The Effects of Therapeutic Exercise for Cardiovascular Rehabilitation in Patients with Inflammatory Rheumatic Diseases: A Narrative Review

Frane Grubišić, Hana Skala Kavanagh, Ines Doko Vajdić and Simeon Grazio

Department of Rheumatology, Physical Medicine and Rehabilitation, Sestre milosrdnice University Hospital Center, Zagreb, Croatia

CORRESPONDENCE TO Frane Grubišić, Department of Rheumatology, Physical Medicine and Rehabilitation, Sestre milosrdnice University Hospital Center, Zagreb, Croatia
+385 1 3787 248
franegrubisic@gmail.com

RECEIVED April 22, 2024
ACCEPTED December 30, 2024

DOI 10.20471/acc.2026.65.01.13

SUMMARY

Inflammatory rheumatic diseases (IRDs), such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) are characterized by functional disability, pain, alteration in body composition and extra-articular comorbidities, among which cardiovascular diseases (CVDs) are the most notable. The affected group of patients is less physically active and exercises less frequently than the general population, possibly due to physical limitations related to their disease. Increasing physical activity can reduce the impact of systemic inflammation. In patients with IRDs and concomitant CVDs, including additional cardiovascular rehabilitation interventions may improve symptoms and patients' overall functioning, increase health-related quality of life and decrease CVD risks.

KEYWORDS

Rheumatoid arthritis; Psoriatic arthritis; Axial spondyloarthritis; Cardiovascular rehabilitation

Introduction

Earlier recognition, improved diagnostics, better access to specialist care and pharmacological treatment (e.g. biologic and targeted synthetic disease-modifying anti-rheumatic drugs (DMARDs)) have significantly improved outcomes in patients with the most common inflammatory rheumatic diseases (IRDs), including decreased levels of inflammation and damage, as well as domains in

the joint field of rheumatologists and rehabilitation medicine specialists, such as disability, work productivity and quality of life.

Another important target in these conditions is the prevention and control of comorbidities. Cardiovascular diseases (CVDs) are among the most notable ones, as they account for a significant part of the still increased morbidity and mortality in IRDs compared to the general population[1-3].

There is abundant evidence that physical activity is crucial in the prevention of arterial hypertension, diabetes and obesity, and even in the reduction of death from CVDs. It improves not only fitness but also quality of life and psychological well-being (anxiety and depression)[4]. This can be applied to patients with IRDs as well.

Apart from trying to achieve disease remission or low disease activity by proper pharmacological treatment, non-pharmacological treatments represent equally important therapeutic modalities. This includes several major interventions: patient education, modifying lifestyle and dietary habits, reducing obesity and encouraging exercise. The latter should be individually tailored and performed under supervision. Considering the recognized risks that obesity carries, as well as the benefits of exercise for the cardiovascular system, the European Alliance of Associations for Rheumatology (EULAR) included physical activity among the recommendations for patients with IRDs[5-7]. There is evidence that cardiomyopathy may be improved by reducing inflammatory activity using drug therapy, while non-pharmacological treatment is equally important, especially in patients in whom biologics or other advanced pharmacological therapies are contraindicated due to a high risk of CVD[8,9].

A combination of these interventions could lead to substantial improvements both in rehabilitation outcomes (e.g. physical function, independence and quality of life) and cardiovascular outcomes (such as improvements in cardiorespiratory fitness)[10,11].

This narrative review will focus on cardiovascular rehabilitation in patients with the most prevalent IRDs — rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) —, as well as its benefits and limitations.

Methods

Our research had two main questions: "To which extent can therapeutic exercise have a positive effect on inflammation in patients with IRDs?"; and "What is the evidence on the effect of cardiorespiratory fitness in patients with rheumatoid arthritis and spondyloarthritis?".

Search strategy

A review of the literature was done using the Scopus and Medline/PubMed databases from September 1, 2003 until December 31, 2023. In order to get as much comprehensive insight into the topic as possible, all types of publications were included in the search (e.g. systematic reviews, narrative reviews, randomized-controlled trials, observational studies, case studies, etc.). Keywords for the search were "rheumatoid arthritis" AND "cardiovascular rehabilitation", "psoriatic arthritis" AND "cardiovascular rehabilitation", "ankylosing spondylitis" AND "cardiovascular rehabilitation", "axial spondyloarthritis" AND "cardiovascular rehabilitation". In order to use two keywords in a single search, the terms were connected by the Boolean operator AND. In total, 77 papers were included in the final version of the manuscript.

Results and discussion

Rheumatoid arthritis

RA is a chronic IRD typically presenting as symmetrical polyarthritis of synovial joints (e.g. radiocarpal joints, metacarpophalangeal joints, knees, etc.), affecting around 1% of the adult working population — predominantly women[6]. Apart from musculoskeletal symptoms, RA is also characterized by systemic and extra-articular symptoms such as fatigue, but also increased atherogenesis and a subsequent elevated risk for CVD. RA is an example of IRD, so it has long been a subject of interest to evaluate the pathogenesis of CV risk, as well as to get better insight into the mechanisms of how exercise influences inflammation. Different mechanisms can explain increased atherosclerosis in RA. One hypothesis is related to the simultaneous effect of arthritis and traditional CV risk factors, such as lipid abnormalities, increased levels of homocysteine, hyperinsulinemia and insulin resistance. On the other hand, studies suggest that systemic inflammation and immune dysregulation play a crucial role in accelerated atherosclerosis[1,9]. A systematic review and meta-analysis performed by Restivo et al. showed that the relative risk of CV events in patients with RA was 1.55 (95% CI: 1.18–2.02)[10]. With exercise, patients can achieve a quick, but also sustained anti-inflammatory response which goes through various physiological mechanisms and, interestingly, is proportional to the intensity of exercise. These mechanisms include the induction of an increase in IL-6 through the amplification of IL-6 mRNA expression, the stimulation of hepatic glycogenolysis and lipolysis to produce more energy for muscles, and the suppression of pro-inflammatory cytokines IL-1 and TNFa. Also, during exercise there is an increase in the anti-inflammatory cytokines IL-10, soluble TNF receptor and IL-1 receptor antagonist. It is believed that the long-term anti-inflammatory effects of exercise are explained by a reduction in the size of adipocytes[11,12]. Moreover, in RA, higher levels of both physical activity and fitness have been associated with reduced insulin resistance (but these mechanisms have not been thoroughly studied in this population), and exercise can modify blood pressure values through different mechanisms (e.g. improved endothelial function, improved resistance to oxidative stress, enhanced baroreceptor sensitivity)[13,14]. RA patients with higher physical activity levels and a higher maximal oxygen uptake have lower blood pressure than RA patients with lower levels of physical activity[15]. The beneficial effects of exercise on lipid-protein changes are achieved in facilitating the synthesis of the antiatherogenic high-density lipoprotein and by increasing the hydrolysis of triglycerides into free fatty acids and glycerol[16]. Overall, studies on RA demonstrate that more physically active patients have significantly better lipid profiles than those who have lower fitness levels[17].

In light of the fact that vascular function may be impaired because of persistent inflammation in RA, it can be significantly improved by exercising for three or six months at intensities of up to 75% of the maximum heart rate, possibly through the effects on increased nitric oxide bioavailability[18]. Therefore, atherosclerosis as the leading cause of CVD could be managed by increasing physical activity and fitness levels.

Evidence on the effect of an exercise program on cardiorespiratory fitness (CRF) in RA patients with higher CVD risk is scarce. A possible reason for that could be the fact that subjects with RA are usually enrolled in clinical studies if they have low CVD risk and better disease control. A study by Sobejana et al. showed that a 12-week medium to high intensity exercise program was safe and improved cardiorespiratory fitness in RA patients with high risk for CVD by 14% with stable C-reactive protein levels in serum, while

withdrawals were not related to exercise[19]. A study by Stavropoulos-Kalinoglou et al. demonstrated significant improvements in aerobic capacity, blood pressure, triglycerides and lipoprotein levels, body mass index, 10-year CVD event probability, CRP level, DAS28 and HAQ in the exercise group compared to the control group. The strongest predictor for the observed improvements in all the assessed CVD risk factors and disease characteristics was change in VO_2 max[20].

A study by Ayeganova et al. showed that in patients with inflammatory arthritis, a 4-week team rehabilitation benefited body composition, levels of physical functioning, activity and CRF for up to 12 months. Measures of physical function and activity were linked to HAQ over time, whereas body composition was linked to CRF[21].

In a study by Peynirci Cersit et al., a supervised exercise program improved physical fitness, disease activity, functional outcomes, systolic blood pressure and resting heart rate, which could reduce the traditional CVD risk factors, although risk reduction could not be demonstrated according to the mSCORE profile in their cohort of patients with RA[22]. Similar conclusions were derived in a study by Cerait et al[23].

Van Zanten et al. performed a study in which the main aim was to explore the effects of exercise and treatment with TNF-alpha inhibitors on CVD risk in RA patients. Outcome measures included markers of disease activity, CVD risk measures and vascular function — all assessed at baseline and after 3 months of exercise intervention. The results of this study showed that both exercise and anti-TNF treatment improved functional ability and fatigue. Anti-TNF treatment was more successful in decreasing inflammation, improving disease activity, functional ability and pain, while exercises resulted in a reduction in overall CVD risk and improvement in vascular function. The conclusion of the study was that exercise and anti-TNF should be combined for optimal CVD risk reduction in patients with RA[24].

Axial Spondyloarthritis

Large-scale meta-analyses reported that hypertension, diabetes mellitus and cardiac diseases are among the most common comorbidities in patients with axSpA, including ankylosing spondylitis (AS). Increased CV risk in AS may be partially explained by an increased prevalence of mainly traditional CV risk factors compared to the general population. However, accelerated atherosclerosis related to chronic systemic inflammation may play an important role in overall CV risk[25,26]. Generally, CVDs are the leading cause of death in patients with AS[27,28]. Mortality from CVDs in AS is as high as 20–40%, while standardized mortality ratios in patients with AS were found to be 1.5–1.9, seemingly as a result of CVDs[29,30]. It is estimated that heart involvement in AS is about 2–10%. While the involvement of the conductive system, aorta, valves and pericardium has already been more extensively described, cardiomyopathy is considered a rare extra-articular manifestation of AS[31-35]. Accelerated atherogenesis in patients with AS is mainly attributed to a lipid metabolism imbalance, combined with chronic systemic inflammation, endothelial dysfunction, enhanced lipid peroxidation and a hyperactive coagulation cascade[36,37]. Some studies showed that despite the low activity of rheumatic disease in patients with AS, subclinical cardiac dysfunction is present[38].

A study by de Mits et al. showed that both strength ($P \leq 0.02$) and mobility ($P \leq 0.001$) were significantly lower for patients with axSpA compared to controls. Strength deficits were comparable between radiographic and non-radiographic groups ($P > 0.05$, except trunk extension ($P = 0.03$)), whereas mobility showed higher deficits in the radiographic group (cervical extension ($P = 0.02$) and rotation ($P = 0.01$), and trunk extension ($P = 0.03$) and rotation ($P = 0.03$)), regardless of symptom duration. Similarly, symptom duration positively affected oxygen pulse ($P = 0.03$),

the relative anaerobic threshold ($P = 0.02$) and aerobic capacity ($P = 0.02$)[39].

According to the recommendations of the Assessment of SpondyloArthritis International Society (ASAS), it is advisable to include physical activity and physical therapy in the treatment of patients with axSpA[40]. In another Cochrane review on exercise programs for AS, which included 14 randomized controlled trials (RCTs) with 1579 participants, the authors concluded that exercise programs may improve function and reduce pain and patient assessment of disease activity. The most frequently used exercises were flexibility, stretching, strength and breathing. The problem with exercises is the lack of an accurate description of the content, dose, intensity, frequency, duration and type of application, and the fact that they are poorly comparable[41]. Just recently, another systematic literature review based on the new ASAS/EULAR recommendations for the management of axSpA was performed. For non-pharmacological treatment, the authors found a moderate or high positive impact on disease activity, function and pain (range in RCTs of exercise for Ankylosing Spondylitis Disease Activity Score (ASDAS): 0.29–0.94, Bath Ankylosing Spondylitis Disease Index (BASDAI): 0.14–1.43, Bath Ankylosing Spondylitis Functional Index (BASFI): 0.04–0.92, Bath Ankylosing Spondylitis Metrology Index (BASMI): 0.06–1.14), although the type, intensity and duration of exercises were very heterogeneous[42].

In a study by Giannotti et al., multimodal treatment supervised by a physiotherapist followed by a home exercise program proved to be an optimal disease management measure in patients with AS[43]. However, a systematic review and meta-analysis by Gravaldi et al. showed that supervised physiotherapy (including cardiorespiratory training) is more effective than usual care in improving disease activity, functional capacity and pain, but did not show superiority of supervised physiotherapy compared to home-based exercise programs[44].

Köseoğlu Tohma et al. pointed to the significance of weight management and prevention of abdominal obesity in CV health of patients with axSpA by improving exercise capacity. They also found HDL-c levels to be significantly lower in the radiographic axSpA group compared to the non-radiographic axSpA group, which can be explained by cumulative inflammation and an altered lipid metabolism in patients with radiographic progression and structural damage[45].

In a more recent study, Giray et al. investigated the impact of an individualized exercise program on CV outcomes. The exercise program was a specially designed program that included stretching, aerobic and strength exercises, and cardiological rehabilitation over 8 weeks. After treatment, the authors noted an improvement in the results of the 6-minute walk test, an increase in metabolic equivalent (MET), and an increase in the myocardial ejection fraction[46].

A randomized study by Niedermann et al. investigated the effect of 12 weeks of CV training on fitness in patients with AS[47]. The fitness level (assessed with a bicycle ergometer) in the training group was significantly higher than in the control group. Improvement in cardiorespiratory fitness is important in reducing cardiovascular morbidity and mortality, and an increase in VO_2 peak corresponds to a decrease in cardiac events in the healthy population[48]. A single blinded randomized controlled pilot study evaluated the efficacy of high intensity exercise on cardiovascular risk and disease activity in patients with axSpA. The exercise plan consisted of 40–60 minutes of supervised training (both endurance and strength) three times a week for 12 weeks. Cardiomyopathy fitness was assessed with a maximal walking treadmill test for peak oxygen uptake (VO_2 peak) estimation. The results showed an improvement in the exercise group in both tools measuring disease activity: the BASDAI and ASDAS score. Also, arterial stiffness was significantly reduced, and significant treatment

effects were seen for VO_2 peak, total body fat, abdominal fat and resting heart rate in the exercise group compared to the control group. This study also showed a decrease in IL-17a and IL-23 in the exercise group compared to the control group[49]. In a systematic review by Verhoeven et al., the authors concluded that aerobic exercises were not more effective than usual physical therapy in reducing disease activity or improving functional status, but they were useful in improving cardiorespiratory outcomes (cardiorespiratory fitness evaluated with VO_2 peak)[50].

A study by Basakci Calik et al. showed significant improvements in BASDAI ($P = 0.002$), BASMI ($P = 0.021$), 6 DYT ($P = 0.036$), VO_2 max ($P = 0.000$), MIP ($P = 0.005$) and MEP ($P = 0.022$) results in the intervention group after 12 weeks of training. When comparing pre-treatment and post-treatment differences, BASDAI ($P = 0.032$) decreased and the VO_2 ($P = 0.001$) max increased, showing significant improvements in the intervention group, and these values were maintained[51].

An assessor-blinded multicenter randomized controlled trial by Sweaas et al. performed on 100 patients with axSpA assessed the effects of cardiorespiratory training and strength exercises at a high intensity on disease activity, inflammatory parameters, physical function and CV health. The authors reported that high-intensity exercise improves disease activity by 23% (for ASDAS estimated mean group difference (95% CI) −0.6 (−0.8 to 0.3), $P < 0.001$). The exercise group improved their VO_2 peak significantly compared to the control group. Together, these improvements prove the safety of high-intensity exercises and efficacy on CV health in patients with axSpA[52].

Psoriatic arthritis

PsA can be a huge burden for patients and their families, especially when it is additionally complicated with CVDs[53]. Some authors found that, in the previous 5 years, the incidence of CVD in PsA patients increased by 43%; more specifically, the incidence of myocardial infarction increased by 68% and of heart failure by 31%[54,55].

Patients with PsA are more commonly obese and have a higher prevalence of hypertension, diabetes mellitus, hyperlipidemia and comorbidities associated with these classic risk factors for CVDs (ischemic heart disease, atherosclerosis, congestive heart failure, peripheral vascular disease and CV accident)[56,57]. These patients also demonstrate an increased prevalence of cardiomyopathy and valvular heart disease[58]. As for CV risk evaluation in PsA, experts suggested the SCORE algorithm in which CV risks are multiplied by 1.5, as was recommended for RA[59,60]. In a multicenter descriptive study of patients with PsA, the authors evaluated carotid artery ultrasound (US) scans in CV risk assessment. Their results showed most abnormalities in US scans in the group with intermediate risk, so they concluded that SCORE charts may underestimate the real CV risk and that a carotid US scan would be advisable in those patients, especially if dyslipidemia, hyperuricemia, axial involvement, or a longstanding skin disease are present[61]. In a recent study by Kavadichanda et al., body composition parameters, serum adipokines and CV risks were observed in PsA and non-psoriatic spondyloarthritis (nPsA–SpA). The authors found that patients with PsA had a higher average carotid intima-media thickness (CIMT) compared to nPsA–SpA patients. However, there are additional unknown factors in PsA resulting in CV diseases besides classic cardiovascular risks. Sarcopenia plays an important role in CV risk due to adipose tissue deposition in skeletal muscles, and this again emphasizes the importance of physical therapy in the prevention of sarcopenia and, consequently, atherosclerosis[62].

CV morbidity in these patients is not mediated solely by the traditional CVD risk factors and it is explained by a complex mechanism involving

chronic systemic inflammation, insulin resistance, dyslipidemia, endothelial dysfunction, angiogenesis and oxidative stress[63]. In patients with PsA and ischemic heart disease, a positive correlation of IL-18 with the atherogenic index (AI) ($\rho = 0.46$ and $\rho = 0.67$) and serum TG concentrations ($\rho = 0.4$ and $\rho = 0.675$), as well as disease activity measured by DAPSA composite index was found, while a negative correlation was found with HDL levels ($\rho = -0.37$ and $\rho = -0.608$)[64].

Metabolic syndrome in PsA is even more present than in SpA and RA[65]. Obesity in PsA is associated with higher disease activity and a reduced response to treatment, and is particularly noted for TNF-alpha inhibitors[66,67].

As for guidelines and CV comorbidities, the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) 2021 guidelines suggest that pharmacological treatment should be chosen according to the individual patient's characteristics and taking into account the presence of CVDs[68]. A Delphi-based consensus of experts for the management of CV comorbidities in PsA patients recommends that rheumatologists advise their patients to do aerobic and strengthening exercises on alternating days as much as possible[69].

Several large studies have shown that patients with psoriasis are more passive than non-psoriatic patients[70]. Many patients avoid sports because of psoriasis alone, and their quality of life measured by the Dermatology Life Quality Index (DLQI) negatively correlates with their level of exercise[71,72]. Psoriasis influences patients' levels of physical activity, and exercise may also influence disease outcomes in a way to improve the disease in patients who are also overweight[73].

Thomsen et al. investigated the effects of high-intensity interval training on a cycle ergometer on CV factors in patients with PsA during 11 weeks. Maximal VO_2, as a predictor of CV morbidity and mortality, was significantly increased after 3 and 9 months in the exercise group (+ 3.72 ml/kg/min CI 95% 2.38–5.06, $P < 0.001$; +3.08 ml/kg/min CI 95% 1.63–4.53, $P < 0.001$) compared to the control group. Truncal fat was significantly reduced after 3 months in the exercise group although it did not show sustained reduction after 9 months (−1.28% CI 95% −2.51 to –0.05, $P = 0.04$)[74,75]. High-intensity physical activity (more than 1 hour per week) additionally reduces the occurrence of psoriasis in obese patients[76].

The commonly reported barriers for physical activity are fatigue and pain[77,78]. The best way to stimulate activity in those patients is to find personal interest and enjoyment in the exercises and to stimulate intrinsic motivation[79].

Conclusion

In conclusion, IRDs are characterized by functional disability, pain, alteration in body composition and extra-articular symptoms, most notably CVDs. The most common among them — such as RA, PsA, AS and axSpA, which were presented in this paper — may be accompanied by CV comorbidities, and research results, though not abundant, show the benefits of rehabilitation interventions on CV health in these patients. To achieve the best possible outcomes, a multidisciplinary approach is necessary, including a physical and rehabilitation medicine specialist and/or a rheumatologist and cardiologist. Although we performed a systematic literature review, a meta-analysis was not conducted due to the heterogeneity of published articles. Still, we believe we provided good insight into this topic. We hope that, in the coming years, we will have more high-quality evidence on the positive effects of rehabilitation on CV conditions in patients with IRDs.

The authors declare no conflicts of interest.

References

1. Hannawi SM, Hannawi H, Al Salmi I. Cardiovascular risk in rheumatoid arthritis: literature review. Oman Med J. 2021;31;36(3):e262. doi: 10.5001/omj.2021.25.
2. Manolis AS, Tzioufas AG. Cardio-rheumatology: Two collaborating disciplines to deal with the enhanced cardiovascular risk in autoimmune rheumatic diseases. Curr Vasc Pharmacol. 2020;18(6):533-537. doi: 10.2174/1570161118666200721145718.
3. Metsios GS, Moe RH, van der Esch M, van Zanten JJCSV, Fenton SAM, Koutedakis Y, et al. The effects of exercise on cardiovascular disease risk factors and cardiovascular physiology in rheumatoid arthritis. Rheumatol Int. 2020;40(3);347-357. doi: 10.1007/s00296-019-04483-6.
4. Warburton DER, Nicol CW, Bredin SSD. Health benefits of physical activity: the evidence. CMAJ. 2006;174(6):801–809. doi: 10.1503/cmaj.051351.
5. GBD 2015 Obesity Collaborators; Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, Lee A, et al. Health effects of overweight and obesity in 195 countries over 25 years. N Engl J Med. 2017;377(1):13–27. doi: 10.1056/NEJMoa1614362.
6. Rausch Osthoff AK, Juhl CB, Knittle K, Dagfinrud H, Hurkmans E, Braun J, et al. Effects of exercise and physical activity promotion: meta-analysis informing the 2018 EULAR recommendations for physical activity in people with rheumatoid arthritis, spondyloarthritis and hip/knee osteoarthritis. RMD Open. 2018;4(2):e000713. doi: 10.1136/rmdopen-2018-000713.
7. Rausch Osthoff AK, Niedermann K, Braun J, Adams J, Brodin N, Dagfinrud H, et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Ann Rheum Dis. 2018;77(9):1251–1260.
8. Metsios GS, Stavropoulos-Kalinoglou A, Treharne GJ, Nevill AM, Sandoo A, Panoulas VF, et al. Disease activity and low physical activity associate with number of hospital admissions and length of hospitalisation in patients with rheumatoid arthritis. Arthritis Res Ther. 2011;13(3):R108. doi: 10.1186/ar3390.
9. Fragoulis GE, Panayotidis I, Nikiphorou E. Cardiovascular risk in rheumatoid arthritis and mechanistic links: from pathophysiology to treatment. Curr Vasc Pharmacol. 2020;18(5):431-446. doi: 10.2174/1570161117666190619143842.
10. Restivo V, Candiloro S, Daidone M, Norrito R, Cataldi M, Minutolo G, et al. A systematic review and meta-analysis of cardiovascular risk in rheumatological disease: symptomatic and non-symptomatic events in rheumatoid arthritis and systemic lupus erythematosus. Autoimmun Rev. 2022;21(1):102925. doi: 10.1016/j.autrev.2021.102925.
11. Saltiel AR, Olefsky JM. Inflammatory mechanisms linking obesity and metabolic disease. J Clin Investig. 2017;127(1):1-4. doi: 10.1172/JCI92035.
12. Benatti FB, Pedersen BK. Exercise as an anti-inflammatory therapy for rheumatic diseases-myokine regulation. Nat Rev Rheumatol. 2015;11(2):86-97. doi: 10.1038/nrrheum.2014.193.
13. Metsios GS, Moe RH, Kitas GD. Exercise and inflammation. Best Pract Res Clin Rheumatol. 2020;34(2):101504. doi: 10.1016/j.berh.2020.101504
14. Hamer M. The anti-hypertensive effects of exercise: integrating acute and chronic mechanisms. Sports Med. 2006;36(2):109-116. doi: 10.2165/00007256-200636020-00002.
15. Metsios GS, Koutedakis Y, Veldhuijzen van Zanten JJ, Stavropoulos-Kalinoglou A, Vitalis P, Duda JL, et al. Cardiorespiratory fitness levels and their association with cardiovascular profile in patients with rheumatoid arthritis: a cross-sectional study. Rheumatology (Oxford). 2015;54(12):2215-2220. doi: 10.1093/rheumatology/kev035.
16. Duggan C, Tapsoba JD, Wang CY, Campbell KL, Foster-Schubert K, Gross MD, et al. Dietary weight loss, exercise, and oxidative stress in postmenopausal women: a randomized controlled trial. Cancer Prev Res (Phila). 2016;9(11):835-843. doi: 10.1158/1940-6207.CAPR-16-0163.
17. Metsios GS, Kitas GD. Physical activity, exercise and rheumatoid arthritis: effectiveness, mechanism and implementation. Best Pract Res Clin Rheumatol. 2018;32:669-682. doi: 10.1016/j.berh.2019.03.013.
18. Sandoo A, Veldhuijzen van Zanten JJ, Metsios GS, Carroll D, Kitas GD. Vascular function

and morphology in rheumatoid arthritis: a systematic review. Rheumatology (Oxford). 2011;50(11):2125-2139. doi: 10.1093/rheumatology/ker275.
19. Sobejana M, van den Hoek J, Metsios GS, Kitas GD, van der Leeden M, Verberne S, et al. Exercise intervention on cardiorespiratory fitness in rheumatoid arthritis patients with high cardiovascular risk: a single-arm pilot study. Clin Rheumatol. 2022;41(12):3725-3734. doi: 10.1007/s10067-022-06343-4.
20. Stavropoulos-Kalinoglou A, Metsios GS, Veldhuijzen van Zanten JJ, Nightingale P, Kitas GD, Koutedakis Y. Individualised aerobic and resistance exercise training improves cardiorespiratory fitness and reduces cardiovascular risk in patients with rheumatoid arthritis. Ann Rheum Dis. 2013;72(11):1819-1825. doi: 10.1136/annrheumdis-2012-202075.
21. Ayeganova S, Wornert M, Hafstrom I. Team rehabilitation in inflammatory arthritis benefits functional outcomes along with improved body composition associated with improved cardiorespiratory fitness. J Rheumatol. 2021;48(9):1371-1378. doi: 10.3899/ jrheum.201301.
22. Peynirci Cerşit H, Yağcı İ, Cerşit S. The improvement in aerobic capacity, disease activity, and function in patients with rheumatoid arthritis following cardiac rehabilitation program: A single-center, controlled study. Turk J Phys Med Rehabil. 2019;66(2):121-133. doi: 10.5606/tftrd.2020.3250.
23. Cerait HP, Yagc I, Cerait S. The improvement in aerobic capacity, disease activity, and function in patients with rheumatoid arthritis following cardiac rehabilitation program: A single-center, controlled study. Turk J Phys Med Rehabil. 2020;66(2):121-133. doi: 10.5606/ TFTRD.2020.3250.
24. Veldhuijzen van Zanten JJCS, Sandoo A, Metsios GS, Stavropoulos-Kalinoglou A, Ntoumanis N, Kitas GD. Comparison of the effects of exercise and anti-TNF treatment on cardiovascular health in rheumatoid arthritis: results from two controlled trials. Rheumatol Int. 2019;39(2):219-225. doi: 10.1007/s00296-018-4183-1.
25. Mathieu S, Soubrier M. Cardiovascular events in ankylosing spondylitis: a 2018 meta-analysis. Ann Rheum Dis. 2019;78(6):e57. doi: 10.1136/annrheumdis-2018-213317.
26. Liew JW, Reveille JD, Castillo M, Sawhney H, Naovarat BS, Heckbert SR, et al. Cardiovascular risk scores in axial spondyloarthritis versus the general population: a cross-sectional study. J Rheumatol. 2021;48(3):361-366. doi: 10.3899/jrheum.200188.
27. Haroon NN, Paterson JM, Li P, Inman RD, Haroon N. Patients with ankylosing spondylitis have increased cardiovascular and cerebrovascular mortality: a population-based study. Ann Intern Med. 2015;163(6):409–416. doi: 10.7326/M14-2470.
28. Dubreuil M, Louie-Gao Q, Peloquin CE, Choi HK, Zhang Y, Neogi T. Risk of myocardial infarction with use of selected non-steroidal anti-inflammatory drugs in patients with spondyloarthritis and osteoarthritis. Ann Rheum Dis. 2018;77(8):1137–1142. doi: 10.1136/annrheumdis-2018-213089.
29. Heeneman S, Daemen MJAP. Cardiovascular risks in spondyloarthritides. Curr Opin Rheumatol. 2007;19(4):358–362. doi: 10.1097/BOR.0b013e328133f58e.
30. Braun J, van den Berg R, Baraliakos X, Boehm H, Burgos-Vargas R, Collantes-Estevez E, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis. 2011;70(6):896–904. doi: 10.1136/ard.2011.151027.
31. Halvorsen S, Vøllestad NK, Provan SA, Semb AG, van der Heijde D, Hagen KB, et al. Cardiorespiratory fitness and cardiovascular risk in patients with ankylosing spondylitis: a cross-sectional comparative study. Arthritis Care Res (Hoboken). 2013;65(6):969–976. doi: 10.1002/acr.21926.
32. Nurmohamed MT, van der Horst-Bruinsma I, Maksymowych WP. Cardiovascular and cerebrovascular diseases in ankylosing spondylitis: current insights. Curr Rheumatol Rep. 2012;14(5):415–421. doi: 10.1007/s11926-012-0270-6.
33. Momeni M, Taylor N, Tehrani M. Cardiopulmonary manifestations of ankylosing spondylitis. Int J Rheumatol. 2011;2011:728471. doi: 10.1155/2011/728471.
34. Ozkan Y. Cardiac involvement in ankylosing spondylitis. J Clin Med Res. 2016;8(6):427–430. doi: 10.14740/jocmr2488w.
35. Papagoras C, Markatseli TE, Saougou I, Alamanos Y, Zikou AK, Voulgari PV, et al. Cardiovascular risk profile in patients with spondyloarthritis.

Joint Bone Spine. 2014;81(1):57–63. doi: 10.1016/j.jbspin.2013.03.019.
36. Sarp Ü, Üstüner E, Kutlay S, Ataman Ş, Kutlay S. Biomarkers of cardiovascular disease in patients with ankylosing spondylitis. Arch Rheumatol. 2020;35(3):435–439. doi: 10.46497/ArchRheumatol.2020.7868.
37. van Eijk IC, Peters MJL, Serné EH, van der Horst-Bruinsma IE, Dijkmans BAC, Smulders YM, et al. Microvascular function is impaired in ankylosing spondylitis and improves after tumour necrosis factor alpha blockade. Ann Rheum Dis. 2009;68(3):362–366. doi: 10.1136/ard.2007.086777.
38. Ozen S, Ozen A, Unal EU, Tufekcioglu O, Ataman S, Yalcin AP. Subclinical cardiac disease in ankylosing spondylitis. Echocardiography. 2018;35(10):1579–1586. doi: 10.1111/echo.14103.
39. De Mits S, Willems MT, Calders P, Danneels L, Varkas G, van den Bosch F, et al. Maximal Exercise Tolerance, Objective Trunk Strength, and Mobility Measurements in Axial Spondyloarthritis. J Rheumatology. 2024;51(6):596-602. doi: 10.3899/jrheum.2023-1046.
40. van der Heijde D, Ramiro S, Landewé R, Baraliakos X, van den Bosch F, Sepriano A, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis. 2017;76(6):978–991. doi: 10.1136/annrheumdis-2016-210770.
41. Regnaux JP, Davergne T, Palazzo C, Roren A, Rannou F, Boutron I, et al. Exercise programmes for ankylosing spondylitis. Cochrane Database Syst Rev. 2019;10(10):CD011321. doi: 10.1002/14651858.CD011321.pub2.
42. Ortolan A, Webers C, Sepriano A, Falzon L, Baraliakos X, Landewé RB, et al. Efficacy and safety of non-pharmacological and non-biological interventions: a systematic literature review informing the 2022 update of the ASAS/EULAR recommendations for the management of axial spondyloarthritis. Ann Rheum Dis. 2023;82(1):142-152. doi: 10.1136/ard-2022-223297.
43. Giannotti E, Trainito S, Arioli G, Rucco V, Masiero S. Effects of physical therapy for the management of patients with ankylosing spondylitis in the biological era. Clin Rheumatol. 2014;33(9):1217–1230. doi: 10.1007/s10067-014-2647-6.
44. Gravaldi LP, Bonetti F, Lezzerini S, de Maio F. Effectiveness of physiotherapy in patients with ankylosing spondylitis: a systematic review and meta-analysis. Healthcare (Basel). 2022;10(1):132. doi: 10.3390/healthcare10010132.
45. Köseoğlu Tohma E, Günendi Z, Özyemişçi Taşkıran Ö, Mengi G, Demirsoy N, Taş N. Exercise capacity in axial spondyloarthritis and associated factors: A cross‐sectional controlled study. Int J Rheum Dis. 2021;24(8):1014–1023. doi: 10.1111/1756-185X.14155.
46. Giray E, Yağcı İ. Cardiac rehabilitation in a patient with ankylosing spondylitis: A single-program, double-effect. Turk J Phys Med Rehabil. 2019;65(2):194–197. doi: 10.5606/tftrd.2019.2401.
47. Niedermann K, Sidelnikov E, Muggli C, Dagfinrud H, Hermann M, Tamborrini G, et al. Effect of cardiovascular training on fitness and perceived disease activity in people with ankylosing spondylitis. Arthritis Care Res (Hoboken). 2013;65(11):1844–1852. doi: 10.1002/acr.22062.
48. Aspenes ST, Nilsen TIL, Skaug EA, Bertheussen GF, Ellingsen Ø, Vatten L, et al. Peak oxygen uptake and cardiovascular risk factors in 4631 healthy women and men. Med Sci Sports Exerc. 2011;43(8):1465–1473. doi: 10.1249/MSS.0b013e31820ca81c.
49. Sveaas SH, Berg IJ, Provan SA, Semb AG, Hagen KB, Vøllestad N, et al. Efficacy of high intensity exercise on disease activity and cardiovascular risk in active axial spondyloarthritis: a randomized controlled pilot study. PLoS One. 2014;9(9):e108688. doi: 10.1371/journal.pone.0108688.
50. Verhoeven F, Guillot X, Prati C, Mougin F, Tordi N, Demougeot C, et al. Aerobic exercise for axial spondyloarthritis – its effects on disease activity and function as compared to standard physiotherapy: A systematic review and meta-analysis. Int J Rheum Dis. 2019;22(2):234–241. doi: 10.1111/1756-185X.13385.
51. Basakci Calik B, Pekesen Kurtca M, Gur Kabul E et al. Investigation of the effectiveness of aerobic exercise training in individuals with ankylosing spondylitis. Mod Rheumatol 2021;31(2):442-450. doi: 10.1080/14397595.2020.1745409.
52. Sveaas SH, Bilberg A, Berg IJ, Provan SA, Rollefstad S, Semb AG, et al. High intensity exercise for 3 months reduces disease activity in axial spondyloarthritis (axSpA): a multicentre randomised trial of 100 patients. Br J Sports Med. 2020;54(5):292–297. doi: 10.1136/bjsports-2018-099943.

53. Lam SH, So H, Cheng IT, Li EK, Wong P, Li TK, et al. Association of C-reactive protein and non-steroidal anti-inflammatory drugs with cardiovascular events in patients with psoriatic arthritis: a time-dependent Cox regression analysis. Ther Adv Musculoskelet Dis. 2021;13:1759720X211027712. doi: 10.1177/1759720X211027712.
54. Polachek A, Touma Z, Anderson M, Eder L. Risk of Cardiovascular Morbidity in Patients With Psoriatic Arthritis: A Meta-Analysis of Observational Studies. Arthritis Care Res (Hoboken). 2017;69(1):67–74. doi: 10.1002/acr.22926.
55. Zheng Z, Guo Q, Ma D, Wang X, Zhang C, Wang H, et al. Related Risk Factors and Treatment Management of Psoriatic Arthritis Complicated With Cardiovascular Disease. Front Cardiovasc Med. 2022;9:835439. doi: 10.3389/fcvm.2022.835439.
56. Verhoven P, Prati C, Demougeot C, Wendling D. Cardiovascular risk in psoriatic arthritis, a narrative review. Joint Bone Spine. 2020:87(5):413-418. doi: 10.2174/1570161117666190619143842.
57. Jamnitski A, Symmons D, Peters MJL, Sattar N, McInnes I, Nurmohamed MT. Cardiovascular comorbidities in patients with psoriatic arthritis: a systematic review. Ann Rheum Dis. 2013;72(2):211–216. doi: 10.1136/annrheumdis-2011-201194.
58. Kibari A, Cohen AD, Gazitt T, Bitterman H, Lavi I, Feldhamer I, et al. Cardiac and cardiovascular morbidities in patients with psoriatic arthritis: a population-based case control study. Clin Rheumatol. 2019;38(8):2069–2075. doi: 10.1007/s10067-019-04528-y.
59. Conroy RM, Pyörälä K, Fitzgerald AP, Sans S, Menotti A, de Backer G, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J. 2003;24(11):987–1003. doi: 10.1016/s0195-668x(03)00114-3.
60. Agca R, Heslinga SC, Rollefstad S, Heslinga M, McInnes IB, Peters MJL, et al. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Ann Rheum Dis. 2017;76(1):17–28. doi: 10.1136/annrheumdis-2016-209775.
61. Martínez-Vidal MP, Andrés M, Jovaní V, Santos-Ramírez C, Romera C, Fernández-Carballido C. Role of carotid ultrasound and systematic coronary risk evaluation charts for the cardiovascular risk stratification of patients with psoriatic arthritis. J Rheumatol. 2020;47(5):682–689. doi: 10.3899/jrheum.181223.
62. Kavadichanda C, Shanoj KC, Ganapathy S, Shah SI, Ananthakrishnan R, Sahoo J, et al. Factors associated with high cardiovascular risk in psoriatic arthritis and non-psoriatic spondyloarthritis. Rheumatol Int. 2022;42(2):251–260. doi: 10.1007/s00296-021-05064-2.
63. Yim KM, Armstrong AW. Updates on cardiovascular comorbidities associated with psoriatic diseases: epidemiology and mechanisms. Rheumatol Int. 2017;37(1):97–105. doi: 10.1007/s00296-016-3487-2.
64. Bonek K, Kuca-Warnawin E, Kornatka A, Zielińska A, Wisłowska M, Kontny E, et al. Associations of IL-18 with altered cardiovascular risk profile in psoriatic arthritis and ankylosing spondylitis. J Clin Med. 2022;11(3):766. doi: 10.3390/jcm11030766.
65. Karmacharya P, Ogdie A, Eder L. Psoriatic arthritis and the association with cardiometabolic disease: a narrative review. Ther Adv Musculoskelet Dis. 2021;13:1759720X21998279. doi: 10.1177/1759720X21998279.
66. Landgren AJ, Bilberg A, Eliasson B, Larsson I, Dehlin M, Jacobsson L, et al. Cardiovascular risk factors are highly overrepresented in Swedish patients with psoriatic arthritis compared with the general population. Scand J Rheumatol. 2020;49(3):195–199. doi: 10.1080/03009742.2019.1672783.
67. Singh S, Facciorusso A, Singh AG, Vande Casteele N, Zarrinpar A, Prokop LJ, et al. Obesity and response to anti-tumor necrosis factor-α agents in patients with select immune-mediated inflammatory diseases: A systematic review and meta-analysis. PLoS One. 2018;13(5):e0195123. doi: 10.1371/journal.pone.0195123.
68. Coates LC, Soriano ER, Corp N, Bertheussen H, Callis Duffin K, Campanholo CB, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. Nat Rev Rheumatol. 2022;18(8):465–479. doi: 10.1038/s41584-022-00798-0.
69. Zarco Montejo P, Almodóvar González R, de Higes-Martínez E, Gorgojo-Martínez JJ, Guijarro Herraiz C, López Navas MJ, et al. Delphi-based recommendations for the management of

cardiovascular comorbidities in patients with psoriatic arthritis and moderate-to-severe psoriasis. Rheumatol Int. 2020;40(6):969–981. doi: 10.1007/s00296-020-04573-w.
70. Schwarz PEH, Pinter A, Melzer N, Barteczek P, Reinhardt M. ERAPSO: revealing the high burden of obesity in german psoriasis patients. Dermatol Ther (Heidelb). 2019;9(3):579–587. doi: 10.1007/s13555-019-0314-1.
71. Ramsay B, O'Reagan M. A survey of the social and psychological effects of psoriasis. Br J Dermatol. 1988;118(2):195–201. doi: 10.1111/j.1365-2133.1988.tb01774.x.
72. Auker L, Cordingley L, Pye SR, Griffiths CEM, Young HS. What are the barriers to physical activity in patients with chronic plaque psoriasis? Br J Dermatol. 2020;183(6):1094–1102. doi: 10.1111/bjd.18979.
73. Yeroushalmi S, Hakimi M, Chung M, Bartholomew E, Bhutani T, Liao W. Psoriasis and Exercise: A Review. Psoriasis (Auckl).2022;12:189–197. doi: 10.2147/ PTT.S349791.
74. Thomsen RS, Nilsen TIL, Haugeberg G, Bye A, Kavanaugh A, Hoff M. Effect of high-intensity interval training on cardiovascular disease risk factors and body composition in psoriatic arthritis: a randomised controlled trial. RMD Open. 2018;4(2):e000729. doi: 10.1136/rmdopen-2018-000729.
75. Kessler J, Chouk M, Ruban T, Prati C, Wendling D, Verhoeven F. Psoriatic arthritis and physical activity: a systematic review. Clin Rheumatol. 2021;40(11):4379–4389. doi: 10.1007/s10067-021-05739-y.
76. Thomsen RS, Nilsen TIL, Haugeberg G, Gulati AM, Kavanaugh A, Hoff M. Adiposity and physical activity as risk factors for developing psoriatic arthritis: longitudinal data from a population-based study in Norway. Arthritis Care Res (Hoboken). 2021;73(3):432–441. doi: 10.1002/acr.24121.
77. Rausch Osthoff AK, Nast I, Niedermann K. Understanding beliefs related to physical activity in people living with axial spondyloarthritis: a theory-informed qualitative study. BMC Rheumatol. 2022;6(1):40. doi: 10.1186/s41927-022-00270-2.
78. Rasmussen JO, Primdahl J, Fick W, Bremander A. Physical activity in people with axial spondyloarthritis and the impact of overall attitudes, barriers, and facilitators: a cross-sectional study. Musculoskeletal Care. 2020;18(4):510–518. doi: 10.1002/msc.1495.
79. Brophy S, Cooksey R, Davies H, Dennis MS, Zhou SM, Siebert S. The effect of physical activity and motivation on function in ankylosing spondylitis: a cohort study. Semin Arthritis Rheum. 2013;42(6):619–626. doi: 10.1016/j.semarthrit.2012.09.007.

SAŽETAK

Učinkovitost terapijskih vježbi za kardiovaskularnu rehabilitaciju bolesnika s upalnim reumatskim bolestima: narativni pregled

Frane Grubišić, Hana Skala Kavanagh, Ines Doko Vajdić i Simeon Grazio

Upalne reumatske bolesti (URB) poput reumatoidnog artritisa (RA), psorijatičnog artritisa (PsA) i aksijalnog spondiloartritisa (axSpA) karakterizirane su funkcionalnom onesposobljenošću, kroničnom boli, promjenama u tjelesnom sastavu i izvanzglobnim komorbiditetima, među kojima su najznačajnije kardiovaskularne bolesti (KVB). Ova skupina bolesnika manje je fizički aktivna i manje vježba u odnosu na opću populaciju, vjerojatno zbog tjelesnih ograničenja vezanih uz njihovu bolest. Povećanje tjelesne aktivnosti može smanjiti utjecaj sistemske upale. U bolesnika s URB i pridruženim KV bolestima uključivanje dodatnih kardiovaskularnih rehabilitacijskih intervencija može smanjiti simptome, poboljšati opće funkcioniranje bolesnika i kvalitetu života vezanu uz zdravlje te smanjiti rizike KV bolesti.

KLJUČNE RIJEČI

Reumatoidni artritis; *Psorijatični artritis*; *Aksijalni spondiloartritis*; *Kardiovaskularna rehabilitacija*