ISSN: 2832-7942
DOI: 10.33552/APHE.2026.03.000561
Annals of Public Health & Epidemiology
Iris Publishers

Research Article

Effects of Physical Rehabilitation on Inflammatory Markers in Patients with Chronic Diseases: A Literature Review

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Received Date: April 15, 2026

Published Date: April 28, 2026

Abstract

Chronic low-grade inflammation is one of the main pathophysiological mechanisms associated with chronic non-communicable diseases (NCDs), contributing to clinical progression and reduced functionality. Physical rehabilitation, especially when supervised by physical therapists, has stood out as an intervention capable of modulating immunological, metabolic, and hemodynamic pathways involved in systemic inflammation. This integrative review analyzed studies published between 2010 and 2025 that investigated the effects of aerobic exercise, resistance training, chest physiotherapy, and combined programs on inflammatory markers such as CRP, IL-6, TNF-α, IL-10, and oxidative stress markers in individuals with cardiovascular, respiratory, metabolic, and osteoarticular diseases. The findings demonstrate consistent reductions in pro-inflammatory mediators and increase in anti-inflammatory biomarkers, as well as significant functional improvements. The strategic role of the physiotherapist in the individualization of protocols and in the enhancement of therapeutic effects is highlighted. It is concluded that physical rehabilitation is an essential intervention in the management of chronic inflammation, with strong translational potential for the areas of Biomedicine, Physical Therapy and Public Health.

Keywords: Physical rehabilitation; Chronic inflammation; Biomarkers; inflammatory; Chronic non-communicable diseases; Therapeutic physical exercise; Physical therapy; Cytokines; Immunometabolic modulation

Introduction

Chronic low-grade inflammation represents a persistent state of immune activation characterized by a continuous but moderate increase in circulating inflammatory mediators such as interleukin-6 (IL-6), C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α), and interleukin-1β (IL-1β). This subclinical inflammatory state arises as the body's response to persistent stimuli, such as metabolic dysfunction, oxidative stress, altered microbiota, cellular aging, and excess visceral adiposity [1]. Unlike acute inflammatory processes, which are self-limiting and physiologically protective, chronic low-grade inflammation operates as a pathological backdrop capable of affecting tissues, metabolic pathways, and fundamental regulatory systems [2].

This prolonged systemic inflammatory condition is recognized as a determining factor in the pathophysiology of chronic

noncommunicable diseases (NCDs), including diabetes mellitus, cardiovascular diseases, obesity, rheumatoid arthritis, chronic obstructive pulmonary disease (COPD), and various metabolic disorders. Persistent activation of pro-inflammatory pathways promotes endothelial dysfunction, insulin resistance, increased protein turnover, and tissue degradation, accelerating the course of established diseases and reducing the body's ability to maintain homeostasis (Libby, 2021). Thus, low-grade inflammation is not only a consequence of these conditions, but a central mechanism of aggravation.

The relationship between systematic inflammation and NCDs is also deeply linked to the process of immunosenescence, which involves functional decline of the immune system associated with aging. Studies show that elderly individuals have naturally elevated levels of IL-6, TNF-α, and CRP, a phenomenon called inflammaging, which increases the risk of cardiovascular and metabolic diseases, in addition to favouring structural changes in muscle, joint, and lung tissues [3]. This scenario underscores the importance of interventions capable of modulating inflammation throughout the life cycle. In addition, adipose tissue plays a crucial role in sustaining low-grade inflammation. Hypertrophied adipocytes infiltrated by M1 macrophages have high production of TNF-α, IL-6, and MCP-1, contributing to systemic inflammation, insulin resistance, and endocrine disruption [4]. This process explains why individuals with obesity or metabolic syndrome exhibit elevated inflammatory markers and a higher risk of developing heart disease, fatty liver, osteoarticular disorders, and worsening COPD. Thus, dysfunctional adipose tissue is recognized as the largest inflammatory organ in the human body in compromised metabolic conditions.

Finally, chronic low-grade inflammation is considered a common biological link between multiple NCDs, which explains the frequent coexistence of comorbidities in the same individual. Integrative health models indicate that this sustained inflammatory state contributes to progressive deterioration of muscle function, decreased cardiorespiratory capacity, and impaired neuroendocrine function, consolidating a vicious circle between disease, sedentary lifestyle, pain, and inflammation [5]. Therefore, understanding this phenomenon is essential for the development of rehabilitation strategies and non-pharmacological interventions capable of modulating inflammatory biomarkers and mitigating the advance of chronic diseases.

Physiological mechanisms of inflammation: cytokines, metabolic pathways, and systemic impact

Chronic inflammation is anchored in a complex network of cytokines, chemokines, and humoral mediators that coordinate persistent immune responses. Among the main pro-inflammatory mediators are TNF-α, IL-1β and IL-6, produced predominantly by activated macrophages, dendritic cells and dysfunctional adipose tissue. These molecules trigger intracellular signaling cascades such as the activation of NF-κB and JAK/STAT pathways that amplify the inflammatory response and induce expression of acute phase proteins, such as CRP and fibrinogen [6]. This set of responses transforms inflammation from a local event into a systemic process with broad metabolic and organic repercussions.

The activation of the NF-κB pathway represents one of the most relevant events in the perpetuation of chronic inflammation. In pathophysiological conditions, such as obesity, insulin resistance, or tissue hypoxia, this pathway is stimulated continuously, leading to the transcription of pro-inflammatory genes and the maintenance of the baseline inflammatory state [7]. At the same time, the NLRP3 inflammasome, activated by intracellular danger signals such as reactive oxygen species, cholesterol crystals, and oxidized lipids, promotes the maturation of IL-1β and IL-18, amplifying tissue damage and favoring the development of CNCD [8]. Thus, the combination of NF-κB and inflammasomes creates a self-sustaining circuit of inflammation.

Another crucial mechanism involves the interface between inflammation and energy metabolism. Low-grade inflammation alters metabolic homeostasis through serine phosphorylation of proteins involved in insulin signaling, such as IRS-1, leading to insulin resistance and glycemic changes typical of metabolic diseases [2]. In addition, cytokines such as TNF-α and IL-6 interfere with mitochondrial function, directly affecting fatty acid oxidation and increasing the production of reactive oxygen species (ROS), which fuel a continuous cycle of inflammatory damage [9]. This metabolic imbalance creates an environment conducive to the progression of chronic diseases. At the systemic level, chronic inflammation compromises multiple physiological systems, including cardiovascular, musculoskeletal, respiratory, and neuroendocrine. In the cardiovascular system, inflammatory cytokines play a direct role in endothelial dysfunction, atherosclerotic plaque instability, and reduced nitric oxide bioavailability, increasing the risk of ischemic events [10]. In muscle tissue, persistent inflammation induces protein catabolism and reduces muscle synthesis, contributing to inflammatory sarcopenia often seen in patients with NCDs and the elderly [11]. This multisystem impact reinforces the role of inflammation as a common point between functional decline and worse clinical prognosis.

Finally, chronic inflammation also profoundly affects the neuroimmune axis. Inflammatory cytokines can cross the blood-brain barrier and modify the function of neurotransmitters related to mood, sleep, and motivation, contributing to symptoms such as chronic fatigue, depression, and reduced exercise tolerance, often reported by patients with chronic diseases [12]. Alterations in serotonin metabolism and microglial activation reinforce the neuroendocrine impact of systemic inflammation. Thus, chronic inflammation is a complex phenomenon that integrates biological systems and plays a central role in the pathophysiology and clinical management of NCDs.

Physical rehabilitation as an immune modulator and anti-inflammatory

Physical rehabilitation has been widely recognized as an intervention capable of acting directly on the modulation of the immune system, promoting adaptations that favor a systemic anti-

inflammatory profile. During therapeutic exercise, skeletal muscle tissue acts as an endocrine organ capable of producing myokines such as anti-inflammatory IL-6, IL-7 and IL-15 that attenuate the activation of pro-inflammatory pathways and contribute to the regulation of energy metabolism [5]. Unlike the pro-inflammatory behavior of IL-6 in chronic states, its acute release during exercise stimulates the production of IL-10 and the IL-1 antagonist receptor (IL-1ra), reducing TNF-α and modulating pathways related to oxidative stress [13]. Thus, exercise plays a dual role: it suppresses systemic inflammation and improves adaptive immune responses.

In addition to myokines, neuroendocrine mechanisms also participate in the inflammatory regulation caused by physical rehabilitation. Activation of the hypothalamic-pituitary-adrenal (HPA) axis during exercise increases the release of cortisol and catecholamines, hormones with recognized anti-inflammatory action, capable of inhibiting the production of cytokines such as TNF-α and IL-1β and reducing the migration of neutrophils and macrophages to peripheral tissues (Nieman; Wentz, 2019). In parallel, regular exercise induces improvement in cortisol sensitivity, preventing compensatory overproduction and reducing inflammation associated with chronic stress. This neuroimmunoendocrine effect contributes to breaking the cycle between stress, inflammation, and clinical worsening in patients with NCDs. Another decisive mechanism of physical rehabilitation involves the modulation of oxidative stress, an intrinsic component of chronic inflammation. Regular exercise increases the activity of endogenous antioxidant enzymes, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase, reducing the accumulation of reactive oxygen species (ROS) that activate inflammatory pathways such as NF-κB [14]. Sustained reduction in oxidative stress decreases inflammasome activation, limits cell damage, and improves mitochondrial functioning, creating a metabolic environment conducive to the reduction of pro-inflammatory cytokines. In this way, exercise becomes an essential therapeutic strategy in the restoration of cellular physiology.

Physical rehabilitation also has a relevant impact on the remodeling of adipose tissue, another critical point in the inflammation-metabolism axis. Regular physical activity reduces visceral fat mass and alters the phenotype of macrophages infiltrated in adipose tissue, promoting the transition from a pro-inflammatory profile M1 to an anti-inflammatory profile M2 [15]. This change decreases the production of TNF-α, IL-6, and MCP-1, while also decreasing the production of TNF-. increases the secretion of diponectin, an adipocytokine with anti-inflammatory and insulin-sensitizing properties [4]. As a result, exercise disrupts one of the pillars of chronic inflammation, acting directly on the body's largest reservoir of inflammatory cytokines. Finally, systemic adaptations promoted by exercise improve endothelial function, capillary expansion, increased cardiac output, increased muscle oxidative capacity, and autonomic regulation contribute to the overall reduction of the inflammatory state and physiological overload associated with chronic diseases [16]. These integrated effects explain why physical rehabilitation programs are considered core therapies in conditions such as cardiovascular disease, diabetes, COPD, and osteoarthritis. By modulating immunological, neuroendocrine, and metabolic pathways, therapeutic exercise is consolidated as an intervention of high clinical relevance in reducing low-grade systemic inflammation.

Impact of physical rehabilitation on inflammatory modulation in different chronic diseases

Physical rehabilitation applied to cardiovascular diseases has shown consistent results in the reduction of systemic inflammatory markers, especially C-reactive protein (CRP), IL-6 and TNF-α. Clinical studies show that structured aerobic exercise programs, even at moderate intensities, promote significant improvements in endothelial function and atherosclerotic plaque stability, mediated by the reduction of vascular inflammation [17]. This modulation occurs through mechanisms such as increasing nitric oxide, reducing oxidative stress, and changing the profile of macrophages infiltrated in the endothelium [18]. These findings justify the inclusion of physical rehabilitation as an essential part of the treatment of patients with coronary artery disease and heart failure. In the respiratory area, especially in individuals with chronic obstructive pulmonary disease (COPD), physical rehabilitation has a relevant impact on the reduction of systemic and local inflammation. Patients undergoing regular aerobic training and muscle strengthening programs show significant reductions in TNF-α, IL-8, and oxidative stress markers, as well as improved mitochondrial biogenesis and exercise tolerance [19]. The improvement of peripheral muscle function reduces the production of inflammatory metabolites derived from fatigued fibers, contributing to breaking the cycle between inflammation, dyspnea, and physical deconditioning [20]. Thus, respiratory rehabilitation not only improves ventilatory mechanisms, but also acts directly on immunometabolic processes.

In metabolic disorders such as type 2 diabetes mellitus and metabolic syndrome, physical rehabilitation promotes intense changes in the inflammation-metabolism axis, acting as a central intervention in reducing inflammation of low grade. Research shows that combined exercise (aerobic + resistance) significantly reduces baseline IL-6, ultrasensitive CRP, and TNF-α, while elevating IL-10, adiponectin, and improving insulin sensitivity [21]. In addition, exercise reduces the size of visceral adipocytes and decreases the infiltration of M1 macrophages into adipose tissue, promoting a more favorable anti-inflammatory microenvironment [15]. These effects explain the strong correlation between physical activity and improved clinical outcomes in metabolic diseases. In osteoarticular diseases, such as osteoarthritis and rheumatoid arthritis, physical rehabilitation reduces both systemic inflammation and intra-articular local inflammation. Supervised exercises, especially strengthening and low-impact exercises, reduce levels of IL-1β, TNF-α, and metalloproteinases in synovial fluid, in addition to decreasing cartilage degradation through modulation of the NF-κB pathway [22]. Meta-analysis studies also show significant improvement in pain, stiffness, and physical function, associated with reduced pro-inflammatory cytokines and increased anti-inflammatory mediators [23]. These findings reinforce the essential role of rehabilitation as a non-pharmacological intervention for the management of osteoarticular diseases.

Finally, the effects of physical rehabilitation on inflammation also extend to systemic chronic diseases of a multifactorial nature, such as chronic kidney failure, autoimmune diseases, and aging-related conditions. In renal patients, for example, intradialytic exercises reduce IL-6 and CRP, in addition to improving muscle strength and functional capacity [24]. In the elderly, regular exercise reduces inflammaging, lowering levels of IL-6 and TNF-α and improving immune function [25]. These cross-sectional effects show that physical rehabilitation acts broadly on inflammatory modulation, presenting benefits that go beyond the musculoskeletal system and reach multiple biological axes.

Clinical importance and gaps in the literature on physical rehabilitation and inflammatory markers

The clinical relevance of physical rehabilitation in the modulation of inflammatory markers is widely recognized, especially in the context of chronic non-communicable diseases, which represent one of the highest global morbidity and mortality burdens. The ability of therapeutic exercise to reduce pro-inflammatory cytokines, improve insulin sensitivity, optimize endothelial function, and promote immunometabolic balance makes this intervention a strategic tool for the management of conditions such as diabetes, heart failure, COPD, and osteoarthritis [5]. Although the role of exercise in functional improvement is already consolidated, recent advances show that its molecular impact is equally determinant for the control of the progression of NCDs, reinforcing their relevance for individualized clinical protocols [13]. Despite progress in understanding exercise-induced anti-inflammatory mechanisms, important gaps related to the heterogeneity of individual responses still persist. Genetic variations, differences in baseline inflammation level, body composition, age, sex, gut microbiota, and the presence of multiple comorbidities influence the magnitude of the inflammatory response to exercise [26]. This diversity highlights the need to develop personalized approaches, considering that some patients exhibit robust anti-inflammatory responses, while others exhibit more discreet or even inconsistent responses, despite similar protocols. Thus, understanding predisposing factors can optimize interventions and improve therapeutic efficacy.

Another relevant gap refers to the standardization of physical rehabilitation protocols used in clinical studies. There is great variability in the intensity, duration, frequency, and type of exercise among the studies, which makes it difficult to compare the results and limits the construction of robust evidence-based guidelines [27]. In addition, many studies use small sample sizes, short intervention periods, and assessments limited to a few inflammatory markers, reducing the ability to extrapolate conclusions to larger populations. The absence of methodological standardization remains one of the main challenges in the consolidation of universal clinical recommendations. There is also a lack of studies addressing the long-term effects of physical rehabilitation on inflammatory modulation, especially in patients with multiple comorbidities, frail older adults, and populations of high clinical complexity. Most research focuses on 8- to 12-week interventions, leaving gaps on the sustainability of anti-inflammatory effects, the persistence of immunometabolic adaptations, and the cumulative impact of exercise over years [25]. Understanding long-term effects is essential to determine whether physical rehabilitation can act as a disease-modifying strategy and not just as an adjunctive intervention.

Finally, despite the growing number of studies, there are still few studies that integrate multiple biological dimensions such as inflammation, mitochondrial function, adipose tissue composition, gut microbiota, and neuroendocrine axes into a single analysis model. The literature tends to study inflammatory markers in isolation, which limits the systemic understanding of the effects of exercise and prevents the construction of integrated pathophysiological models [1]. Thus, the main gap in the area lies in the need for multidimensional, multicentric and longitudinally robust, capable of capturing the complexity of the interactions between exercise, metabolism, and inflammation. Studies of this type would allow the consolidation of exercise as a first-line therapeutic intervention in the management of chronic inflammation.

Role of physical rehabilitation and the role of physical therapists in inflammatory modulation

The role of the physical therapist plays a central role in the prescription, monitoring and therapeutic modulation of physical interventions aimed at reducing systemic inflammation in patients with chronic diseases. While physical exercise can be conducted by different professionals, the physical therapist has specific training in biomechanics, clinical exercise physiology, kinesiology, pathophysiology and rehabilitation, allowing the construction of individualized protocols based on the functional and inflammatory status of each patient [28]. This differential allows the physiotherapist to adapt loads, intensities, volumes, and stimuli safely, preventing joint overloads, adverse events, and exacerbated inflammatory responses. Thus, its action becomes decisive for patients with NCDs, who are often frail, polymedicated, or have significant functional limitations.

Physical rehabilitation guided by the physiotherapist integrates various modalities, such as aerobic exercise, resistance training, therapeutic stretching, functional training, manual techniques and cardiorespiratory approaches, all with evidence of modulation of inflammatory markers. The physiotherapist structures these interventions based on careful assessments, such as submaximal cardiorespiratory tests, dynamometry, functional scales, and muscle performance measures, allowing dynamic adjustments according to clinical evolution [29]. This ability to measure therapeutic response ensures progressive interventions, avoiding insufficient or excessive stimuli, both associated with worse immune responses. In this way, physiotherapy acts not only in functional rehabilitation, but as a biological strategy to control inflammation. Resistance training, when prescribed by physiotherapists, has significant impacts on muscle metabolism and on the release of anti-inflammatory myokines. Studies show that supervised strengthening increases IL-10 production and

reduces circulating TNF-α, in addition to improving muscle structural parameters and reducing inflammatory sarcopenia, which is frequent in the elderly and patients with chronic diseases [30]. Physiotherapeutic supervision ensures correct execution, appropriate load selection, speed control and injury prevention, fundamental aspects to achieve anti-inflammatory responses without generating mechanical stress excessive. Thus, resistance training under physical therapy conduction produces combined functional, metabolic and immunological benefits.

Aerobic exercise also stands out in physical therapy practice for its strong association with the reduction of low-grade systemic inflammation. Supervised aerobic programs reduce CRP, IL-6, and oxidative stress markers, in addition to increasing cardiorespiratory capacities that are fundamental for the management of cardiovascular, metabolic, and respiratory diseases [31]. The physiotherapist adapts intensity and monitors heart rate, peripheral oxygen saturation, ventilation, subjective perception of exertion, and clinical response, ensuring safety especially for at-risk populations, such as cardiac patients, diabetics, and patients with pulmonary limitations. Aerobic intervention, therefore, becomes more effective and safer when integrated with clinical physical therapy reasoning.

In addition to exercise modalities, manual techniques and respiratory therapies applied by the physiotherapist also have indirect effects on inflammation, by improving joint mobility, reducing pain, optimizing ventilation, reducing bronchospasm and favoring global functionality. Studies reveal that chest physiotherapy reduces pro-inflammatory cytokines in COPD patients, while manual interventions reduce inflammatory mediators in chronic musculoskeletal conditions [32]. The integration of these practices with structured exercise keeps the physiotherapist in a strategic position to address chronic inflammation from multiple therapeutic axes. Thus, physical rehabilitation becomes a field in which physical therapy acts as a protagonist in the immunometabolic modulation of chronic diseases.

Relevance and possible impacts of the review for the areas of Biomedicine, Public Health and Physiotherapy

The integration between Biomedicine, Public Health, and Physical Therapy is fundamental to understand the complexity of chronic inflammation and its interfaces with the biological, functional, and social determinants of health. In the field of Biomedicine, this review offers essential elements to deepen the understanding of molecular and immunometabolic pathways modulated by exercise, including the action of myokines, adipokines, inflammatory cytokines, and oxidative stress markers, allowing biomedical professionals to act both in diagnosis and in clinical monitoring based on biomarkers [2]. The systematization of these mechanisms expands the translational potential of laboratory research for clinical practices, strengthening the role of Biomedicine in the management of complex inflammatory and metabolic diseases. From a Public Health perspective, the results of this review highlight exercise and physical rehabilitation as low-cost strategic tools, high effectiveness and population impact, which are fundamental for coping with chronic non-communicable diseases (NCDs), which remain the main causes of global morbidity and mortality. Interventions based on supervised physical activity reduce systemic inflammatory burden, improve functional capacity, reduce hospitalizations, and increase the autonomy of individuals, which is in line with international guidelines for health promotion and disease prevention [33]. Thus, this review reinforces the need for public policies that include physical rehabilitation as a structuring component of primary care and health surveillance.

In Physical Therapy, the findings reinforce the centrality of the physical therapist in inflammatory modulation through individualized, evidence-based interventions based on clinical reasoning. The synthesis presented in this review legitimizes professional performance in protocols that combine aerobic exercise, resistance training, manual therapies, and cardiorespiratory interventions, demonstrating that such practices directly influence immunological, metabolic, and functional pathways [16]. In addition, the review offers subsidies for the qualification of clinical practice, curricular improvement and expansion of applied research, strengthening the role of Physical Therapy in coping with NCDs. Thus, the impact of this review is manifested in a transversal way, contributing to multiprofessional integration and scientific advancement in the three areas.

Methodology

This study is characterized as an integrative review of the literature, a method widely used to synthesize scientific evidence in a systematic and comprehensive way, allowing the integration of results from experimental, clinical and observational studies relevant to the investigated topic. The integrative review makes it possible to identify gaps, compare methodologies and build conclusions based on multiple research designs, giving theoretical robustness to the analysis [34]. This method was chosen due to the complexity of the phenomenon studied: the inflammatory modulation induced by physical rehabilitation, which involves molecular, physiological and functional interactions, requiring a methodological approach capable of integrating different levels of evidence.

Search strategy and databases

The literature search was carried out between August and November 2025 in the following electronic databases: PubMed/MEDLINE, SciELO, Web of Science, Scopus, and PEDro (Physiotherapy Evidence Database). The selection of these databases occurred due to their relevance for research in Biomedicine, Physiotherapy and Health Sciences, in addition to the wide coverage of clinical and experimental studies on inflammation, chronic diseases and physical rehabilitation. Controlled and uncontrolled descriptors (DeCS/MeSH) were used, combined by Boolean operators (AND/OR), such as: “physical rehabilitation”, “exercise therapy”, “inflammation”, “inflammatory biomarkers”, “chronic diseases”, “physiotherapy”, “cytokines”, “IL-6”, “CRP”, “TNF-alpha”, “aerobic

training" and "resistance training". This strategy ensured sensitivity and specificity in the retrieval of the most relevant studies [35].

Inclusion and exclusion criteria

We included studies that: (a) investigated the effects of physical rehabilitation including aerobic exercise, resistance training, functional training, respiratory physiotherapy, and combined programs on inflammatory markers in patients with chronic diseases; (b) presented clinical and experimental designs or systematic reviews with robust evidence; (c) were published between 2010 and 2025; (d) were available in English, Portuguese or Spanish; and (e) used recognized biomarkers, such as CRP, IL-6, IL-10, TNF-α, IL-1β, adiponectin, or oxidative stress markers. Articles were excluded that: (a) did not assess inflammatory outcomes; (b) included only athlete populations; (c) used unsupervised interventions without methodological description; or (d) had methodological insufficiency, such as lack of a control group, absence of randomization, or incomplete description of exercise protocols [36].

Study selection process

The selection took place in three stages: (1) reading of titles and abstracts by two independent evaluators; (2) full reading of potentially eligible articles; and (3) systematic data extraction. Divergences between evaluators were resolved by consensus or by consultation with a third evaluator experienced in review methodologies. Data extraction included sample characteristics, type of chronic disease, physical rehabilitation modality, intensity and duration of interventions, inflammatory markers evaluated, and main outcomes. The process followed recommendations from the PRISMA methodology adapted for integrative reviews, ensuring rigor and transparency [37].

Data synthesis and analysis

After selection and extraction, the studies were organized according to the previously defined thematic axes: (a) cardiovascular diseases; (b) respiratory diseases; (c) metabolic disorders; (d) osteoarticular diseases; and (e) special populations. An integrative qualitative analysis was performed, highlighting convergences and divergences between studies, mechanisms involved, and magnitude of therapeutic effects. The synthesis of the findings considered critical methodological variables, such as exercise intensity and duration, population characteristics, and biomarkers evaluated. This method allowed interpreting the effects of physical rehabilitation from perspective multidimensional, articulating physiological, immunological and clinical aspects [38].

Results and Discussion

Physical rehabilitation in cardiovascular diseases

The analysis of the selected studies demonstrates that supervised aerobic interventions generate consistent reductions in inflammatory markers in patients with cardiovascular diseases, particularly C-reactive protein (CRP), IL-6, and TNF-α. Clinical trials have shown reductions ranging between 15% and 40% in CRP after 8- to 12-week programs of moderate aerobic training, regardless of age or type of heart disease (Lavie et al., 2019). In addition, cohort studies have shown a significant increase in IL-10 and improved endothelial function, indicating that physical rehabilitation plays a direct and indirect anti-inflammatory role by modulating metabolic and hemodynamic pathways. Such evidence reinforces the efficacy of cardiac rehabilitation as a robust anti-inflammatory intervention in patients with heart disease. Additional evidence reveals that resistance training also promotes significant inflammatory reduction in cardiac patients, especially when combined with aerobic exercise. Meta-analyses report that hybrid protocols are more efficient than any modality alone in reducing IL-6 and TNF-α, suggesting that the combination of metabolic and mechanical stimuli enhances immune modulation [18]. The decrease in inflammatory markers was accompanied by an improvement in heart rate variability and an increase in the bioavailability of nitric oxide, reinforcing systemic effects of rehabilitation. Thus, combined programs emerge as a superior therapeutic strategy in cardiovascular inflammation [17,18].

Physical rehabilitation in respiratory diseases (COPD, asthma and restrictive)

The included studies showed relevant reductions in inflammatory markers in patients with COPD after respiratory rehabilitation programs and supervised aerobic exercise. Clinical trials have shown a significant decrease in TNF-α, IL-8, and oxidative stress markers, associated with improved exercise tolerance and peripheral muscle strength [19]. In addition, there was evidence of reduced neutrophil count and positive changes in fatigue-related muscle biomarkers, signaling simultaneous benefits in systemic and local inflammatory pathways. These results strengthen the role of respiratory rehabilitation as a multisystem anti-inflammatory intervention.

Studies involving chest physiotherapy have also reported an impact on inflammatory markers, particularly in patients with frequent exacerbations. Protocols with lung expansion techniques and bronchial hygiene demonstrated a reduction in IL-6 and IL-1β in sputum, in addition to improving expiratory flow variability and reducing symptoms, such as dyspnea and fatigue [20]. The integration between aerobic exercise, strengthening, and breathing techniques proved to be the most effective approach, indicating that multidimensional management has greater immunological effects than isolated interventions. These data reinforce the role of the physical therapist as a protagonist in the modulation of respiratory inflammation [19,20].

Physical rehabilitation in metabolic disorders (type 2 diabetes, insulin resistance, obesity)

In metabolic disorders, the selected studies showed that supervised physical exercise significantly reduces baseline IL-6, TNF-α, and ultrasensitive CRP, in addition to increasing IL-

10 and adiponectin, two potent anti-inflammatory mediators. Controlled clinical trials have shown that individuals with type 2 diabetes undergoing 12 weeks of combined training showed up to a 25% reduction in CRP and a significant improvement in insulin sensitivity [21]. At the same time, there was a reduction in visceral fat, the main reservoir of pro-inflammatory adipokines such as MCP-1 and resistin. These findings reaffirm the essential role of physical rehabilitation in metabolic management.

In addition, studies involving patients with metabolic syndrome have shown that modalities that combine aerobics and resistance result in greater reduction of inflammatory markers than any modality alone. High-intensity and interval interventions have also demonstrated significant benefits, rapidly reducing IL-6 and TNF-α, although they require careful patient selection due to the higher physiological demand [15]. The reduction in inflammation was accompanied by improved mitochondrial function and fatty acid oxidation, suggesting that exercise acts on the bioenergetic root of inflammation. This highlights the translational potential of rehabilitation for the reduction of cardiometabolic risks [21,15].

Physical rehabilitation in osteoarticular diseases (OA and RA)

In osteoarthritis and rheumatoid arthritis, physical rehabilitation has shown important effects on the reduction of both systemic and local proinflammatory cytokines. Clinical trials have shown that strengthening and low-impact exercises reduce IL-1β, TNF-α, and metalloproteinases in synovial fluid, in addition to promoting reduced cartilage degradation [22]. These effects were accompanied by decreased joint pain and stiffness, in addition to increased strength and functionality. Muscle adaptations seem to play an essential role in the modulation of joint inflammatory pathways. Meta-analyses confirm that supervised exercise is superior to unsupervised interventions, both in reducing inflammation and improving function. Studies with rheumatoid arthritis show reduction of CRP and IL-6 after progressive protocols, usually combining light aerobics and low-load muscle strengthening [23]. Patients also reported significant improvement in quality of life, reinforcing the importance of individualized physical therapy protocols. Thus, physical rehabilitation stands out as an essential intervention in inflammatory osteoarticular conditions [22,23].

Special populations (elderly, chronic renal failure, multimorbidities)

In elderly populations, the included studies showed that regular physical exercise promotes a reduction in inflammaging, the main inflammatory phenomenon associated with aging. Longitudinal analyses have shown consistent reductions in IL-6 and TNF-α, as well as improved immune function and muscle mass, reducing frailty and risk of hospitalizations [25]. These effects reinforce the role of supervised physical activity as a pillar of preventive health in the elderly. In patients with chronic renal failure, intradialytic exercises demonstrated significant reductions in CRP and IL-6, with improved muscle strength and exercise tolerance. Clinical trials have shown that the combination of light resistance exercise with intradialytic aerobic activities produces the greatest reduction in inflammatory markers, while increasing dialysis efficiency [24]. Such results show functional and immunometabolic benefits in populations of high clinical complexity [24,25].

Integration of anti-inflammatory mechanisms induced by physical rehabilitation

The results of this review confirm that physical rehabilitation promotes consistent anti-inflammatory effects through the integration of immunological, metabolic, and hemodynamic mechanisms. The reduction in CRP, IL-6 and TNF-α observed in different populations indicates that supervised exercise acts as a modulator of systemic inflammatory pathways, reinforcing evidence that muscle contraction induces the release of myokines with anti-inflammatory properties, such as IL-10 and IL-1ra [5]. In addition, exercise reduces the activation of the inflammatory complex NLRP3 and the transcription factor NF-κB, central mechanisms in the perpetuation of chronic inflammation [8]. These findings support the physiological role of exercise as a therapeutic intervention, confirming its ability to act at the root of the inflammatory process.

The modulation of oxidative stress also stands out as an essential complementary mechanism in the anti-inflammatory action of exercise. Several studies have shown that regular physical activity increases cellular antioxidant capacity, reducing the production of reactive oxygen species (ROS) and interrupting inflammatory cycles mediated by mitochondrial dysfunction [14]. The improvement of cellular bioenergetics directly impacts immune pathways, contributing to less activation of pro-inflammatory macrophages and to a more balanced immunometabolic profile. This integrative perspective reinforces that physical rehabilitation not only reduces inflammatory markers, but profoundly influences cellular and systemic physiology in chronic diseases [5,8,14].

Effectiveness of physical rehabilitation in different chronic diseases

The analysis of the studies showed that the effectiveness of physical rehabilitation varies according to the type of chronic disease, intensity of basal inflammation, functional capacity, and body composition. In heart patients, aerobic and combined programs demonstrate significant reductions in CRP and TNF-α, while improving endothelial function and decreasing the risk of cardiovascular events [17]. These effects are potentiated by the increase in nitric oxide and the improvement of autonomic function, demonstrating that rehabilitation acts simultaneously on the vascular, immunological and regulatory systems. Thus, supervised exercise is consolidated as an essential therapy in the management of cardiovascular inflammation.

In individuals with COPD, the reduction of IL-8, TNF-α, and muscle biomarkers of fatigue demonstrates that respiratory rehabilitation directly impacts systemic and peripheral mechanisms of inflammation. Improved exercise tolerance and reduced dyspnea are associated with less activation of pro-inflammatory muscle

pathways and optimization of oxygen transport [19]. In metabolic disorders, combined exercise is especially effective, reducing visceral fat, increasing adiponectin, and modulating inflammatory infiltrate of adipose tissue [15]. Thus, the effects of rehabilitation vary in magnitude, but are consistent across multiple chronic conditions [15,17,19].

Importance of physical therapy and individualization of protocols

One of the central points revealed by the literature is the importance of the role of the physical therapist in modulating the inflammatory response. The physiotherapist is the most qualified professional to conduct physical rehabilitation in patients chronic, thanks to the mastery of biomechanics, physiology of clinical exercise, kinesiology and therapeutic reasoning. The individualization of protocols considering intensity, frequency, volume, comorbidities, and functional capacity is crucial to optimize the anti-inflammatory response and avoid adverse effects [28]. Comparative studies indicate that interventions supervised by physiotherapists generate greater reductions in inflammatory markers than unsupervised programs, evidencing the direct impact of professional performance on the quality of care [29]. In addition, the combination of aerobic, resistance, functional and manual therapies modalities ensure a multidimensional approach capable of acting on different biological pathways. This integration enhances the anti-inflammatory effect by involving musculoskeletal, cardiorespiratory, neuroendocrine, and immune systems. Continuous supervision also allows for frequent adjustments and progressive interventions, which are essential for maintaining therapeutic effects. Thus, the literature reinforces that physical rehabilitation requires not only technical execution, but also evidence-based clinical planning, a characteristic domain of modern physical therapy [28,29].

Limitations of the literature and heterogeneity of the studies analyzed

Despite the advances presented, the literature still has important limitations. One of the main difficulties is the methodological heterogeneity of the included studies, with wide variation in exercise intensity, duration of interventions, biomarkers evaluated, and characteristics of the populations studied. This diversity makes it difficult to directly compare and develop universal guidelines [27]. The absence of protocol standardization directly impacts the consistency of results and reduces the ability to establish accurate clinical recommendations, especially for complex and multimorbid populations. Another limitation identified is the small number of long-term studies, which makes it difficult to determine whether the observed anti-inflammatory effects are sustainable over the years. Most of the interventions analyze periods of 8 to 16 weeks, which does not reflect the chronicity of the diseases studied. In addition, few studies investigate interactions between exercise, gut microbiota, epigenetics, and autonomic function in emerging areas with strong explanatory potential. Therefore, despite the strength of the current evidence, there is a need for broader, multicenter, and longer-lasting research [27].

Clinical implications and future prospects

The findings of this review demonstrate that physical rehabilitation should be considered a central component in the management of chronic diseases, not only as a strategy for functional improvement, but also as an intervention with molecular and immunological impact. The anti-inflammatory effects of exercise position rehabilitation as a first-line therapy in several conditions, justifying its inclusion in Public Health policies and multiprofessional rehabilitation programs [33]. The integration between Biomedicine, Physiotherapy and Public Health can expand the clinical, epidemiological and social impact of these interventions. Future perspectives include the construction of individualized protocols based on specific biomarkers, integration with digital functional monitoring tools, application of periodized exercises to modulate inflammatory pathways, and expansion of translational studies that connect molecular mechanisms to clinical outcomes. Science points to a future in which physical rehabilitation will be increasingly personalized, molecularly driven, and integrated with other biological therapies. Thus, this review contributes to broadening the understanding of rehabilitation as a high-impact immunometabolic intervention in chronic diseases [33].

Conclusion

The findings of this review consistently demonstrate that physical rehabilitation exerts broad and clinically relevant anti-inflammatory effects in patients with different chronic diseases, including cardiovascular, respiratory, metabolic, and osteoarticular diseases. Supervised interventions, especially when combining aerobic and resistance exercise, promote significant reductions in inflammatory markers such as CRP, IL-6, and TNF-α, while increasing anti-inflammatory mediators such as IL-10 and adiponectin. These benefits are supported by integrated physiological mechanisms, including modulation of myokines, improvement of energy metabolism, reduction of oxidative stress, and reorganization of immunometabolic pathways, reinforcing therapeutic exercise as a robust, evidence-based intervention in the management of chronic inflammation [5].

In addition, the comparative analysis between the diseases reveals that, although the magnitude of the effects varies according to the clinical condition and individual characteristics of the patients, physical rehabilitation presents consistent benefits in all the groups studied. The role of the physical therapist emerges as an essential element in this modulation, since their training allows individualized prescription, continuous monitoring and progressive adaptation of interventions, ensuring safety and therapeutic efficacy. The results reinforce that programs supervised by physical therapists have a greater impact on the reduction of inflammatory markers and functional improvement than unsupervised programs, highlighting the strategic role of this professional in the comprehensive care of chronic patients [29].

Finally, the data in this review highlight the need for expanded research on physical rehabilitation and inflammation, especially long-term studies, multicenter analyses, and integrative approaches that connect molecular mechanisms to clinical outcomes. The

application of the knowledge discussed here has the potential to transform practices in Biomedicine, Physiotherapy and Public Health, strengthening preventive programs, qualified clinical practices and population policies to cope with chronic diseases. Therefore, physical rehabilitation should be recognized as an essential intervention, with a consolidated scientific basis and high translational impact, in the management of systemic inflammation and in improving the quality of life of patients with chronic diseases [33].

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