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Review article

Lifestyle medicine and rheumatoid arthritis: physical exercise as a therapeutic pillar

Medicina do estilo de vida e artrite reumatoide: o exercício físico como pilar terapêutico

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease that primarily affects the joints but can also compromise multiple organ systems. Although pharmacological treatments have advanced, the integration of non-pharmacological approaches has gained increasing attention, particularly within the framework of Lifestyle Medicine (LM). This literature review explores the role of physical exercise as a core therapeutic component in the modern management of RA. Evidence demonstrates that various types of exercise – aerobic, resistance, and mind-body – significantly contribute to reducing systemic inflammation, improving joint function, regulating immune responses, managing pain and fatigue, and enhancing overall well-being. The physiological and immunological mechanisms involved are discussed, including the role of myokines and oxidative stress regulation, alongside practical recommendations for safe exercise implementation. We conclude that physical activity should be incorporated as a therapeutic pillar in rheumatology, fostering patient-centered care aligned with LM principles.-

RESUMO

A artrite reumatoide (AR) é uma doença inflamatória crônica autoimune que afeta articulações e pode comprometer diversos sistemas do organismo. Apesar dos avanços no tratamento farmacológico, a integração de abordagens não farmacológicas vem ganhando destaque, sobretudo no escopo da Medicina do Estilo de Vida (MEV). Nesta revisão de literatura, investigamos o papel do exercício físico como componente terapêutico fundamental na abordagem contemporânea da AR. As evidências demonstram que diferentes modalidades de exercício – aeróbico, resistido e mente-corpo – contribuem significativamente para a redução da inflamação sistêmica, melhora da função articular, regulação imunológica, controle da dor, fadiga e promoção do bem-estar geral. São discutidos os mecanismos fisiológicos e imunológicos envolvidos, incluindo o papel das miocinas e da regulação do estresse oxidativo, além de recomendações práticas para a implementação segura dessas atividades. Concluímos que o exercício físico deve ser incorporado como um pilar terapêutico na reumatologia, promovendo um cuidado centrado no paciente e alinhado com os princípios da MEV.

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic autoimmune inflammatory disease that primarily affects synovial joints, leading to pain, stiffness, functional limitation, and progressive joint destruction. Its pathophysiology is characterized by the activation of T and B cells, the production of autoantibodies (such as rheumatoid factor and anti-CCP), and the release of inflammatory cytokines, including TNF-α, IL-1, and IL-6, which sustain the chronic inflammatory process[1]. RA is estimated to affect approximately 0.5% to 1% of the global population, with a predominance in females and a more common onset between 30 and 50 years of age[2].

Traditionally treated with disease-modifying antirheumatic drugs (DMARDs) and biological agents, the therapeutic approach to RA has expanded with the incorporation of Lifestyle Medicine (LM) strategies, which aim to intervene in the behavioral and environmental determinants of health. Within this context, physical activity has emerged as a safe, accessible intervention with potential immunomodulatory effects, acting to reduce systemic inflammation, improve body composition, control pain, and preserve joint function[3–8].

Lifestyle Medicine is an evidence-based clinical approach that applies structured interventions across six pillars — predominantly plant-based nutrition, physical activity, sleep, stress management, social connections, and avoidance of risky substances — as a central therapeutic strategy to prevent, treat, and, when plausible, reverse chronic diseases. The definition and pillars are described by reference societies; the core competencies for prescription were proposed in 2010 in JAMA and updated in 2022, with the aim of guiding clinical training and practice. From this perspective, Lifestyle Medicine integrates multiprofessional teams and person-centered care[9,10].

Growing evidence demonstrates that different modalities of physical exercise, such as aerobic training, resistance training, and mind–body activities, contribute to clinical improvement in patients with RA. Beyond effects on musculoskeletal function, exercise influences the release of anti-inflammatory myokines (such as IL-10 and IL-1ra), the regulation of the hypothalamic–pituitary–adrenal (HPA) axis, and the profile of circulating cytokines, thereby potentially modulating disease activity[11,12].

In this context, this literature review aims to evaluate the effects of physical activity in patients with RA, focusing on clinical, functional, and immunological outcomes, in light of current evidence and the paradigm of Lifestyle Medicine.

MATERIAL AND METHODS

This study is a narrative literature review conducted with the aim of gathering, analyzing, and synthesizing scientific evidence on the effects of physical exercise in patients with RA, from the perspective of Lifestyle Medicine (LM).

The bibliographic search was carried out in the electronic databases PubMed and the Latin American and Caribbean Health Sciences Literature (LILACS) during May 2025. Studies published between 2020 and 2025, in Portuguese or English, were selected.

The descriptors used in the search were “rheumatoid arthritis” and “physical exercise,” combined to reflect the main themes addressed in the study.

Randomized clinical trials and meta-analyses published in Portuguese or English that addressed the relationship between physical exercise and RA were included. Duplicate articles, studies focused on other non-comparable populations (such as osteoarthritis or lupus), and studies not related to the objective of the present study were excluded (**Figure 1**).

Study selection was performed in two stages: reading of titles and abstracts to assess whether they met the established criteria. After this screening, the included articles were

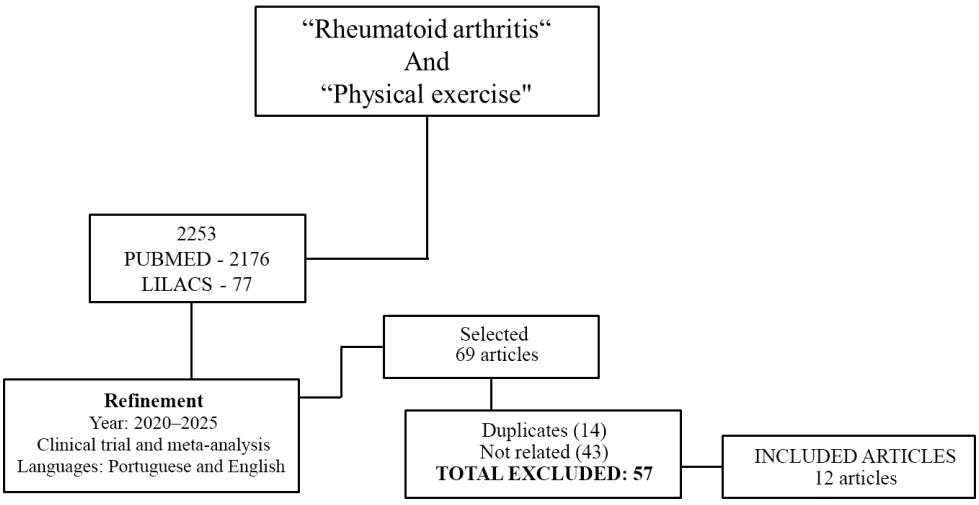

Figure 1. Flowchart of the articles.

qualitatively analyzed, with findings organized into four thematic axes: (1) pathophysiology and clinical manifestations of RA; (2) benefits of physical exercise; (3) physiological and immunological mechanisms involved; and (4) recommended modalities of physical activity.

RESULTS AND DISCUSSION

Fundamentals of Rheumatoid Arthritis

RA is a chronic systemic autoimmune inflammatory disease whose main clinical manifestation is persistent synovitis, leading to progressive joint destruction. The pathogenesis of the disease typically begins years before the onset of clinical manifestations, and its pathophysiology is complex, involving a multifactorial interaction among genetic predisposition, environmental factors, and immunological alterations that determine the development of an inflammatory and destructive autoimmune response in the synovium[2].

Environmental factors contribute to disease development; however, the mechanisms by which this occurs are not yet fully understood. It is known that the autoimmune process is often initiated at mucosal sites, such as the respiratory tract, oral mucosa, and intestinal mucosa, where elements such as smoking and alterations in the microbiota induce protein modifications, particularly the citrullination of arginine residues mediated by peptidyl arginine deiminase enzymes[1,2].

These modified proteins become neoantigens and are presented to the immune system by class II HLA molecules, especially those containing the shared epitope. This process leads to the activation of CD4+ helper T cells and the differentiation of B cells that produce autoantibodies, such as anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF)[13,14].

These autoantibodies can be detected in serum years before the clinical onset of the disease and are associated with a more aggressive phenotype; therefore, they are considered both diagnostic and prognostic markers. However, their presence alone is not sufficient to generate the typical joint inflammation of RA, and the transition to the symptomatic phase requires a second stimulus, such as the formation of immune complexes, activation of the complement system, or microvascular damage, which promotes clinically evident synovial inflammation[2,14,15].

In RA, progression of the inflammatory process is characterized by the infiltration of mononuclear cells into the synovium, including T lymphocytes, macrophages, and plasma cells,

as well as the activation of synovial fibroblasts (FLS), which acquire an invasive phenotype and secrete matrix metalloproteinases and pro-inflammatory cytokines. This cellular response induces significant structural changes in the synovium, such as hyperplasia of the intimal layer, immune cell infiltration, and the formation of ectopic germinal centers, where B-cell maturation and local autoantibody production occur. Continuous FLS activity and osteoclast activation, stimulated by inflammatory mediators such as TNF, IL-1, IL-6, and RANKL, result in extracellular matrix degradation, cartilage destruction, and irreversible bone erosions. The persistence of inflammation is maintained by a complex cytokine network and interactions between innate and adaptive immunity, consolidating RA as a systemic inflammatory syndrome. Clinically, it manifests predominantly as symmetric polyarthritis of small joints, with progressive evolution that compromises joint function, impacts quality of life, and may lead to significant disability if not adequately treated[1,13,14].

Among systemic manifestations, an increased risk of cardiovascular disease and harmful alterations in body composition are notable, favoring increased fat mass and reduced muscle mass, a condition known as "rheumatoid cachexia." All these factors contribute to disease worsening, impairing the ability to perform daily activities[8].

It is important to highlight the potential risk of publication bias, as studies with positive outcomes tend to be published more frequently. Thus, the available evidence may overestimate the beneficial effects of physical exercise in RA.

Benefits of Physical Exercise in RA

Regular physical exercise has been shown to be a therapeutic strategy in the management of RA, as it contributes significantly to the control of overall symptomatology through the development of functional and structural adaptations across different physiological systems[8,16-19].

One of the main benefits is the improvement in joint function and pain[18,20-24]. Activities combining aerobic and muscle-strengthening training have been shown to improve joint mobility, strength, and functionality without exacerbating disease progression. A prospective randomized clinical trial evaluated the effects of different types of physical exercise — resistance training, aerobic training, and a control group — in women with RA with low disease activity or in remission. The study included 66 participants, with a mean age of 42.5 ± 5.6 years, who underwent a 12-week protocol. The exercise groups showed significant improvements in pain, disease activity, quality-of-life parameters, and body composition compared with the control group ($p < 0.05$). Specifically, the resistance training group demonstrated greater gains in muscle thickness (rectus femoris and vastus intermedius), total and lower-limb lean body mass, as well as reductions in body fat and improvements in functional performance assessed by the timed up and go test. These results indicate that resistance exercise may be an effective strategy to improve physical function, body composition, and clinical outcomes in women with RA[18].

The multicenter randomized study conducted by de Jong *et al.* (2003)[25] evaluated the efficacy and safety of a supervised high-intensity exercise program lasting two years, compared with conventional physiotherapy, in 309 patients with RA. The results showed that the RAPIT group (Rheumatoid Arthritis Patients In Training) achieved significant improvement in functional capacity, primarily measured by the MACTAR questionnaire, as well as increased aerobic fitness, muscle strength, and reduced emotional distress over time.

It is important to note that there was no significant increase in radiographic progression of weight-bearing joints, although patients with pre-existing joint damage showed a tendency toward greater progression, suggesting the need for individualized exercise adaptation in such cases. Disease activity remained stable or

showed slight improvement in both groups, reinforcing the safety of the intervention[25].

This study provides evidence that regular practice of vigorous exercise, when properly supervised, is not only safe for individuals with RA but also promotes relevant clinical and psychosocial benefits, reinforcing the therapeutic role of movement in the comprehensive care of these patients. Complementing the findings of de Jong *et al.*[25], the review by Li and Wang (2022)[26] reinforces the role of physical exercise as a safe and beneficial intervention for patients with RA by synthesizing clinical evidence and underlying biological mechanisms. According to the authors, exercise not only improves physical function and quality of life but also modulates the inflammatory response and immune activity, promoting a balance between pro- and anti-inflammatory cytokines. The review highlights that both aerobic and resistance exercise, when performed regularly and in an individualized manner, contribute to the reduction of systemic inflammation characteristic of the disease. These mechanisms corroborate the clinical results observed in studies such as RAPIT, demonstrating that the positive effects of exercise extend beyond functional gains to include a modulatory role in the pathophysiology of RA. Thus, physical exercise has become established as a safe therapeutic tool with a solid physiological basis and important clinical effects, especially when adapted to the patient's needs and limitations[26].

The meta-analysis conducted by Rongen-van Dartel *et al.* (2015)[27] demonstrated that aerobic exercise programs are effective in reducing fatigue in individuals with RA, one of the most impactful symptoms of the disease. Beneficial effects were observed regardless of protocol duration or intervention specificity, indicating that even moderate levels of physical activity promote clinically relevant improvements. Fatigue reduction, in addition to enhancing functionality, contributes to improved quality of life and greater autonomy in daily activities for these patients[27].

De Luna *et al.* (2024)[28] reported that a single session of aerobic exercise was able to significantly reduce resting systolic blood pressure and blood pressure responses to stress in patients with RA. These findings suggest that physical exercise exerts an acute beneficial effect on cardiovascular function, which is particularly relevant given the increased risk of cardiovascular events in this population. The observed physiological response reinforces the cardioprotective potential of exercise even in the short term, supporting its early and regular inclusion in therapeutic strategies[28].

In the review conducted by Katz *et al.* (2020)[23], the authors compiled evidence indicating multiple benefits of physical activity in patients with RA, including improvements in disease activity, pain, fatigue, mental health, sleep quality, and functional capacity. Beyond physiological effects, the study highlighted the importance of appropriate professional guidance to overcome common barriers to exercise practice. Lack of information or fear of worsening joint symptoms still limits adherence, reinforcing the need for educational strategies and continuous support from the healthcare team[23].

Adherence of patients with RA to regular physical activity may be influenced by a combination of individual, clinical, and contextual factors. According to Katz *et al.* (2020)[23], many patients remain physically inactive due to barriers such as pain, chronic fatigue, functional limitations, and fear of exacerbating disease symptoms. In addition, lack of knowledge about the benefits of exercise for arthritis and insufficient guidance from healthcare professionals contribute to low adherence. These barriers reflect an important need for educational interventions and personalized motivational strategies that address both the physical and emotional aspects of these patients[23].

In the same direction, Law *et al.* (2013)[29] identified that patients' beliefs about the effects of exercise and their previous experiences strongly influence their motivation to maintain

a physical activity routine. The study showed that negative perceptions, such as the belief that exercise may cause joint damage, tend to reduce the likelihood of adherence. Moreover, social factors, including family support and encouragement from the healthcare team, are fundamental to promoting self-confidence and commitment to exercise programs. Behavioral strategies based on self-efficacy and continuous encouragement appear promising in strengthening long-term adherence[29].

Gyurcsik *et al.* (2015)[30] emphasized the importance of approaches based on motivational interviewing and personalized interventions, noting that self-efficacy to overcome barriers such as pain or fatigue is positively associated with physical activity practice[30]. In turn, Do *et al.* (2011)[31], when analyzing data from Healthy People 2010, observed that only about 52% of adults with arthritis reported having received clinical counseling for physical activity, a figure below the established target of 67%. The study highlights that although medical counseling is a key factor in stimulating behavior change, there remains a significant gap in the implementation of these guidelines in routine clinical care[31,33].

In light of these findings, it becomes evident that adherence to physical activity among individuals with RA depends not only on the availability of exercise programs, but on an integrated support ecosystem involving trained professionals, health education, motivational strategies, and accessible environments. Reflecting on these multiple dimensions allows not only a better understanding of the challenges faced by patients, but also the direction of health policies and clinical practices toward more humanized and effective approaches that value patient empowerment in the self-care process.

Physiological mechanisms involved in the improvement of rheumatoid arthritis

The clinical improvements observed in patients with RA undergoing physical exercise programs are supported by several physiological mechanisms that modulate inflammation, energy metabolism, cardiovascular health, and muscle integrity. These effects involve complex interactions among the immune system, skeletal muscle, and the cardiovascular system and have been confirmed by experimental studies and clinical reviews.

One of the main mechanisms involves the modulation of inflammatory pathways. Regular physical exercise, especially aerobic exercise and resistance training, has been associated with a reduction in pro-inflammatory cytokines, such as tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β), while simultaneously stimulating an increase in anti-inflammatory cytokines, such as interleukin-10 (IL-10)[26,32-34]. This immunological modulation directly contributes to reduced disease activity. According to Docherty *et al.* (2022)[32], exercise induces the release of cytokines, such as IL-6 — which plays an anti-inflammatory role in this context — promoting systemic beneficial effects on joint inflammation. In addition, Lu *et al.* (2024)[35] highlight that myokine secretion by skeletal muscle during exercise may play an immunomodulatory role, promoting balance between innate and adaptive immunity[35].

Another central mechanism is the potential improvement in oxidative metabolism, which is often impaired in patients with RA due to systemic inflammation and physical inactivity. The review by Li and Wang (2022)[26] indicates that exercise appears to increase the expression of genes related to fatty acid oxidation, such as those encoding the enzyme carnitine acetyltransferase (CrAT), in addition to improving mitochondrial efficiency in skeletal muscles[28]. These changes favor energy utilization and contribute to fatigue reduction, a central symptom of the disease. This metabolic improvement is also associated with greater functional capacity and better physical performance, as observed in clinical trials demonstrating increas-

es in muscle strength and mass with resistance exercise[23,25].

Cardiovascular health also benefits from physical exercise. Patients with RA have an increased cardiovascular risk due to the chronic inflammatory state. The study by de Luna *et al.* (2024)[28] demonstrated that a single session of aerobic exercise was sufficient to reduce resting systolic blood pressure and blood pressure responses to stress. This physiological response indicates a protective role of exercise on the cardiovascular system[28]. Furthermore, other studies indicate that regular physical activity improves endothelial function and reduces classic cardiovascular risk factors, such as arterial hypertension and autonomic dysfunction[26,36,37].

Impact of physical exercise on validated clinical markers in rheumatoid arthritis

Several studies have shown that physical exercise can promote improvements in validated clinical markers used to monitor RA, such as the Disease Activity Score in 28 joints (DAS28), the Health Assessment Questionnaire (HAQ), pain indices, the number of tender and swollen joints, as well as inflammatory laboratory parameters.

The meta-analysis by Ye *et al.* (2022)[38], which included 13 randomized clinical trials involving patients with RA, demonstrated that aerobic exercise led to significant reductions in disease activity, as measured by DAS28, as well as improvements in functional capacity assessed by the HAQ. The authors also highlighted statistically significant decreases in the number of tender and swollen joints, as well as in scores on the visual analog scale (VAS) for pain and fatigue. In addition, a reduction in C-reactive protein (CRP) levels was reported, indicating anti-inflammatory effects of exercise[38].

Corroborating these findings, Karateev *et al.* (2018)[39] observed that patients with RA who underwent a combined intervention consisting of optimized pharmacological treatment and a structured physical activity program showed a clinically significant reduction in DAS28, associated with improved pain perception and an increase in daily step count. Moreover, the study reinforces that regular physical activity is associated with improvements in the HAQ Disability Index (HAQ-DI), suggesting relevant functional gains and greater ability to perform activities of daily living[39].

The study by Sandberg *et al.* (2014)[40] further adds that a high-intensity exercise program lasting 20 weeks promoted significant improvements in HAQ and DAS28 scores, with reductions in the number of tender joints and increases in muscle strength compared with the control group[40]. Similarly, Cerasola *et al.* (2023)[41] demonstrated that home-based interventions involving physical exercise and occupational therapy resulted in improved quality of life and reduced clinical symptoms, as assessed by validated functional scales and questionnaires[41].

These data reinforce the evidence that physical exercise, when appropriately guided and adapted to the profile of patients with RA, has a positive impact on clinical indicators widely used in rheumatology practice. The systematic inclusion of this strategy as an adjunct to pharmacological treatment may contribute to disease activity control, reduction of functional disability, and improvement in quality of life, consolidating an integrative and patient-centered approach.

Recommended exercise modalities

The appropriate selection of physical exercise modalities for patients with RA is essential to ensure clinical, functional, and psychological benefits, while respecting disease-related limitations and promoting patient engagement. Scientific literature provides evidence that both aerobic and resistance exercises, as well as mind–body practices such as Pilates, are safe and effective, provided they are individualized and properly supervised[38,42,43].

Aerobic exercises, such as walking, stationary cycling, and aquatic exercise, have been

widely recommended for promoting improvements in cardiorespiratory capacity and reductions in pain and fatigue, with a positive impact on disease activity indices[44]. Guidelines from the American College of Rheumatology (ACR) strongly recommend the inclusion of moderate-intensity aerobic exercise for adults with RA, three to five times per week, with sessions lasting between 30 and 60 minutes[21]. This type of activity not only contributes to the control of systemic inflammation but also reduces cardiovascular risk, which is frequently elevated in these patients.

Strength or resistance training has also been widely recommended, as it helps prevent the loss of muscle mass associated with chronic inflammation, known as rheumatoid cachexia, in addition to promoting improvements in joint function and quality of life. According to Iversen *et al.* (2012), resistance training programs using light to moderate loads, performed two to three times per week, have demonstrated safety and provide significant gains in muscle strength and functional performance[43].

In addition, Pilates, as a low-impact modality, has demonstrated efficacy comparable to that of traditional aerobic exercises. In a randomized clinical trial, Yentür *et al.* (2021)[42] showed that both Pilates alone and its combination with aerobic activity promoted reductions in pain and morning stiffness, as well as improvements in functional capacity and quality of life, as assessed by the HAQ and VAS instruments[42].

It is important to highlight that interventions based on mobile technologies and digital platforms have also proven to be effective. Guided online programs, as evidenced by Bossen *et al.* (2014)[45], can increase engagement in physical exercise and promote disease self-management[45]. Complementarily, Knitza *et al.* (2020) observed that patients with RA demonstrate high interest in using digital tools for health monitoring and physical exercise, although barriers persist, such as low digital literacy and distrust of digital platforms[46].

Finally, it is essential to emphasize that the success of any intervention depends on the integration of educational and motivational strategies and appropriate support contexts. Recommendations from the European Alliance of Associations for Rheumatology (EULAR) for self-management strategies reinforce that patient-centered interventions involving counseling, continuous support, and personalization promote greater adherence to exercise programs and increased patient empowerment. In this context, Lifestyle Medicine emerges as a consistent and comprehensive approach by incorporating physical exercise as a therapeutic pillar, combined with engagement strategies and interpersonal support. By treating the pa-

Table 1. Practical recommendations for physical exercise in patients with Rheumatoid Arthritis. Adapted from references[45,46].

Modality	Primary focus	Recommended frequency	Practical considerations
Aerobic	Cardiovascular health, fatigue, and pain	3 to 5 times per week	Walking, stationary cycling, or aquatic exercise are well tolerated.
Resistance	Muscle strength and physical function	2 to 3 times per week	Focus on large muscle groups; start with light loads and progress gradually.
Mind–body	Flexibility, well-being, and chronic pain	2 to 3 times per week	Pilates, tai chi, and yoga have demonstrated physical and psychological benefits.

tient in an integrated manner, respecting individual experiences and promoting autonomy, this approach can transform adherence to exercise into a viable pathway toward a more active, functional life with improved quality of life.

In light of this review, it is suggested that physical exercise, as a pillar of Lifestyle Medicine, should be systematically integrated into the care of rheumatoid arthritis, due to its benefits on pain perception, physical function, fatigue, and cardiovascular risk. Among the exercise modalities studied, the most consistent results are associated with aerobic training and resistance training.

Aerobic exercise shows potential to reduce fatigue and disease activity and to improve functional capacity, with indications of a possible anti-inflammatory effect. Resistance training contributes to increases in muscle strength and lean mass, in addition to improving functional performance, without evidence of accelerated structural damage when appropriately supervised. Mind–body practices, such as Pilates, act as adjunct strategies, promoting flexibility, chronic pain management, and overall well-being.

Considering the methodological heterogeneity of the analyzed studies, it is recommended that exercise prescription be individualized, progressive, and continuously monitored, adopting a person-centered approach that is sensitive to the clinical, functional, and psychosocial particularities of each patient.

AUTHOR CONTRIBUTIONS

TPF, VBAT, MPBM and MCGP contributed to the conception and design of the study, data analysis, and manuscript writing. DJM performed the final revision of the text. All authors read and approved the final version of the manuscript and agree to take responsibility for its content.

CONFLICT OF INTEREST

We wish to confirm that there are no known conflicts of interest associated with this publication and that no significant financial support has influenced its results.

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DECLARATION REGARDING THE USE OF GENERATIVE AI

The authors declare that they used the generative artificial intelligence tool ChatGPT to assist with language revision. The editorial board made the decision to utilize ChatGPT, an AI language model developed by OpenAI, for the translation of this manuscript from the original language, Portuguese, to English.

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