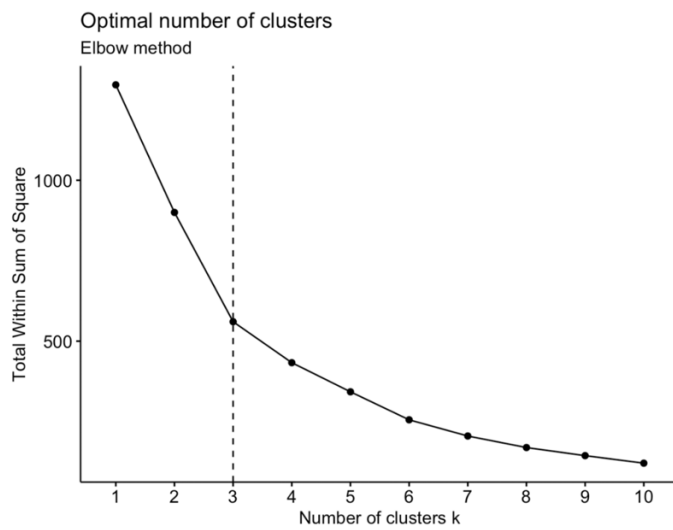
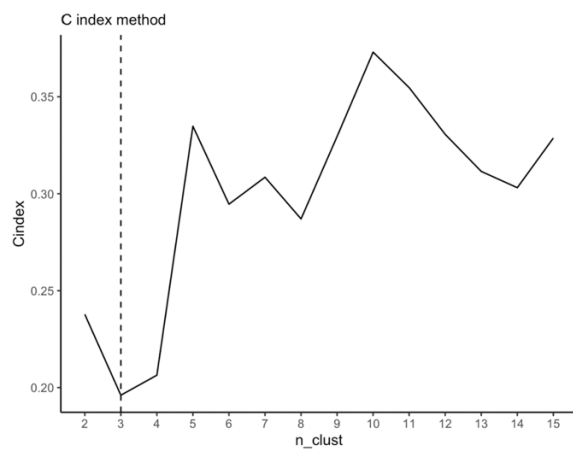
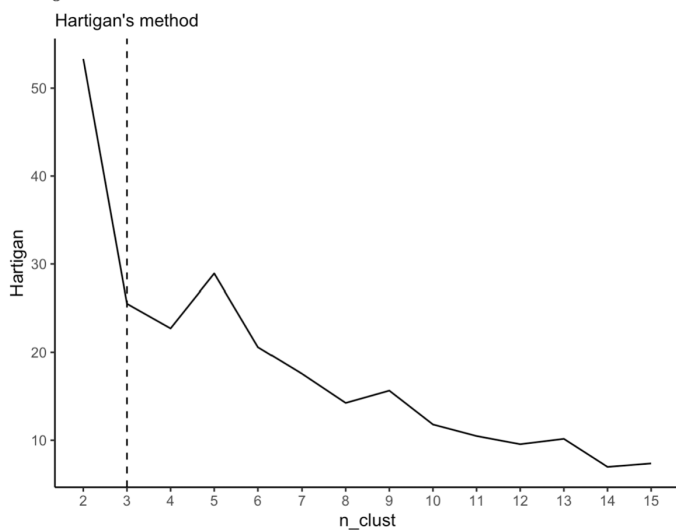


Elbow method**C index method**

HUBERT LJ, LEVIN JR: A General Statistical Framework for Assessing Categorical Clustering in Free Recall. *Psychological Bulletin* 1976; 83(6): 1072-80. <https://psycnet.apa.org/doi/10.1037/0033-2909.83.6.1072>

Hartigan's method

HARTIGAN JA: Clustering Algorithms. (Wiley series in Probability and Mathematical Statistics). John Wiley & Sons Inc, 1975.

Supplementary Fig. S1. Determination of optimal cluster number (k-mean clustering).

We used three different methods to determine the optimal number of clusters. All methods suggested 3 clusters.

Supplementary Table S1. Characteristics of patients with gastro-oesophageal involvement.

Overall n = 90	Without gastro-oesophageal involvement (n=6)	With gastro-oesophageal involvement (n=84)	<i>p</i>
Female, n (%)	6 (100)	70 (83.3)	0.613
Age, year median (IQR)	68.9 (48.1-69.2)	55.3 (45.9-63.7)	0.271
Arterial hypertension, n (%)	3 (50)	23 (27.4)	0.475
Diabetes, n (%)	1 (16.7)	5 (6.0)	0.865
Smoking, n (%)	2 (33.3)	29 (34.5)	1.000
Gougerot-Sjögren syndrome, n (%)	2 (33.3)	12 (14.3)	0.509
Autoimmune thyroiditis, n (%)	0 (0.0)	6 (7.1)	1.000
Primary biliary cholangitis, n (%)	2 (33.3)	4 (4.8)	0.062
lcSSc, n (%)	6 (100)	58 (69)	0.250
BMI, median (IQR)	25.5 (21.7-27.0)	23.6 (20.7-28.1)	0.719
Digital ulcers, n (%)	1 (16.7)	43 (51.2)	0.226
Active digital ulcers, n (%)	1 (16.7)	13 (15.5)	1.000
Telangiectasia, n (%)	3 (50)	50 (59.5)	0.977
mRSS, median (IQR)	3 (0.00-6.75)	8 (4.00-13.00)	0.034
Interstitial lung disease*, n (%)	0 (0.0)	33 (39.3)	0.136
Cardiac disease [∞] , n (%)	0 (0.0)	18 (21.4)	0.460
Pulmonary hypertension [£] , n (%)	0 (0.0)	4 (4.8)	1.000
Articular involvement, n (%)	1 (16.7)	32 (38.6)	0.526
Scleroderma renal crisis history, n (%)	0 (0.0)	1 (1.2)	1.000
Anti-centromere antibodies, n (%)	4 (66.7)	28 (35.9)	0.289
Anti-Scl70 antibodies, n (%)	1 (16.7)	25 (32.1)	0.743
Anti-RNA POL3 antibodies, n (%)	0 (0.0)	7 (9.0)	1.000
Anti-PM/SCL antibodies, n (%)	0 (0.0)	3 (3.8)	1.000
Reflux, n (%)	0 (0.0)	65 (77.4)	<0.001
Dysphagia, n (%)	0 (0.0)	23 (28.0)	0.304
Vomiting, n (%)	0 (0.0)	8 (9.8)	0.947
Abdominal pain, n (%)	3 (50)	25 (30.5)	0.592
Diarrhoea, n (%)	0 (0.0)	35 (42.2)	0.108
Constipation, n (%)	2 (33.3)	42 (50.6)	0.693
POIC, n (%)	0 (0)	3 (3.7)	1.000
SIBO, n (%)	0 (0)	5 (6.2)	1.000
Anal incontinence, n (%)	0 (0)	17 (21.0)	0.473
UCLA reflux, median (IQR)	0 (0.00-0.03)	0.38 (0.12-0.75)	0.011
UCLA distension/bloating, median (IQR)	0.25 (0.25-0.75)	0.75 (0.25-1.50)	0.590
UCLA diarrhoea, median (IQR)	0 (0.00-0.00)	0 (0.00-1.00)	0.110
UCLA faecal soilage, median (IQR)	0 (0.00-0.00)	0 (0.00-0.25)	0.259
UCLA constipation, median (IQR)	0 (0.00-0.12)	0.25 (0.00-0.50)	0.253
UCLA social functioning, median (IQR)	0.25 (0.13-0.37)	0.17 (0.00-0.54)	0.947
UCLA emotional well-being, median (IQR)	0 (0.00-0.11)	0.44 (0.11-0.72)	0.054
UCLA total, median (IQR)	0.08 (0.06-0.21)	0.44 (0.21-0.72)	0.05
s-HAQ, median (IQR)	0.02 (0.00-0.06)	0.20 (0.00-0.70)	0.100
Albumin (g/l), median (IQR)	41.1 (37.7-41.1)	41.0 (36.8-43.0)	0.631
Calprotectin (µg/g), median (IQR)	6.5 (4.5-8.3)	44.5 (17.5-103.3)	0.007
Steroids, n (%)	0 (0.00)	30 (36.1)	0.173
IS treatment without steroids [°] , n (%)	1 (16.7)	37 (44.0)	0.377
Calcium channel blockers, n (%)	4 (66.7)	58 (69.9)	1.000
Bosentan, n (%)	0 (0.0)	7 (8.4)	1.000
Sildenafil, n (%)	1 (16.7)	6 (7.2)	0.965
Proton pump inhibitors, n (%)	0 (0.0)	73 (88.0)	<0.001
Total lung capacity (TLC), % of the theoretical value, median (IQR)	109 (99.0-117.5)	89 (77.0-100.3)	0.009
Forced vital capacity (FVC), % of the theoretical value, median (IQR)	119 (114.5-126.5)	90.5 (68.3-110.0)	0.021
Forced expiratory volume (FEV), % of the theoretical value, median (IQR)	116.5 (115.3-117.0)	87 (73.8-104.2)	0.011
FEV/FVC, median (IQR)	82.5 (77.3-84.0)	80 (76.0-85.3)	0.829
Diffusing capacity for carbone monoxide (DLCO), % of the theoretical value, median (IQR)	81.5 (78.3-86.3)	61 (50.0-72.0)	0.002

*Interstitial lung disease: evaluated by CT-scan.

[∞]Cardiac disease: presence of diastolic ventricular dysfunction or arrhythmia or atrioventricular block or pericarditis.[£]Pulmonary hypertension: measured by right-heart catheterisation.[°]Including cyclophosphamide, mycophenolate mofetil, rituximab and methotrexate.

IS: immunosuppressive; mRSS: modified Rodnan skin score.

Supplementary Table S2. Characteristics of patients with intestinal involvement.

Overall n = 90	Without intestinal involvement (n=29)	With intestinal involvement (n=61)	p
Female, n (%)	25 (86.2)	51 (83.6)	0.994
Age, year median (IQR)	58.7 (49.8-67.7)	54.2 (41.2-63.2)	0.206
Arterial hypertension, n (%)	9 (31)	17 (27.9)	0.951
Diabetes, n (%)	3 (10.3)	3 (4.9)	0.608
Smoking, n (%)	12 (41.4)	19 (31.1)	0.473
Gougerot-Sjögren syndrome, n (%)	3 (10.3)	11 (18)	0.529
Autoimmune thyroiditis, n (%)	2 (6.9)	4 (6.6)	1.000
Primary biliary cholangitis, n (%)	2 (6.9)	4 (6.6)	1.000
lcSSc, n (%)	24 (82.8)	40 (65.6)	0.152
BMI, median (IQR)	25.6 (22.4-28.0)	23.1 (20.4-27.8)	0.192
Digital ulcers, n (%)	11 (37.9)	33 (54.1)	0.227
Active digital ulcers, n (%)	2 (6.9)	10 (16.4)	0.364
Telangiectasia, n (%)	17 (58.6)	36 (59)	1.000
mRSS, median (IQR)	6.0 (2.0-10.0)	8.0 (5.0-13.5)	0.211
Interstitial lung disease*, n (%)	11 (37.9)	22 (36.1)	1.000
Cardiac disease [∞] , n (%)	2 (6.9)	16 (26.2)	0.063
Pulmonary hypertension [£] , n (%)	1 (10)	3 (13.6)	1.000
Articular involvement, n (%)	8 (27.6)	25 (41.7)	0.292
Scleroderma renal crisis history, n (%)	1 (3.4)	0 (0.0)	0.702
Anti-centromere antibodies, n (%)	13 (48.1)	19 (33.3)	0.287
Anti-Scl70 antibodies, n (%)	7 (25.9)	19 (33.3)	0.665
Anti-RNA POL3 antibodies, n (%)	3 (11.1)	4 (7.0)	0.833
Anti-PM/SCL antibodies, n (%)	0 (0.0)	3 (5.3)	0.559
Reflux, n (%)	16 (55.2)	49 (81.7)	0.017
Dysphagia, n (%)	3 (10.3)	20 (33.9)	0.035
Vomiting, n (%)	0 (0.0)	8 (13.6)	0.092
Abdominal pain, n (%)	5 (17.2)	23 (39.0)	0.070
Diarrhoea, n (%)	0 (0.0)	35 (58.3)	<0.001
Constipation, n (%)	2 (6.9)	42 (70.0)	<0.001
POIC, n (%)	0 (0.0)	3 (5.1)	0.558
SIBO, n (%)	0 (0.0)	5 (8.5)	0.274
Anal incontinence, n (%)	1 (3.6)	16 (27.1)	0.022
UCLA reflux, median (IQR)	0.25 (0.06-0.56)	0.38 (0.12-0.75)	0.400
UCLA distension/bloating, median (IQR)	0.25 (0.00-0.50)	1.00 (0.50-1.75)	0.001
UCLA diarrhoea, median (IQR)	0.0 (0.0-0.0)	0.50 (0.0-1.0)	<0.001
UCLA faecal soilage, median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-1.0)	0.027
UCLA constipation, median (IQR)	0.0 (0.0-0.25)	0.25 (0.0-0.75)	0.005
UCLA social functioning, median (IQR)	0.0 (0.0-0.17)	0.33 (0.0-0.67)	0.001
UCLA emotional well-being, median (IQR)	0.22 (0.0-0.44)	0.44 (0.11-0.81)	0.030
UCLA total, median (IQR)	0.16 (0.09-0.29)	0.57 (0.26-0.83)	<0.001
s-HAQ, median (IQR)	0.0 (0.0-0.46)	0.20 (0.05-0.72)	0.040
Albumin (g/l), median (IQR)	41.1 (38.8-42.0)	40.0 (34.6-43.3)	0.558
Calprotectin (µg/g), median (IQR)	28.0 (15.0-75.0)	42.0 (17.0-95.0)	0.412
Steroids, n (%)	8 (27.6)	22 (36.7)	0.542
IS treatment without steroids [°] , n (%)	12 (41.4)	26 (42.6)	1.000
Calcium channel blockers, n (%)	23 (79.3)	39 (65)	0.258
Bosentan, n (%)	0 (0.0)	7 (11.7)	0.135
Sildenafil, n (%)	2 (6.9)	5 (8.3)	1.000
Proton pump inhibitors, n (%)	23 (79.3)	50 (83.3)	0.866

*Interstitial lung disease: evaluated by CT-scan.

[∞]Cardiac disease: presence of diastolic ventricular dysfunction or arrhythmia or atrioventricular block or pericarditis.[£]Pulmonary hypertension: measured by right-heart catheterisation.[°]Including cyclophosphamide, mycophenolate mofetil, rituximab and methotrexate.

IS: immunosuppressive; mRSS: modified Rodnan skin score.

Supplementary Table S3. Characteristics of patients with anorectal involvement.

Overall n = 90	Without anorectal involvement (n=73)	With anorectal involvement (n=17)	p
Female, n (%)	60 (82.2)	16 (94.1)	0.395
Age, year median (IQR)	54.2 (43.6-63.7)	61.7 (47.7-69.4)	0.162
Arterial hypertension, n (%)	22 (30.1)	4 (23.5)	0.807
Diabetes, n (%)	6 (8.2)	0 (0.0)	0.494
Smoking, n (%)	25 (34.2)	6 (35.3)	1.000
Gougerot-Sjögren yndrome, n (%)	11 (15.1)	3 (17.6)	1.000
Autoimmune thyroiditis, n (%)	4 (5.5)	2 (11.8)	0.692
Primary biliary cholangitis, n (%)	5 (6.8)	1 (5.9)	1.000
lcSSc, n (%)	51 (69.9)	13 (76.5)	0.807
BMI, median (IQR)	24.3 (20.7-27.8)	22.4 (20.7-28.12)	0.461
Digital ulcers, n (%)	36 (49.3)	8 (47.1)	1.000
Active digital ulcers, n (%)	7 (9.6)	5 (29.4)	0.077
Telangiectasia, n (%)	43 (58.9)	10 (58.8)	1.000
mRSS, median (IQR)	7.5 (4.0-12.25)	7.5 (2.75-12.25)	0.512
Interstitial lung disease*, n (%)	27 (37.0)	6 (35.3)	1.000
Cardiac disease [∞] , n (%)	10 (13.7)	8 (47.1)	0.006
Pulmonary hypertension [£] , n (%)	3 (12.5)	1 (12.5)	1.000
Articular involvement, n (%)	29 (40.3)	4 (23.5)	0.314
Scleroderma renal crisis history, n (%)	1 (1.4)	0 (0.0)	1.000
Anti-centromere antibodies, n (%)	26 (38.8)	6 (35.3)	1.000
Anti-Scl70 antibodies, n (%)	23 (34.3)	3 (17.6)	0.301
Anti-RNA POL3 antibodies, n (%)	7 (10.4)	0 (0.0)	0.368
Anti-PM/SCL antibodies, n (%)	2 (3.0)	1 (5.9)	1.000
Reflux, n (%)	51 (70.8)	14 (82.4)	0.510
Dysphagia, n (%)	19 (26.8)	4 (23.5)	1.000
Vomiting, n (%)	7 (9.9)	1 (5.9)	0.966
Abdominal pain, n (%)	16 (22.5)	12 (70.6)	<0.001
Diarrhoea, n (%)	22 (30.6)	13 (76.5)	0.001
Constipation, n (%)	31 (43.1)	13 (76.5)	0.027
POIC, n (%)	1 (1.4)	2 (11.8)	0.176
SIBO, n (%)	2 (2.9)	3 (17.6)	0.077
Anal incontinence, n (%)	0 (0.0)	17 (100)	<0.001
UCLA reflux, median (IQR)	0.25 (0.06-0.56)	0.62 (0.25-0.75)	0.015
UCLA distension/bloating, median (IQR)	0.5 (0.25-1.00)	1.25 (1.0-1.75)	0.002
UCLA diarrhoea, median (IQR)	0 (0.0-0.5)	1 (0.0-1.50)	0.002
UCLA faecal soilage, median (IQR)	0 (0.0-0.0)	1 (1.0-1.0)	<0.001
UCLA constipation, median (IQR)	0.0 (0.0-0.5)	0.38 (0.25-1.0)	0.008
UCLA social functioning, median (IQR)	0.17 (0.0-0.33)	0.67 (0.17-0.83)	0.002
UCLA emotional well-being, median (IQR)	0.22 (0.0-0.44)	0.78 (0.44-1.0)	<0.001
UCLA total, median (IQR)	0.25 (0.12-0.53)	0.94 (0.72-1.03)	<0.001
s-HAQ, median (IQR)	0.1 (0.0-0.65)	0.48 (0.24-0.92)	0.014
Albumin (g/l), median (IQR)	41.0 (37.0-43.0)	38.8 (34.0-42.5)	0.360
Calprotectin (µg/g), median (IQR)	37.0 (16.3-108.0)	39.5 (9.0-81.5)	0.429
Steroids, n (%)	21 (29.2)	9 (52.9)	0.114
IS treatment without steroids [°] , n (%)	31 (42.5)	7 (41.2)	1.000
Calcium channel blockers, n (%)	51 (70.8)	11 (64.7)	0.841
Bosentan, n (%)	5 (6.9)	2 (11.8)	0.870
Sildenafil, n (%)	5 (6.9)	2 (11.8)	0.870
Proton pump inhibitors, n (%)	58 (80.6)	15 (88.2)	0.696

*Interstitial lung disease: evaluated by CT-scan.

[∞]Cardiac disease: presence of diastolic ventricular dysfunction or arrhythmia or atrioventricular block or pericarditis.[£]Pulmonary hypertension: measured by right-heart catheterisation.[°]Including cyclophosphamide, mycophenolate mofetil, rituximab and methotrexate.

IS: immunosuppressive; mRSS: modified Rodnan skin score.

Supplementary Table S4. Characteristics of patients with malnutrition at the end of the follow-up.

Overall (n=90)	Without malnutrition (n=62)	With malnutrition (n=28)	<i>p</i>
Female sex, n (%)	53 (85.5)	23 (82.1)	0.928
Age, year median (IQR)	54.6 (46.8-63.6)	60.8 (43.1-67.7)	0.601
Arterial hypertension, n (%)	17 (27.4)	9 (32.1)	0.836
Diabetes, n (%)	5 (8.1)	1 (3.6)	0.738
Smoking, n (%)	19 (30.6)	12 (42.9)	0.374
lcSSc, n (%)	49 (79.0)	15 (53.6)	0.027
BMI (kg/m ²), median (IQR)	25.7 (22.4-30.5)	20.8 (17.8-23.8)	<0.001
Digital ulcers, n (%)	29 (46.8)	15 (53.6)	0.712
Telangiectasia, n (%)	34 (54.8)	19 (67.9)	0.352
mRSS, median (IQR)	6.0 (4.0-10.0)	10.0 (6.5-18.0)	0.057
Interstitial lung disease*, n (%)	17 (27.4)	16 (57.1)	0.013
Cardiac disease [∞] , n (%)	7 (11.3)	11 (39.3)	0.005
Pulmonary hypertension [£] , n (%)	2 (9.5)	2 (18.2)	0.888
Articular involvement, n (%)	26 (41.9)	7 (25.9)	0.231
Scleroderma renal crisis history, n (%)	0 (0.0)	1 (3.6)	0.682
Gastro-oesophageal involvement, n (%)	56 (90.3)	28 (100.0)	0.212
Intestinal involvement, n (%)	40 (64.5)	21 (75.0)	0.458
Anorectal involvement, n (%)	11 (17.7)	6 (21.4)	0.902
Albumin (g/l), median (IQR)	41.1 (37.6-43.4)	38.1 (33.6-42.1)	0.049
Calprotectin (μg/g), median (IQR)	32.0 (10.5-87.5)	81.0 (20.5-122.5)	0.130
Anti-centromere antibodies, n (%)	26 (45.6)	6 (22.2)	0.069
Anti-Scl70 antibodies, n (%)	15 (26.3)	11 (40.7)	0.279
Anti-RNA polymerase 3 antibodies	3 (5.3)	4 (14.8)	0.291
Anti-PM/SCL antibodies	2 (3.5)	1 (3.7)	1.000
Steroids, n (%)	18 (29.0)	12 (44.4)	0.242
IS treatment without steroids [°] , n (%)	24 (38.7)	14 (50.0)	0.439
Calcium channel blockers, n (%)	44 (71.0)	18 (66.7)	0.877
Bosentan, n (%)	4 (6.5)	3 (11.1)	0.747
Sildenafil, n (%)	5 (8.1)	2 (7.4)	1.000
Proton pump inhibitors, n (%)	48 (77.4)	25 (92.6)	0.158
Death at the end of the follow-up, n (%)	0 (0.0)	4 (14.3)	0.013

*Interstitial lung disease: evaluated by CT-scan.

[∞]Cardiac disease: presence of diastolic ventricular dysfunction or arrhythmia or atrioventricular block or pericarditis.[£]Pulmonary hypertension: measured by right-heart catheterisation.[°]Including cyclophosphamide, mycophenolate mofetil, rituximab and methotrexate.

IS: immunosuppressive; mRSS: modified Rodnan skin score.

Supplementary Table S5. Characteristics of patients with composite criteria outcome at the end of the follow up.

Overall (n=90)	Without composite criteria (n=81)	With composite criteria (n=9)	<i>p</i>
Female sex, n (%)	67 (82.7)	9 (100)	0.383
Age, year median (IQR)	56.4 (46.7-67.0)	48.3 (41.0-60.3)	0.164
Arterial hypertension, n (%)	23 (28.4)	3 (33.3)	1.000
Diabetes, n (%)	6 (7.4)	0 (0.0)	0.888
Smoking, n (%)	24 (29.6)	7 (77.8)	0.012
lcSSc, n (%)	59 (72.8)	5 (55.6)	0.485
BMI (kg/m ²), median (IQR)	24.3 (20.8-29.1)	18.6 (17.6-24.7)	0.027
Digital ulcers, n (%)	38 (46.9)	6 (66.7)	0.439
Telangiectasia, n (%)	46 (56.8)	7 (77.8)	0.391
mRSS, median (IQR)	7.5 (4.0-12.25)	7.5 (4.5-9.0)	0.590
Interstitial lung disease*, n (%)	30 (37.0)	3 (33.3)	1.000
Cardiac disease [∞] , n (%)	15 (18.5)	3 (33.3)	0.539
Pulmonary hypertension [£] , n (%)	4 (13.8)	0 (0.0)	1.000
Articular involvement, n (%)	31 (38.3)	2 (25.0)	0.721
Scleroderma renal crisis history, n (%)	0 (0.0)	1 (11.1)	0.180
Gastro-oesophageal involvement, n (%)	75 (92.6)	9 (100)	0.888
Intestinal involvement, n (%)	53 (65.4)	8 (88.9)	0.293
Anorectal involvement, n (%)	15 (18.5)	2 (22.2)	1.000
Albumin (g/l), median (IQR)	41.0 (37.0-43.0)	36.0 (32.4-43.2)	0.387
Calprotectin (µg/g), median (IQR)	37.5 (15.0-94.5)	62.0 (34.8-125.0)	0.290
Anti-centromere antibodies, n (%)	30 (39.5)	2 (25.0)	0.675
Anti-Scl70 antibodies, n (%)	24 (31.6)	2 (25.0)	1.000
Anti-RNA polymerase 3 antibodies	6 (7.9)	1 (12.5)	1.000
Anti-PM/SCL antibodies	3 (3.9)	0 (0.0)	1.000
Steroids, n (%)	25 (30.9)	5 (62.5)	0.157
IS treatment without steroids [°] , n (%)	34 (42.0)	4 (44.4)	1.000
Calcium channel blockers, n (%)	59 (72.8)	3 (37.5)	0.095
Bosentan, n (%)	6 (7.4)	1 (12.5)	1.000
Sildenafil, n (%)	6 (7.4)	1 (12.5)	1.000
Proton pump inhibitors, n (%)	66 (81.5)	7 (87.5)	1.000
Death at the end of the follow-up, n (%)	2 (2.5)	2 (22.2)	0.061

*Interstitial lung disease: evaluated by CT-scan.

[∞]Cardiac disease: presence of diastolic ventricular dysfunction or arrhythmia or atrioventricular block or pericarditis.[£]Pulmonary hypertension: measured by right-heart catheterisation.[°]Including cyclophosphamide, mycophenolate mofetil, rituximab and methotrexate.

IS: immunosuppressive; mRSS: modified Rodnan skin score.