



SYSTEMATIC REVIEW

The effect of exercise intervention on fatigue and quality of life in individuals with sarcoidosis; a systematic review

Masoume Khosropanah¹, Ali Livani², Ebrahim Ebrahimi^{3*}

- 1- Department of Physical Education & Sport Sciences, Faculty of Humanities, Tarbiat Modares University, Tehran, Iran. Email: m_khosropanah@modares.ac.ir, ORCID: 0009-0008-6525-9984
- 2- Department of Exercise Physiology, Shahrood University of Technology, Shahrood, Iran. Email: alivani1371@gmail.com, ORCID: 0009-0001-8139-6961
- 3- Department of Corrective Exercise & Sport Injury, Faculty of Physical Education and Sport Sciences, Al-lameh Tabataba'i University, Tehran, Iran. Email: ebrahim_ebrahimi@atu.ac.ir, ORCID: 0009-0004-2969-2896

Corresponding author: Ebrahim Ebrahimi. Email: ebrahim_ebrahimi@atu.ac.ir

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Abstract. This systematic review synthesized current evidence on the effects of exercise-based interventions on fatigue and health-related quality of life (HR-QoL) in adults with sarcoidosis. Following PRISMA guidelines, PubMed, Scopus, Web of Science, and Google Scholar were searched from inception to December 2025. Six studies comprising 11–57 participants across varying disease stages met inclusion criteria. Exercise interventions were generally safe and feasible, including high-intensity resistance training. Across studies, structured exercise and pulmonary rehabilitation consistently improved exercise capacity, muscle strength, dyspnea, and HR-QoL. Reductions in fatigue were observed in several interventions; however, fatigue outcomes were heterogeneous and not always correlated with physiological improvements. Physical activity levels were more associated with exercise capacity and HR-QoL than with fatigue severity, underscoring the multifactorial nature of fatigue in sarcoidosis. Future research should employ standardized fatigue measures, larger samples, and longer follow-up to optimize exercise prescription and address the complex symptom profile of this population.

Keywords: Pulmonary rehabilitation, Physical activity, Chronic inflammatory disease, Quality of life, Systematic review

Introduction

Sarcoidosis is a systemic inflammatory disorder characterized by the differentiation and proliferation of immune cells, leading to granuloma formation across multiple tissues (Grunewald et al., 2019; Iriarte et al.,



2020). The condition triggers an exaggerated immune response. Inflammatory mediators and oxidative stress impair mitochondrial function and amino acid metabolism in muscle cells. Lipid homeostasis is also affected (Cho et al., 2019). Fatigue is among the most disabling and frequently reported symptoms in patients with sarcoidosis, often persisting even when pulmonary manifestations are well controlled (Marcellis et al., 2011). These processes interact in a complex and dynamic manner, without being driven by a single factor. Clinically, sarcoidosis presents with nonspecific symptoms such as fatigue, arthralgia, reduced exercise tolerance, and dyspnea (Bargagli et al., 2017; Simonen et al., 2016). Gender appears to play a significant role in sarcoidosis, as the condition is more prevalent in women (Musellim et al., 2009), who also report lower health-related quality of life compared to men (Gwadera et al., 2021). Increasing evidence indicates that the disease not only affects organ-specific functions but also leads to nonspecific problems, including low energy, pain, anxiety, depression, and cognitive symptoms, which significantly impair health-related quality of life (HR-QoL) (Drent et al., 2015; Judson, 2015).

Exercise intolerance is a common issue in sarcoidosis and is associated with multiple factors. Several studies have reported that it correlates with reduced quality of life, increased dyspnea, and heightened fatigue in affected individuals (Karadallı et al., 2016; Marcellis et al., 2015). Decreased muscle strength and impaired quality of life are commonly observed in individuals with sarcoidosis, including those with mild forms of the disease (Kallianos et al., 2015). Recent evidence indicates that patients with sarcoidosis engage in significantly lower levels of physical activity compared to healthy individuals (Cho et al., 2019). In various chronic pulmonary and inflammatory conditions, structured physical training has been shown to enhance exercise capacity, alleviate muscle weakness, improve quality of life, and reduce fatigue, without causing adverse effects (Holland et al., 2012; Kullberg et al., 2020). Accumulating evidence in sarcoidosis shows that participation in rehabilitative exercise programs, designed to address the disease's specific pathophysiology, alleviates fatigue, muscle weakness, and dyspnea, and significantly improves patients' quality of life (Karadallı et al., 2016; Marcellis et al., 2015; Mendes et al., 2021; Naz et al., 2018; Strookappe et al., 2015).

Although the pathophysiological mechanisms of interstitial lung disease (ILD) and chronic obstructive pulmonary disease (COPD) differ, patients with ILD often experience fatigue, dyspnea, reduced exercise capacity, and diminished quality of life (Dowman et al., 2021). Utilizing exercises involving small muscle groups has facilitated the differentiation of peripheral muscle dysfunction from central cardiovascular and pulmonary limitations (Heidorn et al., 2023). Therefore, this systematic review aims to synthesize current evidence on the effects of exercise interventions on fatigue and quality of life in individuals with sarcoidosis, highlighting effective approaches and identifying gaps for future research. We applied the PICO framework (Population, Intervention, Comparison, and Outcomes) to filter, select, and review the literature (Amir-Behghadami & Janati, 2020).

Methodology

Search Strategy. This systematic review was conducted according to the PRISMA guidelines (Page et al., 2021). The databases PubMed, Scopus, and Web of Science were searched from the databases' inception until December 2025. Google Scholar was also searched for additional records. Keywords were selected

according to Table 1 and searched using Boolean operators. The search was conducted in English-language databases using English terms.

Inclusion and Exclusion Criteria. Studies were included if they investigated adults diagnosed with sarcoidosis and examined the effects of exercise-based interventions (e.g., resistance training, aerobic exercise, pulmonary rehabilitation, or structured exercise programs) on fatigue and health-related quality of life. Eligible studies comprised randomized controlled trials and quasi-experimental studies, published as original research articles in peer-reviewed journals. Only articles published in English were considered. Studies were excluded if they did not involve an exercise intervention, focused on diseases other than sarcoidosis, or were conference abstracts, review articles, case reports, or editorials. Studies lacking quantitative outcome measures related to fatigue and quality of life were also excluded.

Study selection. After searching the databases, the results were transferred to EndNote 7X software. Then, the titles and abstracts of the articles were screened by two independent researchers (M.KH., A.L.). Relevant articles were selected for full-text review. In case of disagreement, the consensus method was used by the supervisor (E.E.).

Data extraction and quality assessment. After extracting eligible articles, general data, study characteristics, and results were extracted from the articles and summarized in Table 2. Data extraction was performed by two independent researchers (M.KH., A.L.). The quality of the studies was assessed with the JBI tools for quasi-experimental studies (Table 3) (NA, 2017).

Table 1: Search strategy used for this study

Variable	Keywords
exercise intervention	("Exercise" OR "Training" OR "Protocol" OR "Rehabilitation" OR "physical therapy" OR "therapeutic exercise" OR "exercise therapy" OR "Exercise Movement Techniques" OR "physiotherapy")
Sarcoidosis	AND ("Sarcoidosis" OR sarcoidosis OR "sarcoid disease" OR "systemic granulomatous disease" OR "non-caseating granuloma*" OR "noncaseating granuloma*")

Table 2 - Characteristics of the included studies

Authors (Year)	Title	Study Design	Participants	Intervention	Outcome Measures	Key Findings
Grongstad A. et al. (2020)	The acute impact of resistance training on fatigue in patients with pulmonary sarcoidosis	Randomized crossover	41 patients with pulmonary sarcoidosis (mean age 53±11 yrs)	One session high-intensity RT (4×5RM) vs. one session moderate-intensity RT (2×25RM)	Fatigue (VAS-F), blood lactate	High-intensity RT did not induce larger fatigue than moderate RT; both protocols feasible and safe
Bahmer T. et al. (2018)	Physical Activity and Fatigue in Patients with Sarcoidosis	Prospective observational	57 patients with sarcoidosis (mean age 50 yrs, 56% male)	Accelerometry (SenseWear Armband) for 1 week	Steps/day, lung function, 6MWD, QoL (SGRQ, SF-12), fatigue (MFI-20)	Physical activity associated more strongly with exercise capacity and QoL than fatigue; fatigue weak predictor of inactivity
Naz I. et al. (2018)	Efficacy of a Structured Exercise Program for Improving Functional Capacity and QoL in Stage 3–4 Sarcoidosis	Randomized controlled trial	18 patients (stage 3–4 sarcoidosis)	12-week supervised exercise program (breathing, endurance, strength, stretching) vs. usual care	6MWD, muscle strength, dyspnea, fatigue (FSS), QoL (SGRQ, SF-36), anxiety/depression	Exercise improved functional capacity, muscle strength, dyspnea, fatigue, oxygenation, QoL, anxiety
Tahmaz T. et al. (2025)	Comparison of One-Legged and Two-Legged Exercise Training on Exercise Capacity and Fatigue in Sarcoidosis	Randomized controlled trial	26 patients (stage 2–4 sarcoidosis, all female)	8-week cycling program: one-legged vs. two-legged	6MWT, ISWT, ESWT, FAS, MFI-20, blood lactate, muscle strength, QoL (SGRQ)	Both groups improved fatigue, strength, QoL; one-legged cycling superior for activity-related QoL

Table 2 - Characteristics of the included studies

Authors (Year)	Title	Study Design	Participants	Intervention	Outcome Measures	Key Findings
Kullberg S. et al. (2020)	High-intensity resistance training in newly diagnosed sarcoidosis	Exploratory intervention study	11 untreated patients with newly diagnosed sarcoidosis	12-week high-intensity RT (80% 1RM, 2×/week) + inspiratory muscle training	Lung function, muscle strength, fatigue (FSS), dyspnea, QoL (SGRQ), BAL immune cells	Increased muscle strength, reduced fatigue/dyspnea, improved QoL; decreased BAL lymphocytes
Grongstad A. et al. (2020)	Pulmonary Rehabilitation in Patients with Pulmonary Sarcoidosis: Impact on Exercise Capacity and Fatigue	Pre-post study	41 patients with pulmonary sarcoidosis	4-week multidisciplinary PR program (endurance + resistance training, education, psychosocial support)	VO ₂ peak (CPET), fatigue (FAS), 6MWD, QoL	PR improved VO ₂ peak, reduced fatigue; baseline fatigue predicted improvement in VO ₂ peak

Abbreviations: **RT** = Resistance Training, **RM** = Repetition Maximum, **PR** = Pulmonary Rehabilitation, **6MWD** = Six-Minute Walk Distance, **6MWT** = Six-Minute Walk Test, **ISWT** = Incremental Shuttle Walk Test, **ESWT** = Endurance Shuttle Walk Test, **VO₂peak** = Peak Oxygen Uptake, **FAS** = Fatigue Assessment Scale, **MFI-20** = Multidimensional Fatigue Inventory (20 items), **FSS** = Fatigue Severity Scale, **SGRQ** = St. George's Respiratory Questionnaire, **SF-12 / SF-36** = Short Form Health Survey (12 or 36 items), **BAL** = Bronchoalveolar Lavage, **QoL** = Quality of Life, **ACTH** = Adrenocorticotrophic Hormone, **CPET** = Cardiopulmonary Exercise Test

Results

Figure 1 illustrates the study selection process. Initially, 535 articles were identified. After removing

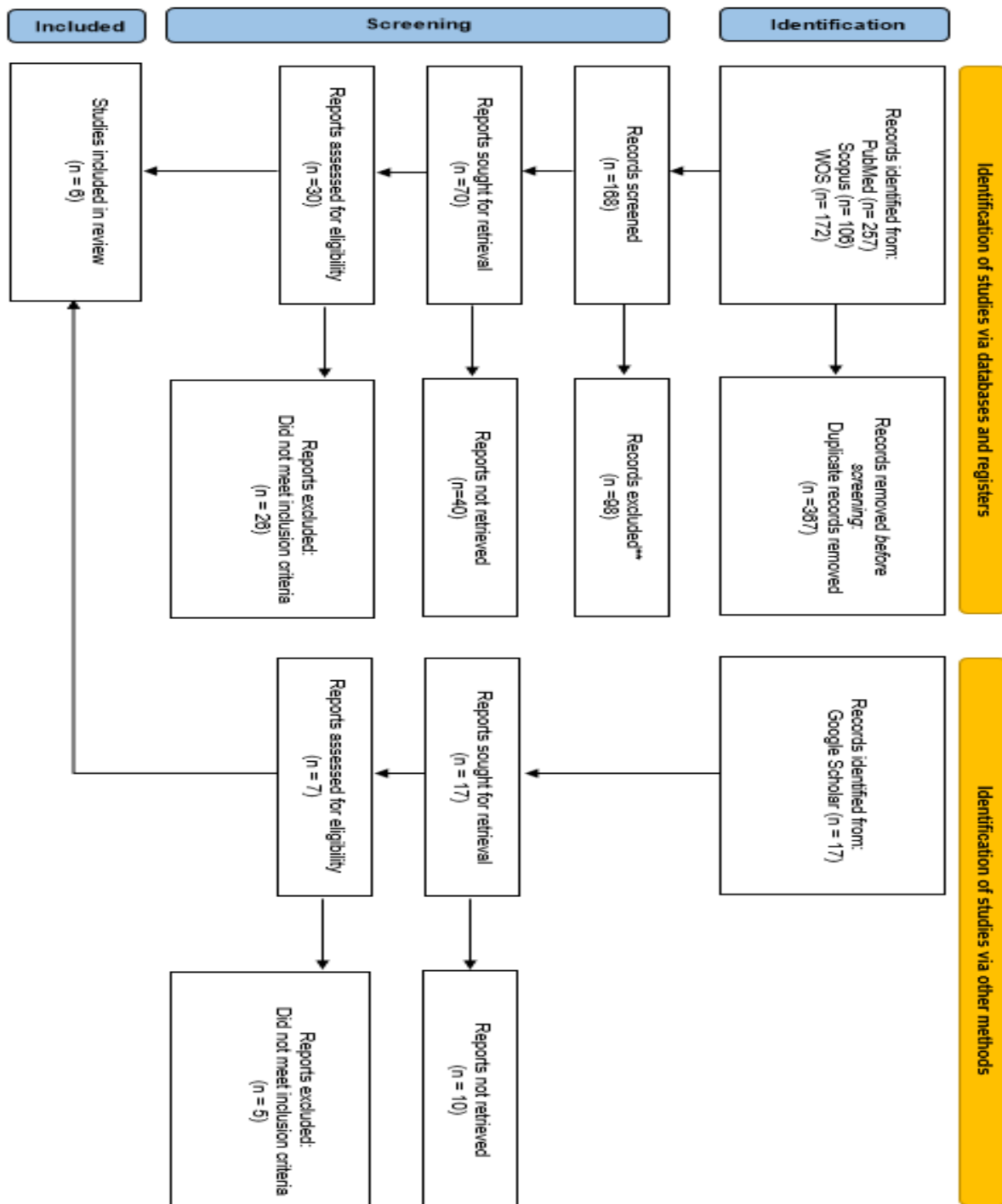


Figure 1. Flow diagram for eligible studies

duplicates, 168 abstracts were screened. Based on the abstract review, 98 studies were excluded, leaving 70 articles for full-text assessment. Following a thorough evaluation of the full texts, 64 articles were excluded, resulting in 6 studies included in the final analysis (Figure 1). Table 2 presents a summary of the findings from these articles.

Study Characteristics. Six studies met the inclusion criteria, encompassing 11–57 participants with sarcoidosis across varying disease stages. Grongstad et al. reported that acute high-intensity RT (5RM) did not exacerbate fatigue compared to moderate-intensity RT (25RM), while Kullberg et al. demonstrated that a 12-week RT program significantly improved muscle strength, reduced fatigue and dyspnea, and enhanced HR-QoL in newly diagnosed patients. Another study by Grongstad et al. found that baseline fatigue predicted the magnitude of improvement in VO_{2peak} . Tahmaz et al. compared one-legged and two-legged cycling, showing that both protocols improved fatigue, muscle strength, and QoL, with superior gains in activity-related QoL in the one-legged group. Naz et al. reported that a structured 12-week exercise program improved functional capacity, muscle strength, dyspnea, fatigue, and psychological outcomes, including anxiety and depression. Bahmer et al. highlighted that physical activity levels were more strongly associated with exercise capacity and HR-QoL than with fatigue, suggesting that fatigue alone is insufficient to explain inactivity. Braam et al. further demonstrated that severely fatigued patients exhibited lower VO_{2max} and workload during repeated cardiopulmonary exercise testing.

Table 3: Critical appraisal results of eligible systematic reviews

	Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Overall Score
1	Grongstad A. et al. (2020)	Y	Y	Y	Y	Y	Y	Y	N	Y	8
2	Bahmer T. et al. (2018)	Y	Y	Y	Y	Y	Y	Y	N	Y	8
3	Naz I. et al. (2018)	Y	Y	Y	Y	Y	Y	Y	N	Y	8
4	Tahmaz T. et al. (2025)	Y	Y	Y	Y	Y	Y	Y	N	Y	8
5	Kullberg S. et al. (2020)	Y	Y	Y	Y	Y	Y	Y	N	Y	8
6	Grongstad A. et al. (2020)	Y	Y	Y	Y	Y	Y	Y	N	Y	8

Quality Assessment. A methodological quality appraisal was conducted for all included studies using the JBI checklist. All six studies demonstrated high methodological rigor, each achieving an overall score of 8 out of 9. The majority of studies fulfilled critical quality domains, including well-defined objectives, appropriate outcome measures, and robust data collection processes, reflecting a moderate to good quality with some limitations. However, a notable limitation was observed in criterion Q8 (Was follow-up complete, and if not, were differences between groups in terms of their follow-up adequately described and analyzed?), which was not satisfied by any of the studies. Despite this issue, the uniformity of high scores across studies highlights the overall strength and reliability of the included research.

Discussion

This systematic review evaluated evidence from six original studies investigating the effects of structured exercise, pulmonary rehabilitation, and repeated exercise testing on exercise capacity, fatigue, and patient-reported outcomes in individuals with sarcoidosis (Bahmer et al., 2018; Braam et al., 2013; Anita Grongstad et al., 2020; A. Grongstad et al., 2020; Kullberg et al., 2020; Tahmaz et al., 2025). Overall, the findings suggest that exercise-based interventions are feasible and generally beneficial for improving functional capacity, although their effects on fatigue are less consistent. Across the included studies, improvements in objective measures of exercise performance were a common finding following structured exercise training or pulmonary rehabilitation programs (Bahmer et al., 2018; Anita Grongstad et al., 2020; Kullberg et al., 2020; Tahmaz et al., 2025). In both randomized controlled and prospective intervention studies, gains were observed in parameters such as peak oxygen uptake, six-minute walk distance, and maximal workload, even among patients with moderate to advanced pulmonary involvement (Anita Grongstad et al., 2020; Kullberg et al., 2020; Tahmaz et al., 2025). These results suggest that impaired exercise capacity in sarcoidosis is at least partly attributable to reversible functional limitations and physical deconditioning rather than fixed disease-related impairment alone.

In contrast, the impact of exercise interventions on fatigue was more heterogeneous. While some studies reported significant reductions in self-reported fatigue following structured exercise or pulmonary rehabilitation (Grongstad et al., 2020; Kullberg et al., 2020; Tahmaz et al., 2025), others found limited or no association between fatigue severity and changes in objective physiological measures (Bahmer et al., 2018; Braam et al., 2013; A. Grongstad et al., 2020). In particular, studies assessing repeated maximal exercise testing demonstrated that exercise-induced physiological and biochemical responses were not correlated with subjective fatigue levels (A. Grongstad et al., 2020). This dissociation indicates that fatigue cannot be fully explained by peripheral physiological stress or acute exercise responses (Shadi et al., 2026). One possible explanation is that sarcoidosis-related fatigue may be driven by central nervous system dysregulation, including altered neurotransmitter balance, neuroinflammatory processes, and impaired central motor drive (Drent et al., 2012). In addition, chronic systemic inflammation and immune activation may contribute to reduced motivation and persistent perceptions of tiredness despite preserved physical capacity (Straub, 2017). Autonomic dysfunction and hypothalamic–pituitary–adrenal (HPA) axis alterations have also been proposed as underlying mechanisms that may influence energy regulation and

stress responses in this population (Tsigos & Chrousos, 2002). The variability in fatigue outcomes across studies highlights the complex and multifactorial nature of fatigue in sarcoidosis. Although exercise training improves physical efficiency and functional performance, fatigue appears to be influenced by additional factors such as sleep disturbances, psychological burden, and central mechanisms, which were not consistently addressed in the included studies (Bahmer et al., 2018; Kullberg et al., 2020). Furthermore, behavioral and cognitive factors such as illness perception, fear of symptom exacerbation, and reduced self-efficacy may mediate the subjective experience of fatigue independently of measurable physiological improvement (Breukers et al., 2019). Consequently, improvements in exercise capacity do not uniformly translate into proportional reductions in fatigue severity.

Several studies also reported favorable effects of exercise-based interventions on health-related quality of life, dyspnea perception, and emotional well-being (Anita Grongstad et al., 2020; Kullberg et al., 2020; Tahmaz et al., 2025). Notably, these improvements were sometimes observed even when changes in fatigue were modest, suggesting that enhanced functional ability and increased confidence in physical performance may independently contribute to better patient-reported outcomes. Enhanced exercise capacity, increased muscle strength, and improved tolerance to physical activity may foster greater functional independence and self-efficacy (Ebrahimi et al., 2025), thereby positively influencing patients' perception of health and well-being. Collectively, these findings indicate that exercise-based interventions can meaningfully enhance quality of life and emotional health in sarcoidosis, underscoring the importance of targeting functional and psychosocial outcomes alongside symptom-specific measures.

Despite the overall positive direction of findings, substantial heterogeneity exists among the included studies. Differences in study design, intervention duration, exercise modality, and outcome measures limit direct comparability and preclude firm conclusions regarding optimal training protocols (Braam et al., 2013; Anita Grongstad et al., 2020; Kullberg et al., 2020; Tahmaz et al., 2025). Sample sizes were generally small, and follow-up periods were relatively short, restricting the assessment of the long-term sustainability of the observed benefits. In addition, the substantial heterogeneity in fatigue assessment instruments across the included studies represents an important methodological limitation. The use of different measurement tools with varying constructs, scoring systems, and sensitivity reduces comparability between studies and limits the ability to draw consistent conclusions or synthesize findings with high confidence (Bahmer et al., 2018; Kullberg et al., 2020). From a clinical perspective, the evidence synthesized in this review supports the integration of structured exercise and pulmonary rehabilitation into the management of sarcoidosis, particularly to improve functional capacity and exercise tolerance (Anita Grongstad et al., 2020; Kullberg et al., 2020; Tahmaz et al., 2025). These findings suggest that individualized, progressive, and supervised exercise programs may be safely incorporated into routine care to enhance physical performance outcomes. However, the inconsistent effects on fatigue indicate that exercise alone may be insufficient to comprehensively address this symptom. Multidimensional and individualized management strategies, potentially incorporating psychosocial support, education, and symptom-targeted interventions, may therefore be required to effectively manage fatigue in this population.

Conclusion

This systematic review demonstrated that exercise-based interventions and pulmonary rehabilitation are safe and effective strategies for improving health-related quality of life in individuals with sarcoidosis. Although reductions in fatigue were observed in several studies, the effects were inconsistent, reflecting the multifactorial nature of fatigue in this population. Future research should focus on standardized outcome measures, larger sample sizes, and long-term follow-up to optimize exercise prescription for this population.

Declarations:

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare no competing interests.

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Authors contributions

MKH and AL contributed to the study design and data collection. MKH, AL, and EE drafted the manuscript and made critical revisions to the manuscript. All authors read and approved the final manuscript.

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Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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