Table 1. Organ-specific manifestations in SSc participants in VCAM-1 Q4 versus Q1-3 (bold font denotes statistically significant associations)

	Above 75th VCAM-1 (n=97)	below 75th VCAM-1 (n=291)	P value
Clinician-defined organ manifestations (present ever)			
PAH	**40 (41.2%)**	**85 (29.2%)**	**0.028**
ILD	35 (36.1%)	103 (35.4%)	0.903
SSc myocardial disease	**19 (19.6%)**	**28 (9.6%)**	**0.009**
Myositis	6 (6.2%)	19 (6.5%)	0.905
Raynaud phenomenon	94 (97.9%)	270 (93.1%)	0.078
Digital ulcers	**60 (62.5%)**	**130 (44.8%)**	**0.003**
Gastro-esophageal reflux	89 (92.7%)	266 (91.7%)	0.758
Gastric antral vascular ectasia	16 (16.5%)	32 (11.0%)	0.154
Calcinosis	57 (59.4%)	162 (56.3%)	0.592
Investigation-defined organ manifestations (*present ever)			
PAH*	16 (16.5%)	29 (10.0%)	0.082
Highest recorded sPAP on right heart catheterisation (mmHg)	**46.00 (37.50-58.50)**	**36.00 (31.00-46.00)**	**<0.001**
NT Pro BNP(pg/ml) at baseline	**221.32 (101.06-966.21)**	**101.70 (60.09-170.45)**	**<0.001**
HRCT defined ILD*	33 (34.0%)	98 (33.7%)	0.951
Lowest FVC%	**83.50 (69.00-97.65)**	**90.00 (75.00-102.00)**	**0.035**
Lowest DLCO %	**51.36 (39.18-65.74)**	**63.50 (47.42-75.65)**	**0.001**

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POS0265

AGE AND TIMING OF ONSET OF RAYNAUD'S PHENOMENON AND FIRST NON-RAYNAUD SIGN/SYMPTOM AS PROGNOSTIC FACTORS IN SYSTEMIC SCLEROSIS: A RETROSPECTIVE ANALYSIS FROM THE SPRING (SYSTEMIC SCLEROSIS PROGRESSION INVESTIGATION) REGISTRY OF THE ITALIAN SOCIETY FOR RHEUMATOLOGY

Keywords: Real-world evidence, Prognostic factors, Observational studies/registry, Outcome measures, Registries

S. Peretti, C. Bruni[1,2], S. L. Bosello, F. Cacciapaglia, C. Campochiaro, V. Codullo, L. Dagna[4], R. De Angelis[5], G. De Luca, D. Giuggioli, S. Guiducci[1], F. Iannone[3], F. Ingegnoli, V. Riccieri, M. Matucci-Cerinic, C. Ferri, S. Bellando-Randone.
[1]*Division of Rheumatology, Scleroderma Unit, Department of Clinical and Experimental Medicine, University of Florence, Careggi University Hospital, Florence, Italy*; [2]*Division of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland*; [3]*Rheumatology Unit, Department of Precision and Regenerative Medicine and Ionian Area (DiMePre-J), University of Bari, Bari, Italy*; [4]*Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UniRAR), Inflammation, Fibrosis and Ageing Initiative (INFLAGE), IRCCS San Raffaele Scientific Institute,& Vita-Salute San Raffaele University, Milan, Italy*; [5]*Rheumatology Unit, Department of Clinical and Molecular Sciences, Polytechnic University of Marche, Ancona, Italy*

Background: Systemic sclerosis (SSc) is a heterogeneous autoimmune disease, affecting mainly females, with variables peaks of incidence depending on sex and ethnicity. Raynaud's Phenomenon (RP) occurs in over 95% of patients and it is commonly described as the initial sign which precedes the onset of the disease, even by several years. However, a small proportion of patients develop the disease presenting with a different sign or symptom.

Objectives: The aim of our study was to determine whether the age and timing of RP onset, as well as the age at onset of the first non-Raynaud sign or symptom, might play a role in defining the disease phenotype and prognosis in SSc patients.

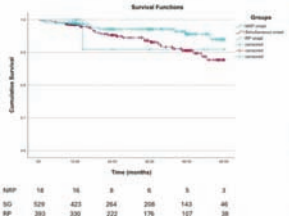
Methods: We performed a cross-sectional study including patients enrolled in the Systemic Sclerosis Progression InvestiGation (SPRING) registry classified as SSc according to the ACR/EULAR 2013 criteria: patients with missing data on age at RP onset (age-RP) and age at onset of non-RP sign or symptom (age-NRP) were excluded. Patients were categorized into 4 groups both for age-RP and age-NRP, based on the quartiles of the distribution in the total population. Additionally, patients were divided into 3 groups based on RP onset timing: 1) RP onset >1 year after the onset of the first NRP sign or symptom (NRP group); 2) RP onset within the same year as NRP sign or symptom onset (Simultaneous group); and 3) RP onset >1 year before NRP sign or symptom onset (RP group). All groups comparison were performed using Chi-square test (with Fisher's correction where applicable), otherwise with ANOVA test. Logistic, linear and multinomial regression models were applied to test the association with dichotomous, continuous and categorical variables. Kaplan-Meier curves and multivariable Cox regression were used to quantify the association with mortality.

Results: A total of 1748/2134 SSc patients were eligible for the study: 682 (39%) in the RP group, 1026 (58.8%) in the Simultaneous group (SG), and 39 (2.2%) in the NRP group. Mean age of RP onset was 39 (± 15 years SD) for the first group, 49 (± 15 years SD) for the simultaneous and 53 (± 12 years SD) for the last group, respectively. Interestingly, the mean age of NRP was similar within the 3 groups (49 ± 14; 48 ± 15 and 48 ± 12, respectively). In the RP group, a higher prevalence of Anti-Centromere Antibodies (ACA) (41.5%) was observed, while the SG had a higher prevalence of Anti-Topoisomerase I Antibodies (ATA) (41.1%), diffuse cutaneous systemic sclerosis (dcSSc, 25,2%) and a higher median Rodnan Skin Score (mRSS) (5, IQR 2-10, p<0,001). Conversely, the NRP group showed no specific autoantibody pattern and a lower prevalence of dcSSc (5.1%) but was characterized by higher rates of pulmonary arterial hypertension (PAH) (15.8%). When the population was divided into 4 groups based on the age of RP onset, the main differences were between the first (18-34 years) and fourth group (> 56 years). The first group had higher prevalence of ATA (42,2%), dcSSc (23,4%), digital ulcers (DU, 29,2%), digital pitting scars (DPS) (58,2%), and joint contractures (17,1%), while the fourth group showed more

Table 1: General characteristics according to RP-NRP onset

	TOTAL	MISSING, n (%)	NRP ONSET	SIMULTANEOUS ONSET	RP ONSET	P-value
Patients, n (%)	1748 (100)	0	39 (2.2)	1026 (58.8)	682 (39)	
Smoking habit, n (%)	530 (33.7)	175 (10)	12 (34.3)	322 (34.5)	196 (32.4)	0.689
Male sex, n (%)	199 (11.4)	4 (0.2)	9 (20.5)	133 (13)	58 (8.5)	**0.004**
Age years mean, y ±SD	59 ± 14	1 (0.06)	60 ± 11	58 ± 13	59 ±14	0.527
Age at RP onset, y ± SD	45± 16	1 (0.06)	53 ± 12	49 ± 15	39 ± 15	**<0.001**
Age at NRP onset, y ± SD	48 ± 14	1 (0.06)	48 ± 12	48 ± 15	49 ± 14	0.892
BMI, n ±SD	24.07 ±4.3	169 (10.7)	25.45 ± 5.7	24.04 ± 4.15	24.04 ±4.43	0.197
CCI, n ± SD	3±2	0	3 ±2	3 ±2	3 ± 2	0.276
RP-NRP time, y ± SD	3.94 ± 7.9	0	-4.74 ± 3.44	0.22 ±0.46	10 ± 9.8	**<0.001**
ESR mm/h, n ± SD	22 ± 18	238 (13.6)	23 ±20	22 ± 19	21 ±16	0.461
CRP mg/dL, n ± SD	1 (0.28-3.10)	157 (9)	1.60 (0.81-2.40)	3.2 (2.4-4.11)	2.6 (2-3.6)	0.611
Skin and vascular						
dcSSc n (%)	351 (20.1)	0	2 (5.1)	259 (25.2)	90 (13.2)	**<0.001**
mRSS, n (IQR)	4 (2-9)	149 (8.5)	3 (0-6)	5 (2-10)	4 (1-8)	**<0.001**
Puffy fingers, n (%)	897 (51.9)	20 (1.1)	15 (40.5)	516 (50.8)	366 (54.1)	0.188
Digital ulcers, n (%)	369 (21.3)	17 (1)	3 (7.9)	220 (21.7)	145 (21.4)	0.113
Pittingscars, n (%)	830 (48.1)	21 (1.2)	16 (43.2)	506 (49.9)	308 (45.6)	0.179
Sclerodactily, n (%)	1216 (70.4)	19 (1.1)	28 (73.7)	746 (73.6)	444 (65.6)	**0.002**
Teleangectasias, n (%)	1052 (60.8)	18 (1)	25 (65.8)	580 (57.1)	447 (66.1)	**<0.001**
Capillaroscopy pattern late, n (%)	409 (26)	176 (10.1)	6 (15.8)	253 (27.7)	150 (24.2)	0.109
Gastrointestinal						
Esophageal involvement, n (%)	885 (51.2)	19 (1.1)	14 (37.8)	550 (54.1)	321 (47.5)	**0.007**
Gastric involvement, n (%)	340 (19.7)	21 (1.2)	5 (13.5)	212 (20.9)	123 (18.2)	0.256
Intestinal involvement, n (%)	350 (20.3)	20 (1.1)	2 (5.4)	205 (20.2)	143 (21.2)	**0.048**
Cardiopulmonary						
Cardiopulmonary manifestation, n (%)	487 (28.2)	22 (1.3)	17 (45.9)	314 (31)	156 (23.1)	**<0.001**
Dyspnea, n (%)	676 (39.3)	26 (1.5)	18 (48.6)	421 (41.6)	237 (35.3)	**0.018**
ILD, n (%)	685 (39.2)	0	16 (41)	428 (41.7)	241 (35.3)	**0.03**
PAH, n (%)	28 (3.9)	0	3 (15.8)	10 (2.3)	15 (5.7)	**0.003**
Conduction block, n (%)	126 (12.2)	716 (41)	3 (16.7)	87 (14.2)	36 (9)	**0.027**
Pericardial effusion, n (%)	100 (7)	319 (18.2)	2 (6.7)	63 (7.4)	35 (8.4)	0.761
Abnormal diastolic function, n (%)	331 (23.5)	339 (19.4)	9 (31)	187 (22.3)	135 (25)	0.316
EF, (%)	61 ±6	383 (21.9)	60 ±9	61 ±5	61 ±5	0.652
sPAP, (mmHg)	22 ±16	321 (18.4)	29 ±19	22 ±16	23 ±16	**0.012**
FVC, (%) ± SD	101 ±23	440(25.2)	97 ±24	100 ±22	104 ±23	**0.004**
DLCO, (%) ± SD	69 ±21	503 (28.8)	65 ±24	68 ±20	69 ±20	0.322
DLCO/VA, (%) ± SD	77 ±19	678 (38.8)	78 ±22	77 ±19	77 ±19	0.901
TLC, (%) ± SD	97± 20	990 (56.7)	89 ±16	96 ±21	99 ±20	**0.025**
6MWT distance, (m) ± SD	470 ±120	1454 (83.2)	353 ±171	474 ±117	470 ±120	0.055
Sat 6MWT, (%) ± SD	95 ±4	1449 (82.9)	95 ±5	95 ±5	96 ±4	0.442
Musculoskeletal						
Calcinosis, n (%)	201 (11.5)	21 (1.2)	5 (13.5)	120 (11.8)	76 (11.3)	0.883
Arthritis, n (%)	199 (11.5)	30 (1.7)	3 (8.1)	123 (12.2)	73 (10.9)	0.662
Muscle weakness, n (%)	247 (14.3)	21 (1.2)	5 (13.5)	155 (15.3)	87 (12.9)	0.37
Joint contractures, n (%)	231 (13.4)	20 (1.1)	2 (5.4)	151 (14.9)	78 (11.5)	0.054
Other symptoms						
Sicca syndrome, n (%)	501 (29)	20 (1.1)	7 (18.4)	290 (28.6)	204 (30.2)	0.263
Renal crisis, n (%)	21 (1.2)	20 (1.1)	1 (2.7)	14 (1.4)	6 (0.9)	0.283
Autoantibodies						
ANA+, n (%)	1664 (97.4)	39 (2.2)	35 (94.6)	975 (97.5)	654 (97.3)	0.574
ATA, n (%)	597 (34.9)	37 (2.1)	9 (21.6)	411 (41.1)	178 (26.4)	**<0.001**
ARA, n (%)	27 (2)	374 (21.4)	0	24 (2.9)	3 (0.6)	**0.007**
ACA, n (%)	508 (31.8)	141 (8.1)	9 (26.5)	239 (25.2)	260 (41.5)	**<0.001**
Therapies						
Ongoing bDMARDs, n (%)	95 (5.4)	0	2 (5.1)	65 (6.3)	28 (4.1)	0.119
Ongoing csDMARDs, n (%)	578 (33.1)	0	18 (46.2)	378 (36.8)	182 (26.7)	**<0.001**
Ongoing Ccs, n (%)	632 (36.2)	0	16 (41)	419 (40.8)	197 (28.9)	**<0.001**
Ongoing ERA, n (%)	399 (22.8)	0	7 (17.9)	238 (23.2)	154 (22.6)	0.745
Ongoing PDE5, n (%)	79 (4.5)	0	0	40 (3.9)	39 (5.7)	0.094
Ongoing Prost, n (%)	996 (57)	0	15 (38.5)	591 (57.5)	390 (57.2)	0.06
Previous ERA, n (%)	393 (22.5)	0	7 (17.9)	237 (23.1)	149 (21.8)	0.666
Previous PDE5, n (%)	66 (3.8)	0	0	32 (3.1)	34 (5)	0.074
Previous Prost, n (%)	870 (49.8)	0	12 (30.8)	523 (50.9)	335 (49.1)	**0.042**
Previous csDMARDS, n (%)	637 (36.4)	0	18 (46.2)	417 (40.6)	202 (29.6)	**<0.001**
Previous bDMARDs, n (%)	61 (3.5)	0	1 (2.6)	40 (4.5)	14 (2.1)	**0.022**
Previous Ccs, n (%)	567 (32.4)	0	16 (41)	378 (36.8)	173 (25.4)	**<0.001**

Figure 1: Kaplan-Meier survival curves between groups and prognostic factors related to mortality in a Cox regression model.
NRP non- Raynaud's phenomenon, RP Raynaud phenomenon, SG Simultaneous group, EUSTAR European Scleroderma Trial a and Research Group



	HR	95% CI Lower Bound	95% CI Upper Bound	p-value
RP group	reference			0.144
NRP group	1.741	0.225	13.493	0.596
Simultaneous group	1.975	1.002	3.893	0.049
Age	1.030	0.992	1.069	0.124
Male sex	1.767	0.832	3.838	0.137
Charlson Comorbidity Index	1.331	1.129	1.570	<.001
EUSTAR revised Activity Index	1.382	1.114	1.477	<.001

cardiopulmonary manifestations (35.3%) and higher sPAP values (25±18 mmHg). Similar data were obtained when dividing our population by the age-NRP. Logistic regression analysis revealed that the SG was associated with a higher prevalence of dcSSc compared to the RP group (OR 1.491, 95% CI 1.032–2.154, p=0.033), independently of ATA and sex. Additionally, we identified earlier age-RP as a negative predictor of sPAP (β -0.149, 95%CI: -0,297, -0,001; p=0.049) and mRSS (β -0.53, 95%CI -0,094, -0,011; p=0.012). No significant association was found when predicting other SSc related manifestations. Among 943 patients with available follow-up (median 24 months, IQR 12-48 months), a comparable estimated survival rate in the RP (97%), the NRP (95%) and the SG (94%) (p=0.09) was observed. However, on multivariable Cox regression, the SG had a significant higher mortality compared to the RP group, independently from patient's age, sex, disease activity and Charlson Comorbidity Index (HR 1.975; 95%CI 1.002- 3.893, p=0.049). Multinomial regression analysis showed that female sex was associated with a higher probability of being included in the RP group (group (OR 2.445; 95% CI 1.052-5.681; p=0.038). Older age at RP onset increased the likelihood of being included in the NRP group (OR 1.067; 95% CI 1.042–1.092; p<0.001) or in the SG (OR 1.048; 95% CI: 1.041–1.056; p<0.001). Additionally, ACA positivity was associated with a higher likelihood of being in the RP group (OR 2.004; 95% CI: 1.550–2.597; p<0.001), while the presence of ATA and Anti-RNA Polymerase III Antibody (ARA) antibodies was linked to a higher likelihood of being included in the SG (OR 1.671; 95% CI 1.295–2.157; p<0.001 and OR 4.002; 95% CI 1.151–13.914; p=0.029, respectively).

Conclusion: Our data highlight the importance of the timing of RP and NRP onset as determinants of disease endotype and survival in SSc. In particular, patients with simultaneous onset of RP and NRP were associated with a more severe disease endotype, as well as higher mortality, even after adjusting for age, antibody status, disease activity, and comorbidities. These findings underline the relevance of the timing of onset of RP-NRP in the disease stratification. Further research is needed to confirm these results to understand whether they may help in the choice of the therapeutic strategy.

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POS0266

DEVELOPMENT OF AN ARTICULAR SCORE IN SYSTEMIC SCLEROSIS (ASSESS): IDENTIFICATION OF CORE INSTRUMENTS TO ASSESS DISEASE ACTIVITY

Keywords: Ultrasound, Synovium, Pain, Patient Reported Outcome Measures, Outcome measures

B. Burja[1], P. M. J. Welsing[2], A. Lescoat, A. Eisenring[3], A. M. Hoffmann-Vold[1,4], C. Leroy David[5], D. Khanna[6], F. Del Galdo, M. Iudici[7], J. Pope[8], J. Spierings[9], M. Vonk[12], M. E. Truchetet[10], M. Clergeau[5], M. Hughes, S. L. Murphy[6], T. Frech[11], O. Distler[1], M. Elhai[1]. [1]*Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland*; [2]*University Medical Center Utrecht, Utrecht University, Department of Rheumatology and Clinical Immunology, Utrecht, Netherlands*; [3]*Patient research partners, Zurich, Switzerland*; [4]*Oslo University Hospital, Department of Rheumatology, Oslo, Norway*; [5]*Patient research partners, Paris, France*; [6]*University of Michigan, Ann Arbor, Department of Internal Medicine, Division of Rheumatology, Michigan, United States of America*; [7]*Faculty of Medicine, Geneva University Hospitals, Division of Rheumatology, Department of Medicine, Geneva, Switzerland*; [8]*University of Western Ontario, Departmnt of Medicine, Ontario, Canada*; [9]*University Medical Centre Utrecht, Department of Rheumatology and Clinical Immunology, Utrecht, Netherlands*; [10]*CHU Bordeaux Hospital, Rheumatology Department, Bordeaux, France*; [11]*Tennessee Valley Health Care System, Veterans Affairs Medical Center and Vanderbilt University Medical Center, Department of Internal Medicine, Division of Rheumatology and Immunology, Nashville, TN, United States of America*; [12]*Radboud University Medical Centre, Department of Rheumatology, Nijmegen, Netherlands*

Background: Inflammatory joint and tendon involvement resulting in pain and reduced joint function affects up to 30% of patients with systemic sclerosis (SSc) and represents a major burden on patient quality of life. The lack of standardized outcome measurements for assessing articular involvement in SSc not only limits the development of evidence-based therapies, but also results in incomplete clinical picture of joint involvement in SSc.

Objectives: We aimed at identifying core instruments for the development of a consensus-based multi-outcome domain: the Articular Score in SystEmic SclerosiS (ASSESS) to assess articular activity among SSc patients for use in both clinical practice and trials.

Methods: A steering committee comprising of 12 rheumatologists, 1 epidemiologist, 1 occupational therapist, and 3 patient research partners, was convened. The articular score was developed through a stepwise iterative process (Figure 1). First, a dedicated scoping review was conducted in PubMed/Medline (January 1960 to April 2023), where two reviewers independently identified eligible studies assessing joint and tendon involvement in SSc and extracted the instruments used to assess outcomes. After expert opinion discussion, instruments were selected if they were considered both feasible and valid by at least 70% of the steering committee. Selected instruments were further assessed by two independent reviewers using OMERACT filters. The results were presented to the steering committee and after a 2-step online Delphi survey, final core instruments to assess articular activity in SSc patients were defined.

Results: Among a total of 770 identified references, 658 were excluded based on their title and/or abstract resulting in 112 articles being examined based on the full text (Figure 1). Overall, 82 studies were included, of which 43 instruments that were used for assessing articular activity in at least two studies were identified. Based on domain match and feasibility, 9 clinical, 1 laboratory, 3 clinico-biological and 3 patient-reported outcomes (Table 1) were selected for consideration in the articular activity score. Based on the measurement property analysis according to OMERACT guidelines, the steering committee voted and selected the 6 instruments to be included in the composite score to assess joint and tendon activity in SSc patients. The ASSESS score will comprise: clinical (tender and swollen joint count, standard 28 joints with the addition of distal interphalangeal joints; the presence of tendon friction rubs), serological (CRP), and patient and physician reported outcome measurements (VAS activity pain patient, VAS activity doctor) instruments.

Conclusion: The steering committee identified 6 meaningful core instruments to assess articular activity in SSc patients. This represents the foundation for further development of a composite score for joint and tendon involvement in SSc for use in both clinical practice and trials. In the subsequent steps, we plan to obtain weight for individual instruments within longitudinal SSc cohorts using the presence of activity in ultrasound and a patient-reported questionnaire (Likert scale 1-5) as anchors.

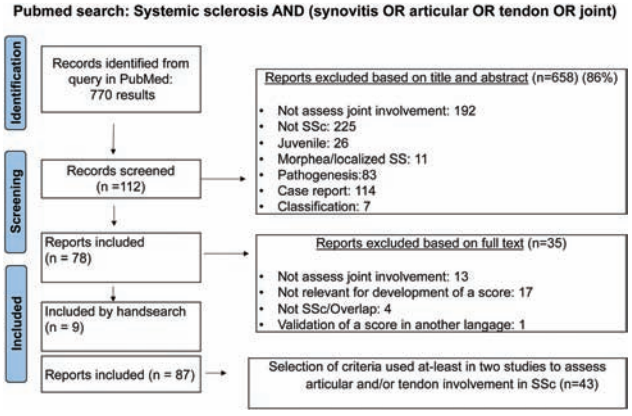

Figure 1. Scoping review search strategy.

Table 1. Identified core instruments for assessing disease articular activity in SSc patients.

Clinical	Serology	Clinico-biological score	Patient reported outcomes
○ *Ritchie articular index* ○ *Number of tender joints* ○ *Number of swollen joints* ○ *Number of synovitis* ○ *Presence of tendon friction rubs* ○ *Number of tendon frictions rubs*	○ *CRP*	○ *DAS28-ESR* ○ *DAS28-CRP* ○ *SDAI*	○ *Visual analogic scale for articular pain (patient)* ○ *Visual analogic scale for disease activity (patient)* ○ *Visual analogic scale for disease activity (physician)*