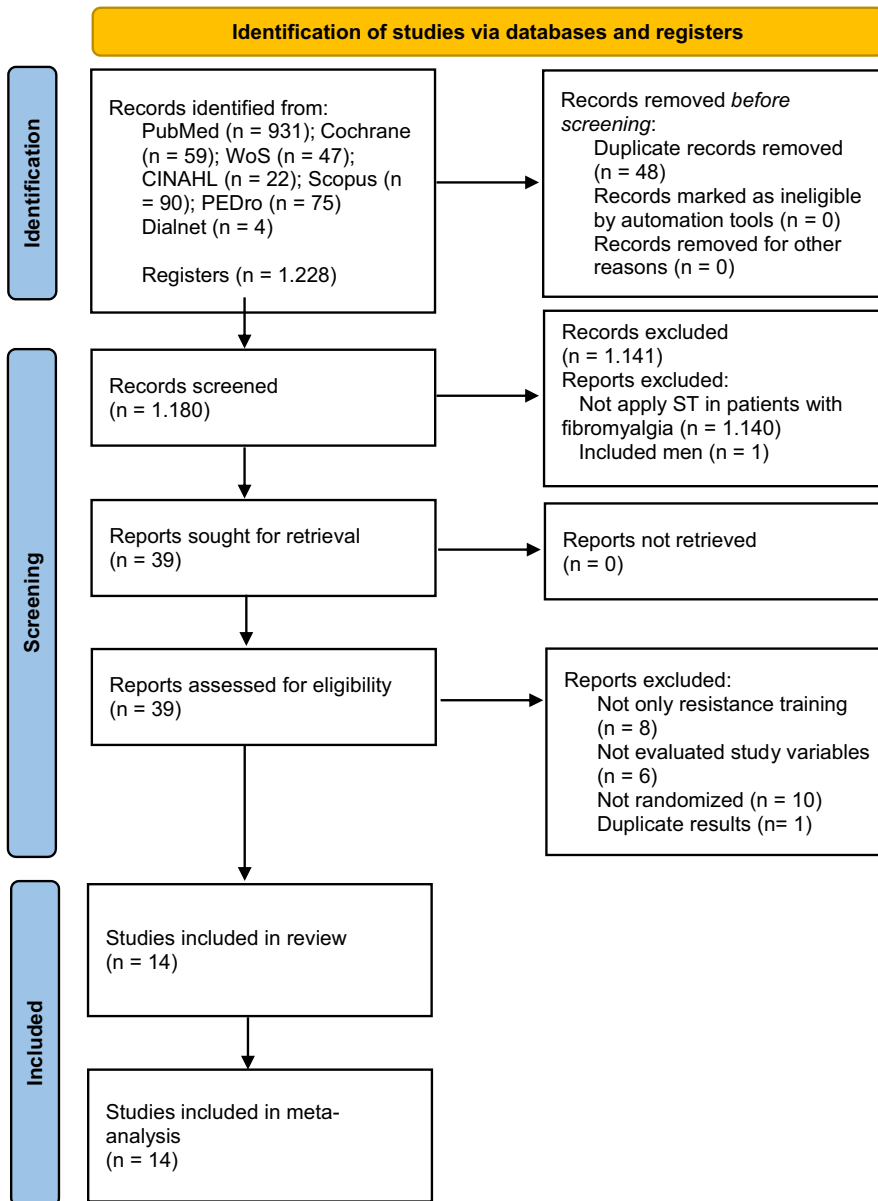
FIGURE 1 PRISMA flowchart of study selection.

3 | RESULTS

Figure 1 describes the study selection process carried out. All (14) articles were included in the qualitative synthesis. The degree of agreement reached between the two reviewers in the selection of the articles was excellent, with Cohen's Kappa coefficient showing a value of 0.89 (standard Error 0.08; CI 0.73 to 1.00; with $p < 0.001$).

3.1 | Characteristics of the studies

All of the studies were published in English between 2001 and 2021. The sample size varied from 21 to 130 patients, with a mean of 55 participants. The total number of patients evaluated was 894 participants. The mean age was approximately 48 years (range = 39–60 years). The sociodemographic and clinical characteristics of the participants in each study, the sample size and the number of participants assigned to each group are shown in Table 1.

3.2 | Intervention characteristics

The duration of the interventions was between 8 and 21 weeks, with the most common being 12 weeks (four studies). Most of the interventions were performed with a training frequency twice a week. Only two studies (Arakaki et al., 2021; Kayo et al., 2011) prescribed the exercise program three times a week. All workouts included 10 min of warm-up, 50 min of RT and 10 min of relaxation at the end, which consisted of stretching exercises. During

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
1.15.1 Resistance training vs aerobic exercise									
Bircan 2008	26.5	14.1	13	21.9	18.8	13	5.5%	0.27 [-0.50, 1.04]	2007
Kayo 2011	-2.77	1.95	30	-3.44	1.81	30	7.9%	0.35 [-0.16, 0.86]	2011
Subtotal (95% CI)			43			43	13.5%	0.33 [-0.10, 0.75]	
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.86); I² = 0%									
Test for overall effect: Z = 1.50 (P = 0.13)									
1.15.2 Resistance training vs flexibility exercise									
Jones 2002	46.1	3.9	28	51.4	4.1	28	7.2%	-1.31 [-1.89, -0.73]	2002
Gavi 2014	-42.68	14.82	35	-42.49	16.53	31	8.2%	-0.01 [-0.50, 0.47]	2014
Assumpção 2017	44	30	16	46	26	14	6.0%	-0.07 [-0.79, 0.65]	2017
Arakaki 2021	33	32	30	53	26	30	7.8%	-0.68 [-1.20, -0.16]	2021
Subtotal (95% CI)			109			103	29.2%	-0.52 [-1.11, 0.07]	
Heterogeneity: Tau² = 0.28; Chi² = 13.14, df = 3 (P = 0.004); I² = 77%									
Test for overall effect: Z = 1.72 (P = 0.09)									
1.15.3 Resistance training vs relaxation group									
Larsson 2015	38.6	25.2	56	53.4	20	49	9.2%	-0.64 [-1.03, -0.25]	2015
Ernberg 2018	-16	40	49	-2	18	43	9.0%	-0.44 [-0.85, -0.02]	2018
Silva 2019	40.6	25.8	30	51	16.2	30	7.9%	-0.48 [-0.99, 0.04]	2018
Jablochkova 2019	37.2	23.7	38	54	19.9	34	8.3%	-0.76 [-1.24, -0.28]	2019
Subtotal (95% CI)			173			156	34.3%	-0.58 [-0.80, -0.36]	
Heterogeneity: Tau² = 0.00; Chi² = 1.21, df = 3 (P = 0.75); I² = 0%									
Test for overall effect: Z = 5.11 (P < 0.00001)									
1.15.4 Resistance training vs control group									
Hakkinen 2001	24	19	11	60	27	10	4.1%	-1.49 [-2.49, -0.50]	2001
Valkeinen 2004	-1.9	2.5	13	0.2	1.2	13	5.1%	-1.04 [-1.86, -0.21]	2004
Kayo 2011 (b)	-2.77	1.95	30	-2.09	1.76	30	7.9%	-0.36 [-0.87, 0.15]	2011
Assumpção 2017 (b)	44	30	16	64	27	14	5.8%	-0.68 [-1.42, 0.06]	2017
Subtotal (95% CI)			70			67	23.0%	-0.77 [-1.24, -0.31]	
Heterogeneity: Tau² = 0.08; Chi² = 4.79, df = 3 (P = 0.19); I² = 37%									
Test for overall effect: Z = 3.26 (P = 0.001)									
Total (95% CI)			395			369	100.0%	-0.49 [-0.74, -0.24]	
Heterogeneity: Tau² = 0.13; Chi² = 35.16, df = 13 (P = 0.0008); I² = 63%									
Test for overall effect: Z = 3.87 (P = 0.0001)									
Test for subgroup differences: Chi² = 15.94, df = 3 (P = 0.001), I² = 81.2%									

FIGURE 2 Effectiveness of resistance training for pain intensity in women with fibromyalgia (forest plot of the meta-analysis).

training, patients were instructed to take 1 min of recovery between each set.

The RT programs used in the studies included a range of 4–12 exercises, but several authors did not report the program used. Although most focused on the main muscle groups, two of the studies focused on working in the lower body (Ernberg et al., 2018; Jablochkova et al., 2019). In terms of intensity, several studies began with 40%–60% of the one repetition maximum (1RM). However, others used increased repetitions to increase intensity. In this way, the number of repetitions was inversely proportional to the intensity. While some started in sets of four to five repetitions and increased to 12 repetitions (Jones et al., 2002), others started in sets of more volume (15–20 repetitions) and at the end of treatment increased the intensity to perform sets of 5–10 repetitions (Valkeinen et al., 2004).

It should be noted that the program designed by Larsson et al. (2015) was replicated by two other studies (Ernberg et al., 2018; Jablochkova et al., 2019). This program included seven exercises (leg press, leg extension, leg curl, biceps curl, hand grip strength, core stability exercise and heel raise) and consisted of 15 weeks of progressive

RT, starting with 15–20 repetitions at 40% of 1RM, progressing to 5–8 repetitions at 80% of 1RM. The last 5 weeks included explosive execution of rapid heel raises and explosive knee extension.

3.3 | Quality assessment

Overall, the quality of the included trials was good, with 14 of the 15 included studies scoring >5 on the PEDro scale. Only one study (Glasgow et al., 2017) had a score of ≤5, and two had an 'excellent' (Arakaki et al., 2021; Kingsley et al., 2005; Table S2).

3.4 | Treatment results

Forest plots represent the effect size calculated for each study by results, as well as the overall effect size obtained for the study results at each time interval. The forest plots also indicate whether the effects obtained in the studies favour the control group or the intervention group.
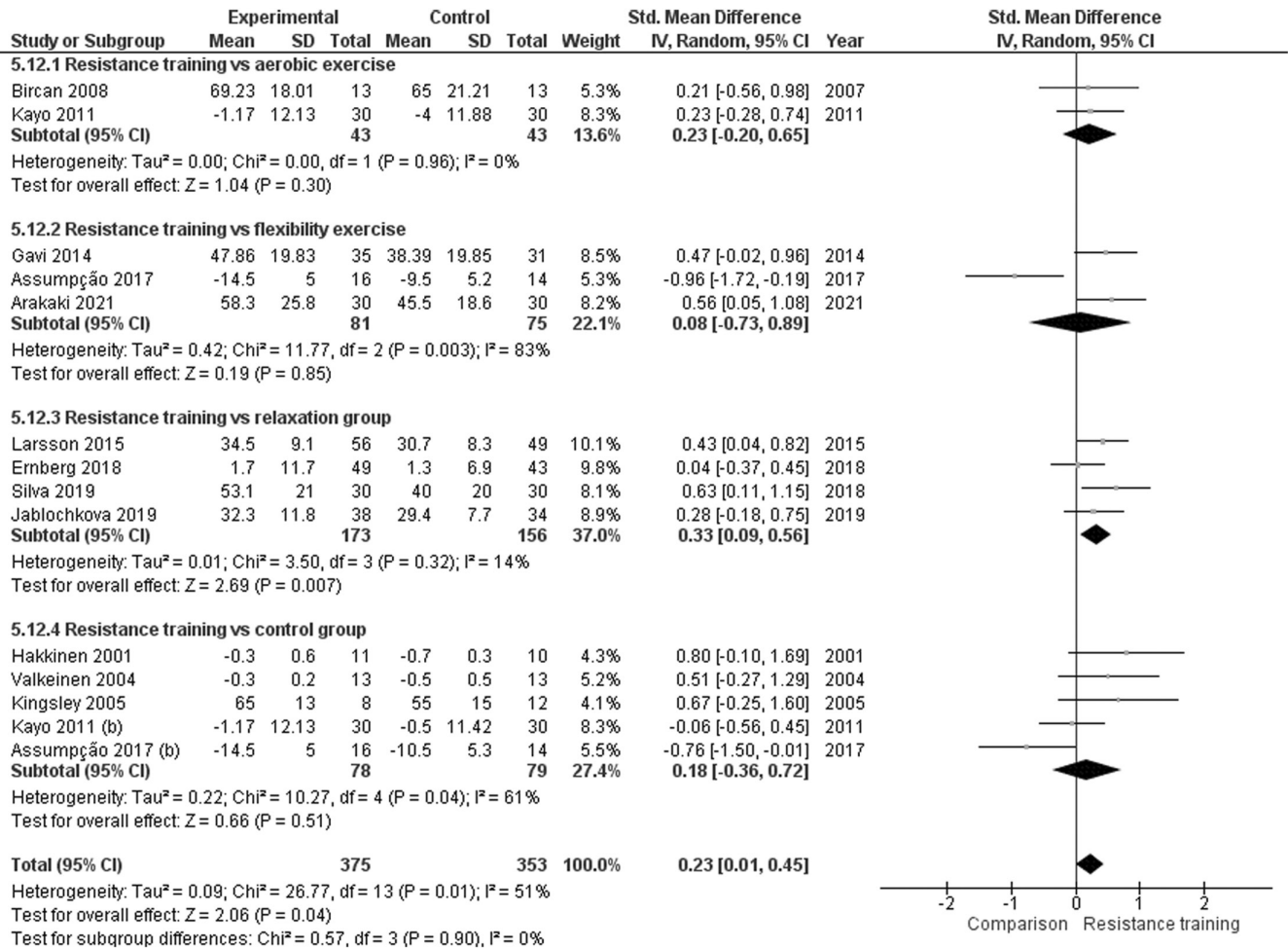
FIGURE 3 Effectiveness of resistance training for functionality in women with fibromyalgia (forest plot of the meta-analysis).

A forest plot was made for each variable by adding the different tools used, and they were divided into subgroups according to the comparison group. Studies that performed usual care (or no intervention) were classified as control groups. Thus, the resulting subgroups were aerobic exercise group, flexibility exercise group, relaxation group and control group. All the variables investigated showed the four groups mentioned.

Of the 14 studies included in the analysis, two studies (Bircan et al., 2008; Kayo et al., 2011) compared RT with aerobic exercise, four studies (Arakaki et al., 2021; Assumpção et al., 2018; Gavi et al., 2014; Jones et al., 2002) compared RT with flexibility exercise, four other studies (Ernberg et al., 2018; Jablochkova et al., 2019; Larsson et al., 2015; Silva et al., 2019) compared it with the relaxation group and five other studies (Assumpção et al., 2018; Glasgow et al., 2017; Kingsley et al., 2005; Valkeinen et al., 2004) compared it with usual care or no intervention (control group).

It is worth noting that two studies (Assumpção et al., 2018; Kayo et al., 2011) had three study groups, so they have two results in some of the forest plots.

3.4.1 | Pain intensity

Twelve of the 14 studies included in the meta-analysis assessed pain intensity. The tools used were the visual analogue scale (VAS) and a subscale of the SF-36 (bodily pain).

Meta-analysis was performed globally, grouped by modalities of comparison groups. Statistically significant differences were found in favour of the RT group compared to the relaxation group (SMD$=-0.58$; 95% CI [-0.80, -0.36], $p < 0.00001$) and the control group (SMD$=-0.77$; 95% CI [-1.24, -0.31], $p = 0.001$). Furthermore, it also showed statistical significance in global measurement (SMD$=-0.49$; 95% CI [-0.74, -0.24], $p = 0.0001$). Figure 2 shows the forest plot of the overall meta-analysis for pain intensity.

3.4.2 | Functionality

Twelve of the 14 studies included in the meta-analysis assessed functionality. The tools used were the
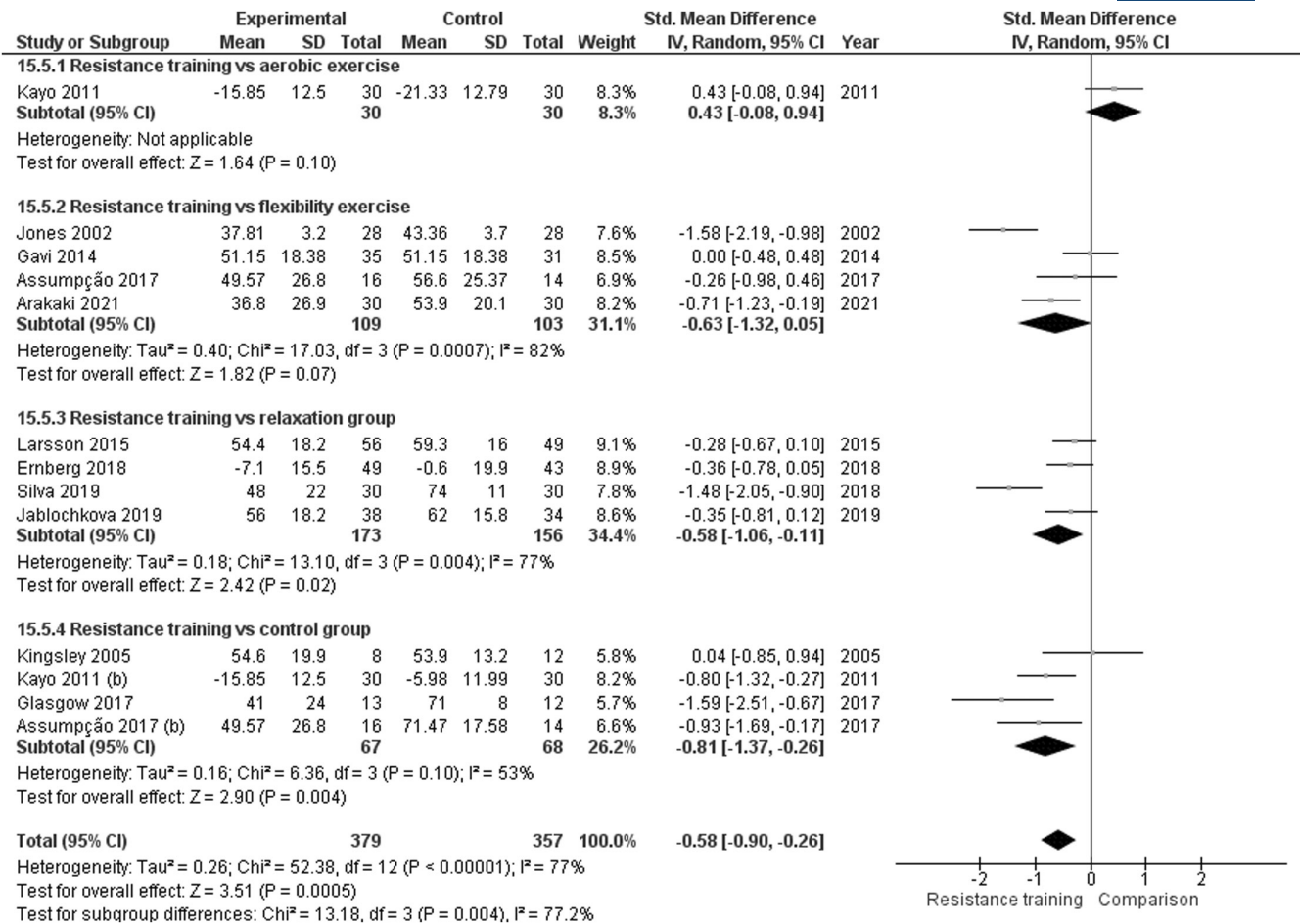
FIGURE 4 Effectiveness of resistance training for severity of the disease in women with fibromyalgia (forest plot of the meta-analysis).

Continuous-Scale Physical Functional Performance (CS-PFP), the Stanford Health Assessment Questionnaire (HAQ) and a subscale of the SF-36 (physical function).

Quantitative synthesis of studies assessing the effectiveness of RT on functionality was performed globally, grouped by modalities of comparison groups. Statistically significant differences were found in favour of the RT group compared to the relaxation group (SMD = 0.33; 95% CI [−0.09, −0.66], $p = 0.07$). Furthermore, it also showed statistical significance in global measurement (SMD = 0.23; 95% CI [0.01, 0.45], $p = 0.04$). Figure 3 shows the forest plot of the overall meta-analysis for functionality.

3.4.3 | Severity of the disease

Eleven of the 14 studies included in the meta-analysis (Figure 4) assessed the impact of fibromyalgia on severity of the disease. The tool used in all studies was the FIQ. Statistically significant differences were found in favour of RT compared to the relaxation group (SMD = −0.58; 95% CI [−1.06, −0.11], $p = 0.004$) and the control group (SMD = −0.81; 95% CI [−1.37, −0.26], $p = 0.004$). The

global measurement also showed statistically significant changes in favour of RT (SMD = −0.58; 95% CI [−0.90, −0.26], $p = 0.0005$).

3.5 | Assessment of the risk of publication bias

The Begg and Eggel tests revealed that there was no statistical evidence of publication bias ($p > 0.05$). These findings are shown in the funnel plot (Figures S1–S3). The sensitivity analysis indicated that the overall results were not substantially modified by the elimination of any outcome.

3.6 | Synthesis of the evidence

The synthesis of the evidence was performed on the overall results of each studied variable and was performed using GRADE Pro/Guideline Development Tool (Table 2). The results for all variables studied were rated as 'not important'. The level of evidence was rated 'very low' for all variables.

TABLE 2 GRADE. Summary of the evidence of the results according to their certainty and their importance using the GRADE tool for pain intensity, functionality and severity of disease.

No. studies	Certainly assessment						No. of patients		Effect		Certainly	Importance
	Study design	Risk of bias	Inconsistency	Indirectly evidence	Imprecision	Others	Intervention	Comparison	Relative (95% CI)	Absolute (95% CI)		
Pain intensity												
14	RTs	Serious[a]	Serious[b]	Not serious	Serious[c]	None	395	369	—	SMD **−0.49** (−074 to −0.24)	⊕○○○ very low	Not important
Functionality												
14	RTs	Serious[a]	Serious[b]	Not serious	Serious[c]	None	375	353	—	SMD **0.23** (0.01–0.45)	⊕○○○ very low	Not important
Severity of the disease												
13	RTs	Serious[a]	Serious[b]	Not serious	Serious[c]	None	379	357	—	SMD **−0.58** (−0.9 to −0.26)	⊕○○○ very low	Not important

Abbreviations: CI, confidence interval; RTs, randomized trials; SMD, standardized mean difference.

The bold value means that SMD is statistically significant.

[a]This variability may be due to the fact that the studies present differences in the interventions.

[b]These differences may be because the studies present differences in the interventions.

[c]The results show differences in the confidence interval.

3.7 | Clinical relevance of outcomes measure

In keeping with the practice of the Philadelphia Panel, we used 15% as the level of clinical relevance (Albright et al., 2001). Due to the heterogeneity of tools found, we evaluated the tool with the highest number of studies per variable.

Clinically important improvements in the overall outcome of the three variables studied in favour of RT were obtained: pain intensity, evaluated with VAS (improvement of 20.52%); functionality (16.30%), assessed with SF-36; and severity of the disease (17.49%), assessed with FIQ. Furthermore, clinically important improvements were obtained in the analysis of the comparison subgroups in pain intensity and severity of the disease in favour of RT compared to the relaxation group (25.91% and 19.28%, respectively) and the control group (55.81% and 26.22%, respectively). In functionality, only clinically important improvements were obtained in favour of RT compared to flexibility exercise (33.07%). Figures S4–S6 and Table S3 show all the results found in relation to the MCID.

4 | DISCUSSION

The objective of this study was to evaluate the clinical relevance and effectiveness of RT for pain intensity, functionality and severity of the disease in women with fibromyalgia. To our knowledge, this is the first systematic review and meta-analysis that evaluated the clinical relevance and effectiveness of RT specifically in women with fibromyalgia. The last systematic reviews with meta-analysis (Albuquerque et al., 2022; Vilarino et al., 2022) conducted in this disease did not exclude studies with men in their sample, raising serious concerns for two reasons. First, because 80%–90% of the affected individuals are female, the efficacy of this intervention should be specifically evaluated in women, since the effectiveness of any intervention is affected by several variables and sex is one of them. The inclusion of men in the analysis adds heterogeneity to the sample, which lowers the level of evidence.

The results of global meta-analyses prove that RT is effective in improving pain intensity, functionality and severity of the disease in women with fibromyalgia. However, the quality of evidence is very low for the three variables studied (Table 2).

In the results of the meta-analysis by comparison subgroups, we observed that RT obtained statistically significant improvements in pain intensity and severity of the disease, compared to the relaxation and control groups. While RT only obtains statistically significant

improvements in functionality when compared to the relaxation group.

As our work is the first systematic review and meta-analysis that studied RT specifically in women with fibromyalgia, we cannot dispute our results with previous meta-analyses in this population. Therefore, we will compare our results with the most current meta-analyses. In this way, a recent meta-analysis (Vilarino et al., 2022) also found that RT is effective in improving pain intensity in patients with fibromyalgia. Although this study included men and women and limited their search to studies that used only the ACR1990 diagnostic criteria; however, these criteria were discarded by their own authors in 2010 due to their low reliability (Wolfe et al., 2011). Thus, the meta-analysis of Vilarino et al., for this variable (pain intensity), has six studies and ours with 12 RCTs. In addition, they found no statistically significant improvements in RT compared to the relaxation and control groups, while our results demonstrate the opposite. This may be because our study had two more studies in the control group. Regarding the relaxation group, the meta-analysis by Vilarino et al. has the same studies as ours, but the discrepancy could be due to Vilarino et al. not using the VAS data offered by one of the studies (Silva et al., 2019), which could imply a bias in the meta-analysis of Vilarino et al.

Regarding the functionality variable, our results only partially coincide with the meta-analysis of Vilarino et al. to obtain statistically significant improvements in favour of RT compared to the relaxation group, although these authors only included three studies, of which one was not a randomized clinical trial (Ernberg et al., 2016), which could imply bias in their results. On the contrary, our study had four RCTs in the relaxation subgroup and 14 RCTs in the global meta-analysis, so our results provide additional evidence of the efficacy of RT in women with fibromyalgia, since Vilarino et al. did not perform a global meta-analysis of this variable.

Regarding the severity of the disease assessed with FIQ, our result coincides with that of a systematic review with meta-analysis (Albuquerque et al., 2022) that also found that RT is effective in improving the severity of the disease in patients (women and men) with fibromyalgia compared to the control group. Although their meta-analysis only had two studies that compared RT with the control group and did not perform a global meta-analysis. Although our meta-analysis had four studies comparing RT with the control group and a total of 14 RCTs in the global meta-analysis.

We should also mention the results of meta-analyses by comparison of subgroups in which no statistically significant changes have been found. Thus, there were no statistically significant changes for any of the variables in the meta-analysis of the comparison of RT with the aerobic exercise group. This may be due to the small number of RCTs that met the inclusion criteria (two RCTs for pain intensity and functionality and one RCT for severity of the disease). Therefore, more studies are needed that specifically clarify this question.

Neither statistically significant changes were found in any of its variables in the meta-analysis of the comparison of RT with the flexibility exercise group, which had four RCTs for pain intensity and severity of the disease, and three RCTs for functionality. However, individually, two studies obtained statistically significant changes in favour of RT in each variable. This apparent discrepancy justifies the need for more studies.

Finally, no statistically significant changes were found in the meta-analysis of the comparison of RT with the control group in the functionality variable, which included five RCTs. In this case, only one study obtained statistically significant changes individually. Therefore, more RCTs are also needed to provide more evidence.

4.1 | Minimal clinically important difference

Regarding MCID, we found clinically important improvements in the overall outcome of the three variables analysed in favour of the RT group. That is, our results prove that RT can produce clinically relevant improvements in pain intensity, functionality and severity of the disease in women with fibromyalgia. The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) recommended the following benchmarks for interpreting changes in pain intensity on a 0–10 numerical rating scale in chronic pain clinical trials: (a) a 10%–20% decrease is minimally important, (b) a decrease greater than 30% is moderately important and (c) a decrease greater than 50% is substantial (Dworkin et al., 2008). Therefore, the improvements obtained by RT compared to the control group (55.81%) in pain intensity in women with fibromyalgia can be considered substantially important. In the same way, the improvements obtained by RT compared to flexibility exercise (33.07%) in functionality in women with fibromyalgia can be considered moderately important.

4.2 | Limitations

This paper presents a series of limitations inherent to the type of intervention used, since none of the included studies fulfilled the conditions of blinding patients and therapists. However, this is not possible in light of the type of intervention applied. Another limitation is the heterogeneity of the studies on the diversity of the RT programs used. Likewise, the number of included trials was

relatively small. Therefore, more studies are needed to determine more conclusively the benefits of RT in women with fibromyalgia. Finally, all studies included in this review analysed the effects of RT in women with fibromyalgia, so these results cannot be extrapolated to men. Therefore, it is necessary to check whether these effects are reproduced only in men with fibromyalgia in future studies.

4.3 | Clinical and research implications

Our results have important clinical and research implications. At the research level, our work has shown the need to carry out more RCTs in both women and men with fibromyalgia, but separately by sex. In the clinical field, our study provides scientific support for practitioners to prescribe RT specifically to women with fibromyalgia to improve pain intensity, functionality and severity of the disease, bearing in mind that the results may be clinically relevant. The evidence that our work has yielded should be shared with women with fibromyalgia to encourage them to trust treatment and make them loyal to the RT program. In this regard, many authors defend that education is a fundamental element of treatment (Dreher et al., 2013; Sarzi-Puttini et al., 2020), as informing the patient of the prognosis improves expectations and adherence to the treatment program.

5 | CONCLUSIONS

Our findings show that RT is an effective intervention method, to improve pain intensity, functionality and severity of the disease in women with fibromyalgia. These improvements are clinically relevant. More clinical trials of RT are needed in women with fibromyalgia to support our results due to the low strength of evidence.

AUTHOR CONTRIBUTIONS

Álvaro-José Rodríguez-Domínguez, Manuel Rebollo-Salas and José-Jesús Jiménez-Rejano contributed to the conception and design of the study and to the acquisition of data. Raquel Chillón-Martínez and Abel Rosales-Tristancho contributed to the acquisition of data and the analysis and interpretation of data. All authors participated in drafting the article or revising it critically for important intellectual content, and all authors approved the final version of the article to be published.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.