

Systematic Review

Is Physical Exercise Beneficial for People with Primary Sjögren's Syndrome? Findings from a Systematic Review

Carlos Ayán-Pérez ^{1,2} , Rocío Carballo-Afonso ^{1,2}, Rodrigo Bueno-Russo ³ and Daniel González-Devesa ^{1,3,*} 

¹ Well-Move Research Group, Galicia Sur Health Research Institute (IIS Galicia Sur), SERGAS-UVIGO, 36310 Vigo, Spain; cayan@uvigo.es (C.A.-P.); rociocarballo@uvigo.gal (R.C.-A.)

² Departamento de Didácticas Especiais, Universidade de Vigo, 36310 Vigo, Spain

³ Grupo de Investigación en Actividad Física, Educación, y Salud (GIAFES), Universidad Católica de Ávila, Canteros, 05005 Ávila, Spain; rodrigo.bueno@ucavila.es

* Correspondence: daniel.gonzalez@ucavila.es

Abstract: Background: The aim of the study was to identify and critically evaluate the best available evidence on the impact of physical exercise on patients with primary Sjögren's syndrome. Methods: Studies were searched in four electronic databases (PubMed, Web of Science, Scopus, and SportDiscus) from their inception up to September 2024. The methodological quality of the included studies was assessed using the 10-point Physiotherapy Evidence Database (PEDro) scale and the Methodological Index for Non-Randomized Studies (MINORS). Results: A total of four randomized controlled trials and one comparative study were analyzed. The training programs evaluated varied in duration, ranging from 12 to 28 weeks. Exercise was found to have a positive intra-group impact on fatigue, quality of life, and functional capacity. However, exercise does not demonstrate superior effects compared to standard treatment for improving quality of life and disease impact. Conclusions: It is essential to increase the number of studies involving individuals with primary Sjögren's syndrome across various exercise conditions to more comprehensively evaluate the potential benefits.

Keywords: fatigue; exercise; quality of life; metabolic syndrome; physical activity; sleep; anxiety; depression



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1. Introduction

Sjögren's syndrome is considered one of the most common systemic autoimmune diseases with a pooled prevalence of 60–82 cases per 100,000 inhabitants; and a female-male ratio of 10:1 [1]. Sjögren's syndrome is identified by symptoms such as keratoconjunctivitis sicca (dry eyes) [2] and xerostomia (dry mouth) [3], often accompanied by swelling of the salivary glands and lacrimal glands [4]. Other common symptoms include fatigue, sleep disturbances [5], musculoskeletal pain [6], and gastrointestinal disturbances [7]. Primary Sjögren's syndrome (pSS) occurs as an isolated autoimmune condition [8,9], while secondary Sjögren's syndrome (sSS) is associated with other autoimmune diseases, such as rheumatoid arthritis [10], systemic sclerosis [11], systemic lupus erythematosus [12,13], or dermatomyositis [14].

This pathology negatively affects the joints, skin, lungs, and peripheral nervous system [15], with disease activity often coupled with fatigue, depression, and pain, leading to a reduced capacity for performing everyday activities and, consequently, an impaired health-related quality of life [16].

Currently, there is no cure for pSS, and the available treatments are primarily symptomatic with limited efficacy [17]. In this context, patients often turn to non-pharmacological therapies (i.e., oral lubricant, acupuncture, lacrimal punctum plugs psychodynamic group therapy) [18], hoping that their use can reduce the impact of symptoms on functionality and lead to an improvement in quality of life [18]. In this regard, physical exercise is widely recognized as a low-cost, non-pharmacological treatment capable of reducing symptom severity in several chronic diseases [19], and it could be considered a therapy of interest for patients with pSS for several reasons.

Firstly, in patients with pSS, fatigue is a disabling symptom that is strongly associated with declining physical function, yet it remains an unmet health need [20,21]. Fatigue, often regarded as the most challenging symptom by pSS patients, is believed to result from genetic and inflammatory factors. It is also thought to be linked to reduced fitness levels and lower physical activity [22]. In this regard, exercise training has consistently demonstrated positive effects in improving both fatigue and physical function in individuals with other autoimmune conditions [23–25]. Therefore, current clinical guidelines strongly recommend the incorporation of exercise into the management strategies for addressing fatigue in patients with pSS [26]. However, it is worth noting that only a limited number of studies have specifically investigated the direct effects of exercise interventions in individuals with pSS [27].

Secondly, patients with pSS often experience physical (e.g., myalgia, arthralgia) and mental (e.g., anxiety, depression) health issues, leading to a lower quality of life compared to the general population [28]. In this regard, exercise has been shown to have a beneficial impact on the quality of life of individuals with autoimmune conditions, positively affecting both their physical and mental health [29–31]. Finally, pSS is associated with a markedly increased risk for the development of non-Hodgkin lymphoma [32], a type of malignancy that has been found to be inversely related to physical activity levels, suggesting that higher levels of physical activity may help reduce this risk [33]. In this regard, previous research has indicated that physical activity levels are lower in individuals with pSS [34], while some authors have emphasized the need to increase these levels beyond the recommended minimum to mitigate the comorbidities associated with the condition [35].

In this context, research focusing on exercise interventions tailored for pSS is crucial, as exercise represents a promising non-pharmacological strategy for managing the diverse symptoms of this condition. Before recommending exercise as a therapeutic approach for patients with pSS, rehabilitation professionals must rely on accurate and current data regarding its potential benefits and side effects to ensure its safe and effective application. One way to achieve this is by conducting systematic reviews that compile and critically analyze the available scientific evidence on the topic. To the best of the authors' knowledge, no systematic review has been published specifically addressing the impact of exercise on patients with pSS. The only identified work on the topic was a narrative review [36]. However, it had several limitations. First, it lacked a quality assessment of the included studies. Second, it did not exclusively focus on patients with pSS. Lastly, it included only a single non-randomized comparative study on pSS. Therefore, the aim of the study was to identify and critically evaluate the best available evidence on the impact of physical exercise on this population.

2. Materials and Methods

This systematic review was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [37]. Furthermore, the protocol for this review was registered with the Open Science Framework (OSF, <https://doi.org/10.17605/OSF.IO/C238N> (accessed on 29 October 2024)).

2.1. Search Strategy

A comprehensive search was performed across four electronic databases: Scopus, Web of Science, SPORTDiscus, and MEDLINE/PubMed, covering the period from their inception to September 2024. Additionally, a manual search was conducted in the PEDro database [38], and the first 200 references retrieved from Google Scholar were also reviewed.

2.2. Eligibility Criteria

Eligible studies for inclusion in this review were randomized controlled trials (RCTs) or comparative studies that examined the effects of exercise on participants with primary Sjögren’s syndrome. The inclusion and exclusion of studies were guided by the Population, Intervention, Comparison, and Outcome (PICO) framework, as summarized in Table 1. Studies were eligible for the initial screening if they were published or accepted for publication in peer-reviewed journals. Abstracts from conference proceedings, books, theses, and dissertations were excluded. An accessible abstract was required for the screening process, and no language restrictions were applied.

Table 1. Search Strategy and Inclusion/Exclusion Criteria Aligned with the PICO Framework (Population, Intervention, Comparison, and Outcome).

Databases	Search Terms	PICO	Inclusion Criteria	Exclusion Criteria
MEDLINE/PubMed Web of Science SPORTDiscus Scopus	("Sjögren" OR "Sjogren") AND ("Exercise" OR "Physical Activity" OR "Sport" OR "Physical Fitness" OR "Aerobic Training" OR "Strength Training")	Population	Participants with Sjögren	Participants without a confirmed diagnosis of Sjögren Studies that included mixed samples, unless separate data were available specifically for the Sjögren subgroup.
		Intervention	Exercise program	Studies that implemented interventions based on a single exercise training session.
		Comparison	Control group or other structured interventions	No comparison between structured interventions or control conditions with pre/post-results.
		Outcome	Quantitative measures	They lacked data regarding the effects of exercise intervention

2.3. Study Selection

Duplicate references were removed using the Rayyan software version 1.5.0. (QCRI, Doha, Qatar) [39] prior to the screening process. The titles and abstracts of all identified studies were independently evaluated by both authors to determine their eligibility. After this initial screening, the selected studies were reviewed in detail by both researchers to confirm their inclusion. Any disagreements were resolved through discussion and mutual agreement. Full-text versions of studies deemed potentially relevant were retrieved for further assessment. Moreover, the reference lists of the included studies, as well as citations identified via Google Scholar, were examined to identify additional studies for potential inclusion in the review.

2.4. Data Extraction

A single researcher carefully extracted detailed information from the original studies, including data on sample characteristics (e.g., age, gender distribution, and diagnostic criteria) and details of the interventions, such as the type, duration, frequency, and intensity of the exercise protocols. Additional data included the assessed outcomes, main findings, reported adverse events, and participant drop-out rates. To ensure accuracy and reliability, a second investigator independently reviewed and verified all extracted data. The collected information was then summarized and presented in Table 2.

Table 2. Descriptive characteristics of the included studies.

First Author (Year), Design, Country	Sample	Intervention	Outcomes	Results	Dropouts and Adverse Events
Dardin et al. (2022) [40]	Participants (<i>n</i>): 59 women with pSS Final sample (<i>n</i>): 56 (EG: 30; CON: 26) Age, years (mean; SD): EG: 62.7 ± 12.95; CON: 58.12 ± 10.21 BMI, kg/m ² (mean; SD): EG: 27.35 ± 4.2; CON: 26.6 ± 4.11 Time since diagnostic, years (mean; SD): EG: 6.15 ± 4.2; CON: 5.73 ± 4.55	Duration: 16 weeks EG: Resistance exercise group Activities: 3 sets of 10 rep. for single-arm row, lateral raise, chest press, triceps extension, biceps curl, knee extension/flexion, hip abduction/adduction, leg press, and squats with dumbbells. Rest intervals were 1 min between sets and exercises. Frequency: 2 days/week Volume: NR Intensity: 60–80% of 1RM CON Received their usual pharmacological treatment and were instructed not to perform any kind of regular physical exercise	Disease activity: • ESSDAI (score)		
			Fatigue: • PROFAD-SSI (score) ➤ Physical ➤ Mental • FACIT-fatigue (score) • ESSPRI (score) ➤ Dryness ➤ Fatigue ➤ Pain Quality of life • SF-36 (score) ➤ Functional Capacity ➤ Physical Aspects ➤ Pain ➤ Vitality ➤ Social Aspects ➤ Emotional ➤ Mental Health ➤ General Health Sleep quality • Actigraphy measures ➤ Sleep latency time(min) ➤ Wake after sleep onset ➤ Sleep efficiency (%) ➤ Total sleep time (min)	Intra-group ($p < 0.05$) ↓ ESSDAI in EG (2.47 ± 3.48 vs. 1.93 ± 3.18) ↓ PROFAD-Phys in EG (2.98 ± 1.72 vs. 1.14 ± 1.21) ↑ ESSPRI-Dryness in CON (6.08 ± 2.93 vs. 6.96 ± 2.49) ↓ ESSPRI-Fatigue in EG (6.5 ± 2.37 vs. 2.23 ± 2.13) ↓ ESSPRI-Pain in EG (5.57 ± 3.13 vs. 2.8 ± 2.83) ↑ FACIT score in EG (33.97 ± 10.07 vs. 42.44 ± 10.29) ↑ SF-36 score in EG (59.93 ± 27.49 vs. 69.63 ± 19.99) ↓ Sleep latency in EG (22.56 ± 13.18 vs. 18.52 ± 10.67) ↓ Wake after sleep onset in EG (39.34 ± 34.43 vs. 34.25 ± 26.92) Inter-group ($p < 0.05$) > PROFAD decrement (physical and mental) in EG than in CON < ESSPRI-Fatigue in EG than in CON > Functional Capacity (SF-36) in EG than in CON > Vitality (SF-36) in EG than in CON	Dropouts: CON: Leg fracture in traffic accident ($n = 1$), Started biologic drugs due to systemic changes ($n = 2$) Adverse events: NR

Table 2. Cont.

First Author (Year), Design, Country	Sample	Intervention	Outcomes	Results	Dropouts and Adverse Events
Garcia et al. (2021) [41]	Participants (<i>n</i>): 60 women with pSS Final sample (<i>n</i>): 53 (EG: 26; CON: 27) Age, years (mean; SD): EG: 60.43 ± 12.2; CON: 55.77 ± 10.42 BMI, kg/m ² (mean; SD): EG: 27.35 ± 4.2; CON: 26.6 ± 4.11 Time since diagnostic, years (mean; SD): EG: 6.15 ± 4.2; CON: 5.73 ± 4.55	Duration: 28 weeks EG: Resistance and aerobic group Activities: 1° Phase-Resistance (16 weeks): 3 sets of 12 rep. for each muscle group. 2° Phase-Ergometer (12 weeks): Intensity and duration gradually increasing. Patients maintained 60–70 rpm, beginning each session with a 5 min warm-up. Frequency: 2 days/week Volume: 40–50 min/session Intensity: 80% of the MVC; 20–84% of the VO _{2max}	Disease activity: ESSDAI (score)		
		CON Received their usual pharmacological treatment and were instructed not to perform any kind of regular physical exercise	Quality of life - SF-36 (score) Functional capacity: - VO_{2max} (ml/kg/min) - AT (ml/kg/min) - HR_{max} (bpm) Glycemic responses: - HbA1c (%) - Fasting glycemia Lipid profile: - Total Cholesterol - HDL - LDL - Triglycerides	Intra-group (<i>p</i> < 0.05) ↓ VO _{2max} in CON (21.96 ± 5.5 vs. 20.2 ± 4.16) ↑ VO _{2max} in EG (19.64 ± 3.47 vs. 22.95 ± 4.01) ↑ AT in EG (16.86 ± 2.86 vs. 19.56 ± 3.18) ↑ SF-36 score in EG and CON ↑ HbA1c in EG (−5.88 ± 0.73 vs. 5.75 ± 0.66) Inter-group (<i>p</i> < 0.05) > VO _{2max} in EG than in CON > AT in EG than in CON > HbA1c in EG than in CON	Dropouts: CON: Did not answer after contact (<i>n</i> = 3) EG: Discontinued intervention (<i>n</i> = 2), Femur fracture not related to exercise (<i>n</i> = 1), Transverse myelitis (<i>n</i> = 1) Adverse events: NO

Table 2. Cont.

First Author (Year), Design, Country	Sample	Intervention	Outcomes	Results	Dropouts and Adverse Events
Miyamoto et al. (2019) [42]	Participants (<i>n</i>): 45 women with pSS Final sample (<i>n</i>): 37 (EG: 18; CON: 19)	Duration: 16 weeks EG: Walking exercise group Activities: Supervised by two trained professionals who alternated weekly, in an outdoor track field (400 m) Frequency: 3 days/week Volume: 30–60 min/session Intensity: 80% HR _{max}	Disease activity:		
			ESSDAI (score)		
Design: RCT	Age, years (mean; SD): EG: 53.4 ± 8.6; CON: 51.3 ± 8.7 BMI, kg/m ² (mean; SD): EG: 26.1 ± 3.5; CON: 27.9 ± 5.5		Fatigue:	Intra-group (<i>p</i> < 0.05) ↑ VO2 _{max} in EG (18.6 ± 8.3 vs. 23 ± 11.5) and CON (21.4 ± 11.4 vs. 22.1 ± 9.4) ↑ Total distance in EG (518.7 ± 207 vs. 672.2 ± 357) ↑ FACIT score in EG (31.4 ± 9.6 vs. 36.9 ± 9.7) ↓ BDI in EG (19.3 ± 9.8 vs. 15.2 ± 9.7) and CON (20 ± 12.2 vs. 15.7 ± 12.1) ↑ Mental component (SF-36) in EG (42.3 ± 12 vs. 46.5 ± 14.3) and CON (37.5 ± 16.9 vs. 42.5 ± 13.9)	Dropouts: CON: Lost to follow-up (<i>n</i> = 1), Discontinued intervention (<i>n</i> = 2) EG: Lost to follow-up (<i>n</i> = 1), Discontinued intervention (<i>n</i> = 4)
Country: Brazil	Time since diagnostic, months (mean): EG: 24; CON: 45	CON Received their usual pharmacological treatment and were instructed not to perform any kind of regular physical exercise	Quality of life		Adverse events: One participant report chest pain in the 1st week
			- SF-36 (score) - Mental component - Physical component		
			Functional capacity:	Inter-group (<i>p</i> < 0.05) > VO2 _{max} in EG than in CON > Total distance in EG than in CON > FACIT score in EG than in CON	
			Depression:		
			BDI (score)		

Table 2. Cont.

First Author (Year), Design, Country	Sample	Intervention	Outcomes	Results	Dropouts and Adverse Events
Minali et al. (2019) [43]	Participants (<i>n</i>): 59 women with pSS Final sample (<i>n</i>): 51 (EG: 26; CON: 25) Age, years (mean; SD): EG: 61.9 ± 11.4; CON: 56.6 ± 10.3 BMI, kg/m ² (mean; SD): EG: 27.7 ± 4.3; CON: 27.2 ± 4.7 Time since diagnostic, years: NR	Duration: 16 weeks EG: Resistance exercise group Activities: 3 sets of 10 rep. for single-arm row, lateral raise, chest press, triceps extension, biceps curl, knee extension/flexion, hip abduction/adduction, leg press, and squats with dumbbells. Rest intervals were 1 min between sets and exercises. Frequency: 2 days/week Volume: NR Intensity: 60–80% of 1RM	Disease activity: • ESSDAI (score)		
		CON Received their usual pharmacological treatment and were instructed not to perform any kind of regular physical exercise	Quality of life • SF-36 (score) ➤ Functional Capacity ➤ Physical Aspects ➤ Pain ➤ Vitality ➤ Social Aspects ➤ Emotional ➤ Mental Health ➤ General Health Functional capacity: • Upper limb strength (rep) • Lower limb strength (rep) • Agility (s) • Aerobic capacity (m) • Upper limb flexibility (cm) • Lower limb flexibility (cm)	Intra-group ($p < 0.05$) ↑ SF-36 score in EG ↑ Upper limb strength in EG ↑ Lower limb strength in EG ↑ Agility in EG ↑ Aerobic capacity in EG ↑ Lower limb flexibility in EG Inter-group ($p < 0.05$) > Upper limb strength in EG than in CON > Lower limb strength in EG than in CON	Dropouts: CON: Lost of follow-up ($n = 2$), Started to exercise (2), Death ($n = 1$) EG: Started to use medicine for fatigue ($n = 2$), Disease became active ($n = 1$) Adverse events: Joint pain ($n = 4$)

Table 2. Cont.

First Author (Year), Design, Country	Sample	Intervention	Outcomes	Results	Dropouts and Adverse Events
Strömbeck et al. (2007) [44] Design: Non-randomized trial Country: Sweden	Participants (<i>n</i>): 21 women with pSS Final sample (<i>n</i>): 19 (EG: 9; CON: 10) Age, years (median; range): EG: 60 (41–65); CON: 56.5 (42–63) BMI, kg/m ² (median; range): EG: 28 (23–32); CON: 25.5 (21–36) Time since diagnostic, years (median; range): EG: 5 (2–14); CON: 8 (3–23)	Duration: 12 weeks Frequency: 3 day/week EG: Nordic Walking group Activities: One day supervised Nordic walking (45 min) and were instructed to walk for 45 min twice more every week at home Volume: 45 min/session Intensity: 60–80% HR _{max} CON-Home exercises Received instructions for a range of motion exercises to be performed at home (light intensity)	Fatigue: • ProF (score) • VAS (mm)		
			Quality of life • SF-36 (score) ➤ Functional Capacity ➤ Physical Aspects ➤ Pain ➤ Vitality ➤ Social Aspects ➤ Emotional ➤ Mental Health ➤ General Health	Intra-group ($p < 0.05$) ↓ Mental Health (SF-36) in EG ↑ VO _{2max} in EG ↓ Depression in EG Inter-group ($p < 0.05$) < Fatigue (VAS) in EG than in CON > VO _{2max} (l/min) in EG than in CON < Depression (HADS) in EG than in CON	Dropouts: EG: Due to misdiagnosis ($n = 1$); Due to family matters ($n = 1$). Adverse events: NR
			Functional capacity: • VO_{2max} (l/min)		
			Anxiety and depression: • HADS (score) ➤ Depression ➤ Anxiety		

>: Greater; <: Lower; ↑: Increment; ↓: Decrement; AT: Aerobic Threshold; BMI: Body Mass Index; BDI: Beck Depression Inventory; CON: Control Group; EG: Experimental Group; ESSDAI: EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index; FACIT: Functional Assessment of Chronic Illness Therapy; HADS: Hospital Anxiety and Depression scale; HbA1c: Glycated Hemoglobin; HDL: High-Density Lipoprotein; HR: Heart Rate; LDL: Low-Density Lipoprotein; MVA: maximum voluntary contraction; NO: Not observed; NR: Not Reported; pSS: Primary Sjögren's Syndrome; ProF: Profile of Fatigue questionnaire; PROFAD-SSI: Profile of Fatigue and Discomfort-Sicca Symptoms Inventory; RPE: Rating of Perceived Exertion; SF-36: quality of life questionnaire; VAS: Visual Analog Scale; VO_{2max}: Maximum Oxygen Uptake.

2.5. Quality Appraisal

The methodological quality of each RCT was obtained from the Physiotherapy Evidence Database (PEDro) [45], where such evaluations were available. For studies not assessed within the PEDro database, their methodological quality was independently evaluated by two researchers utilizing the PEDro scale [46]. The studies were subsequently categorized based on the following thresholds: excellent (scores of 9–10), good (scores of 6–8), fair (scores of 4–5), and poor (scores below 3) [47].

The Methodological Index for Non-Randomized Studies (MINORS) [48] was applied to assess the methodological quality of the comparative studies included. This tool comprises 12 items, each representing a quality criterion relevant to comparative studies. Each item is scored as follows: 0 (not reported), 1 (reported but inadequate), and 2 (reported and adequate). For comparative studies, the maximum achievable score is 24 points. Studies were categorized as high quality if they achieved a total score of 17 or higher, while those scoring below 17 were classified as low quality [49].

3. Results

3.1. Study Selection Results

A total of 541 records were identified through the database search. After the removal of duplicates, 363 records were screened based on their titles and abstracts, resulting in 18 articles being selected for full-text assessment. Ultimately, four RCTs and one comparative study fulfilled the inclusion criteria and were included in the systematic review (Figure 1).

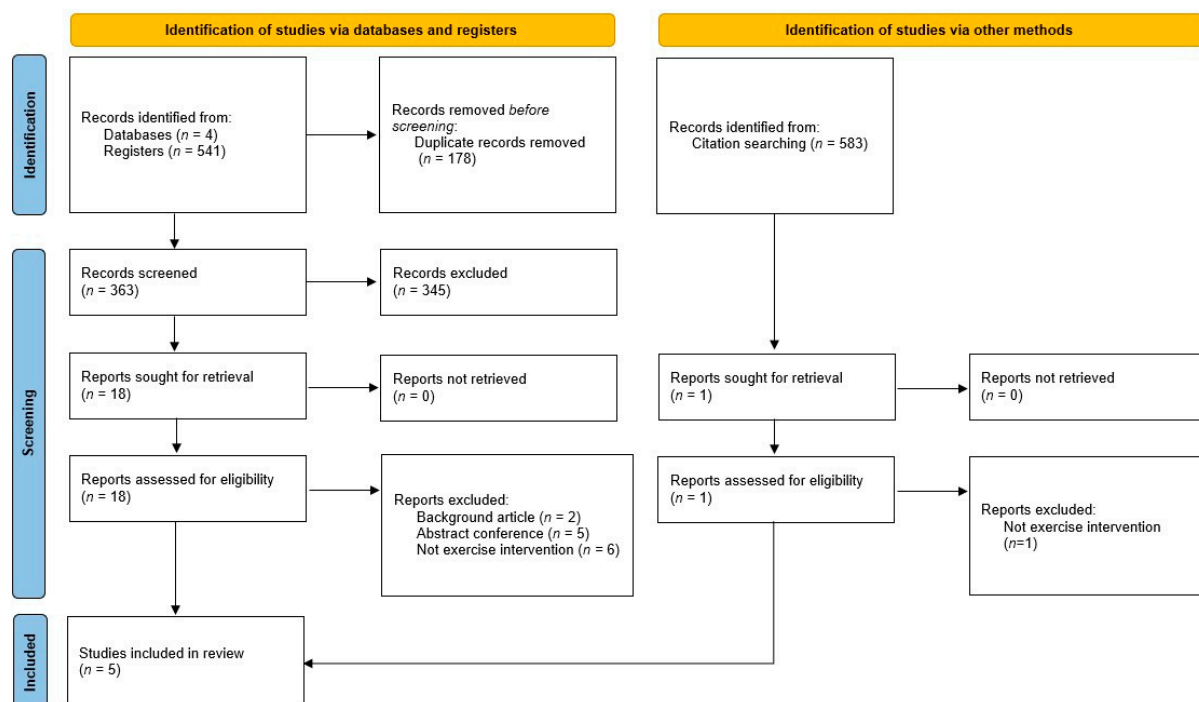


Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) study flow diagram.

3.2. Design and Samples

The combined sample size across all included studies consisted of 244 women. Sample sizes were relatively small, ranging from 21 participants [44] to 60 participants [41]. All study participants were over 40 years old and had been diagnosed with primary pSS for a duration exceeding two years, except for Minali et al. [43], who did not report the time

since diagnosis. The studies were published between 2007 and 2022. A summary of their main characteristics is presented in Table 2

3.3. Intervention Characteristics

Two of the interventions were based on resistance training [40,43], two on aerobic training [42,44], and one on both [41]. Exercise interventions lasted between 12 [40] and 28 [44] weeks. The studies reported frequencies ranging from 2 [46–48] to 3 [42,44] sessions per week. The duration of sessions varied from 30 to 60 min. The studies conducted by Minali et al. [43] and Dardin et al. [40] did not specify the duration of the sessions. Miyamoto et al. [42] and Strömbeck et al. [44] used heart rate to control exercise intensity, while Dardin et al. [40] and Minali et al. [43] used one repetition maximum. Garcia et al. [41] utilized maximum voluntary contraction and maximum oxygen uptake for this purpose.

3.4. Main Outcomes

3.4.1. Quality of Life

All of the studies included analyzed the effects of exercise on the quality of life of the participants using the SF-36 questionnaire and four of them reported significant intra-group improvements after the intervention. However, Strömbeck et al. [44] reported a significant reduction in the mental health score after the intervention

Notably, the effects of exercise were not found to be superior to control conditions in four studies. Only, Dardin et al. [40] showed significant improvements in the vitality and functional capacity subscales after 16 weeks of resistance training, compared to the control group, which was instructed not to engage in any regular exercise.

3.4.2. Disease Activity

Four studies analyzed the effects of exercise on disease activity, measured using the EULAR Sjögren's Syndrome Disease Activity Index [40–43]. In this regard, Dardin et al. [40] observed a significant intra-group reduction after a 16-week resistance exercise intervention, but no inter-group differences were reported. The remaining studies did not report any changes in disease activity scores.

3.4.3. Functional Capacity

Four of the five studies reported information on the effects of exercise on functional capacity measurements [41–44], and all of them reported a significant positive effect derived from these practices compared to baseline measures.

When the inter-group analysis was performed, three studies showed a greater increase in maximum oxygen uptake after the exercise intervention compared to the control group, which did not follow a specific training program [41,42,44]. Additionally, Minali et al. [43] demonstrated that a 16-week resistance training intervention increased upper and lower limb strength more than in the control group.

3.4.4. Fatigue

Three studies aimed to identify the association between exercise practice and changes in fatigue-related parameters [40,42,44]. Significant intra-group improvements were observed in all of them after the exercise programs.

Inter-group analysis revealed that the exercise interventions led to a greater reduction in fatigue outcomes compared to the control group, which did not follow a specific training program [40,42,44].

3.4.5. Anxiety and/or Depression

Two studies evaluated the impact of exercise on anxiety and/or depression using standardized questionnaires. Miyamoto et al. [42] reported a significant reduction in the Beck Depression Inventory score following an aerobic intervention, although no significant differences were observed between the experimental and control groups. In contrast, Strömbeck et al. [44] found a significant decrease in depression scores, measured by the Hospital Anxiety and Depression Scale, within the exercise group compared to baseline. Additionally, the exercise group demonstrated a greater reduction in depression scores compared to the control group, which did not participate in a structured training program. However, no significant changes were observed in the anxiety scores.

3.4.6. Lipid Profile

Resistance and aerobic exercise programs did not have any significant impact on the lipid profile, according to the results reported in the only study investigating these outcomes [41].

3.4.7. Sleep Quality

One study explored the impact of resistance exercise training on sleep quality, assessed using actigraphy [40]. The results indicated that sleep latency and wake after sleep onset were reduced in the experimental group after 16 weeks. However, no significant differences between groups were found after the training period.

3.4.8. Glycemic Responses

According to the findings from the only study that examined this outcome, combined resistance and aerobic training resulted in a significant increase in HbA1c following a 28-week intervention [40]. Additionally, the improvement observed in the intergroup evaluation was statistically significant compared to the control group.

3.5. Dropouts and Adverse Events

Across all included studies, a total of 28 participants dropped out, with 14 of these occurring within the exercise groups. The main reasons for dropouts were health-related issues and/or discontinuation of the intervention. Adverse effects were reported in two of the five studies [42,43], which included one instance of chest pain during the first week of the intervention and four cases of joint pain.

3.6. Methodological Quality

The results of the methodological quality assessment of the RCTs were retrieved directly from PEDro for all of the RCTs [40–43]. The methodological quality was considered good in all of them. The only study evaluated using the MINORS scale was considered to be of high quality [44]. A full description of the quality analysis was also provided in Table 3.

Table 3. Methodological quality appraisal of the included studies.

Randomized Controlled Trials (PEDro Scale)	First Author, Year			
	Dardin et al. (2022) [40]	Garcia et al. (2021) [41]	Minali et al. (2019) [43]	Miyamoto et al. (2019) [42]
1. Random allocation	+	+	+	+
2. Concealed allocation	+	+	+	+
3. Baseline comparability	+	+	+	+
4. Blind subjects	—	—	—	—
5. Blind therapists	—	—	—	—
6. Blind assessors	+	+	+	+

Table 3. Cont.

Randomized Controlled Trials (PEDro Scale)	First Author, Year			
	Dardin et al. (2022) [40]	Garcia et al. (2021) [41]	Minali et al. (2019) [43]	Miyamoto et al. (2019) [42]
7. Adequate follow-up	+	+	+	+
8. Intention-to-treat analysis	—	+	+	+
9. Between-group comparisons	+	+	+	+
10. Point estimates and variability	+	+	+	+
Total score	7/10	8/10	8/10	8/10
Comparative study (MINORS scale)	Strömbeck et al. (2007) [44]			
1. Clearly stated aim	2			
2. Inclusion of consecutive patients	1			
3. Prospective collection of data	2			
4. Endpoints appropriate to the aim of the study	2			
5. Unbiased assessment of the study endpoint	0			
6. Follow-up period appropriate to the aim of the study	2			
7. Loss to follow up less than 5%	0			
8. Prospective calculation of the study size	0			
9. Adequate control group	2			
10. Contemporary groups	2			
11. Baseline equivalence of groups	2			
12. Adequate statistical analyses	2			
Total score	17/24			

4. Discussion

This systematic review aimed to provide scientific evidence on the effectiveness of exercise as a therapeutic approach for patients with pSS. The results may be valuable to professionals looking for rehabilitation strategies to reduce the impact of this condition on patients' overall health. After conducting an extensive and thorough search, only a small number of studies met the criteria for inclusion in this review. However, the majority of the studies analyzed were RCTs of good methodological quality. Considering the existing gap in the literature regarding the prescription of exercise for individuals with pSS, the findings of this review offer valuable and thought-provoking data that merit further discussion.

For instance, it is noteworthy that all the studies included reported on the effects of exercise on quality of life. This is an important topic to address, as treatment goals for patients with pSS should focus not only on extraglandular symptoms but also on improving quality of life outcomes [50]. Fatigue levels have also been considered as a predictor of quality of life in this population, given their detrimental impact on both physical and mental health [51].

Previous systematic reviews have demonstrated that exercise modalities, such as yoga and resistance training, result in significant improvements in the quality of life for patients with rheumatic diseases [52,53]. Interestingly, while intra-group analyses typically showed significant positive effects of exercise on this outcome, inter-group comparisons largely indicated that these effects were not superior to those achieved with standard treatment. This lack of effect of exercise on the usual treatment may be attributed to the limited impact that exercising has on several disease hallmarks that significantly influence the quality of life in this population, including dryness, autonomic responses, pruritus, and both oral and ocular disorders [54]. Additionally, it is important to note that exercise was not found to be superior to standard treatment in alleviating anxiety and depression, both of which are strongly linked to quality of life [55]. Similarly, other systematic reviews have noted that exercise could have a similar but not superior effect to standard treatment for depression [56] or anxiety [57]. Thus, it appears that the impact of exercise on the mental health of patients with pSS is limited.

In this context, most of the analyzed studies indicated that disease severity was not influenced by participation in exercise training programs. The lack of efficacy of exercise in modifying disease activity has also been observed in patients with lupus [58]. This aligns with previous findings suggesting that, among patients with autoimmune diseases, the anticipated changes in inflammation biomarkers resulting from exercise are modest at best [59]. Hence, a reduced effect of exercise on disease activity is expected. Notably, prior research has shown that patient-reported symptoms, which relate to systemic activity, are associated with improved health-related quality of life in individuals with pSS [60]. This finding suggests that since exercise was ineffective in reducing disease severity, it likely also did not have a direct impact on the quality of life. The effects of current pharmacological therapies aimed at alleviating the symptoms of this disease are limited, primarily due to its unknown and complex etiology, with potential treatment targets for disease severity still requiring further research [61]. In this context, it appears that exercise should not be regarded as a more viable option than the existing prescribed drug therapies.

On the other hand, the reviewed studies highlighted a positive impact of exercise on physical function, which is particularly noteworthy given that functional status is often impaired in individuals with pSS [16]. This finding aligns with previous research suggesting that exercise can significantly benefit the physical functioning of patients with rheumatological diseases [62]. Based on the analyzed data, it can be hypothesized that this improvement may stem from increases in fitness levels associated with engaging in physical activity, as this factor is closely linked to the prevention of functional decline [63]. In this regard, it is worth noting that those who experienced a greater increase in their fitness levels compared to their peers undergoing standard treatment showed more pronounced improvements.

Similarly, exercise has also been shown to be effective in reducing the impact of fatigue. This is a significant finding, as patients with pSS often report that fatigue is their most challenging and burdensome symptom to manage [64]. Other published reviews on the effects of exercise in autoimmune and rheumatic diseases have also reported positive outcomes, particularly in reducing fatigue levels [23,65]. Fatigue in Sjögren's disease is believed to be partly driven by pro-inflammatory cytokines. Therefore, it can be hypothesized that exercise may help alleviate fatigue by reducing the concentration levels of these pro-inflammatory cytokines, as has been suggested in other conditions [66]. The obtained results support the notion that, while pharmacological treatments for fatigue have not proven effective in managing this symptom, exercise appears to be a valuable, safer, and more cost-effective option [42].

The reviewed studies that provided data on outcomes related to sleep problems and metabolic health indicated that exercise had a similar effect to standard pharmacological treatment. Similarly, exercise has been shown to yield effects akin to pharmacological therapy in individuals with movement disorders (Franco, 2019), and to offer comparable benefits for metabolic health when evaluated alongside standard pharmacological approaches [67]. However, the limited number of investigations available restricts the ability to draw more definitive conclusions or engage in deeper discussion.

On a final note, it is important to highlight that dropouts due to health issues were reported in the exercise groups by the authors of the studies included in this review, with some cases being directly attributed to the exercise itself. This finding raises concerns about the feasibility of exercise interventions for individuals with pSS and suggests that caution should be exercised when recommending physical activity to this population.

The findings of this systematic review support the use of supervised physical exercise programs, conducted 2 to 3 days per week in sessions of 30 to 60 min, as a complementary, safe, and effective intervention for patients with pSS. Aerobic activities, such as supervised walking or Nordic walking, enhance cardiorespiratory capacity, while resistance training

alleviates fatigue and pain, and improves vitality. Although no clear superiority over standard treatments was observed in areas such as mental health or inflammatory activity, these non-pharmacological interventions contribute significantly to improving physical functionality and daily quality of life, with high safety and adherence rates. Therefore, it is advisable for patients, trainers, and caregivers to consider incorporating this type of treatment.

This appears to be the first systematic review examining the efficacy of exercise for patients with pSS. Despite its originality, several limitations must be acknowledged, as they significantly impact the strength of the findings presented. Firstly, a reduced number of investigations were found. Thus, caution is required when interpreting the obtained results. Secondly, due to the variation in methods and interventions used across studies, it remains unclear which exercise protocol is most beneficial. Additionally, only one study directly compared the effectiveness of two exercise interventions, making it challenging to determine which type of exercise should be recommended. Finally, we could not eliminate the possibility that some studies used the same sample, which prevented the performance of a meta-analysis. Clearly, further RCTs with larger sample sizes are needed to determine whether exercise has superior effects compared to standard therapy on key disease hallmarks, such as disease activity, fatigue, and pain. The findings from these studies should help establish basic guidelines for safely prescribing exercise to individuals with pSS.

5. Conclusions

Exercise does not demonstrate superior effects compared to standard treatment for improving quality of life and disease impact in patients with pSS. However, it can still be recommended for enhancing physical function and reducing fatigue. Nonetheless, the evidence is insufficient to inform clinical decisions regarding exercise prescription for this population due to the limited number of studies identified.

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