Supplementary material

Definitions

SSc onset (first symptom): Starting date of the first symptoms related to SSc (Raynaud's phenomenon or other).

SSc diagnosis: Date on which the patient met the criteria for SSc according to the ACR 1980 classification criteria and/or to the modified LeRoy and Medsger classification criteria.

Diagnostic delay: Time from onset of disease to SSc diagnosis.

Limited scleroderma (lcSSc): Cutaneous sclerosis distal to elbows and knees; may include face/neck.

Diffuse scleroderma (dcSSc): Skin sclerosis proximal to elbows and knees.

Scleroderma sine scleroderma (ssSSc): Patients with visceral involvement characteristic of scleroderma (oesophageal or intestinal hypomotility, interstitial lung disease, PH, heart disease and/or renal crisis) with no skin thickening, Raynaud's phenomenon with positive anti-nuclear antibodies (ANA), and ruling out other diseases that may mimic scleroderma.

Pre-scleroderma (preSSc): Raynaud's presence, altered capillaroscopy and/or anti-centromere antibodies (ACA), anti-topo I antibodies, other specific autoantibodies or ANA with nucleolar immunofluorescence.

Gastrointestinal (GI) involvement, alteration in one or more of the following organs: Oesophagus (impaired motility detected by upper GI series, manometry and isotopic study and/or presence of reflux), stomach (gastric antral vascular ectasia, telangiectasia), bowel (impaired motility detected by upper GI series and/or barium enema and/or bowel manometry; suggestive findings in abdominal CT of intestinal conditions such as dilated loops or intestinal pneumatosis; breath test with glucose or xylose and/or altered intestinal biopsy).

Pulmonary involvement: Defined by the presence of interstitial lung disease (ILD) or pulmonary hypertension (PH). The former was established if evidence consistent with pulmonary fibrosis was present in chest radiograph or high-resolution computed tomography (HRCT), regardless of forced vital capacity (FVC). PH was considered when systolic pulmonary arterial pressure (PAP) was estimated to be >40 mmHg by Doppler echocardiogram or when mean PAP was found to be ≥25 mmHg at rest by right-sided heart catheterisation (RHC). Isolated PH was classified as pulmonary arterial hypertension with no ILD or ILD and FVC percent predicted >60%.

Musculoskeletal involvement: Presence of arthralgia, arthritis, myositis, tendon or osteolysis friction. Inflammatory myopathy: Clinical, analytical, electromyography and biopsy compatible with inflammatory myopathy. Non-inflammatory myopathy: Muscle weakness with impaired muscle enzymes and myogenic EMG pattern without other causes of myopathy (with or without biopsy).

Cardiac involvement: Pericarditis, ischaemic cardiomyopathy without with no other associated cardiovascular risk factors, reversible scintigraphy thallium perfusion defects after cold stimulation, structural abnormalities detected by Doppler ultrasound, ECG abnormalities without another identifiable cause, diastolic dysfunction, ejection fraction of the left ventricle <50% or right ventricle <40% diagnosed by echo-

Epidemiology and clinical subtypes.

Number of patients	n	Total 1506	Male 165	Female 1341	*p*-value
Clinical subtype					
lcSSc	1506	892 (59%)	84 (51%)	808 (60%)	**0.023**
dcSSc	1506	355 (24%)	62 (38%)	293 (22%)	**<0.001**
seSSc	1506	153 (10%)	13 (7.9%)	140 (10%)	0.342
Pre-SSc	1506	106 (7.0%)	6 (3.6%)	100 (7.5%)	0.076
Age at SSc onset	1430	45.6 (16,2)	48 (16,2)	45.3 (16,2)	**0.042**
<30	1430	250 (17%)	17 (11%)	233 (18%)	**0.015**
30-50	1430	612 (43%)	63 (39%)	549 (43%)	0.353
>50	1430	568 (40%)	81 (50%)	487 (38%)	**0.005**
Age at SSc diagnosis	1428	51.7 (15,5)	52.2 (15,2)	51.7 (15,5)	0.662
<30	1428	129 (9.0%)	10 (6.3%)	119 (9.4%)	0.241
30-50	1428	516 (36%)	57 (36%)	459 (36%)	1.000
>50	1428	783 (55%)	91 (58%)	692 (55%)	0.241
Time SSc onset-diagnosis	1384	2.48 (0.71-8.57)	1.30 (0.35-4.02)	2.92 (0.79-9.43)	**<0.001**
Smoking habit	1214	145 (12%)	26 (20%)	119 (11%)	**0.006**
Arterial hypertension	1216	392 (32%)	42 (33%)	350 (32%)	0.841
Deaths	1523	247 (16,4%)	51 (30,4%)	196 (14,6%)	**<0.001**
Follow up from onset	1430	14.2 (11.7)	11.6 (10.2)	14.5 (11.9)	**0.001**
Follow up from diagnosis	1428	8.2 (7.7)	8.1 (8.1)	8.2 (7.7)	0.898
ACR 1980 criteria	1504	942 (63%)	128 (76%)	814 (61%)	**<0.001**
ACR/EULAR 2013 criteria	1237	1211 (98%)	149 (98%)	1062 (98%)	1.000
First symptom					
Raynaud´s	1454	1.185 (81%)	124 (78%)	1.061 (82%)	0.328
Puffy fingers	1454	37 (2.5%)	4 (2.5%)	33 (2.5%)	1.000
Arthralgia	1454	92 (6.3%)	9 (5.7%)	83 (6.4%)	0.863
Cutaneous sclerosis	1454	80 (5.5%)	14 (8.9%)	66 (5.1%)	0.062

Data expressed in (n, %), cuantitative variables in mean and standard deviation (normal distribution) or median and interquartile range (non-normal distribution); n: number of patients with variable recorded; Age/time in years; lcSSc: limited systemic sclerosis; dcSSc: diffuse systemic sclerosis; se-SSc: systemic sclerosis without scleroderma; pre-SSc: pre scleroderma.

Immunological and capillaroscopic parameters.

	n	Total	Male	Female	*p*-value
Autoantibodies					
ANA	1512	1,390 (92%)	142 (85%)	1,248 (93%)	0.001
ACA	1348	615 (46%)	41 (30%)	574 (47%)	<0.001
Anti topo I	1373	301 (22%)	44 (29%)	257 (21%)	0.029
Anti RNA pol III	222	37 (17%)	9 (36%)	28 (14%)	0.018
Anti Pm-Scl	768	58 (7.6%)	11 (12%)	47 (7.0%)	0.141
Anti U1RNP	1332	75 (5.6%)	4 (2.7%)	71 (6.0%)	0.129
Anti Ku	263	12 (4.6%)	1 (3.8%)	11 (4.6%)	1.000
Anti Ro/SSA	1356	179 (13%)	11 (7.3%)	168 (14%)	0.021
Anti La/SSB	1349	44 (3.3%)	2 (1.3%)	42 (3.5%)	0.221
Anti mitocondrial	750	71 (9.5%)	4 (5.1%)	67 (10%)	0.221
Anti Sm	1325	27 (2.0%)	4 (2.7%)	23 (2.0%)	0.529
Lupus anticoagulant	511	34 (6.7%)	5 (10%)	29 (6.3%)	0.358
IgG anticardiolipine	928	53 (5.7%)	6 (6.3%)	47 (5.6%)	0.815
IgM anticardiolipine	928	46 (5.0%)	2 (2.1%)	44 (5.3%)	0.218
Antithyroid	383	103 (27%)	4 (13%)	99 (28%)	0.089
Rheumatoid factor	1120	270 (24%)	22 (19%)	248 (25%)	0.248
Anti citrullinated	148	9 (6.1%)	0 (0.00%)	9 (6.8%)	0.598
Capillaroscopy (Maricq's patterns)					
Slow	1146	600 (52%)	56 (46%)	544 (53%)	0.126
Active	1146	388 (34%)	46 (37%)	342 (33%)	0.420

cardiography, MRI or ventriculography.
Scleroderma renal crisis (SRC), defined by Traub criteria: Severe hypertension, rapidly progressive acute renal failure, microangiopathic haemolysis and thrombocytopenia (<100,000 platelets).
Sicca syndrome: Xerostomia and xerophthalmia with pathological eye and salivary examination.
SSc-related causes of death: Scleroderma renal crisis, high or low gastrointestinal involvement (GI bleeding, occlusive crisis, severe malabsorption), ILD, PH, documented history of heart disease (ventricular dysfunction, arrhythmias, myocardial fibrosis, stroke pericardial, ischaemic heart disease without other associated cardiovascular risk factor).