Acknowledgements: NIL.
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2025-eular.B2137

ABS0574

CHARACTERIZING AND PREDICTING GASTROINTESTINAL INVOLVEMENT IN SYSTEMIC SCLEROSIS: DATA FROM THE NATIONAL SYSTEMIC SCLEROSIS PROGRESSION INVESTIGATION (SPRING) REGISTRY OF THE ITALIAN SOCIETY FOR RHEUMATOLOGY

Keywords: Gastrointestinal tract, Real-world evidence, Prognostic factors, Registries, Observational studies/registry

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Background: Over 80% of systemic sclerosis (SSc) patients are affected by the gastrointestinal (GI) tract, causing significant morbidity and ranking as the third leading cause of death. Symptoms vary widely, affecting any part of the GI tract from the early phases of the disease. No specific treatment exists, and management remains symptomatic. The underlying mechanisms remain unclear, leaving the disease course uncertain and challenging to predict.
Objectives: Our study aimed to identify the SSc endotypes linked to GI involvement and the predictors associated with GI manifestations, as well as to test the association between GI involvement and disease duration, using the SSc Progression INvestiGation (SPRING) registry of the Italian Society for Rheumatology.
Methods: From the SPRING registry, we selected patients fulfilling the 2013 ACR/EULAR classification criteria and excluded cases without available data on GI symptoms. The registry identified the presence or absence of GI symptoms in the esophageal, gastric, and intestinal tracts. The "GI involvement" was defined as the presence of symptoms in at least one tract, while the extent of GI involvement was clustered into "upper GI involvement" (esophageal or gastric symptoms but not intestinal), and "lower GI involvement" (intestinal symptoms regardless of upper GI involvement). Descriptive analyses were performed using Chi-square or Student's T test, as appropriate, to compare SSc patients with and without GI involvement and those with different extents of GI involvement. Logistic regression analysis was performed to identify predictors of presence of GI involvement, while ordinal regression to evaluate which red flags were associated to a more extensive GI disease.
Results: In the Registry, 1917/2178 patients met the inclusion criteria: GI symptoms were reported by 1073/1917 (56%) cases. Patients with GI involvement showed longer disease duration (p<0.001) and a more severe disease phenotype, namely more frequent diffuse skin involvement (dcSSc, p<0.001), interstitial lung disease (ILD, p<0.001), and digital ulcers (DU, p<0.001) (Table 1) when compared to patients without GI involvement. Sex, age and antibody status were similarly distributed. The distribution of GI involvement according to disease duration showed a significant increase in the proportion of patients with GI symptoms, as disease duration increased. Patients with a disease duration of >12 years reported the highest percentage of GI symptoms (62.3%), while those with <3 years of disease duration had the highest rate of no GI symptoms (56.2%) (p<0.001, Figure 1). Similar findings were confirmed when stratifying the analysis for upper or lower GI. Logistic regression identified telangiectasias (OR 1.707, 95% CI 1.357-2.147, p<0.001), tobacco exposure (OR 1.511, 95% CI 1.186-1.925, p<0.001), dcSSc (OR 1.793, 95% CI 1.320-2.434, p<0.001), ILD (OR 1.443, 95% CI 1.142-1.823, p=0.002), DU (OR 1.583, 95% CI 1.182-2.120, p=0.002), and longer disease duration (OR 1.027, 95% CI 1.011-1.043, p=0.001) as independent predictors of GI involvement. Patients with more extensive GI tract involvement (i.e., both upper and lower GI involvement) exhibited a higher prevalence of more severe SSc features, confirming the abovementioned associations of SSc-related features seen for GI involvement. In particular, the prevalence of tobacco exposure (p=0.015), dyspnea (p<0.001), dcSSc (p<0.001), ILD (p<0.001), DU (p<0.001), telangiectasias (p<0.001), longer disease duration (p<0.001, Figure 1) and lower DLCO (p<0.001) progressively increased with the worsening GI extent. Again, sex, age and autoantibody status were not differently distributed among the groups. Based on the assumption of progression from absent to isolated upper or upper and lower GI involvement, we tested several predictors of more severe GI extent using ordinal regression. We identified key predictors in disease duration (OR 1.022, 95% CI 1.009-1.035, p<0.001), female sex (OR 1.654, 95% CI 1.191-2.296, p=0.003), ILD (OR 1.488, 95% CI 1.200-1.842, p<0.001), DU (OR 1.650, 95% CI 1.282-2.123, p<0.001), dcSSc (OR 1.739, 95% CI 1.282-2.262, p<0.001), telangiectasias (OR 1.905, 95% CI 1.531-2.370, p<0.001), and tobacco exposure (OR 1.546, 95% CI 1.244-1.919, p<0.001). When focusing specifically on predictors of progression from upper to lower GI extent, logistic regression revealed that DU (OR 1.698, 95% CI 1.195-2.415, p=0.003), telangiectasias (OR 1.757, 95% CI 1.211-2.551, p=0.003), and anti-centromere antibodies (OR 1.647, 95% CI 1.161-2.342, p=0.005) were significant predictors, while disease duration was not confirmed (OR 1.006, 95% CI 0.987-1.025, p=0.560).
Conclusion: Our data show that the presence and extent of GI involvement may characterize a more severe SSc disease endotype. Independent risk factors for GI involvement were disease duration, dcSSc, ILD, DU, and tobacco exposure. Disease duration was associated with the presence of GI symptoms, but it did not predict the further evolution from upper to lower GI extent involvement, suggesting its pivotal role in the onset rather than in the progression of GI manifestations.
REFERENCES: NIL.

Table 1. Comparison of demographical data and symptoms in SSc patients with different extent of GI involvement.

	GI extent			Total 1917	
	No GI symptoms	Upper GI symptoms	Upper and Lower GI symptoms	Missing	p value
	844 (45.8)	704 (38.2)	293 (15.9)	76	
Female sex, n (%)	742 (88.1)	619 (88.1)	265 (91.1)	81	0.345
Age, mean, (SD)	58.09 (14.05)	59.31 (13.16)	59.45 (12.92)	78	0.147
Disease duration, mean (SD)	8.81 (7.68)	10.77 (8.60)	11.55 (9.48)	264	**<0.001**
Tobacco exposure, n (%)	223 (29.3)	218 (35.3)	98 (37.1)	274	**0.015**
Diffuse cutaneous involvement, n (%)	111 (13.2)	159 (22.6)	82 (28)	76	**<0.001**
Sclerodactyly, n (%)	506 (60.1)	539 (76.6)	225 (76.8)	78	**<0.001**
Puffy fingers, n (%)	442 (52.4)	358 (50.9)	142 (48.6)	78	0.531
Digital pitting scars, n (%)	303 (36)	377 (53.6)	174 (59.4)	78	**<0.001**
Digital ulcers, n (%)	132 (15.6)	164 (23.3)	96 (32.8)	76	**<0.001**
Telangectasias, n (%)	414 (49.1)	455 (64.6)	217 (74.6)	78	**<0.001**
Calcinosis, n (%)	56 (6.7)	88 (12.5)	65 (22.2)	79	**<0.001**
Joints contractures, n (%)	70 (8.3)	95 (13.5)	75 (25.6)	77	**<0.001**
Tendon friction rubs, n (%)	40 (4.7)	62 (8.8)	51 (17.5)	77	**<0.001**
Arthritis, n (%)	76 (9.1)	89 (12.7)	42 (14.5)	88	**0.014**
Anti topoisomerase I, n (%)	286 (34.3)	239 (34.3)	100 (35.1)	100	0.970
Anti RNApolimerase III, n (%)	12 (1.8)	10 (1.8)	6 (2.7)	461	0.685
Anti Centromere, n (%)	264 (34.1)	196 (29.9)	93 (34.2)	215	0.190
Nailfold videocapillaroscopy pattern Late, n (%)	151 (19.8)	177 (28.1)	91 (33.8)	257	**<0.001**
Interstitial lung disease, n (%)	262 (31)	298 (42.3)	138 (47.1)	76	**<0.001**
Dyspnea, n (%)	218 (26)	305 (43.3)	173 (59.5)	83	**<0.001**
DLCO, mean (SD)	72.64 (19.85)	66.23 (19.85)	64.44 (21.49)	618	**<0.001**

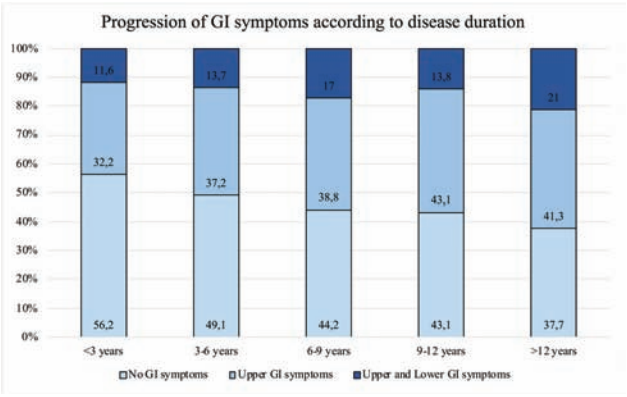

Figure 1. Stratification of GI extent according to disease duration.

Acknowledgements: NIL.

Disclosure of Interests: Francesco Bonomi: None declared, Cosimo Bruni Boeringher Ingelheim, Novartis Foundation for medical-biological research, EMDO foundation, Iten-Kohaut Foundation. Educational grants from Wellcome Trust, Silvia Laura Bosello: None declared, Fabio Cacciapaglia: None declared, Corrado Campochiaro: None declared, Roberto F. Caporali: None declared, Maria Antonietta D' Agostino: None declared, Lorenzo Dagna: None declared, Rossella De Angelis: None declared, Giacomo De Luca: None declared, Dilia Giuggioli: None declared, Serena Guiducci: None declared, Florenzo Iannone: None declared, Francesca Ingegnoli: None declared, Carlomaurizio Montecucco: None declared, Valeria Riccieri: None declared, Giovanni Zanframundo: None declared, Clodoveo Ferri: None declared, Marco Matucci-Cerinic: None declared, Silvia Bellando-Randone: None declared.

DOI: 10.1136/annrheumdis-2025-eular.B215

ABS0575

EXPLORING THE ASSOCIATION BETWEEN AUTOANTIBODY PROFILES AND THE DEVELOPMENT OF DIGITAL ULCERS IN SYSTEMIC SCLEROSIS PATIENTS: A COMPREHENSIVE ANALYSIS

Keywords: Observational studies/registry, Autoantibodies

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Background: Systemic sclerosis (SSc) is a chronic, multisystemic autoimmune disease. Vasculopathy is a prevalent feature in nearly all patients with SSc, and it can manifest as digital ulcers (DUs) in a subset of these individuals. DUs represent a significant complication, with the potential to lead to tissue necrosis, infection, and even auto-amputation, thereby severely impacting patients' daily activities and overall quality of life [1]. The relationship between the development of DUs and the presence of autoantibodies is crucial for understanding disease progression and improving patient management strategies [2].

Objectives: The principal aim of this study was to examine the association between the emergence of DUs and the presence of autoantibodies in patients diagnosed with SSc. Through the analysis of clinical parameters and autoantibody profiles, the objective was to identify potential predictors of DUs development, with a view to enhancing our understanding of the disease's progression and informing therapeutic strategies.

Methods: This study included 305 patients who were diagnosed with SSc within the last year. Clinical parameters such as gender, age, the onset age of Raynaud's phenomenon, the onset age of the first symptom other than Raynaud's phenomenon, disease duration, and organ involvement were meticulously recorded. Furthermore, we collected data on smoking history, the presence of digital ulcers, digital gangrene, calcinosis, the modified Rodnan skin score (mRSS), and existing comorbidities. A thorough statistical analysis of the gathered data was conducted to identify significant relationships among these variables, employing binomial logistic regression to assess the associations between autoantibody profiles and DUs development.

Results: Among the patients diagnosed with SSc, 59 (19.3%) ones had DUs. It is noteworthy that gangrene was observed in two patients (3.4%) in the DUs group. 8 (13.6%) of the patients who had DUs were males and 24 (9.8%) the non-DUs group were males; however, the difference was not significant (p=0.392). The presence of anti-dsDNA antibody positivity was significantly higher in patients with DUs compared to the non-DUs group (n=3 (60%) vs. n=2 (40%); p=0.025). In patients with DUs, anti-Ro antibody positivity was observed in 12 (33.3%), while 44 (17.4%) tested negative (p = 0.024). Additionally, among patients with DUs, anti-Scl70 antibody was positive in 35 (28.7%) and negative in 23 (13.5%) (p < 0.001). Conversely, anti-centromere antibody positivity was found in 13 (10.3%) of patients with DUs, while 44 (26.2%) tested negative (p < 0.001) (Table 1). Notably, among the nine patients with U1RNP positivity, none developed DUs, a finding that did not reach statistical significance (p=0.127). The evaluation of additional antibodies yielded no substantial findings. The binomial logistic regression analysis indicated that the model's fit criteria were a deviance value of 221, Akaike information criterion (AIC) of 237, and McFadden R^2 of 0.130, suggesting a limited explanatory power of the model. A significant relationship was identified between anti-Ro/SSA negativity and the development of DUs (OR: 0.391, 95% CI: 0.1641 - 0.934, p = 0.034). However, no statistically significant relationships were identified for anti-Scl70, anti-centromere, anti-dsDNA antibody positivities, platelet count, and hemoglobin levels (p > 0.05) (Table 2).