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Effects of physical activity on pain, fatigue, inflammation and cardiovascular risk in rheumatoid arthritis

Małgorzata Wirkijowska

Formmed Center for Treatment of Congenital Defects and Malformations, ul. Warszawska 197D, Babice Nowe

https://orcid.org/0009-0003-5857-965X

wirkijowskam@gmail.com

Jakub Wirkijowski

Independent Public Clinical Hospital of Prof. W. Orlowski, Czerniakowska 231, 00-401, Warsaw, Poland

https://orcid.org/0009-0007-9882-9341

k.wirkijowski0@gmail.com

Paulina Woźniak
Central Clinical Hospital, Banacha 1A, 02-097 Warsaw, Poland
https://orcid.org/0009-0006-9626-1062
paulinawoz777@gmail.com

Wiktoria Gajek-Flanczewska
Central Clinical Hospital, Banacha 1A, 02-097 Warsaw, Poland
https://orcid.org/0009-0004-8875-433X
wiktoria.gajek@onet.eu

Sebastian Flanczewski
Central Clinical Hospital, Banacha 1A, 02-097 Warsaw, Poland
https://orcid.org/0009-0006-8461-2806
flanczewskis@gmail.com

Ewa Wietrzykowska
Municipal Polyclinical Hospital, ul. Niepodległości 44, 10-045 Olsztyn, Poland
https://orcid.org/0009-0009-5510-9007
ewawietrzyk99@gmail.com

Martyna Śliwińska
Regional Center of Blood Donation and Blood Treatment, Saska 63/75, 03-948 Warsaw
https://orcid.org/0009-0008-2757-5660
sliwinskamartyna29@gmail.com

Katarzyna Wójtowicz
Central Clinical Hospital, Banacha 1A, 02-097 Warsaw, Poland
https://orcid.org/0009-0009-3914-7804
wojtowicz.katarzyna14@gmail.com

Agata Walczak
National Medical Institute of the Ministry of the Interior and Administration, Wołoska 137, 02-507, Warsaw, Poland

https://orcid.org/0009-0004-7023-634X
walag2410@gmail.com

Dominika Sobolewska
Municipal Polyclinical Hospital, ul. Niepodległości 44, 10-045 Olsztyn, Poland
https://orcid.org/0009-0004-4048-3489
dn.sobolewska@gmail.com

Anna Podraza
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
https://orcid.org/0009-0008-4214-3882
ania.podraza001@gmail.com

Katarzyna Michalczyk-Fraszka
University Clinical Hospital in Olsztyn, Aleja Warszawska 30, 11-041 Olsztyn, Poland
https://orcid.org/0009-0006-5596-6517
kasia.michalczyk6@gmail.com

ABSTRACT

Introduction and aim of the study: The prevalence of rheumatoid arthritis in our society is relatively high. As a result, the number of people requiring some kind of treatment or improvement in quality of life is also increasing day by day. In our study, we aimed to explore the topic of reducing discomfort associated with this condition. We decided to examine the effects of physical activity on individual complaints and systemic symptoms. We summarised the influence of different exercises on pain, fatigue, inflammation, and the cardiovascular system.

Materials and methods: The authors conducted an extensive review of articles available in PubMed, Google Scholar, UpToDate, Science Direct, and Cochrane databases. The keywords rheumatoid arthritis, physical activity, quality of life, pain, inflammation, fatigue, and cardiovascular diseases were the basis of the review. Studies published between 2004 and 2024 were included.

Results: Most studies emphasized the positive effects of exercise, particularly aerobic and resistance training, on improving the clinical conditions and well-being of patients with rheumatoid arthritis. Nevertheless, the papers with inconsistent results underscored the need to delve further into this topic.

Keywords: Rheumatoid arthritis, physical activity, quality of life, pain, inflammation, fatigue, cardiovascular disease

INTRODUCTION

Rheumatoid arthritis (RA) is one of the most common problems occurring in society in the field of autoimmune diseases. It causes inflammation of the joints, gradually leading to bone resorption, cartilage erosion, and destruction of the affected joints. (1), (2) The most commonly affected areas are the metacarpophalangeal joints, proximal interphalangeal joints, and wrists. Further affected are the metatarsophalangeal joints and the shoulders. (3) The most frequent symptoms manifest as musculoskeletal deficits, such as hand deformities, pain, and reduced grip strength and pinching. (4) The pathogenesis of this disease entity is not fully established. It may have several factors, such as genetic or environmental factors, inflammatory conditions of the synovial membrane and immune processes, or even structural damage. (5) Significant progress has been made during the previous several decades in understanding the mechanisms underlying RA, including the role of specific cytokines, immune cells, and genetic markers. (6)

According to 2019 data, approximately 18 million people are living with rheumatoid arthritis worldwide. At least 13 million of them may benefit from rehabilitation to reduce the severity of their disease symptoms. (7), (8) Furthermore, researchers have shown that RA, like other systemic autoimmune diseases, has a strong association with sex hormones. Consequently, the disease affects women two to three times more often than men. (9)

Regarding physical activity among individuals suffering from RA, it is also important to address the barriers that effectively block patients from exercising. Tuulikki Sokka et al. examined physical activity levels in RA patients from 58 centers in 21 countries. They found that only 13.8 percent of RA patients performed physical activity more than three times a week, the current recommended level. (10)

Among the factors that discourage patients from exercising are those that are universal to the rest of society, such as lack of time and high cost. However, the majority of studies also identified disease-related barriers, in particular, pain, fatigue, and functional disability. Surprisingly, the blockages that prevent people from exercising are similar in those RA patients who exercise regularly and those who do not. (11)

This article aims to review the current state of knowledge on the impact of exercise on the RA course, explore advances in diagnostic and therapeutic approaches, and highlight new strategies to improve patient care.

METHODS

The authors extensively reviewed articles in PubMed, Google Scholar, UpToDate, Science Direct, and Cochrane databases. The keywords rheumatoid arthritis, physical activity, quality of life, pain, inflammation, fatigue, and cardiovascular disease were the basis of the review. Studies published between 2004 and 2024 were included.

PHYSICAL EXERCISE

Workouts can benefit RA symptoms, as activity is a source of stimuli that leads to many adaptations in the patient's physiology. Increasing physical activity levels positively affects both systemic and disease-related symptoms.

Influence on pain

Overall, physical activity leads to an increase in beta-endorphin expression and has an anti-inflammatory effect, which contributes to pain reduction. (12), (13) The American College Rheumatology Guidelines, published in 2022, recommend aerobic exercise for patients with RA. This activity focuses on improving cardiorespiratory fitness (CRF) and muscular endurance, for example, walking, running, cycling, hiking, using an elliptical machine, swimming, rowing, and aerobics. Authors emphasize its effectiveness in improving physical function, but they point out that the effect of aerobic exercise on pain is negligible. (14) There are studies supporting the claim that this form of exercise induces a pain-relieving effect on RA patients. (15), (16) However, Hu et al., in their meta-analysis from 2020, indicated that they cannot conclusively state that aerobic exercise has a significant impact on pain. (17) Strength training aims to increase muscle strength and includes free weights, exercise machines, resistance bands, and pilates. (14) A review from 2004 confirmed that this type of activity may be helpful in pain reduction in individuals suffering from RA. (18) Although Baillet et al., in another review from 2012, didn't report that correlation. (19) In another meta-analysis, resistance training has also been proven to help reduce joint pain and shorten the duration of morning stiffness among patients. (20) In addition, it improves overall health-related quality of life (HR-QoL). It reduces body pain in people with rheumatic diseases, as shown in a meta-analysis by Siateczkowska et al.. (21) Rheumatology Guidelines recommend consistent resistance exercise, as it leads to a reduction in pain. However, this recommendation is conditional as the confidence level of the evidence was considered low. (14) Water exercises combine aerobic and resistance exercise elements, including swimming, water aerobics, water walking, or jogging, which have been shown not to affect pain reduction in RA patients. (22) American College Guidelines agree but point out the positive impact of these exercises on physical functioning. (14) Hand exercises tailored to improve hand mobility and strength (14) were studied in a systematic review of the Cochrane database. (23) Williams et al.'s research included seven studies involving 841 people and found that it was uncertain whether hand exercises alleviate pain in the short term and that there was no difference in its occurrence in the medium and long term. (23) However, according to the Guidelines for Rheumatoid Arthritis, hand therapy is conditionally recommended for RA patients with hand involvement, resulting in pain reduction. (14)

Influence on fatigue

A prevalent symptom in individuals with RA is fatigue, which has been demonstrated in studies from different countries. (24) Among those people, fatigue is the main difficulty, perceived as a reason for their low physical activity and non-participation in exercise programs. (11) Meta-analysis from 2021 found a positive effect of aerobic exercise on reducing fatigue in RA patients when duration time was 3 months but reported no difference after 6 months. The researchers, therefore, classified this recommendation as evidence of very low quality. Furthermore, Hu et al. also proved that combining aerobic exercise with strength training has a fatigue-reducing effect. (17) Interestingly, American College Rheumatology Guidelines state that we may help to control fatigue by using activity pacing. It involves finding a balance between activity and rest to perform an activity. It includes activity planning, energy conservation, modification, and fatigue management techniques. The mentioned technique is safe; however, it is emphasized that there is a lack of evidence to make a conditional recommendation for it. (14)

Influence of inflammation

Patients with rheumatoid arthritis exhibit states of chronic inflammation. A sedentary lifestyle and reduced muscle function, as well as the frequent presence of atherosclerosis and other comorbidities, contribute to this. (25) Many studies have examined the anti-inflammatory effects of physical activity, which have been well-proven in recent years. Exercise can reduce inflammation in both an acute and long-term manner. This phenomenon is dose-dependent, i.e., the higher the intensity, the better the possible effects can be obtained. (25)

IL-1 and IL-6, as well as tumor necrosis factor (TNF-a), are mediators that majorly impact inflammatory symptoms in rheumatoid arthritis. Their production, co-occurrence, and interactions shape the acute phase response. Physical activity has been shown to inhibit the production of IL-1 and tumor necrosis factors, mediators of inflammation and sepsis. During muscle activity, exercise-induced IL-6 is produced. Surprisingly, it is not a pro-inflammatory factor, but it promotes hepatic glycogenolysis and lipolysis, which results in energy delivery to the muscles. An increase in anti-inflammatory IL-1, soluble TNF receptor, and IL-1 receptor antagonist accompanies the increase in exercise-induced IL-6. (25) Thus, this mechanism is responsible for the acute pro-inflammatory effect of workouts.

Another important aspect is the beneficial effect of physical activity on the weight and body composition of patients suffering from RA. Studies indicate that implementing exercise has a long-term positive impact, attributed to reducing inflammation by decreasing the size of adipocytes. (25) Obese patients often present a state of systemic inflammation without inflammatory disorder. (26) It has been proven that inflammatory processes are activated during the expansion and progression of adiposity. (27) Hayashino et al.'s meta-analysis of diabetic patients showed that physical activity reduced adipocyte size. This relationship was noticeable even though diabetes is a low-grade inflammatory disease. (28) Workout triggers the production of myokines, which participate in preventing abdominal obesity. (25) Verheggen et al. proved that exercises lead to loss of visceral fat without weight loss. (29) Hence, the conclusion is that the long-term reduction in inflammation in RA patients who are physically active is due to the reduction in adipocyte size.

Influence on cardiovascular disease

Another important aspect of people suffering from RA is the increased risk of cardiovascular disease (CVD). Myocardial infarction and congestive heart failure due to atherosclerotic events in those patients result in higher cardiovascular morbidity and mortality. (30)

Cardiorespiratory fitness is a commonly used measure of the efficiency of the body delivering oxygen to muscles. Stavropoulos et al. conducted a clinical study that showed that CRF is also a significant indicator of cardiovascular disease. (31)

A recent clinical trial by Bilberg et al. involved 87 people affected by RA and tested for the effects of high-intensity interval training (HIIT) and strength training on cardiovascular health. The study significantly improved CRF, pulse O2, and abdominal fat reduction. (32) Nordén et al. conducted a randomized controlled trial involving 60 patients with inflammatory arthritis who participated in a 12-week HIIT program delivered as part of their primary physiotherapy care. This study also showed improved CRF, which was measured as peak oxygen uptake. The beneficial effect was maintained in these patients for six months. (33) Importantly, none of the studies showed increased disease activity, and the exercises were well tolerated by those participating in the trials. (32), (33) Other studies have

also confirmed that the risk of CVD comorbidities is reduced in RA patients doing aerobic and endurance exercise. (31), (34), (35)

The most relevant risk factors for the development of CVD are insulin resistance, hypertension, and hypercholesterolemia. (36) Workouts can benefit insulin resistance by improving glycemic control, which has been well-studied in the diabetic population. (25) The positive effects of increased physical activity and maximal oxygen uptake on reduced insulin resistance have also been reported among patients with RA. (37), (38) Exercises also reduce elevated blood pressure due to a reduction in peripheral vascular resistance immediately after training. (39), (40) In the long term, working out positively increases baroreceptor sensitivity, endothelial function, vasodilation, and resistance to oxidative stress and reduces peripheral vascular resistance. (40) Physical activity has also been shown to benefit the lipoprotein profile, producing antiatherosclerotic high-density lipoprotein. (41) Studies have indicated this association occurs in hypercholesterolaemic and healthy individuals. (42) Among people suffering from RA, this trend was also confirmed, with more physically active patients showing better lipid profiles compared to those who were less physically active. (37) In conclusion, exercises reduce the risk of comorbid cardiovascular events.

Conclusions

To summarize, physical activity in people with RA has a stimulating effect, leading to many adaptive changes in the patient's body. It positively impacts manifestations directly related to the disease, such as pain or fatigue and systemic symptoms.

Studies we analyzed either show a beneficial influence of physical activity on pain or no difference. This applies to aerobic, strength, and aquatic exercise and is probably due to differences in the methodology used. Among individuals with RA-related hand problems, hand therapy exercises are an effective method to improve pain and hand function. The quality of evidence for this treatment is moderate and low for pain and hand function, respectively. (17)

Regarding fatigue in RA patients, studies have shown that aerobic and strength exercise combinations provide benefits in this area. However, the quality of the evidence is considered to be very low for aerobic exercise and low for its combination with strength exercise. (14)

Workout has also been demonstrated to reduce inflammation in individuals diagnosed with RA. The anti-inflammatory impact is obtained in both an acute and long-term manner and is dose-dependent, so the higher the intensity of the activity, the better results can be obtained. (25)

The other advantage of exercise is that it decreases the prevalence of cardiovascular events due to improved cardiorespiratory fitness. This rate is significantly higher in patients who engage in physical activity. (32), (33) Workout also reduces insulin resistance, hypertension, and hypercholesterolemia, which are the most critical risk factors for the development of CVD. (36)

It should be emphasized that none of the forms of physical training resulted in exacerbation of disease activity or pain. It demonstrates that exercising is safe for patients with RA. (43)

However, it is essential to remember that the types of training should be selected individually for each patient based on their symptoms. This will allow the best results to be achieved. Ultimately, it is crucial to mention that for people with RA, any form of activity will be more profitable than being inactive at all.

Nonetheless, we still have insufficient information to determine the most optimal exercise parameters, such as frequency, intensity, period, duration, and mode. Further research on this subject, especially randomised controlled trials with different training parameters, would allow the establishment of an appropriate exercise programme.

ABBREVIATIONS

RA	Rheumatoid arthritis
CRF	Cardiorespiratory fitness
CVD	Cardiovascular disease
HIIT	High-intensity interval training

DISCLOSURE

Author's contribution:

Conceptualization: Jakub Wirkijowski, Małgorzata Wirkijowska

Methodology: Katarzyna Michalczyk-Fraszka, Sebastian Flanczewski

Software: Ewa Wietrzykowska, Dominika Sobolewska

Check: Katarzyna Wójtowicz, Wiktoria Gajek-Flanczewska

Formal analysis: Anna Podraza, Agata Walczak

Investigation: Jakub Wirkijowski, Małgorzata Wirkijowska

Resources: Martyna Śliwińska, Paulina Woźniak

Data curation: Paulina Woźniak, Anna Podraza

Writing - rough preparation: Jakub Wirkijowski, Małgorzata Wirkijowska

Writing - review and editing: Dominika Sobolewska, Agata Walczak

Visualization: Katarzyna Michalczyk-Fraszka, Martyna Śliwińska

Supervision: Agata Walczak, Wiktoria Gajek-Flanczewska

Project administration: Jakub Wirkijowski, Małgorzata Wirkijowska

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