

Comment on: The 2024 British Society for Rheumatology guideline for management of systemic sclerosis.

MITROPOULOS, Alexandros http://orcid.org/0000-0002-9453-0808 and KLONIZAKIS, Markos http://orcid.org/0000-0002-8864-4403

Available from Sheffield Hallam University Research Archive (SHURA) at: https://shura.shu.ac.uk/34604/

This document is the Accepted Version [VoR]

Citation:

MITROPOULOS, Alexandros and KLONIZAKIS, Markos (2024). Comment on: The 2024 British Society for Rheumatology guideline for management of systemic sclerosis. Rheumatology (Oxford, England), keae657. [Article]

Copyright and re-use policy

See http://shura.shu.ac.uk/information.html

Comment on: The 2024 British Society for Rheumatology guideline for management of systemic sclerosis

Alexandros Mitropoulos¹, Markos Klonizakis¹

¹ Lifestyle, Exercise and Nutrition Improvement (LENI) Research Group, Department of Nursing and Midwifery, Sheffield Hallam University, Sheffield, UK

Corresponding author details:

Markos Klonizakis

Postal address: Sheffield Hallam University, Collegiate Hall, Collegiate Crescent Rd, S10 2BP, Sheffield,

Email address: m.klonizakis@shu.ac.uk

ORCID

Alexandros Mitropoulos: https://orcid.org/0000-0002-9453-0808

Markos Klonizakis: https://orcid.org/0000-0002-8864-4403

Dear Editor,

It is with great interest that we read, the recently published article entitled 'The 2024 British Society for Rheumatology guideline for management of systemic sclerosis' by Denton and colleagues¹. Although the article comprehensively describes the medical treatment options for the management of systemic sclerosis (SSc) it only briefly attends to the non-pharmacological, SSc treatments, in general and to exercise in specific. As the latter has demonstrated several benefits in this population, we are writing this short critique to draw your readers' attention to those.

Physical activity and exercise are universally recommended, but for connective tissue diseases, their impact is especially significant in reducing inflammation, aiding recovery, and improving cardiovascular health². Exercise helps address key disease mechanisms by reducing inflammatory and fibrotic pathways in both the blood and tissues, while also enhancing circulation and promoting vascular repair through muscle and blood vessel responses².

Digital microvasculature

Digital vasculopathy leads to Raynaud's phenomenon and digital ischaemia with the concomitant development of severe complications (e.g., ulceration and infection of superficial and deep tissues including gangrene). Exercise (aerobic and resistance training) has demonstrated the potential to improve the digital microvascular function in people with limited cutaneous SSc preventing simultaneously the development of digital ulcers, gangrene and potential concomitant digital amputations^{3,4}.

Cardiac function

Vascular dysfunction and its concomitant multi-organ involvement, including cardiac involvement, affects prognosis in systemic sclerosis (SSc) patients. Exercise in PwSSc has demonstrated to significantly increase the global right ventricular (RV) free wall longitudinal systolic strain, RV free wall longitudinal systolic strain of the basal segment, and global RV four-chamber longitudinal systolic strain as those assessed by a two-dimensional speckle tracking echocardiography (2DSTE) focused on RV morphology and function⁵.

Pain, fatigue, depression and quality of life

A recent six-centre European large cohort (n=170) definitive research clinical trial showed that a combined exercise protocol (see detailed training dose below) in PwSSc can significantly improve two of the most debilitating symptoms in SSc (i.e., pain and fatigue) including depressive symptoms and QoL compared to no exercise (i.e., control group)⁶. Interestingly, most of the improvements were maintained at the 6-month follow up (i.e., 3 months post-exercise intervention).

Physical fitness and functional capacity

Physical fitness is strongly linked to SSc-related QoL leading to an improved daily activities capacity in PwSSc, physical independency, increased energy levels⁷. Regular exercise can also improve the cardiorespiratory fitness (as assessed by peak oxygen uptake tests) and upper body musculoskeletal strength and endurance^{3,6,4}.

Feasibility and safety of exercise

Exercise has demonstrated to be feasible, enjoyable and safe in PwSSc⁷. Namely, a combined exercise protocol was feasible for people with limited cutaneous SSc, with no adverse events, resulting in high adherence and low attrition rates, high enjoyment levels and intentions for future engagement to exercise⁷.

Non-pharmacological recommendations for the management of systemic sclerosis

Exercise has also been recommended as a non-pharmacological treatment for SSc by the recently published European Alliances of Association for Rheumatology (EULAR) recommendations⁸. Exercise has found to significantly improve health-related QoL in PwSSc.

Recommended exercise guidelines

The minimum effective training period and frequency is suggested to be around 12 weeks, twice per week. Although, the included studies have mainly tested an upper body exercise protocol, a whole-body training approach is recommended for future studies and/or strategic exercise treatment. A whole-body training approach would add musculoskeletal strength and endurance to the lower limbs which are commonly used for daily activities.

It is also recommended that the exercise protocol should be a combination of aerobic and resistance training. For the aerobic training, an individualised high-intensity interval training (HIIT; 30 s at 100% of peak power output and 30-s passive recovery) of 30 minutes has been shown to be feasible, safe, enjoyable and effective in PwSSc^{7,6,4,5}. The resistance training an upper body (5 exercises of main muscle groups) circuit (3 circles) training has found to be effective of an intensity of 75–80% of one repetition maximum performing 10 repetitions of each exercise interspersed by 20–30 s to allow for safe movement between exercises. Both for the aerobic and resistance training, the individualised progression shall be monitored based on the daily corresponding heart rate and ratings of perceived exertion via the Borg scale (6-20 points).

It is important to emphasize that exercise shall be treated as a long-term lifestyle change in PwSSc adjunct to pharmacotherapy and not as a short-term (i.e., \geq 12 weeks) temporary prevention and/or rehabilitation non-pharmacological treatment.

Future directions

The current evidence concerning the effects, feasibility and safety of exercise as a non-pharmacological treatment adjunct to pharmacotherapy for PwSSc highlight the need for the implementation of exercise in SSc to improve PwSSc QoL. The extensive inclusion of exercise as a non-pharmacological treatment for the management of SSc in the future British Society for Rheumatology and National Institute for Health and Care Excellence guidelines is warranted.

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

Disclosure statement: The authors have declared no conflicts of interest.

Data availability statement: No new data were generated or analysed in support of this article.

References

- 1. Denton CP, De Lorenzis E, Roblin E, et al. The 2024 british society for rheumatology guideline for management of systemic sclerosis. *Rheumatology (Oxford)*. 2024:keae394. https://doi.org/10.1093/rheumatology/keae394. doi: 10.1093/rheumatology/keae394.
- 2. Pettersson H, Alexanderson H, Poole JL, et al. Exercise as a multi-modal disease-modifying medicine in systemic sclerosis: An introduction by the global fellowship on rehabilitation and exercise in systemic sclerosis (G-FoRSS). *Best Pract Res Clin Rheumatol*. 2021;35(3):101695. doi: 10.1016/j.berh.2021.101695.
- 3. Mitropoulos A, Gumber A, Crank H, Akil M, Klonizakis M. The effects of upper and lower limb exercise on the microvascular reactivity in limited cutaneous systemic sclerosis patients. *Arthritis Res Ther*. 2018;20(1):112–0. doi: 10.1186/s13075-018-1605-0.
- 4. Mitropoulos A, Gumber A, Akil M, Klonizakis M. Exploring the microcirculatory effects of an exercise programme including aerobic and resistance training in people with limited cutaneous systemic sclerosis. *Microvasc Res.* 2019;125:103887. doi: 10.1016/j.mvr.2019.103887.
- 5. Anifanti M, Teloudi A, Mitropoulos A, et al. Right ventricular morphology and function after exercise training in people with systemic sclerosis: A randomized controlled pilot study. *Life (Basel)*. 2023;13(2):545. doi: 10.3390/life13020545.
- 6. Mitropoulos A, Boström C, Mattsson M, et al. Op0117-hpr preliminary findings of a combined high intensity interval training (hiit) programme on pain and fatigue in people with systemic sclerosis: A multi-centre randomised controlled trial. *Ann Rheum Dis.* 2024;83:213. http://ard.bmj.com/content/83/Suppl_1/213.1.abstract. doi: 10.1136/annrheumdis-2024-eular.5604.
- 7. Mitropoulos A, Gumber A, Crank H, Akil M, Klonizakis M. Exploring the feasibility of an exercise programme including aerobic and resistance training in people with limited cutaneous systemic sclerosis. *Clin Rheumatol*. 2020;39(6):1889–1898. doi: 10.1007/s10067-019-04921-7.
- 8. Parodis I, Girard-Guyonvarc'h C, Arnaud L, et al. EULAR recommendations for the non-pharmacological management of systemic lupus erythematosus and systemic sclerosis. *Ann Rheum Dis.* 2024;83(6):720–729. doi: 10.1136/ard-2023-224416.