Annals of the Rheumatic Diseases

The EULAR Journal

BMJ

ard.bmj.com

Regression of skin fibrosis can be predicted using mRSS scores

People with advanced skin fibrosis are more likely to regress in the next year than those with milder skin fibrosis.

INTRODUCTION

Systemic sclerosis is a rare but serious disease of the connective tissue. An initial potential damage to the tissue due to yet unknown triggers causes the activation of the immune system (autoimmunity) and affects the blood vessels leading to scar-like changes (also called fibrosis). This can cause thickening and hardening of the skin or of the internal organs. Skin fibrosis can happen in two different patterns. It can affect just a person's extremities below the elbows and knees (the "limited" disease subtype), or it can extend to other body areas like the upper arms or legs, chest and abdomen (the "diffuse" subtype).

WHAT DID THE AUTHORS HOPE TO FIND?

It is known that after an initial "active" period, skin fibrosis often tends to get better, but this varies between different people. The goal of this project was to see if there are any markers that would help to identify people with diffuse systemic sclerosis who are likely to experience an improvement of their skin fibrosis within a year of first seeing a doctor about their disease. Recognising people who are most likely to improve could help doctors to tailor how they manage patients. It could also help to make clinical trials more efficient, precise and reliable by helping investigators to choose the right endpoints to study, respectively to identify the patients who could benefit most from the study.

WHO WAS STUDIED?

The study looked at 919 people with diffuse systemic sclerosis. All patients were over 18 years of age and had given consent for information from their regular medical visits to be recorded and analysed for scientific purposes.

HOW WAS THE STUDY CONDUCTED?

The data used were from the EUSTAR registry (short for European Scleroderma Trials and Research) – an international, observational cohort. This means that information is collected on a set of patients, but there are no interventions and no medicine under investigation.

This study looked at two consecutive visits 1 year apart. The extent of skin fibrosis was assessed using a score called the modified Rodnan skin score (shortened to mRSS). The mRSS assesses the thickness of the skin in 17 body areas on a scale of 1–3. The higher the score, the more advanced the skin fibrosis is. After 1 year, a decrease in mRSS of more than 5 points or at least 25% was considered a significant improvement.

Eleven "test" parameters thought to possibly play a role in determining whether someone would have skin improvement were chosen by a group of experts in systemic sclerosis. These included clinical signs that a doctor could see in an examination, or laboratory tests such as blood tests. Statistical tests were used to see whether the presence of the selected markers at the first visit was predictive of a person having improvement in their skin fibrosis after 1 year.

WHAT WERE THE MAIN FINDINGS?

Of the 919 patients included, 218 (24%) saw an improvement in their skin fibrosis, and 95 (10%) worsened. Having a high mRSS score at the first visit was the strongest predictor of improved skin fibrosis after 1 year. For example, in this group the authors found that a person with an mRSS score of 22 points at their first visit was more than twice as likely to experience an improvement in his/her skin fibrosis after 1 year than someone with an mRSS score of 14 points. The authors also found that people who did not have signs of inflamation in their tendons or did not have a certain type of antibodies (called Anti-Scl70) in their blood were more likely to see an improvement in their skin fibrosis after 1 year than people who did have these changes.

In addition, the authors could confirm data from a previous study by Maurer et al., showing that patients with a lower mRSS score at the first visit were more likely to experience worsening of their skin fibrosis after 1 year.

Keeping these two complementary roles of mRSS in mind, in this study, the subgroup of patients having an mRSS at the first visit in the range between 18 and 25 points included the highest number of patients at risk of progression and the minimum number of patients likely to spontaneously improve.

ARE THESE FINDINGS NEW?

This is the first report of an evidence-based prediction of skin improvement in a group of people with systemic sclerosis being treated in normal clinics. The most relevant and novel finding is that a higher mRSS skin score at the first visit is the strongest predictor of an improvement in skin fibrosis after 1 year. There was one previous study by Steen et al that looked at predictors of improvement of skin thickening in diffuse SSc, but which only included patients with early disease and higher mRSS, making the comparison of the results difficult.

ARE THERE ANY LIMITATIONS?

One limitation is that, although it is very detailed, the EUSTAR database has some missing values. This can make it difficult to analyse some of the information, but it is normal for a registry to have some information missing. In addition, there might be other factors that we don't yet know about besides the mRSS that are important in working out what will happen to a person's skin fibrosis. Finally, there are geographical differences between systemic sclerosis in different groups of people. As the majority of the EUSTAR database is from Europe, the results will need to be tested in other groups of people to see if they are relevant.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

This information has already been used to help design clinical trials in systemic sclerosis. In clinical trials, it is important to include people who are at risk of their skin fibrosis getting worse, and less those who might naturally get better anyway.

To confirm the results, another study of the analysis is underway. This study is looking at a different group of people with diffuse systemic sclerosis.

WHAT DOES THIS MEAN FOR ME?

If you are a patient with diffuse systemic sclerosis, it is important to realize that there is a "window of opportunity" in the earlier phases of the disease when skin fibrosis is progressing but has not reached very high values to discuss with your treating physician possible treatments. Your doctor will use clinical assessments and laboratory results to attempt to predict how your disease might develop, and decide at which point and which treatments are needed.

FUTHER READING

1. Maurer B, Graf N, Michel BA, *et al*. Prediction of worsening of skin fibrosis in patients with diffuse cutaneous systemic sclerosis using the EUSTAR database. *Ann Rheum Dis* 2015;74:1124–1131.

Date prepared: October 2016

Summary based on research article published on: 25 March 2016

From: Dobrota, R. *et al*. Prediction of improvement in skin fibrosis in diffuse cutaneous systemic sclerosis: a EUSTAR analysis. *Ann Rheum Dis* 2016;75:1743–8. doi: 10.1136/annrheumdis-2015-208024.