Sclérodermie systémique: Manifestations musculo-squelettiques

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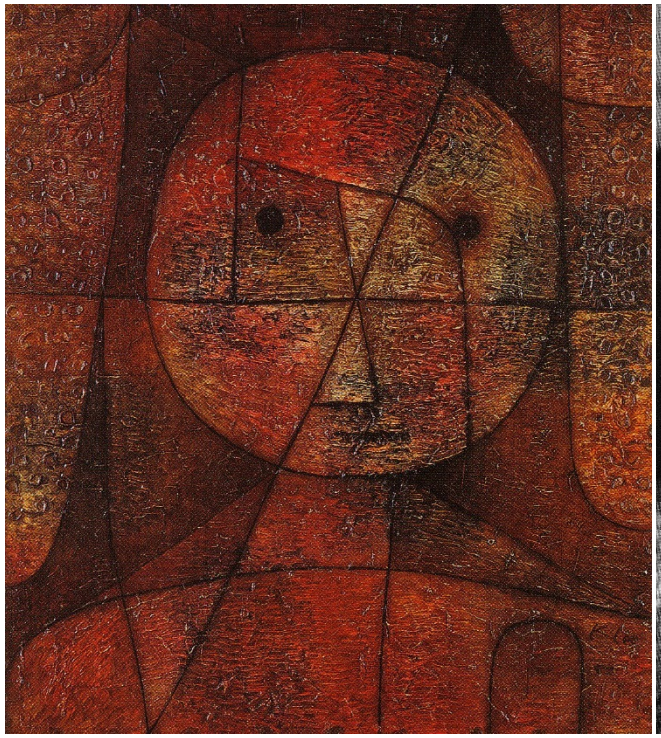
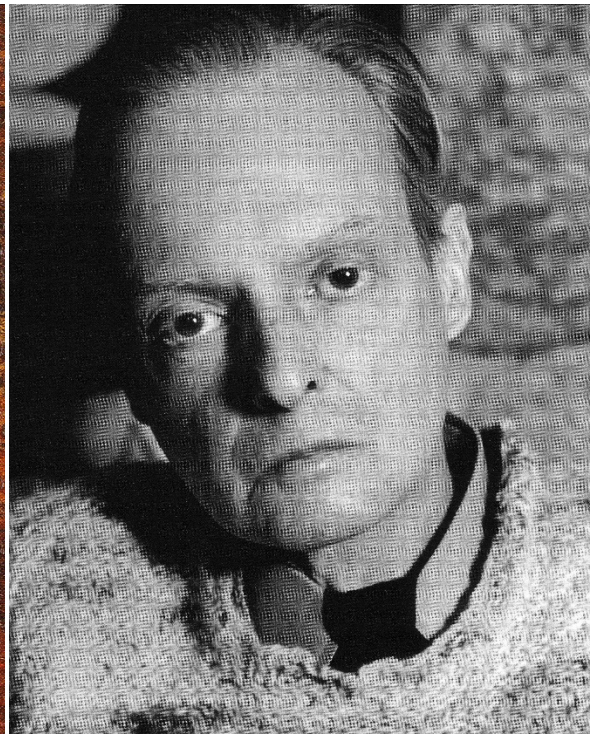
Paul Klee : 1879-1940 (I)





Gezeichneter 1935
„portant la marque de la mort“

1933 Raynaud‘s phenomenon

1934 Fatigue, dyspnea, thickened skin

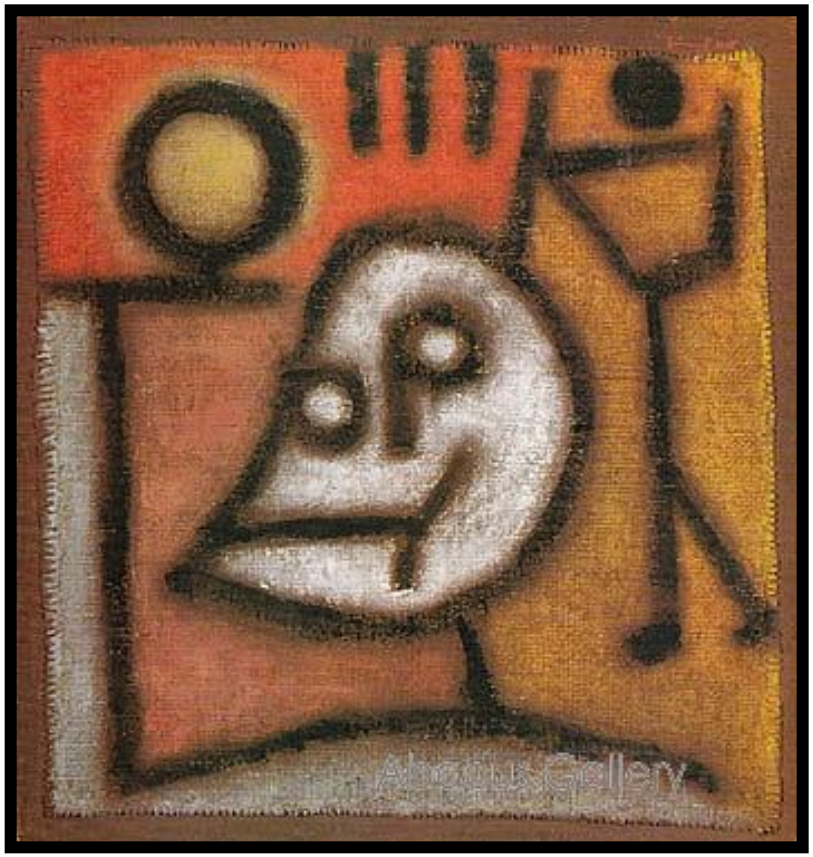
1936 Extension of skin fibrosis

1940 Hospitalisation at Sant‘ Agnes, Locarno (worsening of dyspnea)

Died in June 1940

Paul Klee: 1879-1940 (2)

Mask – 1921



Death and Fire – 1940

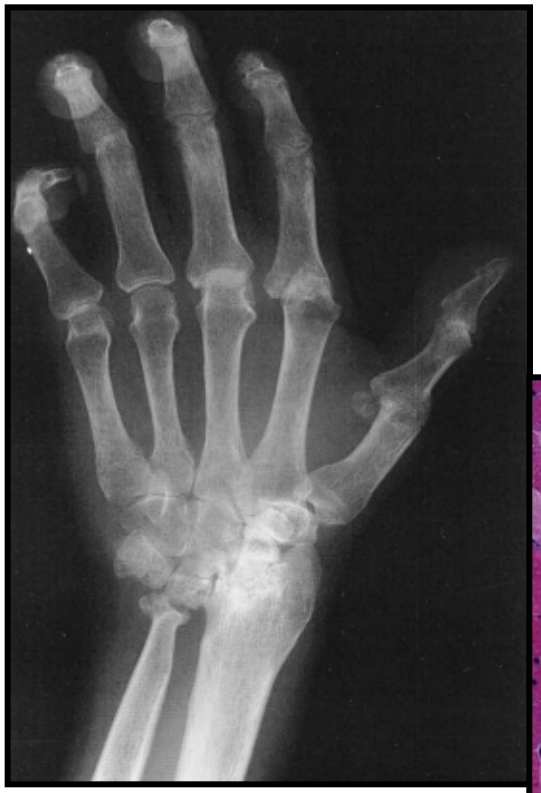
***Paul Klee* Polyphonies, Cité de la *musique*, Paris**
18 October 2011 – 15 January 2012

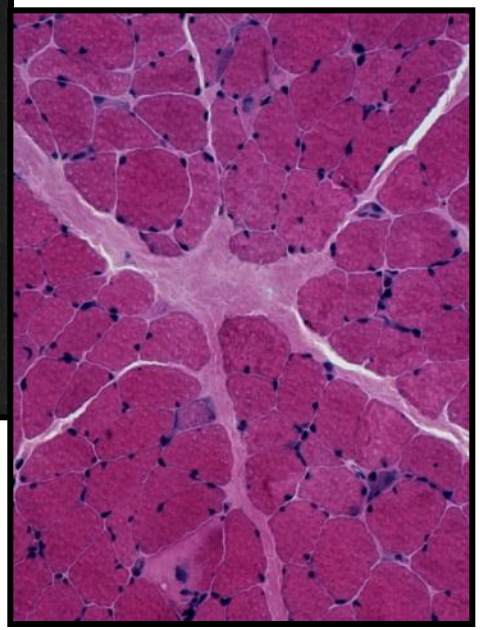
Musculoskeletal manifestations of SSc: Diffuse versus limited disease

	dcSSc	lcSSc	dcSSc vs. lcSSc
RP	96%	96%	0.58
Digital ulcers	43%	33%	< 0.001
Synovitis	21%	14%	< 0.001
Contractures	47%	24%	< 0.001
Friction rubs	22%	7%	< 0.001
Muscle weakness	37%	23%	< 0.001
CK elevation	11%	4%	< 0.001

Walker UA, *et al*. *Ann Rheum Dis* 2007; 66:754-63.

Musculoskeletal manifestations of SSc





- A major cause of morbidity and disability in SSc
- Includes
  - Muscle involvement (inflammatory myopathy)
  - Arthralgias
  - Arthritis
  - Flexion contractures
  - Nerve entrapment

Pope JE, *Rheum Dis Clin North Am* 2003; 29:391-408.

Skeletal muscle involvement in SSc

- Common feature in SSc
- Muscle weakness is found in up to 90% of SSc patients when systematically assessed
- Muscle clinical, biological and electromyographic features are similar to those of polymyositis or dermatomyositis, except for a higher proportion of mild symptoms
- SSc-associated myopathy is more prevalent in dcSSc and is associated with cardiomyopathy

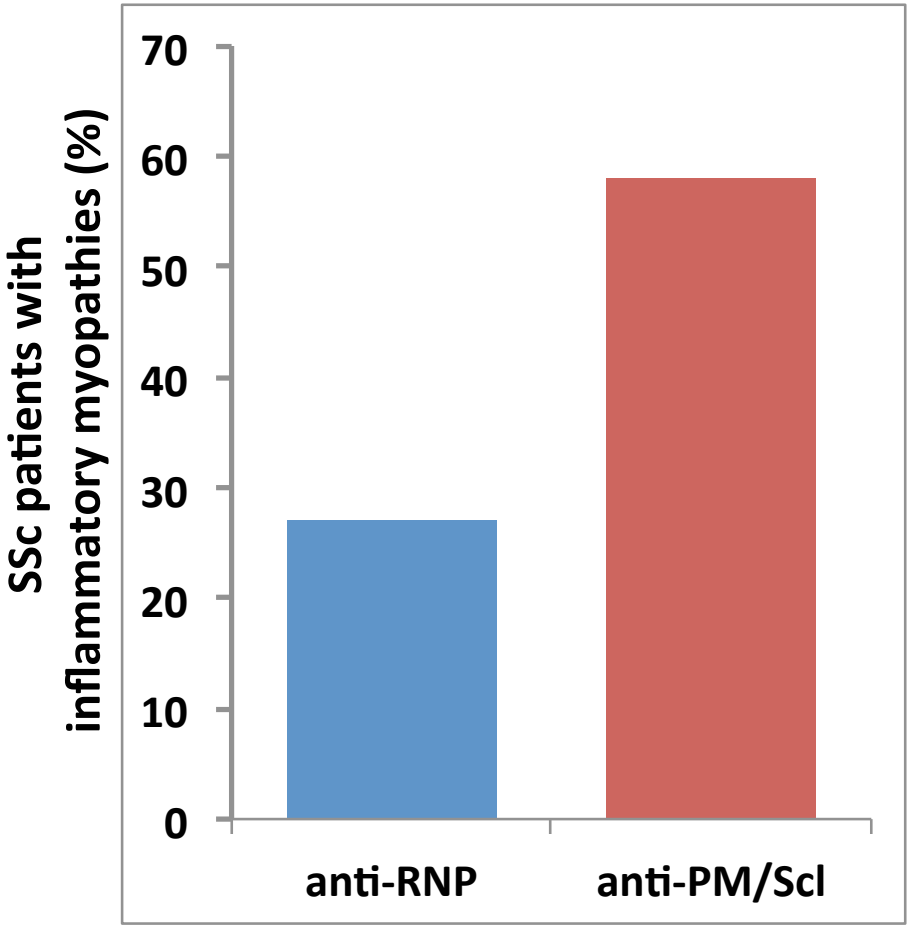
Follansbee WP, *Am Heart J* 1993; 125:194-203.
Ranque B, *et al*. *Ann N Y Acad Sci* 2007; 1108:268-82.

Features of SSc patients with skeletal myopathy

Variables	Cases *n* = 40	Controls *n* = 80	Univariate analysis		Multivariate analysis	
			p	OR [95%CI]	*p*	OR [95%CI]
Arthralgia: *n* (%)	20/39 (51)	49/79 (62)	0.222	0.7 [0.3-1.4]	-	-
Calcinosis: *n* (%)	4/40 (10)	15/79 (19)	0.213	0.4 [0.1-1.5]	-	-
FVC <75%: *n* (%)	26/39 (67)	30/75 (40)	0.007	3.5 [1.3-9.0]	0.025	3.1 [1.3-9.8]
ILD: *n* (%)	27/40 (68)	41/80 (51)	0.082	2.1 [0.9-4.8]	ns	ns
Systolic PAP>50 mmHg: *n* (%)	11/39 (28)	21/74 (28)	0.715	0.9 [0.4-2.0]	-	-
Heart involvement	16/40 (40)	14/80 (18)	0.011	2.9 [1.3-6.5]	0.045	2.5 [1.1-7.5]
SRC: *n* (%)	6/40 (15)	4/80 (5)	0.045	3.0 [1.3-34.9]	ns	ns
Gastrointestinal tract involvement: *n* (%)	4/40 (10)	16/80 (20)	0.170	0.5 [0.1-1.4]	-	-
anti-Scl70: *n* (%)	7/39 (18)	19/68 (28)	0.149	0.5 [0.1-1.4]		
anti-centromere: *n* (%)	2/39 (5)	21/66 (32)	0.002	0.1 [0.0-0.5]	0.002	0.1 [0.0-0.5]
anti-PM/Scl: *n* (%)	4/39 (11)	1/62 (2)	0.042	6.9 [1.1-64.4]	ns	ns

Ranque B, *et al. Scand J Rheumatol* 2010.

Autoantibodies associated with muscular involvement in SSc



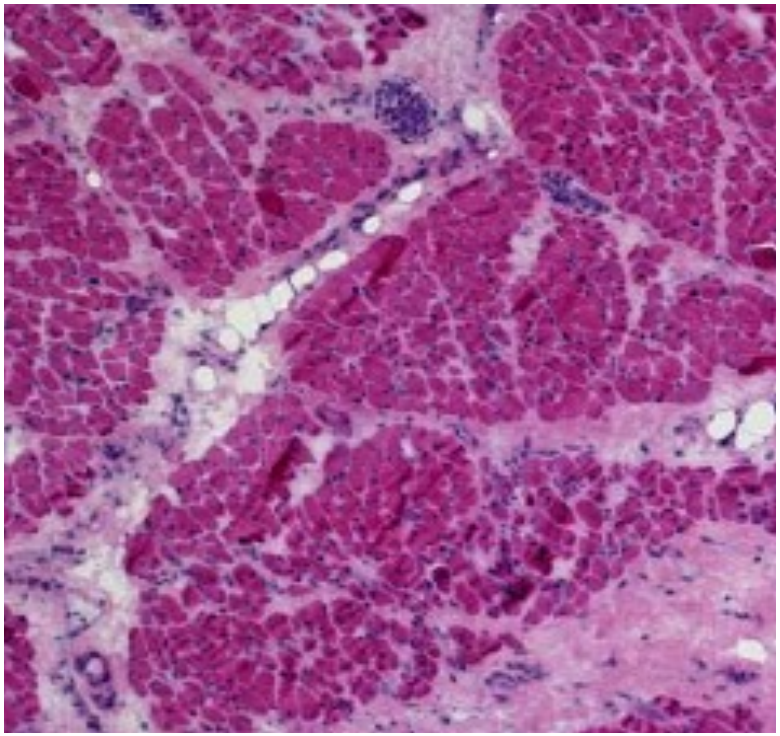
SSc	Myositis	Anti-PM/Scl
+	+	43-58%
-	+	5-8%
+	-	3-10%

Steen VD. *Semin Arthritis Rheum* 2005; 35:35-42.

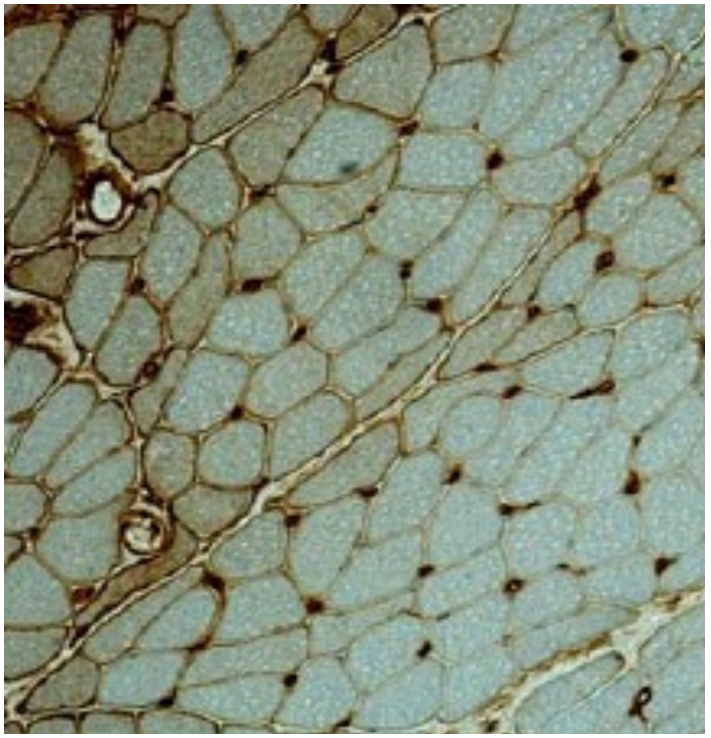
Ranque B, *et al. Ann N Y Acad Sci* 2007; 1108:268-82.

Muscle involvement in systemic sclerosis

Histopathology: Muscle fibre involvement



HE staining
Necrosis, atrophy, fibrosis
Perimysial inflammation

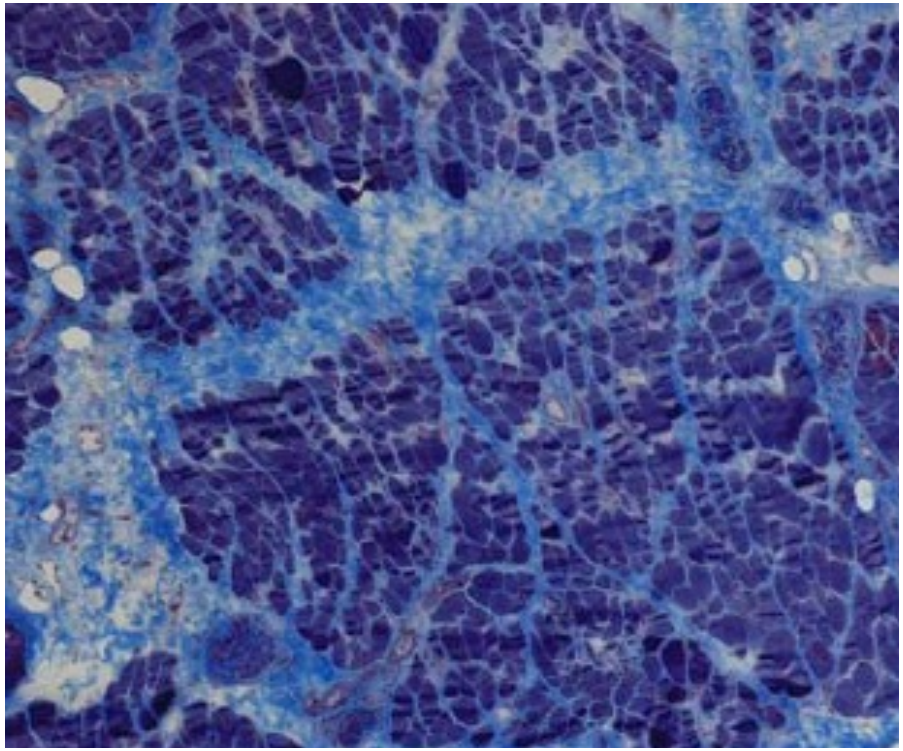


Class I MHC staining
Heterogeneous re-expression of class I MHC by myocytes

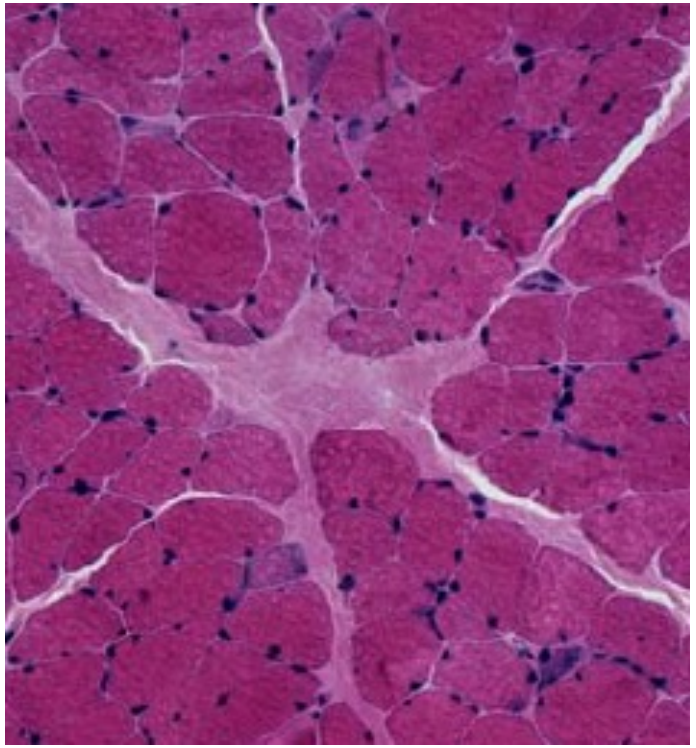
Courtesy F.J. Authier, Créteil, France

Muscle involvement in systemic sclerosis

Histopathology: Interstitial fibrosis



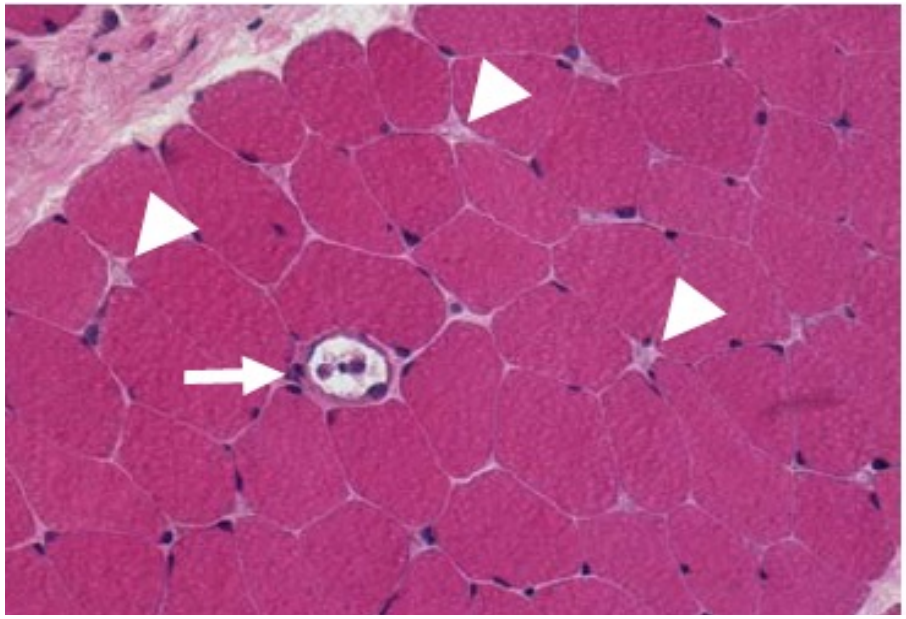
Masson trichrome staining
Collagen deposition



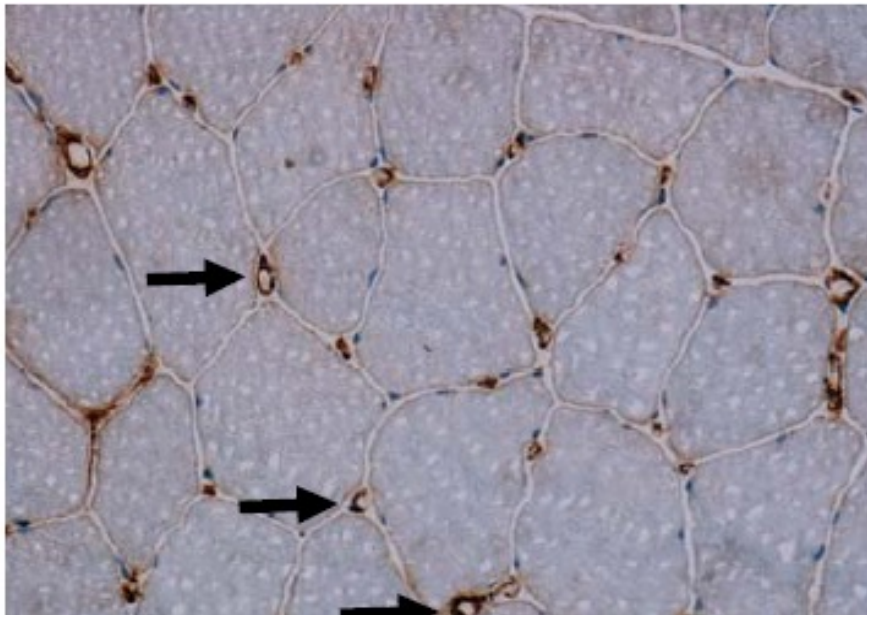
HE staining
Fibroblasts loss
Interstitial fibrosis

Courtesy F.J. Authier, Créteil, France

Muscle involvement in systemic sclerosis
Histopathology: Microangiopathy



HE staining



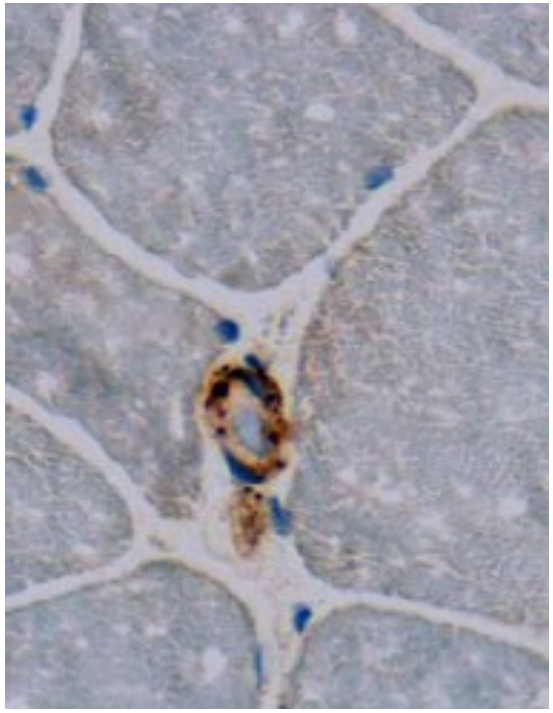
Staining of smooth muscles (actin)

Lumen dilation (arrows)
Thickening of vascular walls (triangles)

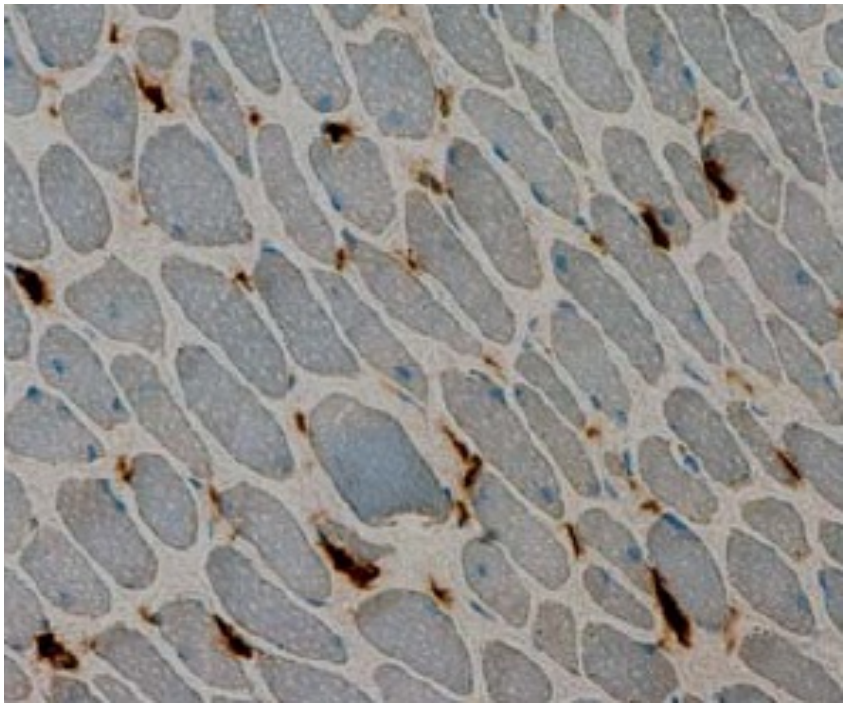
Courtesy F.J. Authier, Créteil, France

Muscle involvement in systemic sclerosis

Histopathology: Microangiopathy



CD5b-9 staining
Membrane attack
Complex deposition



CD 31 staining (endothelium)
Capillary loss

Courtesy F.J. Authier, Créteil, France

Therapeutic Advances in Musculoskeletal Disease *Original Research*

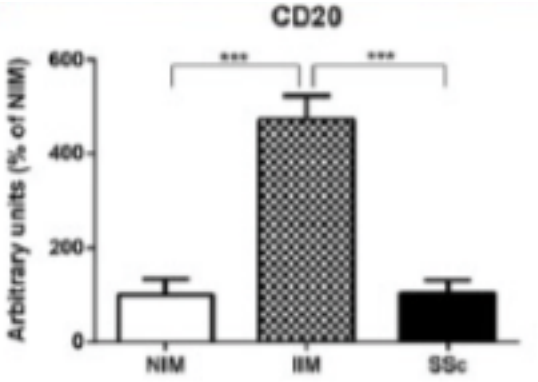
Histopathological findings in systemic sclerosis-related myopathy: fibrosis and microangiopathy with lack of cellular inflammation

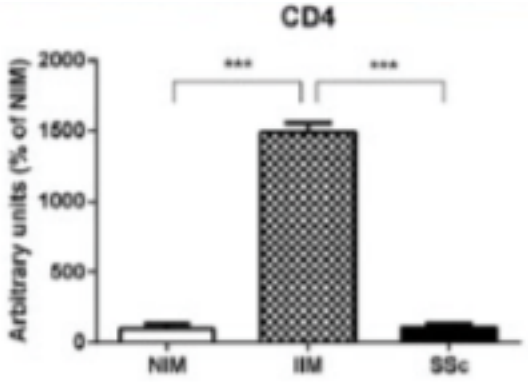
Ther Adv Musculoskel Dis

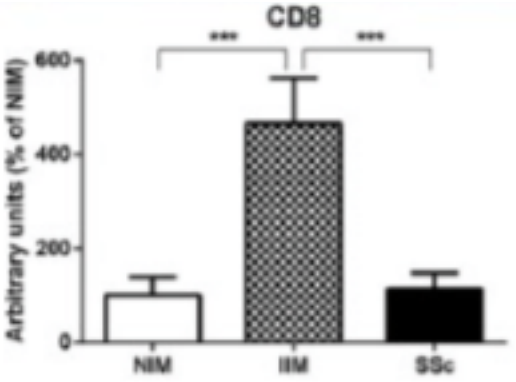
2017, Vol. 9(1) 3–10

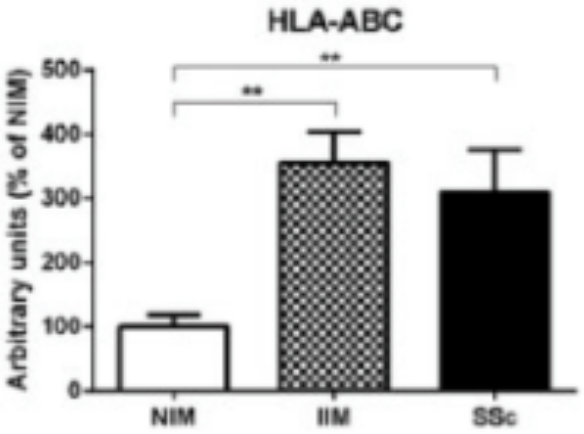
DOI: 10.1177/1759720X16671928

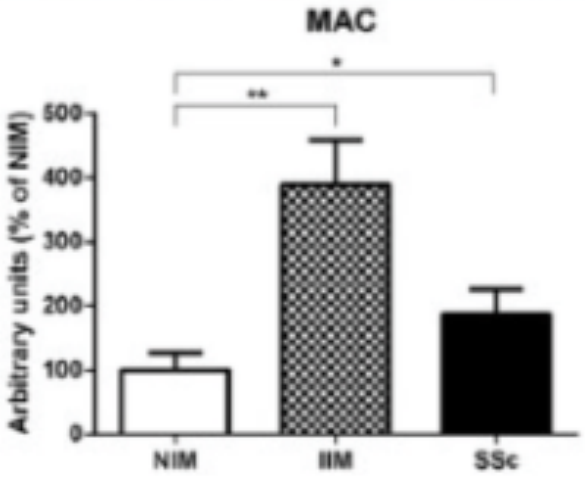
Claudio Corallo, Maurizio Cutolo, Nila Volpi, Daniela Franci, Margherita Aglianò, Antonio Montella, Chiara Chirico, Stefano Gonnelli, Ranuccio Nuti and Nicola Giordano

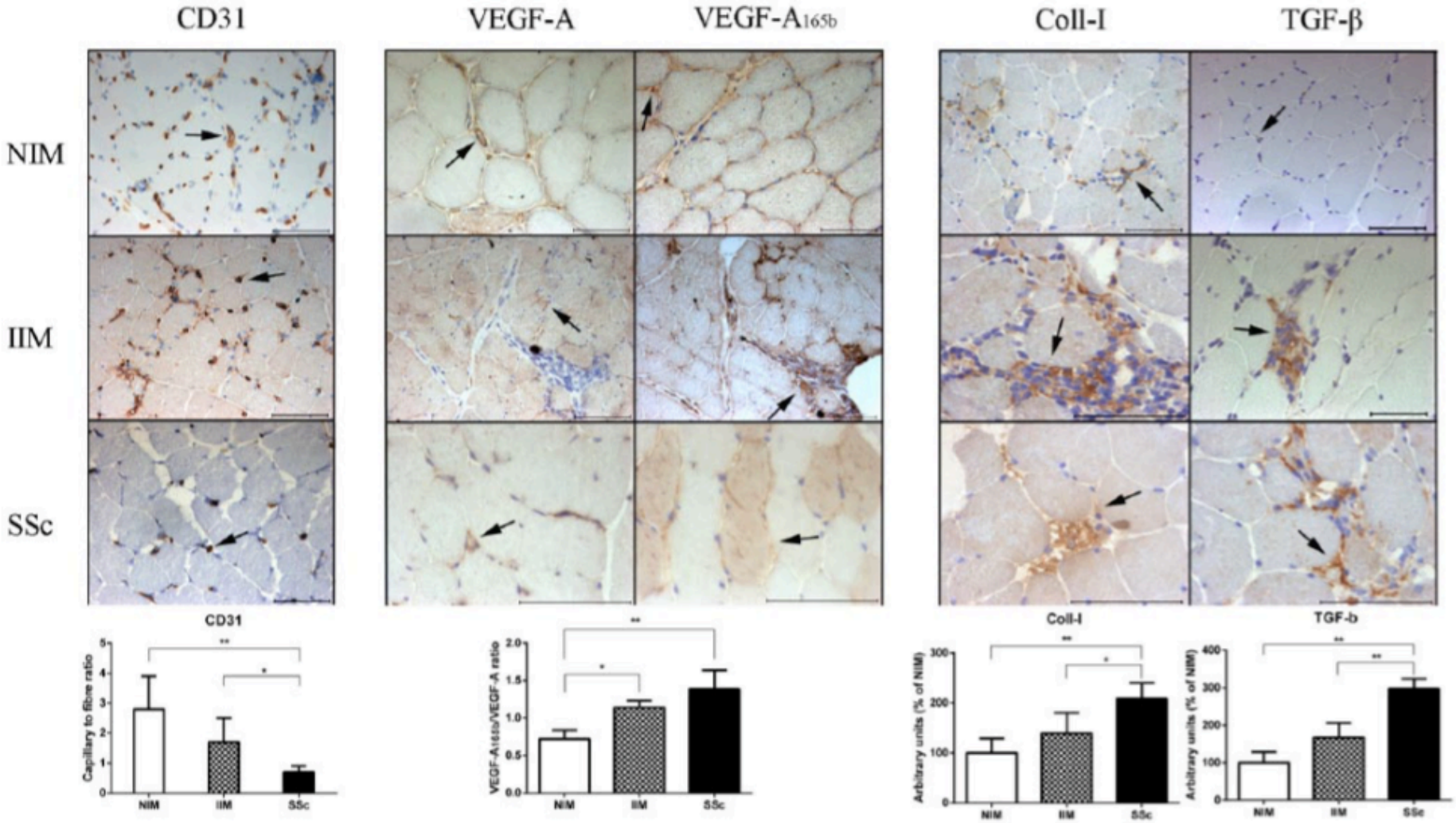

CD20
Arbitrary units (% of NIM)
600
400
200
0
***
***
NIM
IIM
SSc


CD4
Arbitrary units (% of NIM)
2000
1500
1000
500
0
***
***
NIM
IIM
SSc


CD8
Arbitrary units (% of NIM)
600
400
200
0
***
***
NIM
IIM
SSc


HLA-ABC
Arbitrary units (% of NIM)
500
400
300
200
100
0
**
**
NIM
IIM
SSc


MAC
Arbitrary units (% of NIM)
500
400
300
200
100
0
*
**
NIM
IIM
SSc


CD31
VEGF-A
VEGF-A165b
Coll-I
TGF-β
NIM
IIM
SSc
CD31
Capillary to fibre ratio
NIM
IIM
SSc
VEGF-A165b/VEGF-A ratio
Coll-I
Arbitrary units (% of NIM)
TGF-b

Response to corticosteroid treatment according to muscle histological parameters

Variable	Favourable muscle response		Univariate analysis		Multivariate analysis	
	in presence of the variable	in absence of the variable	*p* value	OR [95% CI]	*p* value	OR [95% CI]
Myopathology						
Inflammation	**18/20 (90%)**	**3/8 (38%)**	**0.004**	**15.0 [1.9-116.0]**	**0.004**	**15.0 [1.9-116.0]**
Necrosis	**16/18 (89%)**	**5/10 (50%)**	**0.034**	**8.0 [1.2-54.7]**	**-**	**-**
Regeneration	**8/10 (80%)**	**12/17 (71%)**	**0.592**	**1.7 [0.3-10.8]**	**-**	**-**
Atrophy	**13/16 (81%)**	**7/11 (64%)**	**0.312**	**2.5 [0.4-14.3]**	**-**	**-**
Microangiopathy	**4/7 (57%)**	**17/21 (81%)**	**0.220**	**0.3 [0.1-2.0]**	**-**	**-**
Fibrosis	**5/6 (83%)**	**16/22 (73%)**	**0.599**	**1.9 [0.2-19.5]**	**-**	**-**

Ranque B, *et al. Ann Rheum Dis* 2008.

Arthritis Care & Research
DOI 10.1002/acr.23291

Fibrosing myopathy in systemic sclerosis associates with higher mortality

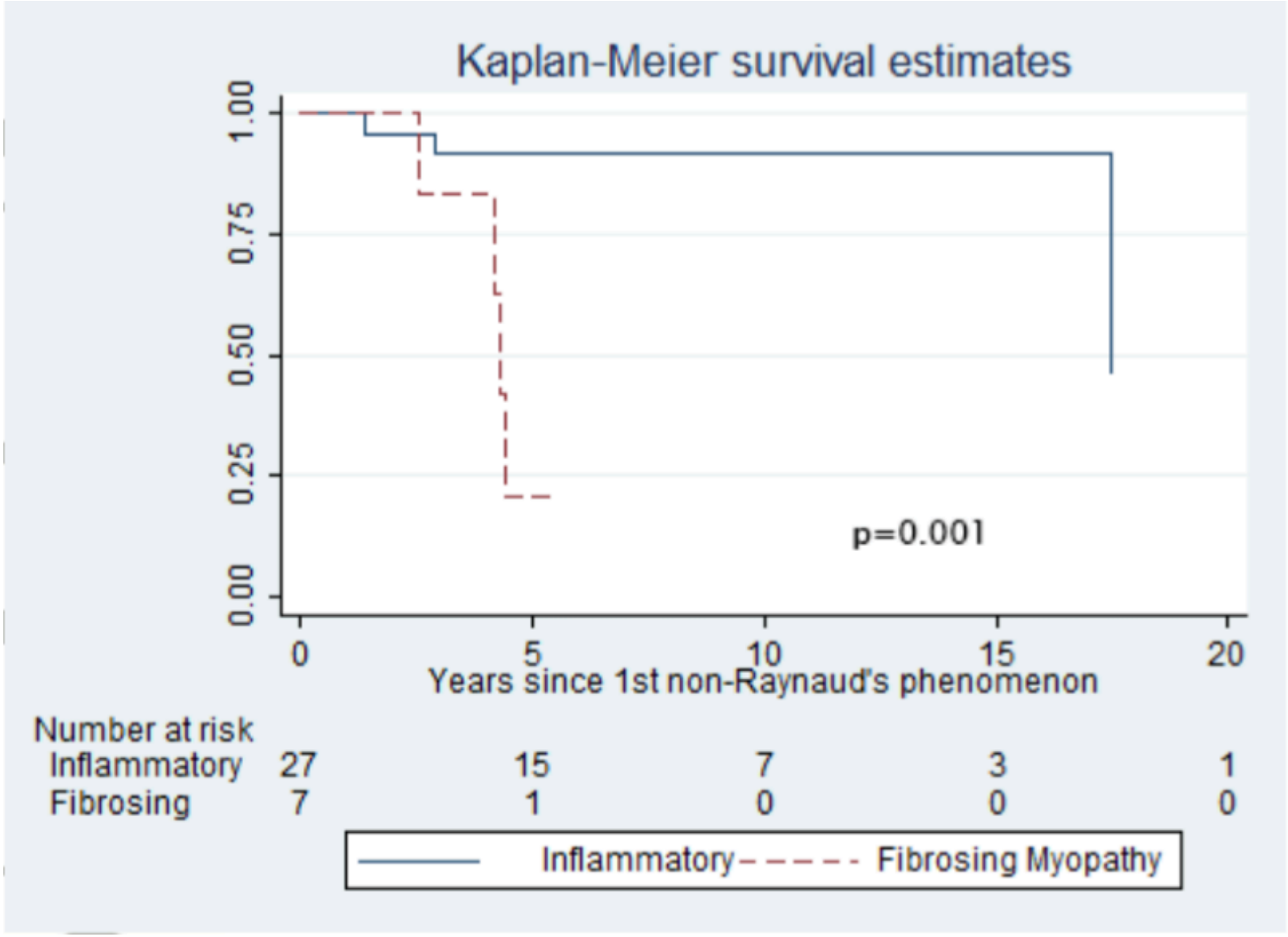
Julie J. Paik, MD, MHS[1], Fredrick M. Wigley, MD[1], Ami A. Shah, MD, MHS[1], Andrea M. Corse, MD[3], Livia Casciola-Rosen, PhD[1], Laura K. Hummers, MD, ScM[1]* and Andrew L. Mammen, MD, PhD [1,2,3]*

OBJECTIVE: To determine if a unique subtype of scleroderma muscle disease exists by comparing the clinical features of systemic sclerosis (SSc) patients with predominant fibrosis on muscle biopsy to those with inflammatory muscle histopathology.

METHODS: This retrospective, cross-sectional study included SSc patients with muscle weakness and an available muscle biopsy. Biopsies with fibrosis but without inflammation/necrosis were designated as "fibrosing myopathy" and those with inflammation and/or necrosis were assigned a category of "inflammatory myopathy". Clinical data including features of SSc, serum creatine kinase (CK) levels, electromyography (EMG), autoantibody profile, and survival were compared between the 2 groups.

RESULTS: The study population consisted of 37 weak SSc patients, 8 with fibrosing myopathy, and 29 with inflammatory myopathy. Compared to those with inflammatory myopathy, patients with fibrosing myopathy were more likely to have diffuse SSc skin subtype (87% vs. 62%, p=0.18), African-American race (62.5% vs. 37.9%; p=0.20), and a lower FVC (55.5 ± 31.9 vs. 66.4 ± 17.6; p=0.23). They also had lower CK values (516 ± 391 vs. 2477 ± 3511, p=0.007) and lower aldolase values (13.8 ± 4.7 vs. 27.3 ± 4.7, p=0.01). Patients with fibrosing myopathy had a significantly higher mortality (5 of 8; 62.5% vs 4 of 29 (14.3%), p=0.005).

CONCLUSION: Fibrosing myopathy is a unique histological subtype of muscle disease among weak patients with SSc and is associated with significantly worse mortality compared to those with inflammation and/or necrosis on muscle biopsy.


Kaplan-Meier survival estimates
1.00
0.75
0.50
0.25
0.00
p=0.001
0
5
10
15
20
Years since 1st non-Raynaud's phenomenon
Number at risk
Inflammatory 27 15 7 3 1
Fibrosing 7 1 0 0 0
Inflammatory
Fibrosing Myopathy

Muscle involvement in systemic sclerosis: Treatment not standardised

- Glucocorticoids
  - Used in most of the cases (80%)
  - Global response 60-80%
  - Prediction of response to treatment: Histopathological evidence of inflammation
    - Remission = 90% if present vs 38% if absent[1]

Renal crisis

- Immunosuppressants
  - Cyclophosphamide (if pulmonary fibrosis)
  - Methotrexate
  - Azathioprine, mycophenolate mofetil

- Intravenous immunoglobulins
  - Very good short term response (10/11)
  - High rate relapses (4/10)

Ranque B, *et al. Ann Rheum Dis* 2008.

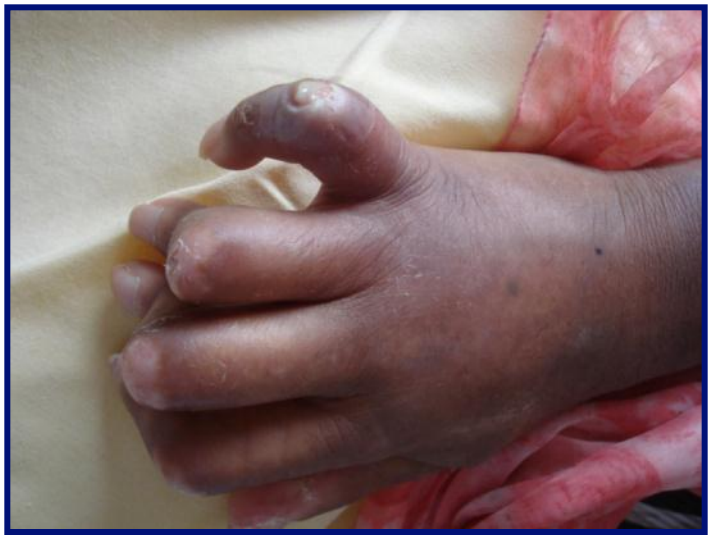
Radiological hand involvement in systemic sclerosis

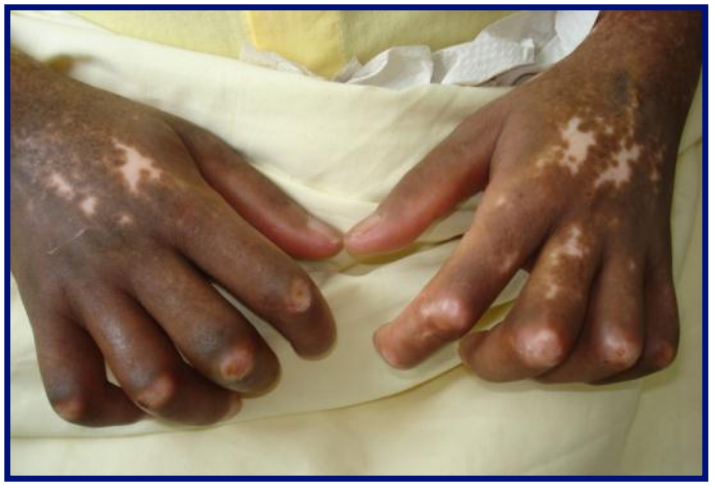
- 120 consecutive SSc patients
- Radiological abnormalities in SSc:
  - Erosion (21%)
  - Joint space narrowing (28%)
  - Arthritis (erosion and joint space narrowing) (18%)
  - Demineralisation (23%)
  - Acro-osteolysis (22%)
  - Flexion contracture (27%)
  - Calcinosis (23%)

Avouac J, *et al. Ann Rheum Dis* 2006; 65:1088-92.

Flexion contractures

- Common, especially in hands
  - MCP, PIP, DIP joints and wrists
- Often related to skin, fascia and tendon involvement
- Responsible for functional disability
- May favour digital ulcerations

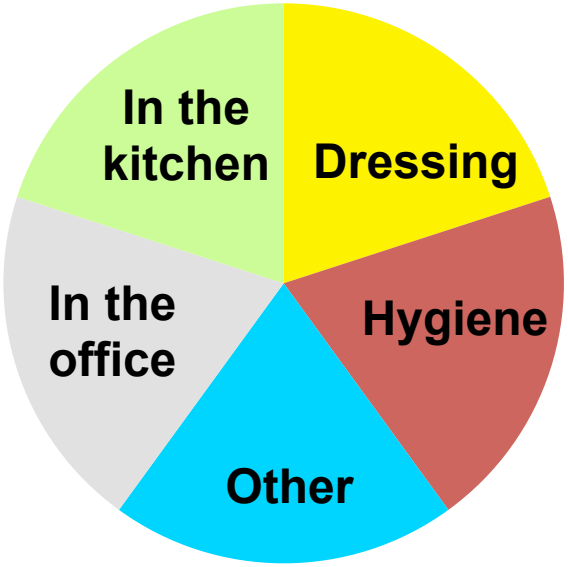




Cochin hand function scale (CHFS)

Without the help of adapted instruments, in the past two weeks, did you:

- Categories for assessment



- The scale is based on the following answer scores
  - 0 = Yes, without difficulty
  - 1 = Yes, with a little difficulty
  - 2 = Yes, with some difficulty
  - 3 = Yes, with much difficulty
  - 4 = Nearly impossible to do
  - 5 = Impossible

Hand disability contributes to 75% of the variance of the HAQ

Duruöz MT, *et al. J Rheumatol* 1996; 23:1167-72.
Rannou, *et al. Arthritis & Rheum* 2007.

EXTENDED REPORT

Joint and tendon involvement predict disease progression in systemic sclerosis: a EUSTAR prospective study

Jérôme Avouac,[1] Ulrich A Walker,[2] Eric Hachulla,[3] Gabriela Riemekasten,[4] Giovanna Cuomo,[5] Patricia E Carreira,[6] Paola Caramaschi,[7] Lidia P Ananieva,[8] Marco Matucci-Cerinic,[9] Laszlo Czirjak,[10] Christopher Denton,[11] Ulf Müller Ladner,[12] Yannick Allanore,[1] the EUSTAR collaborators*

Ann Rheum Dis 2016;**75**:103–109. doi:10.1136/annrheumdis-2014-205295

Disease characteristics at baseline of the 1301 included patients

Patients with synovitis (n=234)	Patients with TFRs (n=166)

Disease progression

Table 2 Predictors of overall disease progression as determined by univariate and multivariate analysis

	Univariate analysis		Multivariate analysis	
Baseline characteristics	**p Value**	**HR (95% CI)**	**p Value**	**HR (95% CI)**
Age (years)	0.097	0.99 (0.98 to 1.01)	NA	NA
Women (n=1079)	0.074	0.79 (0.64 to 1.01)	NA	NA
Time since diagnosis (years)	0.401	0.96 (0.89 to 1.05)	NA	NA
Joint synovitis (n=234)	<0.001	1.43 (1.17 to 1.74)	0.039	1.26 (1.01 to 1.59)
TFRs (n=166)	<0.001	1.61 (1.29 to 2.01)	0.030	1.32 (1.03 to 1.70)
Diffuse cutaneous subset (n=500)	<0.001	1.58 (1.33 to 1.88)	0.014	1.30 (1.05 to 1.61)
mRSS >14 (n=382)	<0.001	1.54 (1.29 to 1.82)	–*	–
Lung fibrosis (n=361)	0.250	1.11 (0.93 to 1.34)	NA	NA
Positive for antitopoisomerase-I antibodies (n=457)	<0.001	1.48 (1.25 to 1.75)	0.029	1.25 (1.02 to 1.53)
Increased CK levels (n=147)	0.015	1.35 (1.06 to 1.72)	0.703	1.06 (0.79 to 1.41)
Elevated acute phase reactants (n=311)	0.638	1.05 (0.87 to 1.26)	NA	NA
Muscle weakness (n=330)	0.006	1.30 (1.08 to 1.57)	0.550	1.07 (0.86 to 1.34)
FVC <75% predicted (n=305)	<0.001	1.46 (1.22 to 1.76)	0.070	1.22 (0.98 to 1.50)
DLCO <75% predicted (n=490)	<0.001	1.41 (1.19 to 1.67)	–†	–

Age, sex, time since diagnosis, cutaneous subset, lung fibrosis, reduced DLCO and acute phase reactants were systematically assessed as covariates in univariate analysis, together with joint synovitis and TFRs. This table also mentions all other variables that have been identified as predictors in univariate analysis.
*Variable not entered in the multivariate model since it has a high association with the diffuse cutaneous subset (Cramer's V=0.66).
†Variable not entered in the multivariate model since it has a high association with FVC<75% predicted (Cramer's V=0.53).
CK, creatine kinase; FVC, forced vital capacity; mRSS, modified Rodnan Skin Score; NA, not applicable; TFRs, tendon friction rubs.

Skin progression

Table 3 Predictors of skin progression as determined by univariate and multivariate analyses

Baseline characteristics	Univariate analysis		Multivariate analysis	
	p Value	HR (95% CI)	p Value	HR (95% CI)
Age (years)	0.110	0.98 (0.97 to 1.02)	NA	NA
Women (n=1037)	0.252	0.75 (0.47 to 1.21)	NA	NA
Time since diagnosis (years)	0.201	0.79 (0.67 to 1.05)	NA	NA
Joint synovitis (n=234)	<0.001	1.99 (1.21 to 1.43)	0.024	1.67 (1.06 to 2.64)
TFRs (n=166)	<0.001	2.23 (1.25 to 4.03)	0.035	1.69 (1.02 to 2.77)
Diffuse cutaneous subset (n=489)	0.021	1.58 (1.07 to 2.44)	0.343	0.98 (0.65 to 1.50)
Positive for antitopoisomerase-I antibodies (n=450)	<0.001	2.10 (1.41 to 3.12)	0.030	1.72 (1.09 to 2.62)
History of digital ulcers (n=354)	0.003	1.42 (1.02 to 2.15)	0.049	1.50 (1.01 to 2.23)
Lung fibrosis (n=355)	0.786	0.94 (0.73 to 1.51)	NA	NA
DLCO <75% predicted (n=468)	0.078	1.32 (0.95 to 1.79)	NA	NA
Elevated acute phase reactants (n=301)	0.407	1.20 (0.78 to 1.85)	NA	NA

Age, sex, time since diagnosis, cutaneous subset, lung fibrosis, reduced DLCO and acute phase reactants were systematically assessed as covariates in univariate analysis, together with joint synovitis and TFRs. This table also mentions all other variables that have been identified as predictors in univariate analysis.
NA, not applicable; TFRs, tendon friction rubs.

Table 4 Predictors of vascular progression as determined by univariate and multivariate analyses

Baseline characteristics	Univariate analysis		Multivariate analysis	
	p Value	HR (95% CI)	p Value	HR (95% CI)
New Digital Ulcer				
Age (years)	0.092	0.99 (0.98 to 1.01)	NA	NA
Women (n=1077)	0.821	1.04 (0.72 to 1.50)	NA	NA
Time since diagnosis (years)	0.547	0.96 (0.85 to 1.09)	NA	NA
Joint synovitis (n=233)	<0.001	1.68 (1.15 to 2.34)	0.003	1.45 (1.08 to 1.96)
TFRs (n=166)	0.003	1.65 (1.09 to 2.51)	0.293	1.23 (0.84 to 1.80)
Diffuse cutaneous subset (n=497)	<0.001	1.76 (1.33 to 2.31)	0.108	1.30 (0.94 to 1.78)
mRSS >14 (n=380)	0.0002	1.64 (1.26 to 2.14)	–*	–
Lung fibrosis (n=360)	0.083	1.35 (0.97 to 1.78)	NA	NA
Positive for antitopoisomerase-I antibodies (n=456)	<0.001	1.96 (1.49 to 2.58)	0.002	1.76 (1.30 to 2.40)
Elevated acute phase reactants (n=311)	0.94	1.01 (0.75 to 1.36)	NA	NA
History of digital ulcers (n=364)	<0.001	3.01 (1.28 to 4.57)	0.001	1.99 (1.51 to 2.64)
FVC <75% predicted (n=304)	<0.001	1.65 (1.09 to 2.51)	0.234	1.21 (0.88 to 1.67)
DLCO <75% predicted (n=488)	0.232	1.18 (0.90 to 1.54)	NA	NA
Reduction of LVEF				
Age (years)	0.547	1.00 (0.98 to 1.03)	NA	NA
Women (n=994)	0.063	0.41 (0.20 to 1.00)	NA	NA
Time since diagnosis (years)	0.493	0.89 (0.65 to 1.22)	NA	NA
Joint synovitis (n=205)	0.004	2.64 (1.08 to 6.44)	0.01	2.20 (1.06 to 4.57)
Diffuse cutaneous subset (n=448)	0.002	2.82 (1.42 to 5.59)	0.3	1.59 (0.72 to 3.52)
Lung fibrosis (n=330)	<0.001	3.11 (1.56 to 6.67)	0.04	2.21 (1.09 to 4.47)
Muscle weakness (n=299)	0.001	2.84 (1.26 to 6.43)	0.04	2.25 (1.08 to 4.56)
History of digital ulcers (n=341)	0.032	1.75 (1.02 to 3.59)	0.3	1.50 (0.75 to 3.00)
Positive for antitopoisomerase-I antibodies (n=439)	0.002	2.71 (1.34 to 5.48)	0.5	1.36 (0.62 to 2.97)
Elevated acute phase reactants (n=257)	0.209	1.56 (0.78 to 3.11)	NA	NA
DLCO <75% predicted (n=422)	0.396	1.34 (0.68 to 2.63)	NA	NA

Age, sex, time since diagnosis, cutaneous subset, lung fibrosis, reduced DLCO and acute phase reactants were systematically assessed as covariates in univariate analysis, together with joint synovitis and TFRs. This table also mentions all other variables that have been identified as predictors in univariate analysis.
*Variable not entered in the multivariate model since it has a high association with the diffuse cutaneous subset (Cramer's V=0.66).
FVC, forced vital capacity; LVEF, left ventricular ejection fraction; mRSS, modified Rodnan Skin Score; NA, not applicable; TFRs, tendon friction rubs.

Handicap

RHEUMATOLOGY

Original article

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Functional disability and its predictors in systemic sclerosis: a study from the DeSScipher project within the EUSTAR group

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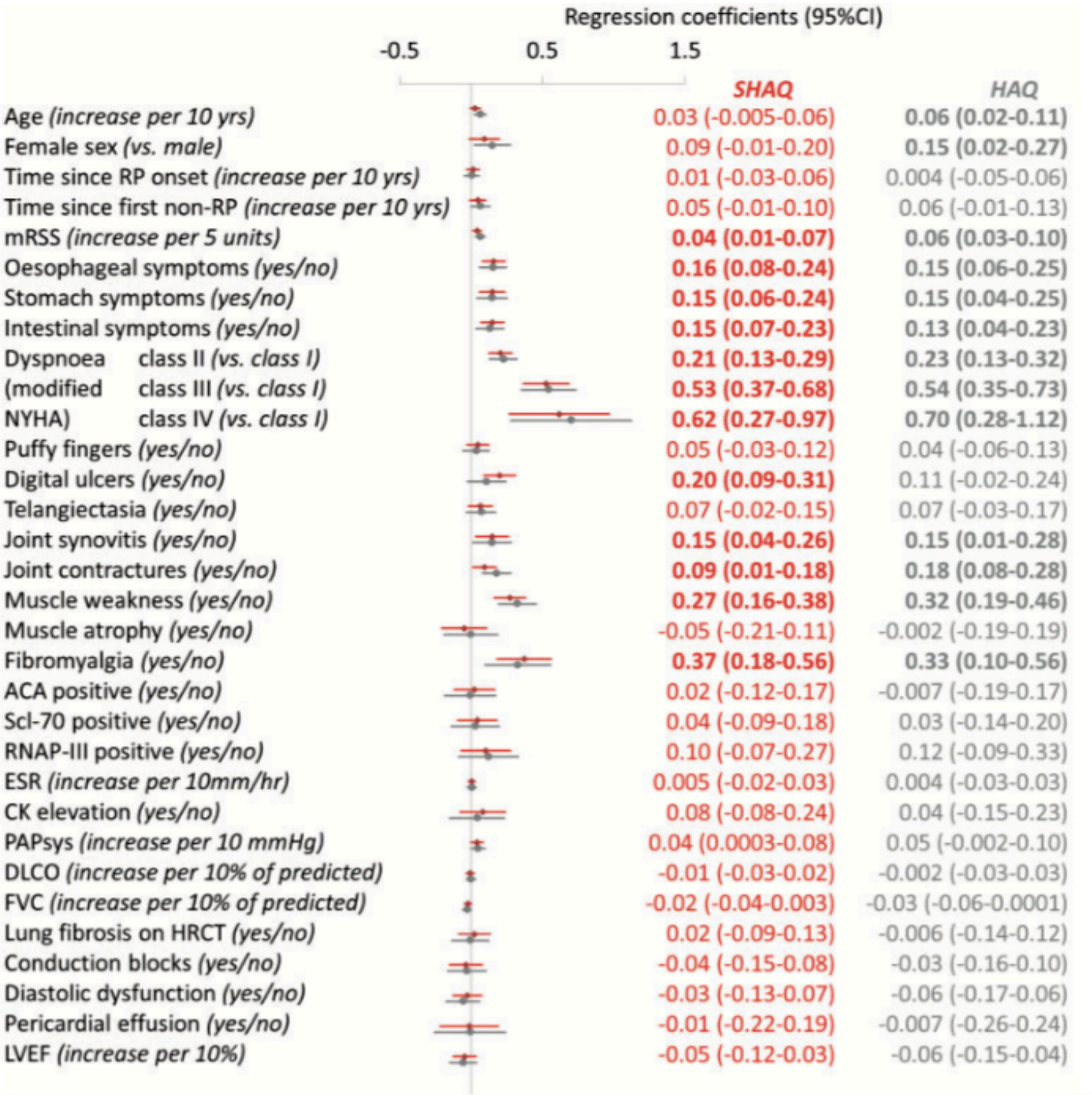
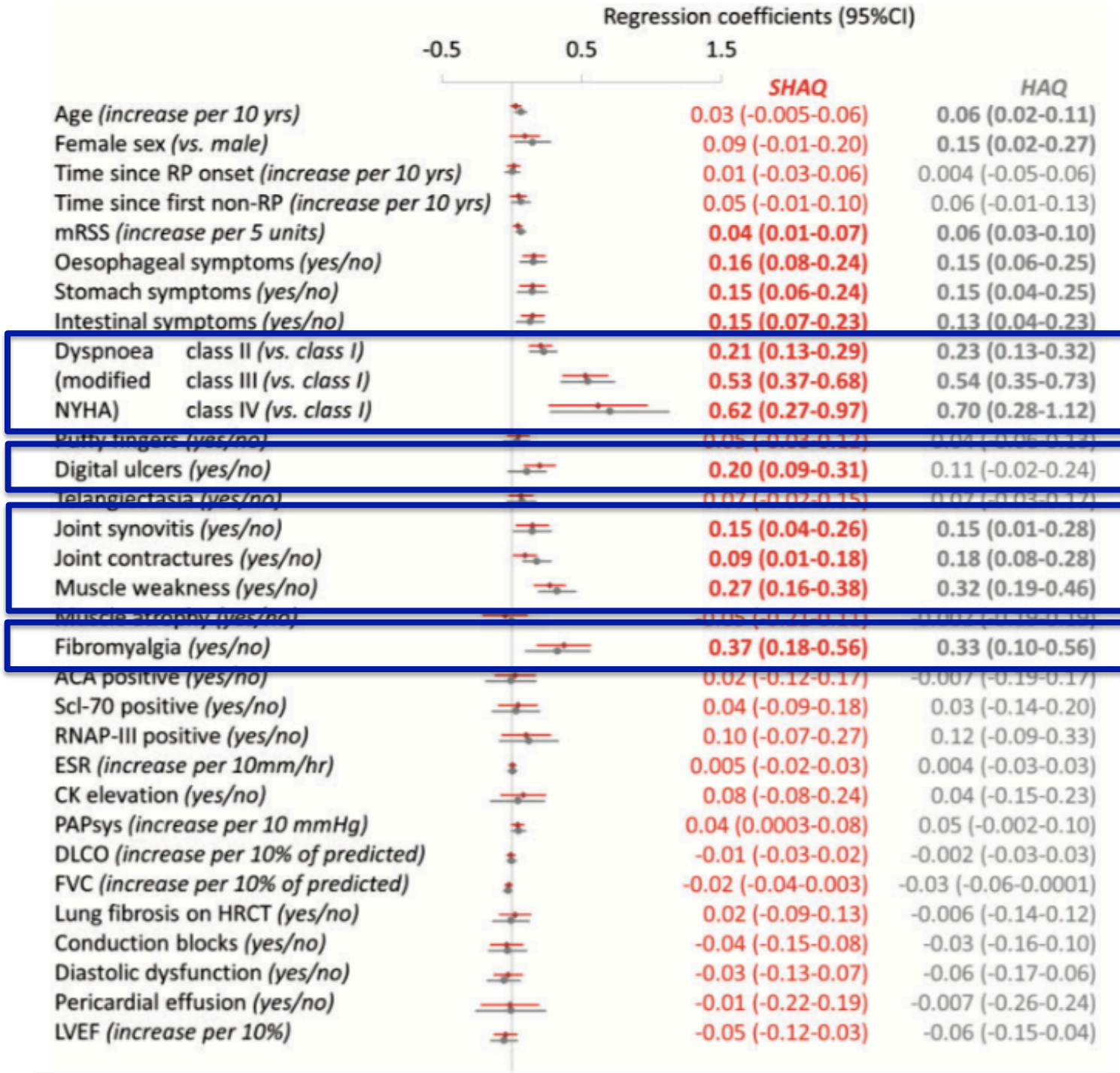
2017



	SHAQ	HAQ
Age *(increase per 10 yrs)*	0.03 (-0.005-0.06)	**0.06 (0.02-0.11)**
Female sex *(vs. male)*	0.09 (-0.01-0.20)	**0.15 (0.02-0.27)**
Time since RP onset *(increase per 10 yrs)*	0.01 (-0.03-0.06)	0.004 (-0.05-0.06)
Time since first non-RP *(increase per 10 yrs)*	0.05 (-0.01-0.10)	0.06 (-0.01-0.13)
mRSS *(increase per 5 units)*	**0.04 (0.01-0.07)**	**0.06 (0.03-0.10)**
Oesophageal symptoms *(yes/no)*	**0.16 (0.08-0.24)**	**0.15 (0.06-0.25)**
Stomach symptoms *(yes/no)*	**0.15 (0.06-0.24)**	**0.15 (0.04-0.25)**
Intestinal symptoms *(yes/no)*	**0.15 (0.07-0.23)**	**0.13 (0.04-0.23)**
Dyspnoea (modified NYHA) class II *(vs. class I)*	**0.21 (0.13-0.29)**	**0.23 (0.13-0.32)**
Dyspnoea (modified NYHA) class III *(vs. class I)*	**0.53 (0.37-0.68)**	**0.54 (0.35-0.73)**
Dyspnoea (modified NYHA) class IV *(vs. class I)*	**0.62 (0.27-0.97)**	**0.70 (0.28-1.12)**
Puffy fingers *(yes/no)*	0.05 (-0.03-0.12)	0.04 (-0.06-0.13)
Digital ulcers *(yes/no)*	**0.20 (0.09-0.31)**	0.11 (-0.02-0.24)
Telangiectasia *(yes/no)*	0.07 (-0.02-0.15)	0.07 (-0.03-0.17)
Joint synovitis *(yes/no)*	**0.15 (0.04-0.26)**	**0.15 (0.01-0.28)**
Joint contractures *(yes/no)*	**0.09 (0.01-0.18)**	**0.18 (0.08-0.28)**
Muscle weakness *(yes/no)*	**0.27 (0.16-0.38)**	**0.32 (0.19-0.46)**
Muscle atrophy *(yes/no)*	-0.05 (-0.21-0.11)	-0.002 (-0.19-0.19)
Fibromyalgia *(yes/no)*	**0.37 (0.18-0.56)**	**0.33 (0.10-0.56)**
ACA positive *(yes/no)*	0.02 (-0.12-0.17)	-0.007 (-0.19-0.17)
Scl-70 positive *(yes/no)*	0.04 (-0.09-0.18)	0.03 (-0.14-0.20)
RNAP-III positive *(yes/no)*	0.10 (-0.07-0.27)	0.12 (-0.09-0.33)
ESR *(increase per 10mm/hr)*	0.005 (-0.02-0.03)	0.004 (-0.03-0.03)
CK elevation *(yes/no)*	0.08 (-0.08-0.24)	0.04 (-0.15-0.23)
PAPsys *(increase per 10 mmHg)*	0.04 (0.0003-0.08)	0.05 (-0.002-0.10)
DLCO *(increase per 10% of predicted)*	-0.01 (-0.03-0.02)	-0.002 (-0.03-0.03)
FVC *(increase per 10% of predicted)*	-0.02 (-0.04-0.003)	-0.03 (-0.06-0.0001)
Lung fibrosis on HRCT *(yes/no)*	0.02 (-0.09-0.13)	-0.006 (-0.14-0.12)
Conduction blocks *(yes/no)*	-0.04 (-0.15-0.08)	-0.03 (-0.16-0.10)
Diastolic dysfunction *(yes/no)*	-0.03 (-0.13-0.07)	-0.06 (-0.17-0.06)
Pericardial effusion *(yes/no)*	-0.01 (-0.22-0.19)	-0.007 (-0.26-0.24)
LVEF *(increase per 10%)*	-0.05 (-0.12-0.03)	-0.06 (-0.15-0.04)



	SHAQ	HAQ
Age *(increase per 10 yrs)*	0.03 (-0.005-0.06)	0.06 (0.02-0.11)
Female sex *(vs. male)*	0.09 (-0.01-0.20)	0.15 (0.02-0.27)
Time since RP onset *(increase per 10 yrs)*	0.01 (-0.03-0.06)	0.004 (-0.05-0.06)
Time since first non-RP *(increase per 10 yrs)*	0.05 (-0.01-0.10)	0.06 (-0.01-0.13)
mRSS *(increase per 5 units)*	**0.04 (0.01-0.07)**	0.06 (0.03-0.10)
Oesophageal symptoms *(yes/no)*	**0.16 (0.08-0.24)**	0.15 (0.06-0.25)
Stomach symptoms *(yes/no)*	**0.15 (0.06-0.24)**	0.15 (0.04-0.25)
Intestinal symptoms *(yes/no)*	**0.15 (0.07-0.23)**	0.13 (0.04-0.23)
Dyspnoea (modified NYHA) class II *(vs. class I)*	**0.21 (0.13-0.29)**	0.23 (0.13-0.32)
Dyspnoea (modified NYHA) class III *(vs. class I)*	**0.53 (0.37-0.68)**	0.54 (0.35-0.73)
Dyspnoea (modified NYHA) class IV *(vs. class I)*	**0.62 (0.27-0.97)**	0.70 (0.28-1.12)
Puffy fingers *(yes/no)*	0.05 (-0.02-0.12)	0.04 (-0.06-0.13)
Digital ulcers *(yes/no)*	**0.20 (0.09-0.31)**	0.11 (-0.02-0.24)
Telangiectasia *(yes/no)*	0.07 (-0.02-0.15)	0.02 (-0.08-0.12)
Joint synovitis *(yes/no)*	**0.15 (0.04-0.26)**	0.15 (0.01-0.28)
Joint contractures *(yes/no)*	**0.09 (0.01-0.18)**	0.18 (0.08-0.28)
Muscle weakness *(yes/no)*	**0.27 (0.16-0.38)**	0.32 (0.19-0.46)
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Fibromyalgia *(yes/no)*	**0.37 (0.18-0.56)**	0.33 (0.10-0.56)
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PAPsys *(increase per 10 mmHg)*	0.04 (0.0003-0.08)	0.05 (-0.002-0.10)
DLCO *(increase per 10% of predicted)*	-0.01 (-0.03-0.02)	-0.002 (-0.03-0.03)
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Pericardial effusion *(yes/no)*	-0.01 (-0.22-0.19)	-0.007 (-0.26-0.24)
LVEF *(increase per 10%)*	-0.05 (-0.12-0.03)	-0.06 (-0.15-0.04)

Joint involvement in systemic sclerosis: Treatment

- ✓ Colchicine
- ✓ Low dose prednisone
- ✓ Methotrexate
- ✓ Biologics
- ✓ Surgical procedures
- ✓ Physiotherapy
- ✓ Occupational therapy

Outcomes of patients with systemic sclerosis-associated polyarthritis and myopathy treated with tocilizumab or abatacept: an EUSTAR observational study

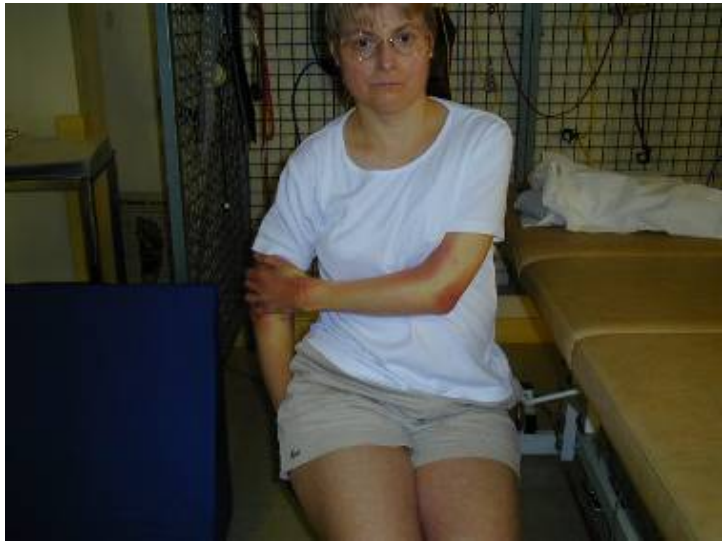
- 20 patients with SSc with refractory polyarthritis and 7 with refractory myopathy:
  - 15 patients received tocilizumab
  - 12 patients received abatacept
- All patients with SSc-myopathy received abatacept
- After 5 months tocilizumab: significant improvement in the DAS-28, with 10/15 patients achieving a EULAR good response
- After 11 months abatacept, joint parameters improved significantly, with 6/11 patients fulfilling EULAR good-response criteria
- Abatacept did not improve muscle outcome measures
- No significant change was seen for skin or lung fibrosis
- Both treatments were well tolerated

Elhai M *et al. Ann Rheum Dis* 2013; 72: 1217-20.

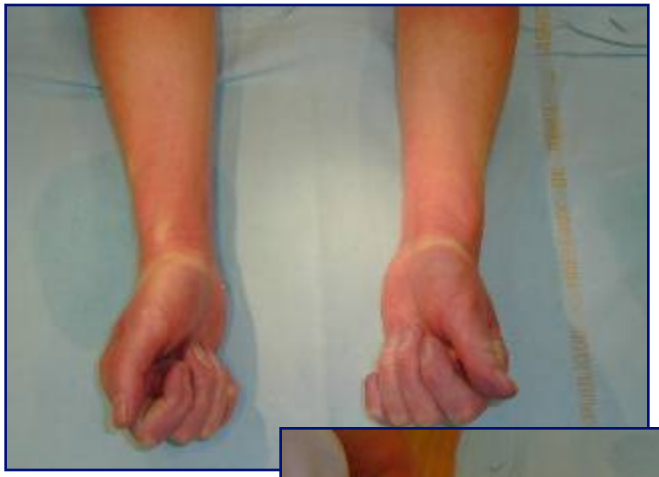
Rehabilitation in SSc patients with musculoskeletal involvement

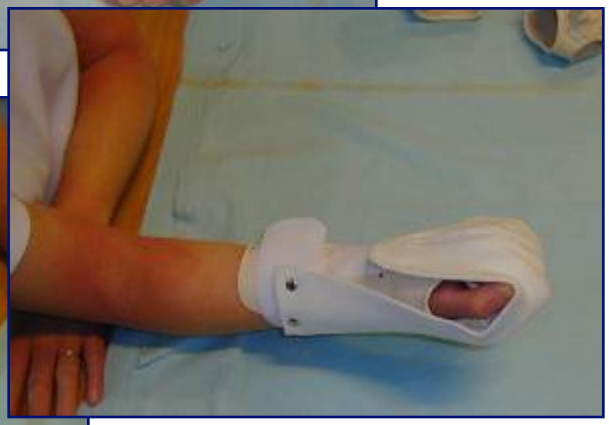
- Increasing articular range of motion
  - Massotherapy
  - Active and passive mobilisation
  - Posture
    - Shoulders
    - Elbows
    - Wrists
    - Fingers
    - Hips
    - Knees
- Correction of microstomia posture
  - Massage
  - Active mobilisation
  - Gum chewing

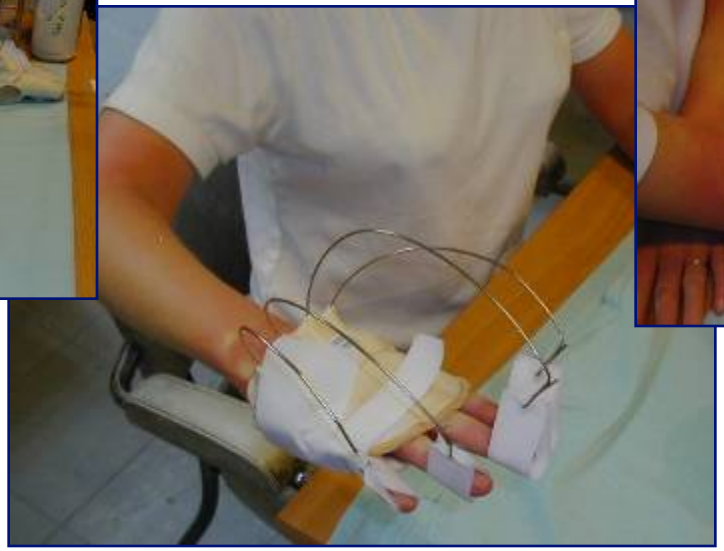
Increasing articular range of motion



Orthoses







Occupational therapy

Personalized Physical Therapy Versus Usual Care for Patients With Systemic Sclerosis: A Randomized Controlled Trial

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Arthritis Care & Research
Vol. 69, No. 7, July 2017, pp 1050–1059

Objective. To compare a physical therapy program to usual care of systemic sclerosis (SSc) patients on disability.
Methods. A 12-month followup, parallel-group randomized controlled trial involving a modified Zelen design was conducted in 4 tertiary-care hospitals. Patients were enrolled if they had a disability rating ≥0.5 on the Health Assessment Questionnaire disability index (HAQ DI) or symptoms of decreased mouth opening or limited range of motion of at least 1 joint. The experimental intervention (n = 112, of which 110 were analyzed) was a 1-month personalized supervised physical therapy program provided by trained care providers followed by home sessions. The comparator (n = 108, and all 108 were analyzed) was usual care that could include ambulatory physical therapy. The primary outcome was the HAQ DI score.
Results. There was no statistically significant difference in disability at 12 months (HAQ DI score between-group difference −0.01 [95% confidence interval (95% CI) −0.15, 0.13]; $P = 0.86$). Disability was reduced at 1 month for patients in the physical therapy group (HAQ DI between-group difference −0.14 [95% CI −0.24, −0.03]; $P = 0.01$); at 6 months the HAQ DI score between-group difference was −0.12 (95% CI −0.23, 0.01); $P = 0.054$. There was a statistically significant difference for hand mobility and function, and for pain, at 1 month. Microstomia was lower in the physical therapy group at 1, 6, and 12 months (between-group difference at 12 months 1.62 [95% CI 0.32, 2.93]; $P = 0.01$). No differences in adverse effects were observed.
Conclusion. A personalized physical therapy program did not reduce disability at 12 months but had short-term benefits for patients with SSc.

Tendon friction rubs (TFR)

- Detected by physical examination
- Highly associated with dcSSc
  - 91% of patients with TFR classified as dcSSc
- Associated with poor prognosis
  - e.g. scleroderma renal crisis
- May aid early diagnosis of dcSSc and identification of patients at high risk for serious organ-based complications

Steen VD and Medsger TA Jr, *Arthritis Rheum* 1997; 40:1146-51.

Nerve entrapment

- Carpal tunnel syndrome
  - Patients with early SSc are likely to develop median nerve entrapment secondary to oedema and inflammation
  - Often settles spontaneously
- Ulnar nerve entrapment
- Brachial plexopathy

Pope JE, *Rheum Dis Clin North Am* 2003; 29:391-408.
Mouthon L*, et al. Rheumatology* 2000; 39:682-3.
Mouthon L, *et al. Ann Med Intern* 2000; 151:303-5.

Conclusion

- Manifestations musculo-squelettiques fréquentes au cours de la sclérodermie systémique (jusqu'à 96%)
- Handicap des mains au premier plan
- Arthrites, myosites: méthotrexate
- Eviter les fortes doses de corticoïdes
- Rééducation fonctionnelle

Merci pour votre attention!

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