Patients with rare scleroderma have deadlier organ damage, despite getting standard treatment

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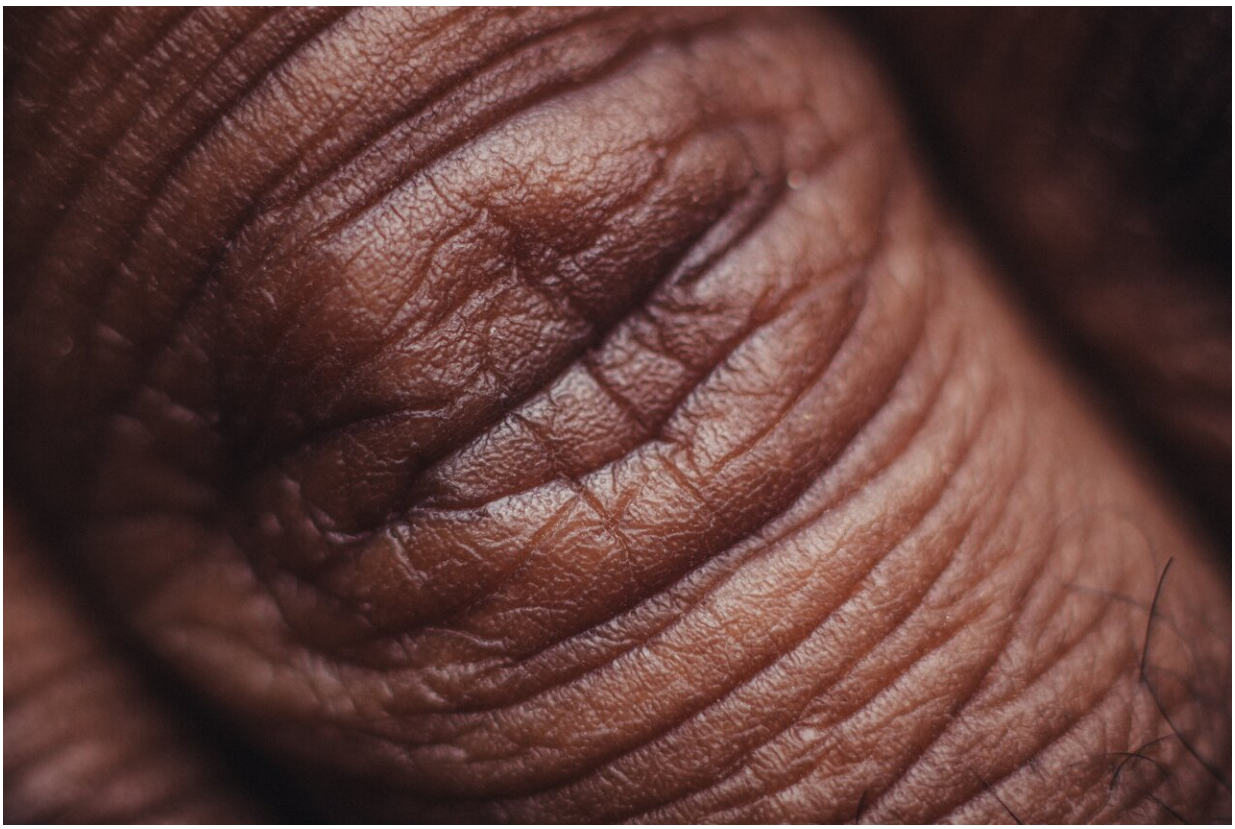

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A Michigan Medicine-led study found that patients in the United States with a rare form of scleroderma have a greater chance of dying from

related kidney, heart and lung problems, despite taking medications used to treat most patients with the disease.

The research team assessed more than 300 patients diagnosed with or at risk for early diffuse systemic sclerosis, a form of the autoimmune condition marked by more tightening of the skin that can also affect internal organs. The participants were treated at 12 different scleroderma centers in the U.S. between 2011 and 2020—one of the largest sub-populations of individuals with the orphan disease ever studied in the U.S.

The results, published in *Arthritis Research & Therapy*, reveal that the immunosuppressive therapies given to most patients with early diffuse systemic sclerosis have minimal effects at changing the progression of the disease in the long term.

"Despite using the standard of care therapies, patients continue to have worse thickening of their skin and internal organ involvement, including lung scarring that has an impact on their disability, function and survival," said Dinesh Khanna, M.B.B.S., M.Sc., corresponding author of the paper, professor of rheumatology at Michigan Medicine and director of U-M's Scleroderma Program. "This leads to significant damage to the internal organs and an increased likelihood of death due to heart, gut and lung involvement."

Nearly two-thirds of the subjects were treated with Mycophenolate Mofetil, commonly referred to as MMF. The immunosuppressive therapy is not FDA-approved but is used by most physicians for the management of the condition.

Of all participants, 23% lost forced vital capacity by 10% or more. Just over 6% of the subjects died from causes including cardiac failure and progressive lung disease.

"This multi-center U.S. cohort demonstrates the progression of skin and lung involvement despite immunosuppressive therapy, and high mortality due to cardiac involvement," said Sara Jaafar, M.D., lead author of the paper and a physician working at the U-M Scleroderma Program. "Our results confirm the overall high progressive trajectory for the worsening of forced vital capacity due to lung scarring, the third most common cause of systemic sclerosis-related deaths."

Two drugs are currently FDA approved to treat lung scarring, or pulmonary fibrosis, that occurs as a result of scleroderma: Nintedanib and tocilizumab. The latter, an anti-inflammatory drug used to treat rheumatoid arthritis, recently showed promising results in preserving lung function in systemic sclerosis patients when detected early.

The trial suggests a window of opportunity for tocilizumab to prevent irreversible health consequences. But Khanna believes this information should also inspire continued, targeted drug development for early diffuse scleroderma.

"This form of scleroderma has the highest fatality rate of any rheumatic disease," he said. "This is a clear opportunity to find new therapies that would improve patients' quality of life, decrease the internal organ involvement, and therefore, improve survival rates."

More information: Sara Jaafar et al, Clinical characteristics, visceral involvement, and mortality in at-risk or early diffuse systemic sclerosis: a longitudinal analysis of an observational prospective multicenter US cohort, *Arthritis Research & Therapy* (2021). DOI: 10.1186/s13075-021-02548-1

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