Significant weight loss in systemic sclerosis: a study from the EULAR Scleroderma Trials and Research (EUSTAR) database

Gastrointestinal (GI) involvement is almost universal in patients with systemic sclerosis (SSc) and is associated with significant disease-related morbidity and mortality.[1] The entire GI tract can be involved and other disease features (eg, low mood, terminal organ failure and functional hand impairment) can result in significant nutritional impairment. Severe GI involvement has been reported to occur in ~10% of patients with SSc and often occurs early in the course of the disease.[2] However, identification of patients at high risk of clinically significant weight loss is extremely challenging, including from the high prevalence of GI symptoms in patients with SSc. Therefore, there is a need to understand high-risk patients including potentially modifiable risk factors, with a view to early intervention strategies. Against this background, the aim of this study was to examine potential clinical risk factors of significant weight loss in patients with SSc.

We performed an analysis of patients with SSc enrolled in the multinational, longitudinal European League Against Rheumatism (EULAR) Scleroderma Trials and Research (EUSTAR) database. In our study, we defined significant weight loss as 4.5 kg and/or least 5% of their body weight at 5 months onwards.[3] Patients with a recorded second visit after 3 months and before 12 months were included in the analysis. We adopted a pragmatic approach (relevant to clinical practice) in order to identify sufficient numbers of patients with a clinical diagnosis of SSc and therefore we examined all eligible patients enrolled in the EUSTAR database (~15% did not fulfil the American College of Rheumatology (ACR)/EULAR SSc classification criteria). We included all those for whom we had enough data to meet (or not meet) the weight loss criteria. To compare characteristics between patients with significant weight loss versus those who did not significantly lose weight we used a χ^2 test of independence for categorical variables, Mann-Whitney test for non-normally distributed continuous variables and an independent samples t-test for the only normally distributed continuous variable age. All statistical analyses were conducted using Stata V.14.

We compared 438 patients with significant weight loss compared with 3169 patients without significant weight loss. The median (IQR) significant and relative weight loss was 6 (4.3–8) kg and 8 (6–12)%, respectively. No difference in age was observed between the groups at baseline (54.1 vs 54.6 years). Clinical features (table 1) associated with significant weight loss were male sex, diffuse cutaneous SSc, digital ulcer disease, shorter disease duration, elevated erythrocyte sedimentation rate (ESR)/C-reactive protein, elevated creatine kinase (CK), pulmonary hypertension, abnormal diastolic dysfunction and interstitial lung disease. After using Holm-Bonferroni correction to account for multiple testing, only shorter disease duration, ESR, elevated CK, pulmonary hypertension and interstitial lung disease remained statistically significant. GI (oesophageal, stomach and intestinal) symptoms were not associated with significant weight loss.

Our study has a number of important considerations, many of which are related to undertaking registry-based research.[4] A key strength of our study is that we examined clinical data including investigations which are collected in routine clinical practice. Of note, the predictor of malnutrition in systemic sclerosis has been recently proposed as a validated score of future weight loss in SSc.[5] However, this employs the malnutrition universal screening tool (including calculation of body mass index) and measurement of serum adiponectin to lectin ratio.

In conclusion, our study has identified a number of clinically relevant associations with significant weight loss in patients with SSc. Our findings suggest that the presence of GI symptoms is insensitive to identify patients at high risk of significant weight loss. Further research is required to confirm these findings including prospective studies to develop predictive models for routine clinical practice and to examine potential biomarkers of significant weight loss in SSc.

Table 1 Baseline characteristics of patients with and without significant weight loss

	Significant weight loss (n=438)	Non-significant weight loss (n=3169)	P value
Age (mean, SD)	54.1 (14.5)	54.6 (13.5)	0.331
Sex (female) %	349 (80%)	2658 (84%)	0.022
Disease subtype			0.009
Diffuse	109 (25%)	616 (19%)	
Limited	229 (52%)	1876 (59%)	
Digital ulcers (current/previous)	232 (51%)	1452 (45%)	0.017
mRSS (median (IQR))	7 (2 to 15)	8 (4 to 14)	0.685
Disease duration (median (IQR))	1697 (577 to 3631)	1826.5 (726 to 4015)	0.002
Raynaud's phenomenon	419 (95%)	3036 (96%)	0.940
ANA positive	405 (92%)	2947 (93%)	0.748
Anticentromere positive	138 (31%)	1026 (32%)	0.865
Anti-Scl-70 positive	155 (35%)	1075 (34%)	0.805
Anti-U1-RNP positive	14 (3%)	70 (2%)	0.418
ESR (mm in first hour)	19 (10 to 32.5)	15 (8 to 27)	<0.001
CRP (mg/L)	3 (1 to 7.5)	5.1 (1 to 5.4)	0.029
Elevated CK	59 (13%)	250 (8%)	<0.001
Pulmonary hypertension	82 (19%)	407 (13%)	<0.001
Cardiac conduction blocks	53 (12%)	309 (10%)	0.189
Abnormal diastolic function	90 (21%)	517 (16%)	0.010
Synovitis	60 (14%)	405 (13%)	0.570
Lung disease/ILD	57 (13%)	265 (8%)	0.001
GI symptoms			
Reflux	279 (64%)	1946 (61%)	0.347
Vomiting	106 (24%)	688 (22%)	0.502
Constipation	115 (26%)	734 (23%)	0.368

Organ involvement is collected in the MEDS of the EULAR Scleroderma Trials and Research database.[6] Lung disease/ILD was defined as forced vital capacity (FVC) <70%. P values are presented as uncorrected values for multiple testing due to the exploratory nature of the analysis. Associations of significant weight loss after application of Holm-Bonferroni correction are presented within the body of the text. ANA, anti-nuclear antibody; CK, creatine kinase; CRP, C-reactive protein; GI, gastrointestinal; ILD, interstitial lung disease; MEDS, minimal essential data set; mRSS, modified Rodnan skin score.

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