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OP0251

THE EULAR SYSTEMIC SCLEROSIS IMPACT OF DISEASE (SCLEROID) SCORE – A NEW PATIENT-REPORTED OUTCOME MEASURE FOR PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Patient reported outcome measures (PROM) are important for clinical practice and research. Given the unmet need for a comprehensive PROM for systemic sclerosis (SSc), the ScleroID questionnaire was developed by a joint team of patients with SSc and medical experts. This is intended as a brief, specific, patient-derived, disease impact score for research and clinical use in SSc.

Objectives: Here, we present the validation and final version of the ScleroID.

Methods: This EULAR-endorsed project involves 9 European expert SSc centers. Patients fulfilling the ACR/EULAR 2013 criteria were prospectively included since 05/16 in a large observational cohort study. Patients completed the ScleroID and comparators SHAQ, EQ5D, SF36. They also weighted the 10 dimensions of the ScleroID by distributing 100 points according to the perceived impact on their health. The final score calculation is based on the ranking of the weights. The validation study included a reliability arm and a longitudinal arm, looking at sensitivity to change at follow-up.

Results: Of the 472 patients included at baseline, 109 patients also had a reliability visit and 113 patients a follow-up visit. 84.5% of patients were female, 29.8% had diffuse SSc, mean age was 54.6 years, and mean disease duration 9.5 years. The highest weights were assigned by the patients to Raynaud's phenomenon, fatigue, hand function and pain, confirming our previous results. The total ScleroID score showed good Spearman correlation coefficients with the comparators (SHAQ, 0.73; EQ5D -0.48; Patient's global assessment, VAS 0.77; HAQ-DI 0.62; SF36 physical score -0.62; each p<0.001). The internal consistency was good: Cronbach's alpha 0.866, similar to SS-HAQ (0.88) and higher than EQ5D (0.77). The ScleroID had a very good reliability: intra-class correlation coefficient 0.839 (ranging 0.608 to 0.788 for the individual items), superior to all comparators. Twenty of 113 patients reported a change in their disease status at follow up. Sensitivity to change: the standardized response mean was 0.34 for the total ScleroID score and highest for lower GI (0.633) and life choices domains (0.521), superior to all other PROM. Figure 1 shows the final ScleroID.

The EULAR Scleroderma Impact of Disease Score (ScleroID)

How much have the different aspects of systemic sclerosis affected you during the last week? Please mark your responses on the scale by choosing the appropriate number for each of the following dimensions:

Raynaud's phenomenon:

Circle the number that best describes the severity of your Raynaud's phenomenon during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Hand function:

Circle the number that best describes your hand function limitations due to your systemic sclerosis during the last week:

No limitation 0 1 2 3 4 5 6 7 8 9 10 Extreme limitation

Upper gastrointestinal tract symptoms (e.g. swallowing difficulties, reflux, vomiting):

Circle the number that best describes the severity of your upper gastrointestinal tract symptoms due to your systemic sclerosis during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Pain:

Circle the number that best describes the pain you felt due to your systemic sclerosis during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Fatigue:

Circle the number that best describes the impact of overall fatigue due to your systemic sclerosis during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Lower gastrointestinal tract symptoms (e.g. bloating, diarrhea, constipation, anal incontinence):

Circle the number that best describes the severity of lower gastrointestinal tract symptoms during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Limitations of life choices and activities (e.g. social life, personal care, work):

Circle the number that best describes how severe the limitations of life choices and activities due to your systemic sclerosis were during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Body mobility:

Circle the number that best describes how much your body mobility was affected due to your systemic sclerosis during the last week:

Not affected 0 1 2 3 4 5 6 7 8 9 10 Extremely affected

Breathlessness:

Circle the number that best describes how severe your breathlessness due to systemic sclerosis was during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Digital ulcers:

Circle the number that best describes how much your digital ulcers affected you overall during the last week:

None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Figure 1.

Conclusion: The EULAR ScleroID is a novel PROM designed for use in clinical practice and clinical trials to reflect the disease impact of SSc, showing good performance in the validation study. Importantly, Raynaud syndrome, impaired hand function, pain and fatigue were the main patient reported drivers of disease impact.

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OP0252

CIRCULATING COLLAGEN TURNOVER MARKERS ARE SPECIFICALLY CHANGED IN VERY EARLY SYSTEMIC SCLEROSIS

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Background: Timely diagnosis of patients with very early systemic sclerosis (veSSc) is essential for their personalized and optimal management. We hypothesise that changes in serum-based extracellular matrix (ECM) turnover biomarkers are already detectable in patients with veSSc, even before occurrence of specific clinical signs.

Objectives: To investigate circulating ECM turnover markers as potential biomarkers for veSSc.

Methods: Patients with veSSc, n=42, defined as presence of Raynaud's syndrome and at least one of puffy fingers, positive antinuclear antibodies or pathological nailfold capillaroscopy, who did not meet any classification criteria for SSc, were compared to healthy controls (HC, n=29). Longitudinal assessment, data and sera collection were conducted by EUSTAR standards. ECM-degradation (BGM, C3M, C4M, C6M) and ECM-formation biomarkers (PRO-C3, PRO-C4, PRO-C5) were measured in serum using ELISA assays. The statistical analyses included Mann-Whitney U, Spearman correlation and ROC analysis. Using Kaplan-Meier plots and univariable Cox regression, we explored if biomarkers can predict progression towards definite SSc (fulfillment of ACR/EULAR criteria or minimum two points increase in the criteria score) during the longitudinal follow-up.

Results: Compared to HC, veSSc patients showed a deregulated turnover of type III and IV collagen, with higher degradation (higher C3M, C4M, both $p < 0.0001$ and PRO-C3, $p = 0.004$, Figure 1a, resulting in lower turnover ratios PRO-C3/C3M and PRO-C4/C4M, both $p < 0.0001$). The biglycan degradation biomarker BGM was also higher in veSSc ($p = 0.006$), whereas the degradation biomarker for type VI collagen, C6M, was lower than in HC ($p = 0.002$). In the ROC analysis, biomarkers of type III and IV collagen distinguished between veSSc and HC: C3M, AUC=0.95, $p < 0.0001$; C4M, AUC=0.97, $p < 0.0001$; turnover ratios PRO-C3/C3M, AUC=0.80, $p < 0.0001$; PRO-C4/C4M, AUC=0.97; $p < 0.0001$ (Figure 1b).

Median follow up was 4.5 years (range 0.5-7.9 years), mean age was 50 ± 2.2 years, 88% female gender, 24% with puffy fingers, 92% were ANA positive, 64% had an abnormal capillaroscopy, none had organ involvement or skin fibrosis. 14/42 veSSc patients fulfilled the ACR/EULAR classification criteria at follow-up (time to fulfilment of criteria ranged between 0.5 and 6.8 years from inclusion) and in addition, 18/42 veSSc patients gained at least two classification criteria-points. This resulted in 14, respectively 18 progressors for the longitudinal analysis. However, in univariable Cox regression, the baseline levels of the markers did not predict progression over time.

Figure 1a. Levels of biomarkers in healthy controls (HC), and very early SSc (veSSc)

Figure 1b. ROC analysis in healthy controls (HC) vs. very early SSc (veSSc)

Conclusion: ECM turnover is already altered in veSSc patients compared to HC. Biomarkers of type III and IV collagen distinguished between veSSc patients and HC, which may indicate them as potential biomarkers for the detection of veSSc in addition to the established immunological and capillaroscopic criteria.

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OP0253

AUTOANTIBODY STATUS IN DERMATOMYOSITIS AND POLYMYOSITIS PATIENTS DEFINES BOTH CANCER RISK AND SURVIVAL WITH ANA NEGATIVITY IN CASES WITH CONCOMITANT CANCER HAVING A WORSE SURVIVAL

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Background: We previously reported that ANA-negative cases with systemic sclerosis (SSc) and concomitant cancer had a worse survival than ANA-positive cases with associated cancer possibly suggesting that humoral mediated autoimmunity conferred a survival advantage (1). Dermatomyositis (DM) and polymyositis (PM) are two immune-mediated myopathies associated with numerous autoantibodies.

Objectives: The present large-scale, population-based study tested the hypothesis that humoral autoimmunity associated with cancer in solid/haematological malignancies impacted on DM/PM patient survival.

Methods: Over 2000 cases with either DM or PM were recruited from the Clalit Health Service (CHS) chronic diseases registry, one of the largest healthcare maintenance Israeli organization, serving approximately half of the entire country's population. Over 10000 matched controls were recruited. The data collected range from 2000 to 2018.

Results: Altogether 12,278 subjects were recruited (2,085 cases, and 10,193 controls, 5,042 males, 41.1%, and 7,236 females, 58.9%). Among cases, 1,475 individuals (70.7%) were diagnosed with DM, whereas 610 (29.3%) with PM. Mean age was 47.81 ± 22.51 years. 1,379 cases of cancers (11.2%) were diagnosed. At the univariate analysis and as expected, the rate of malignancies was