New Systemic Sclerosis Classification Created

BY BRUCE JANCIN
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KYOTO — One in five patients with clinical symptoms characteristic of systemic sclerosis do not fit into the popular classification scheme that divides the disease into the diffuse and limited cutaneous subtypes, according to Dr. Thomas Krieg.

This major limitation of the conventional bimodal classification system was among the key findings from the prospective German Network for Systemic Scleroderma registry, which includes 2,007 systemic sclerosis patients at 41 centers, Dr. Krieg said at an international investigative dermatology meeting.

The discovery that so many patients were excluded under the conventional two-subtype scheme prompted a joint committee of German dermatologists and rheumatologists who oversee the registry to create a new, more inclusive classification system by adding three more systemic sclerosis disease subtypes: overlap syndrome, undifferentiated scleroderma, and scleroderma sine scleroderma, explained Dr. Krieg, a dermatologist at the University of Cologne (Germany).

Overlap syndrome was defined as a disease feature major syndrome of scleroderma simultaneously with those of other autoimmune diseases such as dermatomyositis, lupus erythematosus, or Sjögren's syndrome.

Scleroderma sine scleroderma consists of Raynaud's phenomenon, pulmonary arterial hypertension, and cardiac or gastrointestinal involvement in the absence of skin alterations.

Undifferentiated scleroderma was defined as Raynaud's phenomenon and at least one additional major feature of systemic sclerosis in patients not meeting the full American College of Rheumatology criteria.

Such features include nail-fold capillary changes, pulmonary hypertension, puffy fingers, or having scleroderma-specific autoantibodies.

Using the extended classification, 48% of the 2,007 patients have the limited cutaneous systemic sclerosis subtype, 31% have the diffuse cutaneous subtype, 11% have overlap syndrome, 8% have undifferentiated scleroderma, and less than 2% have scleroderma sine scleroderma, Dr. Krieg reported at the meeting of the European Society for Dermatological Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

The uniquely large and inclusive scleroderma registry has had surprising findings, said Dr. Krieg.

A family history of rheumatic diseases, present in almost 20% of patients, was associated with a significantly younger age of symptom identification by 1.5 years, along with a significantly earlier age at the onset of internal organ involvement. This suggests the importance of shared genes in the pathophysiology of a range of rheumatic diseases, according to Dr. Krieg.

Patients who had overlap syndrome were more frequently managed by dermatologists and rheumatologists, but the nearly 80% of registry participants with the diffuse or limited cutaneous subtypes were seen equally by the two specialties.

German patients with pulmonary hypertension, pulmonary fibrosis, digital ulcers, or conduction blocks were equally likely to be managed by dermatologists and rheumatologists, however, those with prominent gastrointestinal or musculoskeletal symptoms were more often cared for by rheumatologists.

The authors also noted a lack of published evidence that corticosteroids or immunosuppressive agents are effective in systemic sclerosis, Dr. Krieg said, 48% of patients treated by rheumatologists received steroids and 46% received immunosuppressive drugs, compared with 33% and 25%, respectively, of patients treated by dermatologists. Dr. Krieg said that he and his coworkers plan to pursue these specialty-based differences in treatment preferences by using them as the basis for controlled clinical trials.

The prevalence of joint contractures, nail-fold capillary changes, pulmonary fibrosis, and stom- ach and intestinal involvement rose significantly within 1 year of follow-up. Rates of renal involvement and pulmonary hypertension remained stable.

Of all the patients, 60% had esophageal involvement and 50% had musculoskeletal involvement. Pulmonary fibrosis was present in more than 33% of the patients, oral mastectomy involvement in 25%, involvement with the heart in 15%, the stomach in 15%, and the kidneys in 10%.

The specific organs involved varied according to disease subtype. Kidney, heart, and lung involvement were most common in the diffuse cutaneous subset. For example, the frequency of pulmonary fibrosis was 61% in the diffuse subgroup, compared with 31% in overlap syndrome and 24% in limited cutaneous systemic sclerosis. Musculoskeletal involvement was most common in overlap syndrome, with 69% of patients affected.

The systemic sclerosis registry is still ongoing.

It is supported by the German Federal Ministry of Education and Research.

SSc Trend in Eastern Europe Not Explained by Geography

BY LEANNE SULLIVAN
Associate Editor

Patients who have severe manifestations of systemic sclerosis are seen more often in Eastern Europe than in other parts of Europe, according to a recent large database study.

However, referral bias precluded the identification of genetic or environmental factors contributing to the disease, wrote the authors.

Baseline data from the European League Against Rheumatism Scleroderma Trials and Research database were used to identify 3,661 systemic sclerosis (SSc) patients from a total of 61 European cities.

Of these, a total of 1,390 (38%) had diffuse systemic sclerosis and 2,271 (62%) had limited systemic sclerosis. The specific type of systemic sclerosis was unknown for just eight patients.

The mean age of all the patients was 55 years, and 87% were female, according to Dr. Ulrich A. Walker, of the Department of Rheumatology at the University of Basel (Switzerland), and his coworkers on the study.

In an attempt to identify geographic, genetic, or environmental factors underly- ing the disease, the researchers analyzed data from 2004-2007 to discover whether there were any specific geographic differences in systemic sclerosis organ involvement as reflected by the presence of anticitrullinated autoantibodies and antitopoisomerase 1 (Scl-70).


On bivariate analysis, no association was found between clinical subtype or autoantibodies and geographic location.

However, one interesting finding was that there were more female patients with systemic sclerosis found in Western regions.

Additionally, Scl-70 was found more frequently in patients in Eastern Europe, the researchers said.

For partial correlations, data were adjusted for variables previously shown to determine particular organ manifesta- tions, including autoantibody status, clinical subtype (either diffuse or limited), and the age at onset of Raynaud's phenomenon.

The association between female patients and Western European centers remained significant after adjustment for autoantibody status.

However, the link did not remain significant after subsequent adjustment for clinical subset.

“The highest correlation coefficient between disease presentations and geo-