International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	THE ROLE OF PHYSICAL EXERCISE IN REDUCING INFLAMMATION IN PATIENTS WITH SYSTEMIC SCLEROSIS
ARTICLE INFO	Aleksandra Gradek, Marcin Sawczuk, Dominika Nowak, Adam Zarzycki, Julia Tarnowska, Filip Szydzik, Bartosz Żegleń, Katarzyna Kozon, Monika Grudzień, Anna Leśniewska. (2025) The Role of Physical Exercise in Reducing Inflammation in Patients With Systemic Sclerosis. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3488
DOI	https://doi.org/10.31435/ijitss.3(47).2025.3488
RECEIVED	10 June 2025
ACCEPTED	16 July 2025
PUBLISHED	21 July 2025
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

THE ROLE OF PHYSICAL EXERCISE IN REDUCING INFLAMMATION IN PATIENTS WITH SYSTEMIC SCLEROSIS

Aleksandra Gradek *(Corresponding Author, Email:) aleksandragradek99@gmail.com)*
University Clinical Center in Gdansk, ul. Dębinki 7, 80-952 Gdańsk, Poland
ORCID ID: 0009-0000-5112-3439

Marcin Sawczuk
University Clinical Center in Gdansk, ul. Dębinki 7, 80-952 Gdańsk, Poland
ORCID ID: 0009-0003-1204-0624

Dominika Nowak
University Clinical Hospital No. 4 in Lublin, ul. Doktora Kazimierza Jaczewskiego 8, 20-090 Lublin, Poland
ORCID ID: 0000-0002-0195-1102

Adam Zarzycki
University Clinical Hospital No. 4 in Lublin, ul. Doktora Kazimierza Jaczewskiego 8, 20-090 Lublin, Poland
ORCID ID: 0009-0004-9589-1842

Julia Tarnowska
University Clinical Center in Gdansk, ul. Dębinki 7, 80-952 Gdańsk, Poland
ORCID ID: 0009-0000-3231-669X

Filip Szydzik
University Clinical Center in Gdansk, ul. Dębinki 7, 80-952 Gdańsk, Poland
ORCID ID: 0009-0003-3291-4923

Bartosz Żegleń
University Clinical Center in Gdansk, ul. Dębinki 7, 80-952 Gdańsk, Poland
ORCID ID: 0009-0008-6150-6191

Katarzyna Kozon
Masovian Brodnowski Hospital, ul. Ludwika Kondratowicza 8, 03-242 Warszawa, Poland
ORCID ID: 0009-0009-6536-946X

Monika Grudzień
University Clinical Hospital No. 4 in Lublin, ul. Doktora Kazimierza Jaczewskiego 8, 20-090 Lublin, Poland
ORCID ID: 0000-0002-4855-8308

Anna Leśniewska
Copernicus Hospital in Gdansk, ul. Nowe Ogrody 1/6, 80-803 Gdansk, Poland
ORCID: 0009-0006-3272-3467

ABSTRACT

Introduction and Aim: Systemic sclerosis (SSc) is a chronic, progressive disease that leads to multi-organ failure. In its pathogenesis, inflammation plays a significant role, particularly due to the reduced frequency of regulatory T cells that modulate this process. The aim of this paper was to analyze the available scientific evidence to determine how physical activity influences the reduction of inflammation and its relevance in the therapy of systemic sclerosis.
Results: Systemic sclerosis is associated with a chronic inflammatory state, as indicated by elevated inflammatory markers such as C-reactive protein and ferritin, which correlate with disease severity and symptom progression. Physical activity demonstrates potential in modulating inflammation by lowering inflammatory markers and improving overall bodily function. Regular, supervised exercise in patients with SSc yields measurable benefits, enhancing exercise capacity, muscle strength, quality of life and respiratory function.
Materials and Methods: During the writing of this paper, data analysis was conducted based on a review of available articles published in the PubMed database. The following combination of keywords was used: „sport in systemic sclerosis", „physical exercise in systemic sclerosis", "sport in systemic sclerosis", „inflammation in systemic sclerosis" „inflammation and exercise". The following filters were applied: Free full text, Clinical Trial, Randomized Clinical Trial and within the last 10 years.
Conclusion: Chronic inflammation in systemic sclerosis accelerates the development of complications, while regular, moderate physical activity under supervision can improve physical capacity, microcirculation, and reduce inflammatory symptoms. However, further research is necessary to confirm the beneficial effects of exercise as a therapeutic intervention in systemic sclerosis.

KEYWORDS

Systemic Sclerosis, Inflammation, Sport, Physical Exercise, Exercise

CITATION

Aleksandra Gradek, Marcin Sawczuk, Dominika Nowak, Adam Zarzycki, Julia Tarnowska, Filip Szydzik, Bartosz Żegleń, Katarzyna Kozon, Monika Grudzień, Anna Leśniewska. (2025) The Role of Physical Exercise in Reducing Inflammation in Patients With Systemic Sclerosis. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3488

Introduction.

Systemic sclerosis (SSc) is a chronic autoimmune disease. It is associated with impaired immune system response, excessive collagen production, endothelial dysfunction, and progressive fibrosis, which lead to multi-organ failure. In patients with SSc, regulatory T cells (Tregs), responsible for controlling inflammation and tissue repair, are present at reduced frequency and exhibit impaired function. The pathogenesis of SSc is not yet fully understood, and available therapies do not achieve the desired outcomes. [1,2] Several clinical forms are distinguished: limited cutaneous systemic sclerosis (lcSSc), diffuse cutaneous systemic sclerosis (dcSSc), systemic sclerosis without skin involvement, and systemic sclerosis in overlap syndromes. The most common clinical manifestations include Raynaud's phenomenon, skin thickening, telangiectasia, pulmonary arterial hypertension, and interstitial lung disease. [3] The prevalence of systemic sclerosis is estimated at approximately 0.02%, with a higher incidence in women. In recent years, an improvement in survival has been observed, with a 10-year survival rate of around 66%. [4]

Historically, physical activity accompanied humanity during daily tasks essential for survival, such as obtaining food or water. The survival of the human species depended on the body's adaptation to walking, running, and swimming long distances, which required good physical fitness and respiratory capacity. [5] Currently, regular physical activity is not apparently necessary for survival; however, it offers numerous health benefits, such as lowering blood pressure, preventing atherosclerosis, and reducing insulin resistance, which directly translate into improved quality and length of life. Recommendations regarding physical activity should be communicated to every patient at each visit, based on the principle that it is better to prevent diseases than to treat them. [6]

In this paper, we will analyze and present research findings on the impact of physical activity on reducing inflammation and, consequently, improving the quality of life of patients suffering from systemic sclerosis. We will summarize the etiology, pathophysiology, and treatment methods of systemic sclerosis, as well as the role of exercise in its therapy.

Results

1. Inflammation in the course of systemic sclerosis.

Among patients with systemic sclerosis (SSc), elevated levels of inflammatory markers such as C-reactive protein (CRP) and ferritin are observed. Additionally, increased ferritin levels induce the formation of autoantibodies in SSc. The pathogenesis of SSc involves oncostatin M (OSM), overexpression of the C-C chemokine ligand (CCL24), neutrophil activation, and the formation of neutrophil extracellular traps (NETs). The immune response in SSc is associated with type 2 helper T cells and interleukins IL-4 and IL-13. [7]

Feldmann et al. investigated whether inflammatory arthritis in SSc is associated with increased CRP levels. Approximately 25% of patients with systemic sclerosis exhibit elevated CRP levels. The study participants were divided into two groups: CRP-positive and CRP-negative. They were then assessed using the modified Rodnan skin score (mRSS) and the number of painful/swollen joints. Additionally, examinations of the hands and feet were performed, along with laboratory tests determining CRP levels and antibody status. The results showed that patients with a disease duration of less than 3 years had higher CRP levels and more frequently presented anti-Scl70 antibodies, joint effusion, and synovitis in the wrist and metacarpophalangeal joints. Furthermore, arthritis was more common in the CRP-positive group than in the CRP-negative group. [8]

Stock et al. examined the association between elevated CRP levels and 5-year mortality in patients with interstitial lung disease, including those with systemic sclerosis. They conducted a retrospective study collecting demographic data, CRP levels, and lung function measurements from patients at the Royal Brompton Hospital between 2010 and 2019. Their analysis determined that higher CRP levels were associated with shorter 5-year survival across all studied groups of patients with SSc. [9]

Allanore et al. investigated the effects of treating skin lesions in systemic sclerosis with romilkimab, an antibody neutralizing IL-4 and IL-13, which inhibits fibrotic processes. The study participants were patients with diffuse cutaneous systemic sclerosis (dcSSc) who received subcutaneous romilkimab at a dose of 200 mg or placebo once weekly for 24 weeks. Outcomes were assessed based on changes in the mRSS. This study demonstrated significant effects of romilkimab on skin lesions in early dcSSc, suggesting the involvement of IL-4 and IL-13 in the inflammatory pathogenesis of systemic sclerosis. [7]

Mor et al. described the association between overexpression of the C-C chemokine ligand (CCL24) and inflammatory and fibrotic diseases, including in patients with SSc. To investigate this, they employed therapy with the humanized antibody CM-101, with safety, tolerability, and pharmacokinetic parameters of CM-101 in serum as the primary endpoints. Following administration, levels of biomarkers of inflammation, fibrosis, and collagen turnover in serum decreased in the treated group. [10]

Kule et al. investigated the role of N-formylmethionine (fMet) in the pathogenesis of SSc associated with neutrophil-mediated inflammation. They found elevated levels of neutrophil activation markers (calprotectin, NETs) in patients with SSc compared to the control group, which correlated with the clinical characteristics of the disease. Additionally, patients with SSc exhibited increased fMet levels compared to healthy controls. The collected data clearly indicated that neutrophils undergo activation and cell death in SSc. [11]

Jiang et al. analyzed the clinical significance of serum ferritin as an inflammatory marker in patients with systemic sclerosis. Among the studied SSc patients, serum ferritin levels were significantly higher than in healthy individuals. Additionally, elevated ferritin levels correlated with increased CRP, inflammation, more frequent occurrence of the diffuse cutaneous form of SSc, joint pain, and cardiac involvement. [12]

The pathogenesis of systemic sclerosis is multifactorial. After analyzing numerous studies, it can be concluded that one of the most important pathogenic factors is inflammation, which occurs as a result of abnormalities in various pathophysiological mechanisms. Certainly, further research and technological development are necessary to better understand these relationships and their molecular basis.

2. The role of physical exercise in modulating inflammation.

As we know, chronic inflammation accelerates the aging process, which in turn leads to the earlier onset of age-related diseases such as cancer, cardiovascular diseases, diabetes, and Alzheimer's disease. Since physical activity is a recognized factor in reducing the risk of the aforementioned diseases, there is a growing body of research investigating the impact of physical exercise on reducing inflammation. [13]

Uzeloto et al. investigated the effect of physical exercise on cytokine expression in CD4+ lymphocytes in patients with chronic obstructive pulmonary disease. Twenty-three participants were enrolled in a randomized controlled trial. They were divided into two groups: one underwent strength aerobic training, while eight participants performed breathing exercises. After 8 weeks, peripheral blood was collected from the participants, and flow cytometry was used to analyze inflammatory cytokines, including interleukins 2, 6, 8, 10, 13, 17, and tumor necrosis factor TNF-α from CD4+ lymphocytes. Both the strength training and breathing exercise groups showed a decrease in IL-8 concentration and an increase in IL-13 and TNF-α concentrations. [14]

Sandsdal et al. conducted a randomized, placebo-controlled trial investigating the effects of combining physical exercise with GLP-1 receptor agonist treatment on reducing the severity of metabolic syndrome, abdominal obesity, and inflammation. They assigned 166 obese participants to four random groups: one group performed moderate physical activity, consisting of 150 minutes per week or 75 minutes per week of vigorous aerobic activity or a combination of both; the second group received liraglutide at a dose of 3 mg daily; the third group engaged in moderate physical activity and received 3 mg of liraglutide daily; and the fourth group served as the placebo control. They then measured weight loss and levels of the inflammatory marker high-sensitivity C-reactive protein (hsCRP). After one year, hsCRP levels did not change in the exercise-only and placebo groups. [15]

In their study, Tadayon et al. examined the effect of physical exercise on inflammatory marker levels in female patients with multiple sclerosis. The training lasted eight weeks and included endurance and balance exercises. Blood samples were collected from participants before and after the eight-week training period to measure levels of inflammatory markers: interleukin 6 (IL-6) and C-reactive protein (CRP), as well as the anti-inflammatory cytokine interleukin 10 (IL-10). The results showed a significant decrease in IL-6 and CRP concentrations, while IL-10 levels increased following physical exercise. These findings suggest that physical activity reduces inflammatory markers, thereby contributing to the reduction of inflammation in the body. [16]

Hiensch et al. hypothesized that physical exercise reduces inflammation. They formed a group of 240 women registered for chemotherapy treatment for breast cancer. The participants were randomly divided into three groups: one performed high-intensity interval and resistance training, the second engaged in moderate-intensity aerobic and interval training, and the third did not perform any physical exercise. Blood samples were collected at baseline and after sixteen weeks of training to assess levels of inflammatory markers, including IL-6 and TNF-α. Following chemotherapy, inflammatory marker levels were significantly elevated; however, a smaller increase was observed in the high-intensity exercise group compared to the non-exercising group. No significant differences were found between the aerobic training group and the non-exercising group. This study suggests that intense physical exercise counteracts the increase in inflammation. [17]

After analyzing the above studies, it can be concluded that physical activity offers significant health benefits. However, there is a need for more clinical trials to definitively demonstrate the impact of exercise on modulating inflammatory markers and, consequently, on inhibiting the inflammatory process in the body.

3. The role of physical exercise in the therapy of systemic sclerosis.

Yakut et al. compared the effects of physical exercises performed at home and under the supervision of a physiotherapist in patients with systemic sclerosis. The exercises included respiratory and resistance training. Participants were assessed before the study and after twelve weeks based on functional capacity, lung function, respiratory muscle strength, dyspnea severity, and health-related quality of life (HRQoL) questionnaires. Both the supervised group and the home exercise group showed improvements in functional capacity, muscle strength, and reduced fatigue. However, respiratory function significantly improved only in the supervised group. This study demonstrates that physical exercise can be beneficial in the treatment of systemic sclerosis, particularly when performed under professional supervision. [18]

Waszczykowski et al. investigated how comprehensive upper limb rehabilitation under the supervision of a qualified professional, compared to home exercises, affects long-term limb mobility, hand function including grip strength and range of motion in patients suffering from SSc. Patients were assessed using the following scales and questionnaires: Disability of the Arm, Shoulder and Hand Questionnaire (DAHS), Visual Analog Scale of pain (VAS), Cochin Hand Function Scale (CHFS), Health Assessment Questionnaire

Disability Index (HAQ-DI), Scleroderma-HAQ (SHAQ), Delta Finger to Palm - Kapandji finger opposition test (d-FTP). The supervised exercise group showed improvement in upper limb function compared to the control group performing exercises independently. Moreover, these effects persisted for up to six months, suggesting that regular rehabilitation sessions every 3 to 6 months are recommended to achieve optimal outcomes. [19]

Mitropoulos et al. compared the effects of high-intensity interval training (HIIT) on microcirculation in patients with limited cutaneous systemic sclerosis. Participants were divided into three groups that performed the following exercises for twelve weeks: cycling, arm cranking, and a control group. Physical and functional fitness, transcutaneous oxygen tension (ΔTcpO2), body composition, and patient-assessed quality of life were evaluated before and after the study. Additionally, endothelium-dependent and -independent vasodilation in the index and middle fingers was measured using Laser Doppler Flowmetry (LDF) with acetylcholine and sodium nitroprusside. ΔTcpO2 increased significantly in the arm cranking group ($p < 0.05$). Endothelium-dependent vasodilation was greater in the arm cranking group. Performing aerobic exercises combined with resistance training was effective in improving endothelium-dependent reactivity. Both intervention groups showed improvements in quality of life. These results suggest that interval exercises such as arm cranking may enhance endothelial function and thus provide significant health benefits for patients with limited cutaneous systemic sclerosis. [20,21,22]

Filippetti et al. conducted a randomized controlled trial in patients with systemic sclerosis to compare a home-based exercise program under partial supervision with standard care. Patients performed stationary cycling, upper limb stretching, and muscle strengthening exercises for six months. Assessments were made before the study, after three months, and after six months using the 6-minute walk test, hand mobility in scleroderma test, muscle strength measurements of hand grip, biceps, and triceps, and the HAQ-DI questionnaire assessing disability. After six months, the exercise group increased their average distance in the 6-minute walk test by 46 meters, while the control group decreased by an average of 5 meters. The exercise group also showed increased muscle strength and improved HAQ-DI scores. This study demonstrates that even minimal physical activity can improve endurance and reduce disability in patients with systemic sclerosis. [23]

Cetin et al. examined the impact of Tai Chi training on trunk endurance, balance, fatigue, sleep quality, anxiety, and depression in patients with systemic sclerosis. They divided 28 patients into two groups: the intervention group performed Tai Chi exercises, while the control group did home exercises. Assessments were conducted before and after 10 weeks using the Trunk Lateral Endurance Test, Berg Balance Scale, Pittsburgh Sleep Quality Index, Fatigue Severity Scale and Fatigue Impact Scale, and Hospital Anxiety and Depression Scale. The Tai Chi group showed statistically significant improvements in trunk endurance, balance, sleep quality, and reductions in anxiety and depression. These results suggest that Tai Chi positively affects both somatic and psychological symptoms in systemic sclerosis patients and should be considered as part of rehabilitation programs for this population. [24]

After analyzing the above studies, it can be concluded that physical activity may lead to significant health benefits in patients with systemic sclerosis.

Conclusions

Systemic sclerosis is a disease that causes numerous adverse effects, including limited limb mobility, reduced physical capacity, decreased quality of life, and premature death. Patients with systemic sclerosis exhibit elevated inflammatory markers such as TNF-α, interleukins, and ferritin, with higher ferritin levels correlating with joint pain and cardiac involvement. Chronic inflammation accelerates aging, leading to earlier onset of conditions like hypertension, cancer, diabetes, and neurodegenerative diseases. Treating inflammation in systemic sclerosis reduces fibrosis and serum collagen turnover. Given reports on the beneficial effects of physical exercise in lowering the risk of these diseases, we examined the relationship between exercise and inflammation reduction. Scientific data indicate that moderate, regular training is safe and beneficial, improving microcirculation and overall fitness, which may indirectly reduce inflammation. Additionally, regular physical activity is associated with decreased anxiety and depression, which is especially important for patients with progressive diseases and uncertain prognosis, such as systemic sclerosis. In light of the above results, it appears that regular physical activity, especially when performed under supervision, should be recommended to every patient with systemic sclerosis and individually tailored to the needs and clinical condition of the patient. Such actions can bring significant health benefits, even though they are not associated with any pharmacotherapy. However, larger-scale studies are needed to directly assess the impact of physical exercise on inflammation reduction and inflammatory marker levels in systemic sclerosis patients.

Disclosures

Author's contribution:
Conceptualization: A.G., M.S., D.N., A.Z.
Formal analysis: J.T., F.Sz., B.Ż., K.K., M.G., A.L.
Methodology: A.G., M.S., F.Sz., A.Z., A.L.
Investigation: K.K., D.N., M.G., B.Ż., J.T.
Resources: B.Ż., F.Sz., A.L., A.Z., M.S.
Writing-rough preparation: A.G., A.L., K.K., J.T., D.N., M.G.
Writing-review and editing: A.G., B.Ż., M.S., D.N., A.Z., J.T., F.Sz., K.K.
Supervision: A.G.

All authors have read and agreed with the published version of the manuscript. Funding statement: Not applicable.
Institutional Review Board Statement: Not applicable.
Informed Consent Statement: Not applicable.
Data Availability: Not applicable.
Acknowledgments: Not applicable.
Conflict or interest statement: Authors declare no conflict of interest.

Declaration of generative AI and AI-assisted technologies in the writing process During preparing this work the authors have used ChatGPT for the purpose of improving language and readability. After using this tool, the authors have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

Abbreviations

SSc - systemic sclerosis
Tregs - regulatory T cells
lcSSC - limited cutaneous systemic sclerosis
dcSSc - diffuse cutaneous systemic sclerosis
CRP - C-reactive protein
OSM - oncostatin M
CCL24 - chemokine ligand C-C
IL - 4 interleukin 4
IL - interleukin
fMet - N-formylomethionine
NETs - neutrophil extracellular traps
anty-Scl70 - anti-topoisomerase I antibody
mRSS - modified Rodnan skin score
MTP - metacarpophalangeal joints
TNFα - tumor necrosis factor α
CD4+ - cluster of differentiation 4
GLP-1 - glucagon-like peptide-1
hsCRP - high sensitivity C-reactive protein
HRQol - health-related quality of life
DAHS - Disability of the Arm, Shoulder and Hand Questionnaire
VAS - Visual Analog Scale
CHFS - Cochin Hand Function Scale
HAQ-DI - Health Assessment Questionnaire Disability Index
SHAQ - Scleroderma-HAQ
d-FTP - Delta Finger to Palm
HIIT - high-intensity interval training
ΔTcpO2 - transcutaneous oxygen tension

REFERENCES

1. Barde, F., Lorenzon, R., Vicaut, E., Rivière, S., Cacoub, P., Cacciatore, C., Rosenzwajg, M., Daguenel-Nguyen, A., Fain, O., Klatzmann, D., & Mekinian, A. (2024). Induction of regulatory T cells and efficacy of low-dose interleukin-2 in systemic sclerosis: interventional open-label phase 1-phase 2a study. *RMD open*, *10*(2), e003500. https://doi.org/10.1136/rmdopen-2023-003500
2. Maehara, T., Kaneko, N., Perugino, C. A., Mattoo, H., Kers, J., Allard-Chamard, H., Mahajan, V. S., Liu, H., Murphy, S. J., Ghebremichael, M., Fox, D., Payne, A. S., Lafyatis, R., Stone, J. H., Khanna, D., & Pillai, S. (2020). Cytotoxic CD4+ T lymphocytes may induce endothelial cell apoptosis in systemic sclerosis. *The Journal of clinical investigation*, *130*(5), 2451–2464. https://doi.org/10.1172/JCI131700
3. Twardzina układowa – rekomendacje diagnostyczno-terapeutyczne Polskiego Towarzystwa Dermatologicznego. Część 1: diagnostyka i monitorowanie Dorota Krasowska, Lidia Rudnicka, Aleksandra Dańczak-Pazdrowska, Grażyna Chodorowska, Anna Woźniacka, Anna Lis-Święty, Joanna Czuwara, Joanna Maj, Sławomir Majewski, Anna Sysa-Jędrzejowska, Anna Wojas-Pelc https://www.termedia.pl/Twardzina-ukladowa-rekomendacje-diagnostyczno-terapeutyczne-Polskiego-Towarzystwa-Dermatologicznego-Czesc-1-diagnostyka-i-monitorowanie,56,30931,1,0.html
4. Twardzina układowa - Otylia Kowal-Bielecka, Marek Bielecki https://podyplomie.pl/wiedza/wielka-interna/1377,twardzina-ukladowa
5. Wasfy, M. M., & Baggish, A. L. (2016). Exercise Dose in Clinical Practice. *Circulation*, *133*(23), 2297–2313. https://doi.org/10.1161/CIRCULATIONAHA.116.018093
6. Adamu, B., Sani, M. U., & Abdu, A. (2006). Physical exercise and health: a review. *Nigerian journal of medicine : journal of the National Association of Resident Doctors of Nigeria*, *15*(3), 190–196. https://doi.org/10.4314/njm.v15i3.37214
7. Allanore, Y., Wung, P., Soubrane, C., Esperet, C., Marrache, F., Bejuit, R., Lahmar, A., Khanna, D., Denton, C. P., & Investigators (2020). A randomised, double-blind, placebo-controlled, 24-week, phase II, proof-of-concept study of romilkimab (SAR156597) in early diffuse cutaneous systemic sclerosis. *Annals of the rheumatic diseases*, *79*(12), 1600–1607. https://doi.org/10.1136/annrheumdis-2020-218447
8. Feldmann, D., Jandova, I., Heilmeier, U., Kollert, F., Voll, R. E., & Finzel, S. (2023). Inflammatory arthritis in systemic sclerosis is associated with elevated C-reactive protein and requires musculoskeletal ultrasound for reliable detection. *Frontiers in medicine*, *9*, 933809. https://doi.org/10.3389/fmed.2022.933809
9. Stock, C. J. W., Bray, W. G., Kouranos, V., Jacob, J., Kokosi, M., George, P. M., Chua, F., Wells, A. U., Sestini, P., & Renzoni, E. A. (2024). Serum C-reactive protein is associated with earlier mortality across different interstitial lung diseases. *Respirology (Carlton, Vic.)*, *29*(3), 228–234. https://doi.org/10.1111/resp.14609
10. Mor, A., Friedman, S., Hashmueli, S., Peled, A., Pinzani, M., Frankel, M., & Safadi, R. (2024). Targeting CCL24 in Inflammatory and Fibrotic Diseases: Rationale and Results from Three CM-101 Phase 1 Studies. *Drug safety*, *47*(9), 869–881. https://doi.org/10.1007/s40264-024-01436-2
11. Kuley, R., Stultz, R. D., Duvvuri, B., Wang, T., Fritzler, M. J., Hesselstrand, R., Nelson, J. L., & Lood, C. (2022). N-Formyl Methionine Peptide-Mediated Neutrophil Activation in Systemic Sclerosis. *Frontiers in immunology*, *12*, 785275. https://doi.org/10.3389/fimmu.2021.785275
12. Jiang, Y., Li, X., Zhou, W., Jin, M., Li, S., Lao, Y., Zhu, H., & Wang, J. (2022). Clinical significance of serum ferritin in patients with systemic sclerosis. *Journal of clinical laboratory analysis*, *36*(8), e24597. https://doi.org/10.1002/jcla.24597
13. Zheng, G., Qiu, P., Xia, R., Lin, H., Ye, B., Tao, J., & Chen, L. (2019). Effect of Aerobic Exercise on Inflammatory Markers in Healthy Middle-Aged and Older Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Frontiers in aging neuroscience*, *11*, 98. https://doi.org/10.3389/fnagi.2019.00098
14. Uzeloto, J. S., de Toledo-Arruda, A. C., Silva, B. S. A., Braz, A. M. M., de Lima, F. F., Grigoletto, I., Ramos, D., Golim, M. A., & Ramos, E. M. C. (2022). Effect of physical training on cytokine expression in CD4+ T lymphocytes in subjects with stable COPD. *Therapeutic advances in respiratory disease*, *16*, 17534666221091179. https://doi.org/10.1177/17534666221091179
15. Sandsdal, R. M., Juhl, C. R., Jensen, S. B. K., Lundgren, J. R., Janus, C., Blond, M. B., Rosenkilde, M., Bogh, A. F., Gliemann, L., Jensen, J. B., Antoniades, C., Stallknecht, B. M., Holst, J. J., Madsbad, S., & Torekov, S. S. (2023). Combination of exercise and GLP-1 receptor agonist treatment reduces severity of metabolic syndrome, abdominal obesity, and inflammation: a randomized controlled trial. *Cardiovascular diabetology*, *22*(1), 41. https://doi.org/10.1186/s12933-023-01765-z
16. Tadayon Zadeh, F., Amini, H., Habibi, S., Shahedi, V., Isanejad, A., & Akbarpour, M. (2020). The Effects of 8-Week Combined Exercise Training on Inflammatory Markers in Women with Multiple Sclerosis. *Neuro-degenerative diseases*, *20*(5-6), 212–216. https://doi.org/10.1159/000518580
17. Hiensch, A. E., Mijwel, S., Bargiela, D., Wengström, Y., May, A. M., & Rundqvist, H. (2021). Inflammation Mediates Exercise Effects on Fatigue in Patients with Breast Cancer. *Medicine and science in sports and exercise*, *53*(3), 496–504. https://doi.org/10.1249/MSS.0000000000002490

18. Yakut, H., Özalevli, S., Aktan, R., Özgen Alpaydın, A., Merih Birlik, A., & Can, G. (2021). Effects of supervised exercise program and home exercise program in patients with systemic sclerosis: A randomized controlled trial. *International journal of rheumatic diseases*, *24*(9), 1200–1212. https://doi.org/10.1111/1756-185X.14177
19. Waszczykowski, M., Dziankowska-Bartkowiak, B., Podgórski, M., Fabiś, J., & Waszczykowska, A. (2021). Role and effectiveness of complex and supervised rehabilitation on overall and hand function in systemic sclerosis patients-one-year follow-up study. *Scientific reports*, *11*(1), 15174. https://doi.org/10.1038/s41598-021-94549-y
20. Mitropoulos, A., Gumber, A., Crank, H., Akil, M., & Klonizakis, M. (2018). The effects of upper and lower limb exercise on the microvascular reactivity in limited cutaneous systemic sclerosis patients. *Arthritis research & therapy*, *20*(1), 112. https://doi.org/10.1186/s13075-018-1605-0
21. Mitropoulos, A., Gumber, A., Akil, M., & Klonizakis, M. (2019). Exploring the microcirculatory effects of an exercise programme including aerobic and resistance training in people with limited cutaneous systemic sclerosis. *Microvascular research*, *125*, 103887. https://doi.org/10.1016/j.mvr.2019.103887
22. Mitropoulos, A., Gumber, A., Crank, H., Akil, M., & Klonizakis, M. (2020). Exploring the feasibility of an exercise programme including aerobic and resistance training in people with limited cutaneous systemic sclerosis. *Clinical rheumatology*, *39*(6), 1889–1898. https://doi.org/10.1007/s10067-019-04921-7
23. Filippetti, M., Cazzoletti, L., Zamboni, F., Ferrari, P., Caimmi, C., Smania, N., Tardivo, S., & Ferrari, M. (2020). Effect of a tailored home-based exercise program in patients with systemic sclerosis: A randomized controlled trial. *Scandinavian journal of medicine & science in sports*, *30*(9), 1675–1684. https://doi.org/10.1111/sms.13702
24. Cetin, S. Y., Calik, B. B., & Ayan, A. (2020). Investigation of the effectiveness of Tai Chi exercise program in patients with scleroderma: A randomized controlled study. *Complementary therapies in clinical practice*, *40*, 101181. https://doi.org/10.1016/j.ctcp.2020.101181.