

INTEGRATING EXERCISE AND REHABILITATION IN RHEUMATOLOGY: ADVANCING THERAPEUTIC STRATEGIES FOR OPTIMAL PATIENT OUTCOMES

A. Angelov

Rheumatology Sector, Department of Internal Medicine, Hospital Burgasmed – Burgas, Bulgaria
Physiotherapy and Rehabilitation Centre, Vita – Burgas, Bulgaria

Abstract. *This review examines the integration of exercise and rehabilitation into rheumatologic care, highlighting their synergistic effects alongside pharmacological treatment. Exercise modalities such as aerobic, resistance, and flexibility training enhance physical function, alleviate pain, and reduce systemic inflammation, primarily through the activity of exercise-induced myokines which support immune regulation and tissue repair. Despite demonstrated benefits, adoption is hindered by barriers, including limited adherence, healthcare access, and absence of standardized guidelines. This review suggests personalized exercise protocols, interdisciplinary collaboration, and telehealth innovations to promote accessibility and adherence. Expanding exercise and rehabilitation as standard practices in rheumatology may optimize patient outcomes and long-term disease management, with future research needed to refine protocols and validate rehabilitation strategies.*

Key words: exercise, rehabilitation, therapeutic strategies

INTRODUCTION

Rheumatic diseases encompass a diverse range of chronic inflammatory and degenerative conditions affecting joints, muscles, and connective tissues, such as rheumatoid arthritis (RA), osteoarthritis (OA), spondyloarthritis (SpA) and systemic lupus erythematosus (SLE). These conditions often result in chronic pain, reduced physical function, and decreased quality of life, imposing a significant burden on patients and healthcare systems alike [1]. While pharmacological treatments such as synthetic and biological disease-modifying antirheumatic drugs (DMARDs), have advanced the management of rheumatic diseases, they do not fully address the functional limitations and disability that many patients experience [2]. Consequently, non-pharmacological interventions, particularly exercise and rehabilitation, have gained recognition as critical components of comprehensive care in rheumatology [3].

Exercise and rehabilitation strategies offer numerous benefits, including improved muscle strength, enhanced joint mobility, reduced pain, and better overall physical function. Furthermore, these interventions have been shown to positively impact mental health, reducing symptoms of depression and anxiety commonly associated with chronic rheumatic conditions [4]. Despite these benefits, exercise and rehabilitation remain underutilized in routine clinical practice. Integration of exercise and rehabilitation into routine rheumatologic care remains

inconsistent, partly due to concerns over exacerbating symptoms, low patient adherence, and a lack of standardized guidelines.

This review aims to synthesize the current evidence on the role of exercise and rehabilitation in the management of rheumatic diseases, with a focus on their potential to complement pharmacological treatments. By exploring the biological mechanisms, clinical outcomes, and practical challenges associated with these interventions, this paper seeks to provide a comprehensive understanding of how exercise and rehabilitation can be more effectively integrated into therapeutic strategies to optimize patient outcomes.

SEARCH METHODOLOGY

We adhered to established guidelines for writing narrative reviews, following the framework of previously published recommendations [5]. We conducted a comprehensive search of PubMed, Scopus, and Web of Science databases up to August 2024, focusing on studies evaluating the role of exercise and rehabilitation in rheumatic disease management. Initial search terms included “exercise”, “rehabilitation”, “rheumatic diseases”, “rheumatoid arthritis”, “spondyloarthritis”, “ankylosing spondylitis”, “systemic lupus erythematosus” and “myokines.” MeSH terms and relevant free-text terms were used accordingly.

References of identified studies and systematic reviews were manually checked for further rele-

vant studies. Emphasis was placed on randomized controlled trials (RCTs), systematic reviews, and meta-analyses reporting physical function, pain reduction, and inflammatory markers as primary outcomes. Non-modifiable risk factors and pharmacological-only interventions were excluded.

THE ROLE OF EXERCISE IN RHEUMATOLOGY

Exercise plays a pivotal role in the management of rheumatic diseases, offering multifaceted benefits that extend beyond traditional pharmacological treatments. Incorporating structured physical activity into the therapeutic regimen of patients with rheumatic conditions such as RA, OA, SLE, and SpA can significantly enhance joint function, improve mobility, and alleviate pain [6, 7]. This section explores the various types of exercise – aerobic, resistance, and flexibility training and their specific impacts on individuals suffering from different rheumatic diseases.

Aerobic exercise, characterized by activities that increase heart rate and improve cardiovascular endurance, is fundamental in managing rheumatic diseases. Exercises such as walking, cycling, swimming, and aerobic classes help reduce systemic inflammation, a key contributor to disease progression. Regular aerobic activity has been associated with decreased levels of inflammatory markers, such as C-reactive protein, thereby mitigating disease activity [8]. Additionally, aerobic exercise enhances cardiovascular health, which is particularly important given the increased risk of cardiovascular comorbidities in patients with chronic inflammatory rheumatic conditions. Improved cardiovascular fitness also translates to better overall stamina and reduced fatigue, common complaints among rheumatic disease patients [9,10].

Resistance training involves exercises that strengthen muscles by working against a force, such as weightlifting, resistance band exercises, and body-weight training. In the context of rheumatology, resistance training is crucial for preserving and enhancing muscle mass, which is often compromised due to chronic inflammation and prolonged inactivity. Stronger muscles provide better support to affected joints, thereby reducing mechanical stress and preventing further joint damage. Studies have demonstrated that resistance training can lead to significant improvements in muscle strength and endurance, pain reduction, which, in turn, enhance functional capacity and quality of life [11, 12]. Moreover, resistance exercises contribute to bone densi-

ty maintenance, offering protective benefits against osteoporosis – a common complication in rheumatic diseases [13, 14].

Flexibility exercises, including stretching and range-of-motion (ROM) activities, are essential for maintaining and improving joint mobility. Rheumatic diseases frequently result in joint stiffness, reduced ROM, and decreased overall flexibility, which can severely limit a patient's ability to perform everyday tasks. Engaging in regular flexibility training helps to alleviate stiffness, increase joint lubrication, and enhance the elasticity of muscles and connective tissues surrounding the joints. Practices such as yoga and Tai Chi not only improve physical flexibility but also incorporate elements of balance and mindfulness, which can further aid in pain management and mental well-being. Enhanced flexibility contributes to better posture, reduced risk of injury, and improved overall functional movement, thereby enhancing the quality of life for individuals with rheumatic conditions [15].

MYOKINE SIGNALING: EXERCISE AS A MOLECULAR MODULATOR IN RHEUMATIC DISEASES

The biological underpinnings of exercise in rheumatic disease management are increasingly centered on the role of myokines, cytokines released by skeletal muscle in response to contraction. There are currently more than 600 identified myokines [16]. These molecules mediate several systemic effects, including immune modulation, anti-inflammatory activity, and metabolic regulation, making them a cornerstone of exercise's therapeutic benefit [17, 18]. Among these myokines, interleukin-6 (IL-6), irisin, and brain-derived neurotrophic factor (BDNF) are particularly interesting, each contributing uniquely to the body's response to exercise and offering specific advantages in the context of rheumatic diseases.

IL-6 serves as a paradoxical player in both pro-inflammatory and anti-inflammatory pathways. Produced transiently during exercise, IL-6 shifts from a pro-inflammatory cytokine in disease states to an anti-inflammatory mediator when derived from contracting muscle. The exercise-induced form of IL-6 suppresses the release of TNF- α and IL-1 β . This IL-6-mediated suppression reduces inflammatory processes, contributing to lower disease activity and symptom relief, while also promoting tissue repair. However, in chronic inflammatory conditions, persistently elevated IL-6 exacerbates inflammation, promoting joint degradation. Therefore, exercise of-

fers a natural means to harness IL-6's transient anti-inflammatory benefits, while IL-6-targeted drugs address its chronic effects [19, 20].

Irisin, another pivotal myokine formed during exercise, is involved in metabolic regulation. It induces the browning of white adipose tissue, thereby increasing energy expenditure and improving insulin sensitivity [21]. This becomes particularly relevant for rheumatic disease patients, who often experience metabolic dysregulation and increased cardiovascular risk [22, 23]. Irisin's role extends beyond metabolism to musculoskeletal health, as it promotes osteoblast activity and bone formation, counteracting osteoporosis. This dual action on metabolism and bone integrity offers a protective mechanism, potentially mitigating the risk of fractures and improving overall physical function in these patients [24, 25].

BDNF, though primarily known for its effects on the central nervous system, is increasingly recognized for its peripheral benefits in muscle regeneration. Exercise-induced BDNF enhances muscle repair by stimulating satellite cells, the progenitors of new muscle fibers. This process is critical in rheumatic diseases where muscle atrophy and weakness are common. Additionally, BDNF's neuroprotective effects are relevant in chronic pain management, a significant concern in conditions where long-term pain can lead to central sensitization and reduced pain thresholds. By improving both muscle and neural function, BDNF levels management can potentially offer a comprehensive recovery mechanism, aiding both physical and cognitive health [26, 27].

Exercise triggers a broader anti-inflammatory response beyond myokines alone. Physical activity increases levels of anti-inflammatory cytokines such as IL-10 while reducing the concentrations of pro-inflammatory markers like CRP and TNF- α [28, 29]. This shift towards an anti-inflammatory profile is especially beneficial for patients with high disease activity, as it can reduce the frequency and intensity of flares. Exercise also enhances the function of regulatory T cells, further contributing to immune balance. The cumulative effect of these anti-inflammatory responses slows disease progression [30].

Exercise induces molecular adaptations in muscle and connective tissue that mitigate inflammation and support tissue health. Key mechanisms include shifts in muscle fiber composition, with increased type I:II fiber ratios and hypertrophy of type II fibers, enhancing muscle endurance and resistance to damage. Additionally, resistance training reduces the expression of inflammation-related genes, such as those involved in fibrosis, and mechanical loading

suppresses proinflammatory cytokine expression in chondrocytes. These molecular responses support local tissue resilience and systemic anti-inflammatory effects, warranting further research into optimizing these therapeutic pathways [31].

BARRIERS TO IMPLEMENTATION AND SOLUTIONS

Despite the proven benefits of exercise and rehabilitation in managing rheumatic diseases, several barriers hinder their integration into standard rheumatologic care. These challenges can be grouped into patient-related factors and healthcare system limitations.

Patient-related barriers primarily involve low adherence due to fear of exacerbating symptoms, fatigue, and psychological resistance, often linked to misconceptions about the effects of exercise on disease progression. Many patients are also hindered by co-existing physical limitations, such as joint deformities, chronic pain, or severe disability. Moreover, socioeconomic factors, such as lack of access to specialized facilities or financial constraints, can prevent patients from engaging in regular rehabilitation [32, 33]. Studies indicate that fatigue, a common symptom in rheumatic conditions, significantly decreases patient motivation to exercise, creating a cycle of inactivity that worsens physical function and increases pain levels [34, 35]. Addressing these concerns requires targeted patient education to dispel myths about exercise and rheumatic diseases and to emphasize the importance of movement for long-term joint health and function.

Healthcare system barriers are multifaceted, including insufficient referral practices, lack of interdisciplinary care coordination, and limited access to rehabilitation services. In many healthcare settings, exercise and rehabilitation are viewed as adjuncts rather than core components of treatment. Consequently, referrals to physical therapy or specialized rehabilitation programs are inconsistent, and when made, patients may encounter long wait times, discordance between rheumatologist and rehabilitation specialist expectation, or geographical barriers that limit access to qualified providers. Additionally, the cost of ongoing rehabilitation may not be fully covered by insurance, deterring patients from adhering to prescribed exercise programs. Another significant barrier is the lack of standardized guidelines within healthcare systems for incorporating exercise as a regular, structured component of rheumatologic care. There is long term data that supervised care is more effective [36].

Addressing these barriers requires a multifaceted approach. First, personalized exercise programs should be developed to meet the individual needs of patients, taking into account disease severity, physical limitations, and comorbidities. Personalized plans increase adherence by ensuring that exercises are both achievable and tailored to the patient's functional level [37]. For example, patients with severe joint damage or pain may benefit from aquatic therapy, which reduces joint stress, while those with lower disease activity could engage in weight-bearing exercises to improve muscle strength and joint stability.

Moreover, interdisciplinary care models, involving rheumatologists, physiatrists, physical therapists, occupational therapists, and mental health professionals, are critical in providing comprehensive care. These teams can collaborate to address both the physical and psychological barriers to exercise. Cognitive-behavioral therapy has been shown to improve patient attitudes toward exercise and increase adherence by helping patients manage the fear of exacerbating symptoms and chronic pain. Mental health support is also essential, as depression and anxiety are prevalent in rheumatic disease patients, often exacerbating physical inactivity [38, 39].

Healthcare systems must also invest in improving access to rehabilitation services. Tele-rehabilitation, which uses digital platforms to deliver physical therapy remotely, has emerged as a viable solution to overcome geographical and logistical barriers. Studies have demonstrated that tele-rehabilitation can lead to comparable outcomes to in-person therapy, offering patients a convenient and cost-effective alternative to traditional rehabilitation [40]. Additionally, integrating wearable technologies and mobile applications that provide real-time feedback on patient activity can foster greater engagement and accountability, leading to sustained physical activity and improved outcomes [41].

Patient education and empowerment remain crucial in overcoming these barriers. Healthcare providers must emphasize the long-term benefits of exercise in reducing pain, improving joint function, and preventing further disability. Educational initiatives should also focus on teaching patients about energy conservation techniques, joint protection strategies, and gradual exercise progression to build confidence and encourage self-management of their disease. Effective education can also clarify misconceptions, such as the belief that exercise will exacerbate joint damage, replacing these with evidence-based information on the protective benefits of regular physical activity [42, 43].

Finally, policy-level changes are needed to prioritize exercise and rehabilitation as essential components of rheumatologic care. Insurance coverage for rehabilitation services should be expanded, and guidelines for exercise prescriptions should be standardized across healthcare systems. Furthermore, healthcare providers need to be trained in the importance of early referral to rehabilitation programs, ensuring that patients receive timely and appropriate interventions before irreversible joint damage occurs.

FUTURE DIRECTIONS AND EMERGING THERAPIES

The field of exercise and rehabilitation for rheumatic diseases is evolving rapidly with the advent of innovative technologies, such as virtual rehabilitation and telemedicine. These emerging technologies hold promise in revolutionizing the way care is delivered, particularly in overcoming logistical and geographical barriers that traditionally limit access to rehabilitation services.

Virtual rehabilitation platforms leverage motion-sensing technologies and interactive software to deliver tailored exercise programs, allowing patients to perform exercises in their own homes while receiving real-time feedback from healthcare providers. This approach offers an effective alternative for individuals who face difficulties attending in-person therapy sessions due to mobility issues or long distances from rehabilitation centers. Studies have demonstrated that virtual rehabilitation can lead to comparable outcomes to traditional in-clinic therapies in terms of improving physical function and pain management [44]. Telemedicine platforms enable healthcare providers to remotely monitor patients, assess their progress, and adjust their rehabilitation programs as needed. The COVID-19 pandemic accelerated the adoption of telemedicine in rheumatology, demonstrating its potential to provide ongoing care without the need for frequent in-person visits. Research has indicated that telemedicine can effectively deliver rehabilitation programs for patients with rheumatic diseases, improving their physical function and reducing disease activity. Importantly, telemedicine allows for a more personalized and adaptive approach to rehabilitation, as clinicians can modify exercise prescriptions based on real-time feedback and patient-reported outcomes [45].

Wearables, such as activity trackers, accelerometers, and smart clothing, provide continuous monitoring of a patient's physical activity levels,

joint mobility, and exercise adherence. These devices can collect data on daily movements and exercise performance, offering insights into the patient's progress and enabling healthcare providers to make data-driven decisions about their rehabilitation plans. For example, wearable devices equipped with sensors can detect joint movements and provide feedback on the quality of exercises, encouraging patients to engage in proper techniques and avoid harmful postures. Studies have demonstrated that patients using wearable technologies as part of their rehabilitation program exhibit higher levels of adherence and improved outcomes compared to those who do not utilize these devices [46].

The integration of gamification into rehabilitation is an intriguing development. Virtual reality (VR) platforms and video games are being incorporated into rehabilitation programs to increase patient engagement and motivation. These gamified platforms offer interactive and immersive environments, in which patients can perform therapeutic exercises while being rewarded for their progress [47].

One promising, yet underutilized and easily available area within rehabilitation is weight-bearing exercise. These exercises have shown to improve muscle strength, hypertrophy and bone density while providing joint stabilization benefits essential for patients with rheumatic conditions. Despite their proven benefits in healthy populations, weight-bearing exercises remain less emphasized, potentially due to misconceptions about their safety but they have been proven to be safe and effective in patients with rheumatic disease [12, 48–51]. Although there is a lack of high quality clinical trial data about specific protocol efficacy in this patient population. New information about optimal protocols for muscle hypertrophy in healthy adults should be carefully tested [52, 53]. There is evidence that a moderate volume of 12-20 sets per muscle group per week divided into several training sessions leads to optimal results [54]. As evidence grows around these benefits, there is a need for healthcare providers to include and promote weight-bearing exercise as an essential part of rehabilitation.

As the evidence base supporting these emerging therapies expands, future research and clinical trials should focus on long-term efficacy and strategies to integrate these tools within standard rheumatologic care. Collectively, these innovations offer a pathway to highly personalized, accessible, and effective care that may redefine exercise and rehabilitation in rheumatology, ultimately enhancing patient outcomes, adherence, and quality of life.

CONCLUSION

Integrating exercise and rehabilitation into the management of rheumatic diseases is essential for enhancing patient outcomes, addressing both physical limitations and systemic inflammation. Evidence supports that aerobic, resistance, and flexibility exercises not only improve mobility, reduce pain, and strengthen muscle function but also influence molecular pathways to decrease inflammation and promote tissue repair. Despite these benefits, challenges such as limited patient adherence and healthcare access persist. Personalized exercise programs, interdisciplinary collaboration, and advancements in telemedicine can help overcome these barriers, ensuring exercise and rehabilitation become core components of rheumatologic care. Embracing these strategies will ultimately foster improved long-term outcomes and quality of life for patients with rheumatic diseases.

RECOMMENDATIONS

Based on current literature and available evidence, here are the author's recommendations for integrating exercise and rehabilitation into rheumatologic care:

1. **Individualize Exercise Plans:** Design individualized programs incorporating aerobic, resistance, and flexibility exercises to patient-specific disease activity, limitations, and personal goals.

2. **Promote Multidisciplinary Collaboration:** Foster teamwork among rheumatologists, physiatrists, physiotherapists, kinesiotherapists, occupational therapists, and mental health professionals, ensuring comprehensive support and alignment of therapeutic goals.

3. **Empower Patients Through Education:** Equip patients with knowledge on the benefits and safety of exercise in managing rheumatic conditions to foster adherence and reduce anxiety related to symptom exacerbation.

4. **Address Psychological Barriers:** Incorporate cognitive and behavioral support to address fears, depression, and fatigue, which can hinder long-term engagement in exercise.

5. **Utilization of Telehealth and Digital Tools:** Leverage telemedicine, wearable technology, and mobile applications to provide continuous monitoring, feedback, and remote support, especially for patients with geographic or mobility barriers.

These recommendations aim to make exercise and rehabilitation accessible and integral parts of rheumatologic treatment, ultimately enhancing patient outcomes and quality of life.

Библиография//References:

1. Salaffi F, Di Carlo M, Carotti M et al. The impact of different rheumatic diseases on health-related quality of life: a comparison with a selected sample of healthy individuals using SF-36 questionnaire, EQ-5D and SF-6D utility values. *Acta Biomed.* 2019;89: 541–557. doi:10.23750/abm.v89i4.7298
2. Taylor PC, Woods M, Rycroft C et al. Targeted literature review of current treatments and unmet need in moderate rheumatoid arthritis in the United Kingdom. *Rheumatol (Oxford).* 2021;60: 4972–4981. doi:10.1093/rheumatology/keab464
3. Luttosch F, Baerwald C. Rehabilitation in rheumatology. *Internist (Berl).* 2010;51: 1239–1245. doi:10.1007/s00108-010-2626-1
4. Fedorchenko Y, Mahmudov K, Abenov Z et al. Rehabilitation of patients with inflammatory rheumatic diseases and comorbidities: unmet needs. *Rheumatol Int.* 2024;44: 583–591. doi:10.1007/s00296-023-05529-6
5. Gasparyan AY, Aivazyan L, Blackmore H, Kitas GD. Writing a narrative biomedical review: considerations for authors, peer reviewers, and editors. *Rheumatol Int.* 2011;31: 1409–1417. doi:10.1007/s00296-011-1999-3
6. Calabrese L, Neiman DC. Exercise, infection and rheumatic diseases: what do we know? *RMD Open.* 2021;7: e001644. doi:10.1136/rmdopen-2021-001644
7. Georgiev T, Angelov AK. Modifiable risk factors in knee osteoarthritis: treatment implications. *Rheumatol Int.* 2019;39: 1145–1157. doi:10.1007/s00296-019-04290-z
8. Swift DL, Johannsen NM, Earnest CP et al. Effect of exercise training modality on C-reactive protein in type 2 diabetes. *Med Sci Sports Exerc.* 2012;44: 1028–1034. doi:10.1249/MSS.0b013e31824526cc
9. García-Correa HR, Sánchez-Montoya LJ, Daza-Arana JE, Ordoñez-Mora LT. Aerobic physical exercise for pain intensity, aerobic capacity, and quality of life in patients with chronic pain: A systematic review and meta-analysis. *J Phys Act Health.* 2021;18: 1126–1142. doi:10.1123/jpah.2020-0806
10. Ye H, Weng H, Xu Y et al. Effectiveness and safety of aerobic exercise for rheumatoid arthritis: a systematic review and meta-analysis of randomized controlled trials. *BMC Sports Sci Med Rehabil.* 2022;14: 17. doi:10.1186/s13102-022-00408-2
11. Siczekowska SM, Coimbra DR, Vilarino GT, Andrade A. Effects of resistance training on the health-related quality of life of patients with rheumatic diseases: Systematic review with meta-analysis and meta-regression. *Semin Arthritis Rheum.* 2020;50: 342–353. doi:10.1016/j.semarthrit.2019.09.006
12. Wen Z, Chai Y. Effectiveness of resistance exercises in the treatment of rheumatoid arthritis: A meta-analysis: A meta-analysis. *Medicine (Baltimore).* 2021;100: e25019. doi:10.1097/MD.00000000000025019
13. Hong AR, Kim SW. Effects of resistance exercise on bone health. *Endocrinol Metab (Seoul).* 2018;33: 435–444. doi:10.3803/EnM.2018.33.4.435
14. Benedetti MG, Furlini G, Zati A et al. The effectiveness of physical exercise on bone density in osteoporotic patients. *Biomed Res Int.* 2018;2018: 4840531. doi:10.1155/2018/4840531
15. Kocyigit BF, Sagtaganov Z, Yessirkepov M. The effectiveness of yoga as a form of exercise in the management of rheumatic diseases. *Rheumatol Int.* 2023;43: 795–801. doi:10.1007/s00296-023-05291-9
16. Lee JH, Jun H-S. Role of myokines in regulating skeletal muscle mass and function. *Front Physiol.* 2019;10: 42. doi:10.3389/fphys.2019.00042
17. Gomasasca M, Banfi G, Lombardi G. Myokines: The endocrine coupling of skeletal muscle and bone. *Adv Clin Chem.* 2020;94: 155–218. doi:10.1016/bs.acc.2019.07.010
18. Severinsen MCK, Pedersen BK. Muscle-organ crosstalk: The emerging roles of myokines. *Endocr Rev.* 2020;41: 594–609. doi:10.1210/endrev/bnaa016
19. Scheller J, Chalaris A, Schmidt-Arras D, Rose-John S. The pro- and anti-inflammatory properties of the cytokine interleukin-6. *Biochim Biophys Acta.* 2011;1813: 878–888. doi:10.1016/j.bbamcr.2011.01.034
20. Ostrowski K, Rohde T, Asp S et al. Pro- and anti-inflammatory cytokine balance in strenuous exercise in humans. *J Physiol.* 1999;515 (Pt 1): 287–291. doi:10.1111/j.1469-7793.1999.287ad.x
21. Machado SA, Pasquarelli-do-Nascimento G, da Silva DS, et al. Browning of the white adipose tissue regulation: new insights into nutritional and metabolic relevance in health and diseases. *Nutr Metab (Lond).* 2022;19: 61. doi:10.1186/s12986-022-00694-0
22. Angelov AK, Markov M, Ivanova M, Georgiev T. The genesis of cardiovascular risk in inflammatory arthritis: insights into glycocalyx shedding, endothelial dysfunction, and atherosclerosis initiation. *Clin Rheumatol.* 2023;42: 2541–2555. doi:10.1007/s10067-023-06738-x
23. Georgiev T, Dimitrov S, Kabakchieva P. Aging gracefully in osteoarthritis: Impact of comorbidities. *Anti-Aging Eastern Europe.* 2024;3: 124–134. doi:10.56543/aaeeu.2024.3.3.03
24. Yu Y, Ma M, Li C et al. Irisin mitigates rheumatoid arthritis by suppressing mitochondrial fission via inhibiting YAP-Drp1 signaling pathway. *Int Immunopharmacol.* 2024;127: 111443. doi:10.1016/j.intimp.2023.111443
25. Gamez-Nava JI, Ramirez-Villafañá M, Cons-Molina F et al. Serum irisin concentrations and osteoporotic vertebral fractures in women with rheumatoid arthritis: A cross-sectional study: A cross-sectional study. *Medicine (Baltimore).* 2022;101: e28799. doi:10.1097/MD.00000000000028799
26. Wang N, Tian B. Brain-derived neurotrophic factor in autoimmune inflammatory diseases (Review). *Exp Ther Med.* 2021;22: 1292. doi:10.3892/etm.2021.10727
27. Rentería I, García-Suárez PC, Fry AC et al. The molecular effects of BDNF synthesis on skeletal muscle: Amini-review. *Front Physiol.* 2022;13: 934714. doi:10.3389/fphys.2022.934714
28. Kasapis C, Thompson PD. The effects of physical activity on serum C-reactive protein and inflammatory markers: a systematic review. *J Am Coll Cardiol.* 2005;45: 1563–1569. doi:10.1016/j.jacc.2004.12.077
29. Petersen AMW, Pedersen BK. The anti-inflammatory effect of exercise. *J Appl Physiol.* 2005;98: 1154–1162. doi:10.1152/jappphysiol.00164.2004
30. Li Z, Wang X-Q. Clinical effect and biological mechanism of exercise for rheumatoid arthritis: A mini review. *Front Immunol.* 2022;13: 1089621. doi:10.3389/fimmu.2022.1089621
31. Lundberg IE, Nader GA. Molecular effects of exercise in patients with inflammatory rheumatic disease. *Nat Clin Pract Rheumatol.* 2008;4: 597–604. doi:10.1038/ncprheum0929
32. Canning J, Williams R, de Souza S. Patient experiences of physical activity and exercise in rheumatoid arthritis. *Rheumatol Adv Pract.* 2023;7: rkac098. doi:10.1093/rap/rkac098
33. Löf H, Johansson U-B. "A body in transformation"-An empirical phenomenological study about fear-avoidance beliefs towards physical activity among persons experiencing moderate-to-severe rheumatic pain. *J Clin Nurs.* 2019;28: 321–329. doi:10.1111/jocn.14606

34. Overman CL, Kool MB, Da Silva JAP, Geenen R. The prevalence of severe fatigue in rheumatic diseases: an international study. *Clin Rheumatol*. 2016;35: 409–415. doi:10.1007/s10067-015-3035-6
35. Musumeci G. Effects of exercise on physical limitations and fatigue in rheumatic diseases. *World J Orthop*. 2015;6: 762–769. doi:10.5312/wjo.v6.i10.762
36. Van Wissen MAT, Van den Ende CHM, Gademan MGJ et al. One-year effectiveness of long-term exercise therapy in people with axial spondyloarthritis and severe functional limitations. *Rheumatology (Oxford)*. 2024; keae323. doi:10.1093/rheumatology/keae323
37. Feddersen H, Søndergaard J, Andersen L et al. Barriers and facilitators for coherent rehabilitation among people with inflammatory arthritis – a qualitative interview study. *BMC Health Serv Res*. 2022;22: 1347. doi:10.1186/s12913-022-08773-x
38. Shen B, Li Y, Du X et al. Effects of cognitive behavioral therapy for patients with rheumatoid arthritis: a systematic review and meta-analysis. *Psychol Health Med*. 2020;25: 1179–1191. doi:10.1080/13548506.2020.1736312
39. Swärdh E, Opava CH, Nygård L, Lindquist I. Understanding exercise promotion in rheumatic diseases: A qualitative study among physical therapists. *Physiotherapy Theory and Practice*. 2021;37: 963–972. doi:10.1080/09593985.2019.1672226
40. Pani D, Piga M, Barabino G et al. Home tele-rehabilitation for rheumatic patients: impact and satisfaction of care analysis. *J Telemed Telecare*. 2017;23: 292–300. doi:10.1177/1357633X16632950
41. Ocaglı H, Agarinis R, Azzolina D et al. Physical activity assessment with wearable devices in rheumatic diseases: a systematic review and meta-analysis. *Rheumatology (Oxford)*. 2023;62: 1031–1046. doi:10.1093/rheumatology/keac476
42. Law R-J, Breslin A, Oliver EJ et al. Perceptions of the effects of exercise on joint health in rheumatoid arthritis patients. *Rheumatology (Oxford)*. 2010;49: 2444–2451. doi:10.1093/rheumatology/keq299
43. de Jong Z, Munneke M, Zwinderman AH et al. Long term high intensity exercise and damage of small joints in rheumatoid arthritis. *Ann Rheum Dis*. 2004;63: 1399–1405. doi:10.1136/ard.2003.015826
44. Bilika P, Karamatsou N, Stavarakis G et al. Virtual reality-based exercise therapy for patients with chronic musculoskeletal pain: A scoping review. *Healthcare (Basel)*. 2023;11. doi:10.3390/healthcare11172412
45. Barnett R, Shakaib N, Ingram TA et al. Rehabilitation interventions delivered via telehealth to support self-management of rheumatic and musculoskeletal diseases: A scoping review protocol. *PLoS One*. 2024;19: e0301668. doi:10.1371/journal.pone.0301668
46. Davergne T, Rakotozafiarison A, Servy H, Gossec L. Wearable activity trackers in the management of rheumatic diseases: Where are we in 2020? *Sensors (Basel)*. 2020;20: 4797. doi:10.3390/s20174797
47. Alfieri FM, da Silva Dias C et al. Gamification in musculoskeletal rehabilitation. *Curr Rev Musculoskelet Med*. 2022;15: 629–636. doi:10.1007/s12178-022-09797-w
48. Rall LC, Meydani SN, Kehayias JJ et al. The effect of progressive resistance training in rheumatoid arthritis. Increased strength without changes in energy balance or body composition. *Arthritis Rheum*. 1996;39: 415–426. doi:10.1002/art.1780390309
49. England BR, Smith BJ, Baker NA et al. 2022 American College of Rheumatology guideline for exercise, rehabilitation, diet, and additional integrative interventions for rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2023;75: 1603–1615. doi:10.1002/acr.25117
50. Abrahão MI, Gomiero AB, Peccin MS et al. Cardiovascular training vs. resistance training for improving quality of life and physical function in patients with systemic lupus erythematosus: a randomized controlled trial. *Scand J Rheumatol*. 2016;45: 197–201. doi:10.3109/03009742.2015.1094126
51. Blaess J, Geneton S, Goepfert T et al. Recommendations for physical activity and exercise in persons living with Systemic Lupus Erythematosus (SLE): consensus by an international task force. *RMD Open*. 2024;10. doi:10.1136/rmdopen-2024-004171
52. Bernárdez-Vázquez R, Raya-González J, Castillo D, Beato M. Resistance training variables for optimization of muscle hypertrophy: An umbrella review. *Front Sports Act Living*. 2022;4: 949021. doi:10.3389/fspor.2022.949021
53. Krzysztofik M, Wilk M, Wojdała G, Gołaś A. Maximizing muscle hypertrophy: A systematic review of advanced resistance training techniques and methods. *Int J Environ Res Public Health*. 2019;16: 4897. doi:10.3390/ijerph16244897
54. Baz-Valle E, Balsalobre-Fernández C, Alix-Fages C, Santos-Concejero J. A systematic review of the effects of different resistance training volumes on muscle hypertrophy. *J Hum Kinet*. 2022;81: 199–210. doi:10.2478/hukin-2022-0017

Постъпил за печат: 11.11.2024 г.

Submitted: 11.11.2024

✉ Адрес за кореспонденция:

А. Ангелов
тел.: +359899840591
e-mail: alexkangelov@gmail.com
ORCID: <https://orcid.org/0000-0003-3062-9478>

✉ Correspondence address:

A. Angelov
tel.: +359899840591
e-mail: alexkangelov@gmail.com
ORCID: <https://orcid.org/0000-0003-3062-9478>