Sclérodermie systémique: pronostic

Luc Mouthon

Service de Médecine Interne, hôpital Cochin,

Centre de Référence Maladies Systémiques Autoimmunes Rares d'Ile de France

Assistance publique-Hôpitaux de Paris, Paris

Université Paris Descartes, Inserm U1016, Institut Cochin, Paris

Skin sclerosis > 90%

Interstitial lung disease 40%

Pulmonary arterial hypertension 10%

Gastro-intestinal complications 90%

Musculoskeletal involvement 65% (myositis 5%)

Renal crisis 5%

Raynaud's 90%

Calcinosis 23%

Digital ulcers 40%

Complication frequency in SSc

PAH

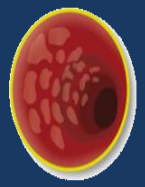
7.85% to 13% [1,2]

ILD

19% to 47% [3]

Renal crisis

< 5% [4]



GORD

80% [5]

Heart involvement

20% to 25% [6,7]

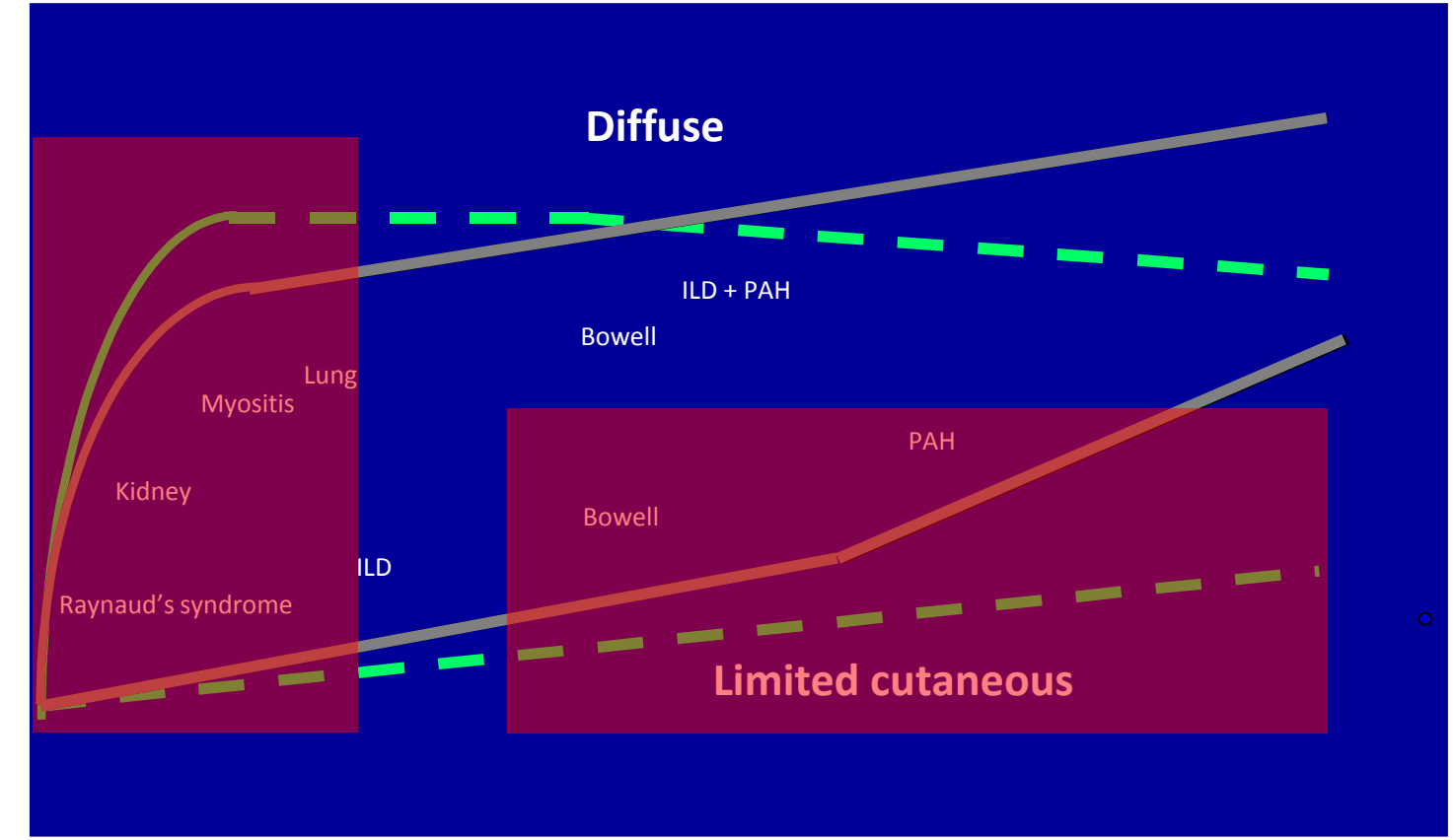
DUs

43% [8]

0 20 40 60 80 100 %

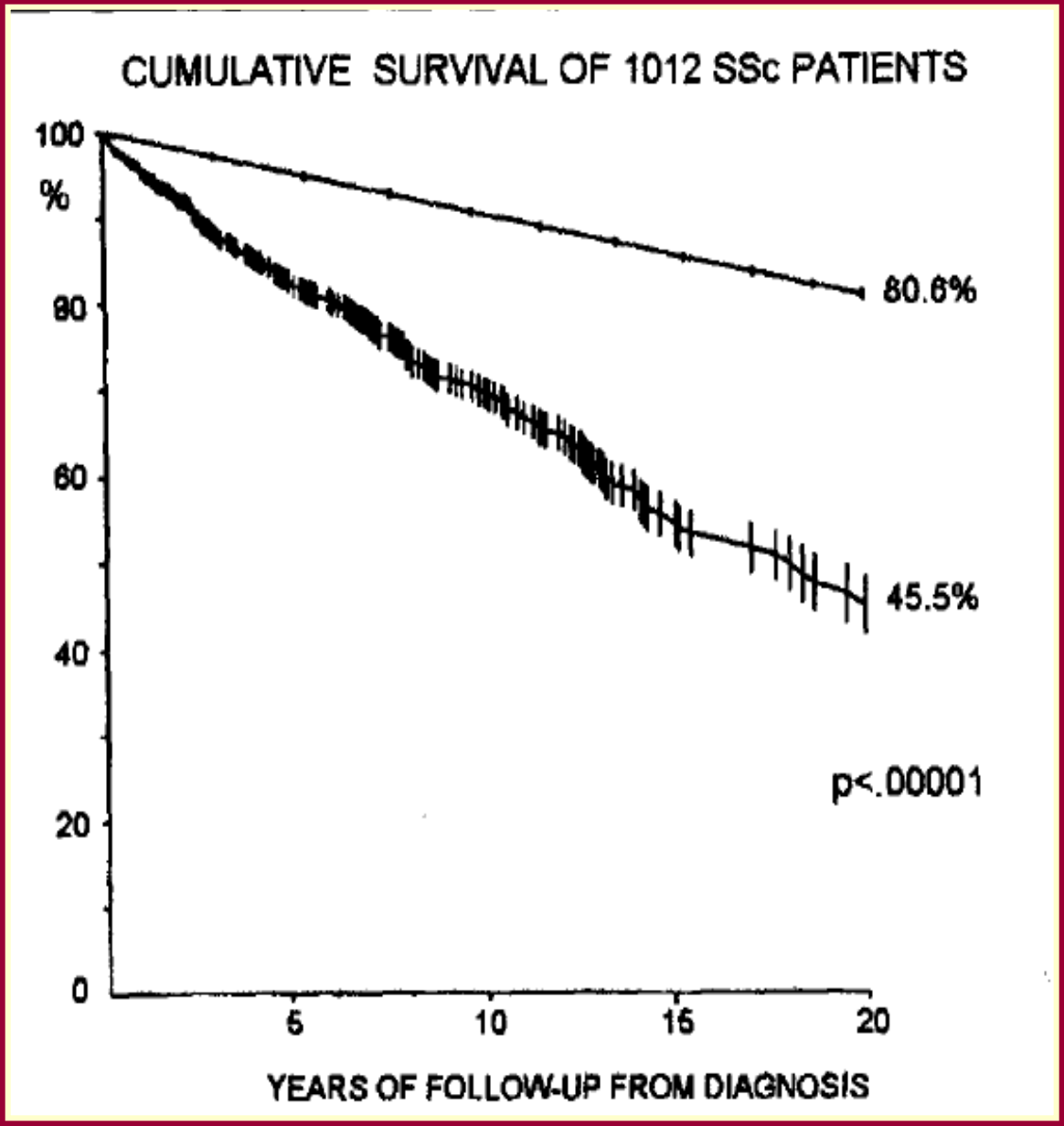
1. Hachulla *et al. Athrit Rheum* 2005; 2. Mukerjee *et al. Ann rheum Dis* 2003; 3. Vonk *et al. Ann Rheum Dis* 2009; 4. Teixeira *et al. Ann Rheum Dis* 2008; 5. Domsic *et al. Dig Dis Scie* 2006; 6. Deswal *et al. Rheum Dis Clin N Am* 1996; 7. Champion *Rheum Dis Clin N Am* 2009; 8. Hachulla *et al. J Rheum* 2007.

SYSTEMIC SCLEROSIS : EVOLUTION



Mortalité

Surmortalité liée à la ScS



Ferri et al, Medicine, 2002

Changes in causes of systemic sclerosis related deaths between 1972 and 2001

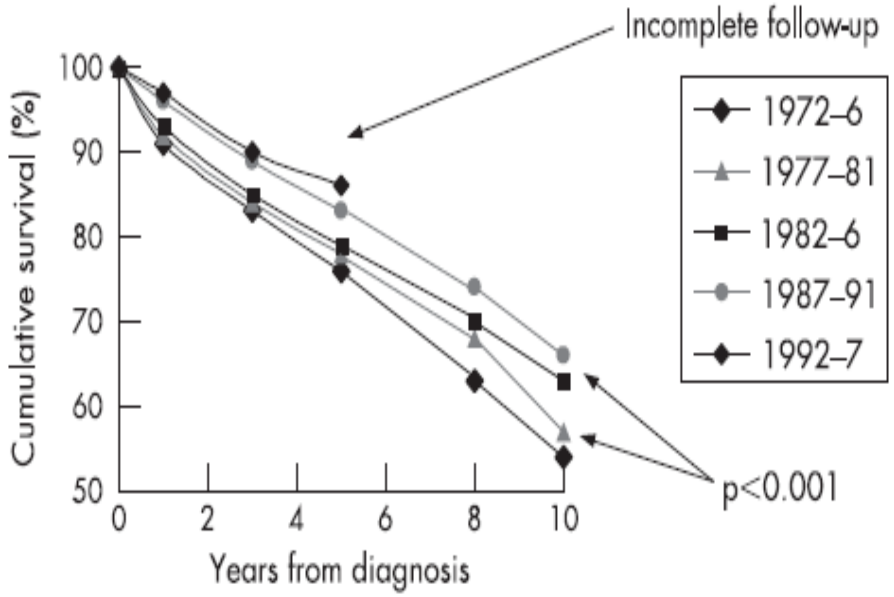


Figure 1 Survival of patients with systemic sclerosis between 1972 and 2002.

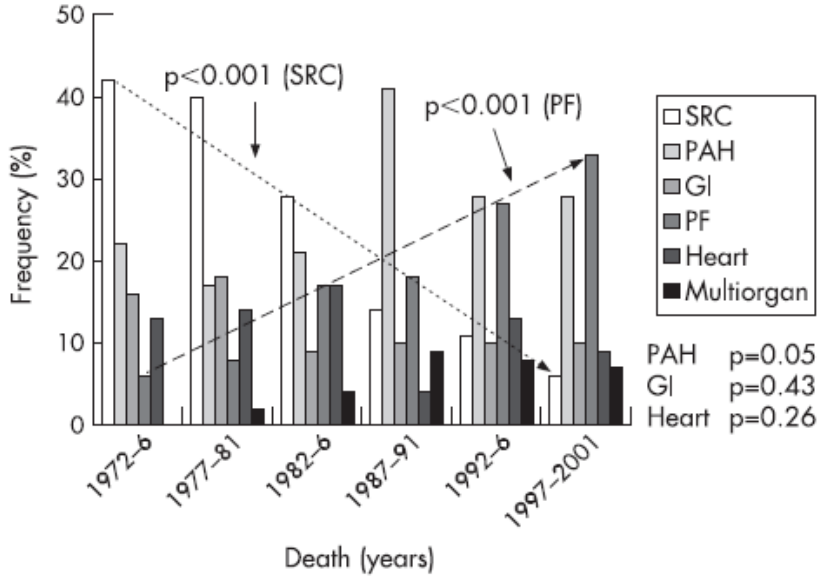


Figure 2 Changes in causes of systemic sclerosis-related deaths between 1972 and 2001. GI, gastrointestinal; PAH, pulmonary arterial hypertension; PF, pulmonary fibrosis; SRC, scleroderma renal crisis.

Steen VD, Medsger T, Ann Rheum Dis 2007, Feb 28 EPub

ScS diffuse et atteinte d'organe

Table 1. Causes and timing of death in patients with systemic sclerosis and diffuse scleroderma*

Cause of death	Time from disease onset: Years 0–5 (n = 148)	Time from disease onset: Years 5–10 (n = 204)	Odds ratio; *P* (95% CI)
Scleroderma-related			
Renal	45 (30)	17 (8)	
Cardiac	20 (14)	20 (10)	
Pulmonary	9 (6)	32 (16)	
Gastrointestinal	13 (9)	21 (10)	
Multiple systems	12 (8)	12 (6)	
Total	99 (67)	102 (51)	2.02; <0.001 (1.27–3.20)

Steen , Arthr Rheum 2000; 43: 2437-2444 2000

Autoanticorps

Survie à 10 ans des patients atteints de ScS

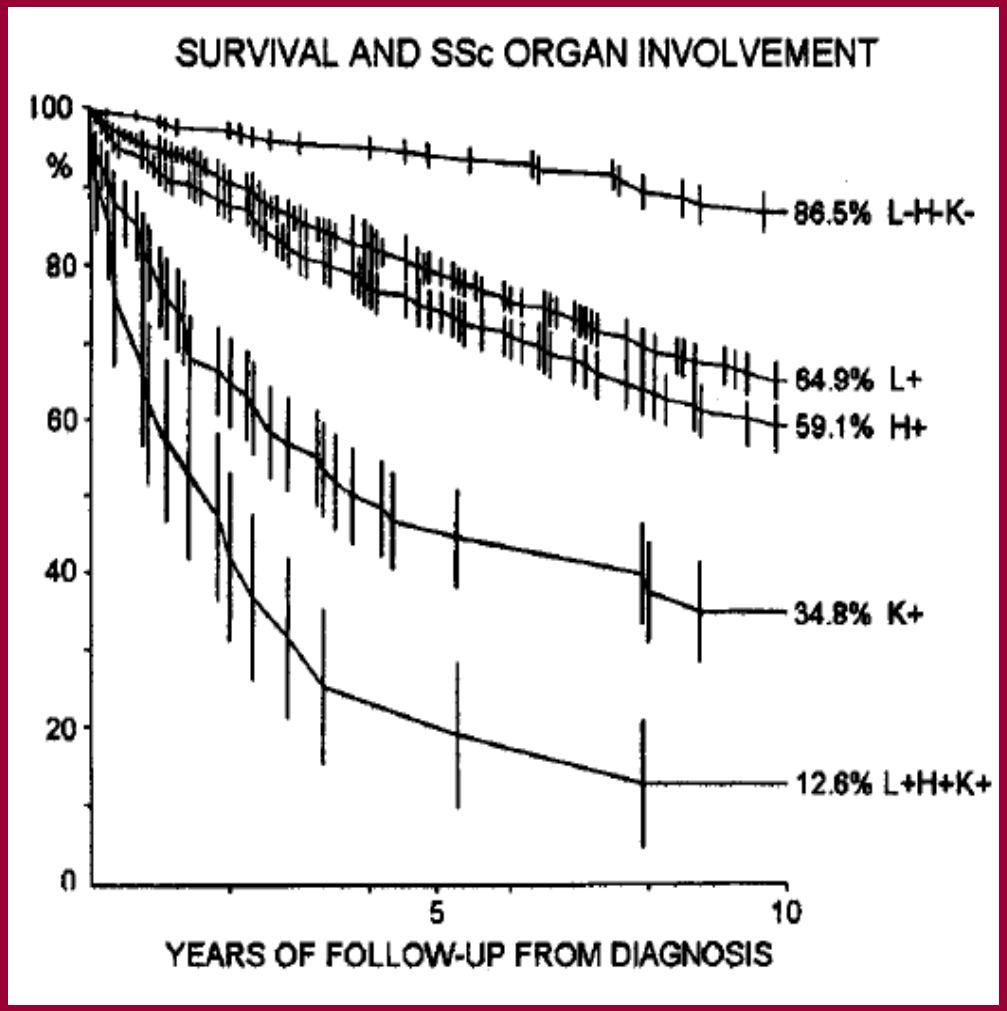
- **93 % avec anticorps anticentromère**
- **66 % avec Ac anti-Scl70**
- **30 % chez les patients ayant des anti-ARN polymérase.**

Kuwana M, Arthritis Rheum 1994; 37: 75-83

Pronostic en fonction du type d'atteinte viscérale

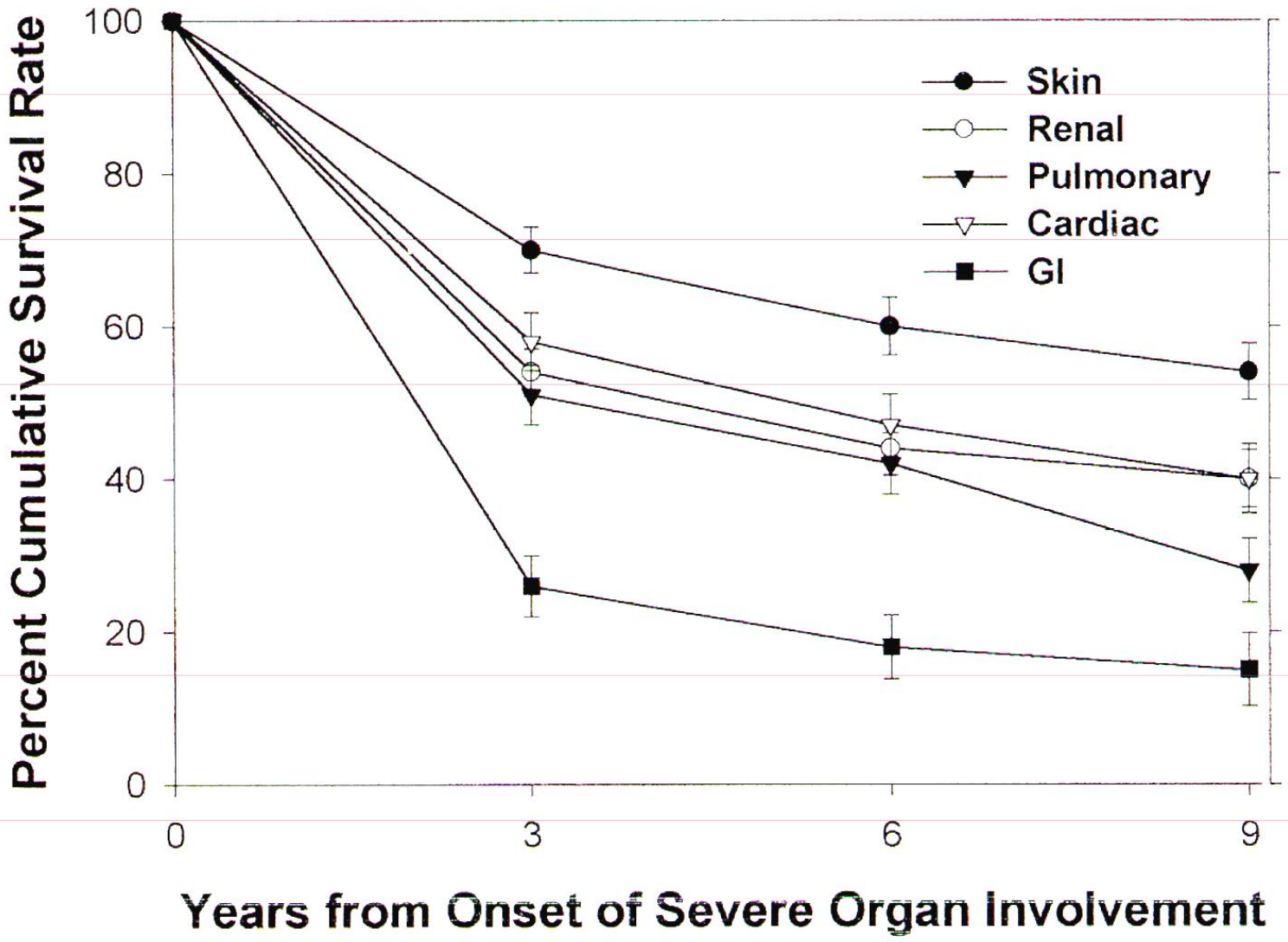
SYSTEMIC SCLEROSIS

- When major visceral involvement occurs in scleroderma, the outcome is poor
  - Lung fibrosis
  - Cardiac involvement
  - Renal insufficiency
  - Pulmonary hypertension



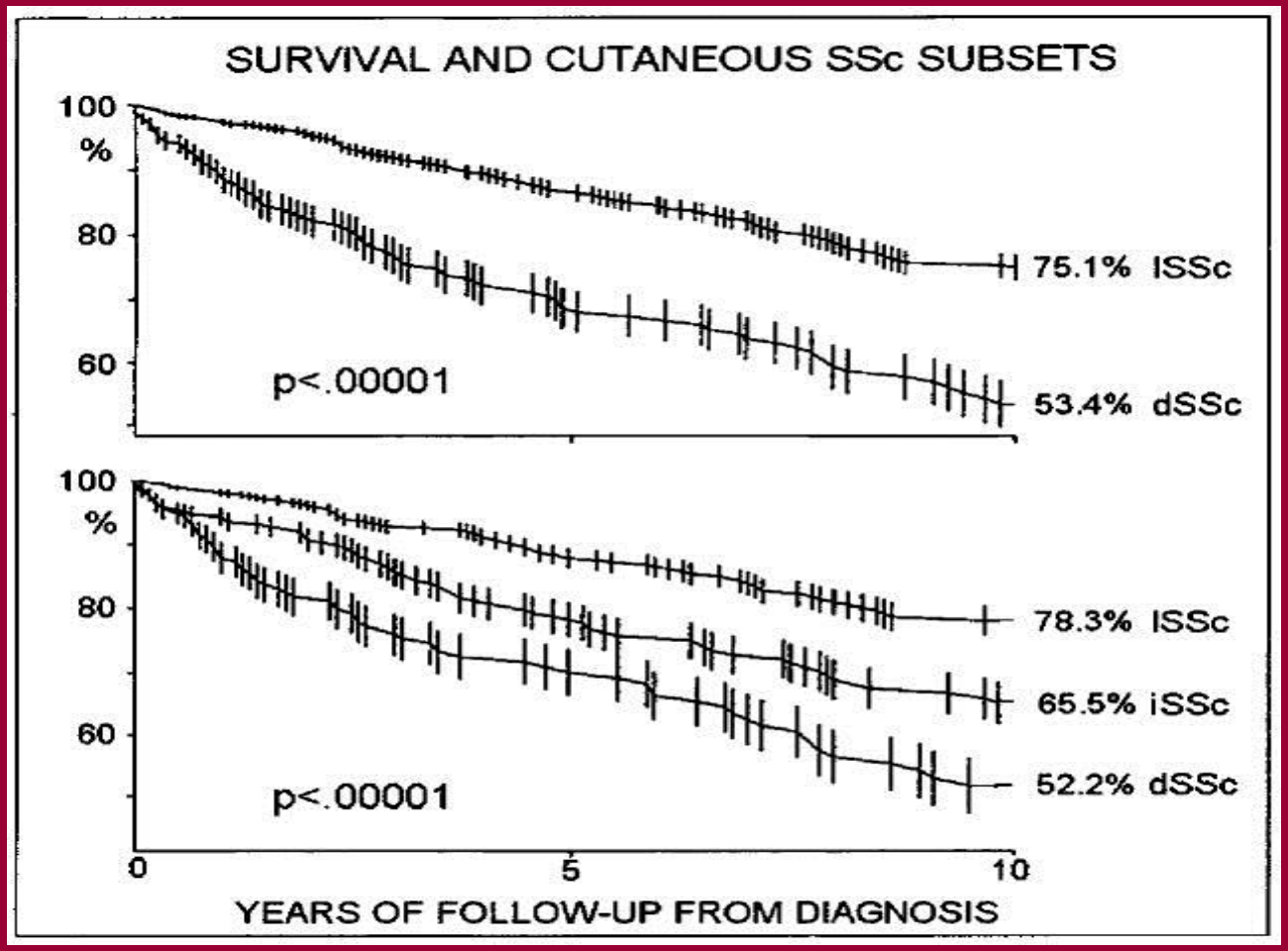
Ferri et al, Medicine, 2002

Severe organ involvement in SSc with diffuse scleroderma



Steen VD, Medsger T, Arthr Rheum 2000; 43: 2437-2444

Pronostic: l'atteinte cutanée proximale et la rapidité d'installation sont les éléments pronostiques importants



Ferri et al, Medicine, 2002

Identify early diffuse SSC

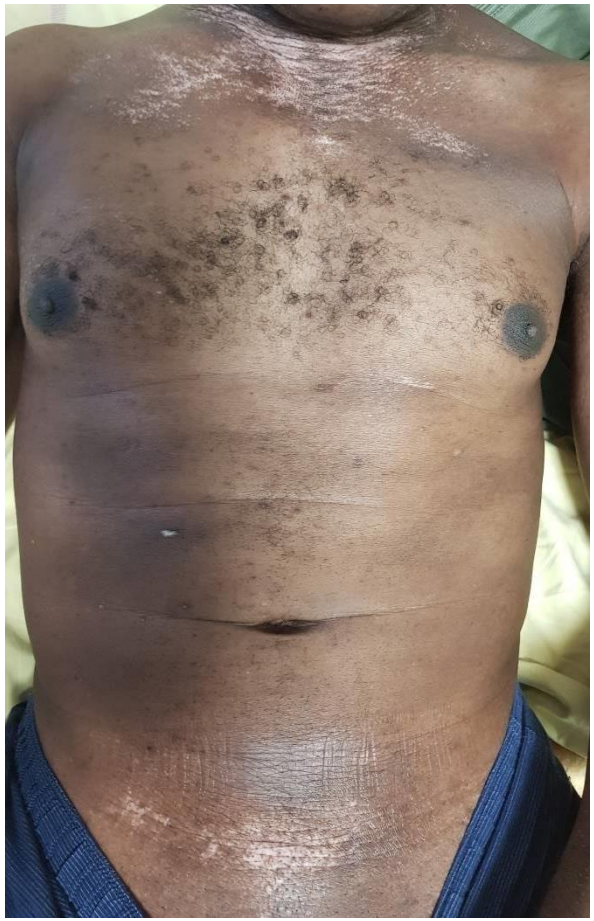
Oedema (weight gain)
Swelling hands
Joint/muscle pain

Later on…..
Raynaud's phenomenon

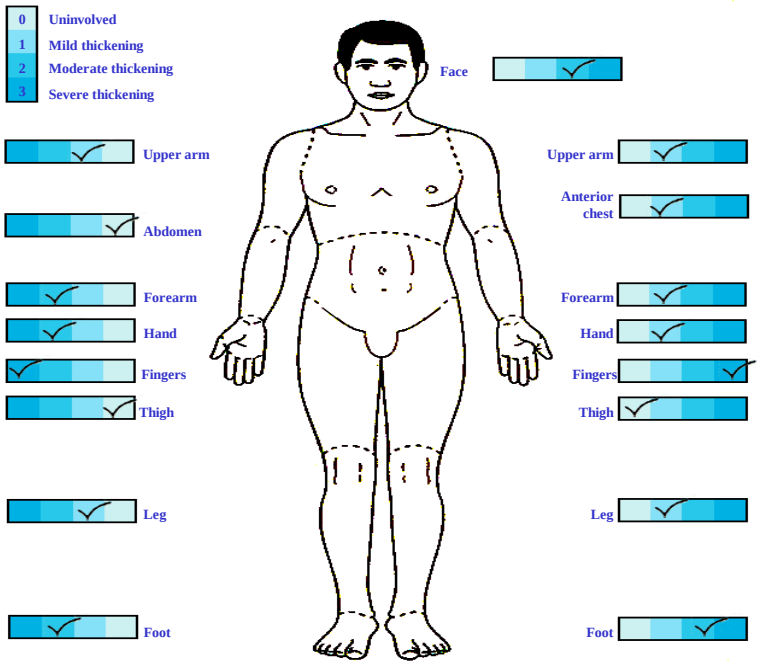
Later on…
Sclerodactyly

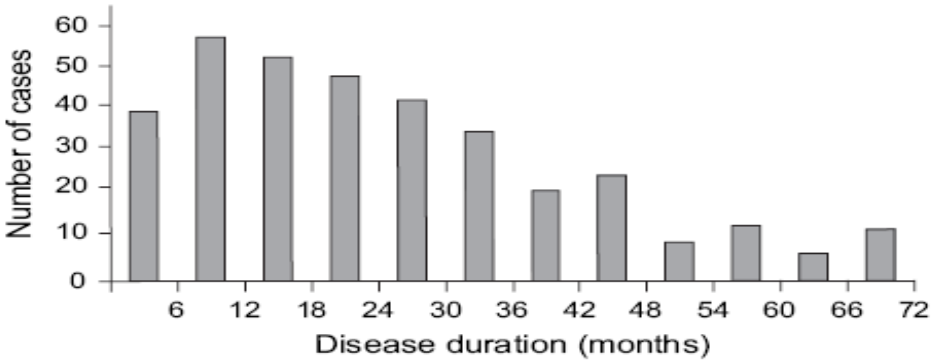
Sometimes:
Myositis
Renal crisis
Before skin sclerosis

Always touch the skin !



The modified Rodnan skin score (MRSS)



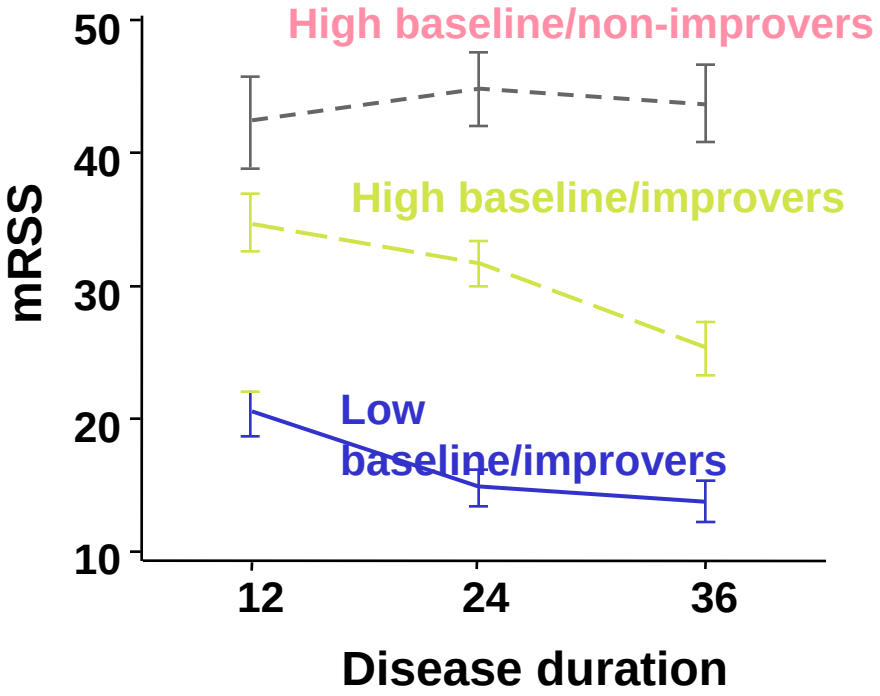


Disease duration at peak skin score of the patients who had dcSSc from the Royal Free Hospital scleroderma database.

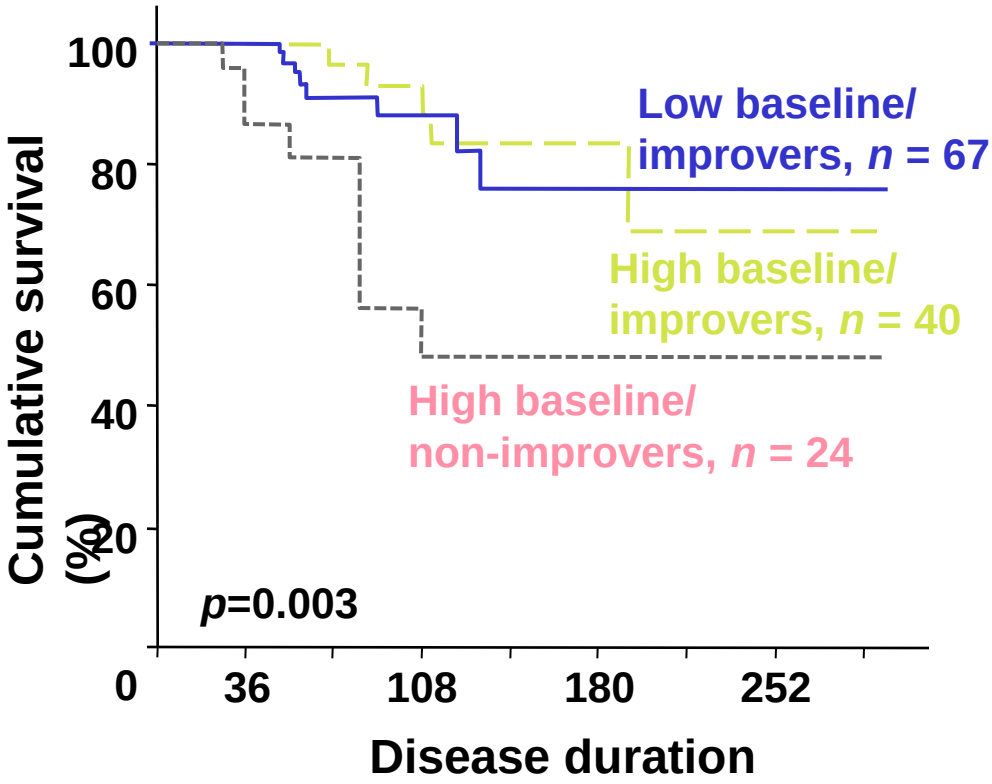
Nihtyanova SI, Denton CP. Rheum Dis Clin N Am 34 (2008) 161–179

Disease duration and skin score in dcSSc

Change in skin score over 3 years in the subgroups

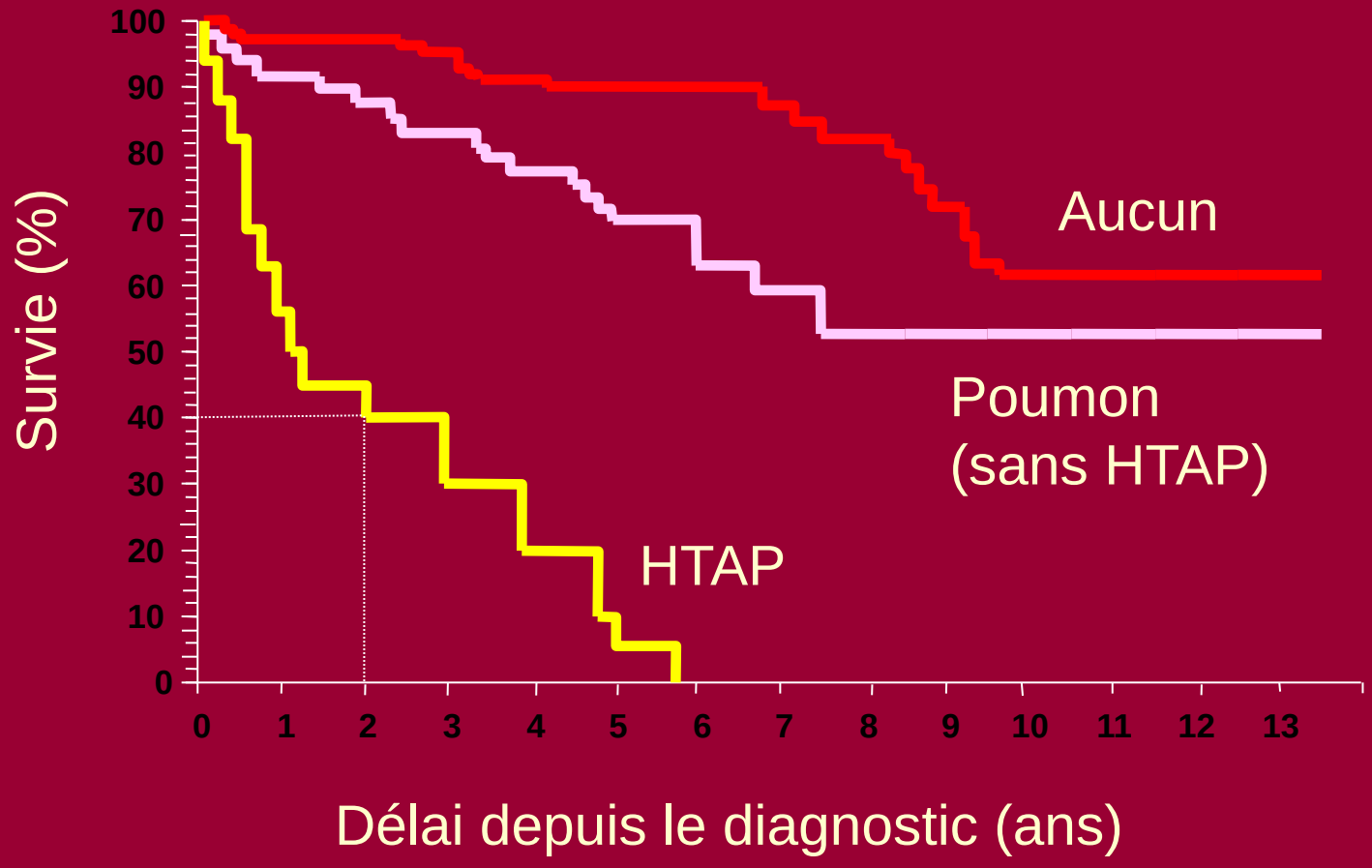


Survival in the subgroups



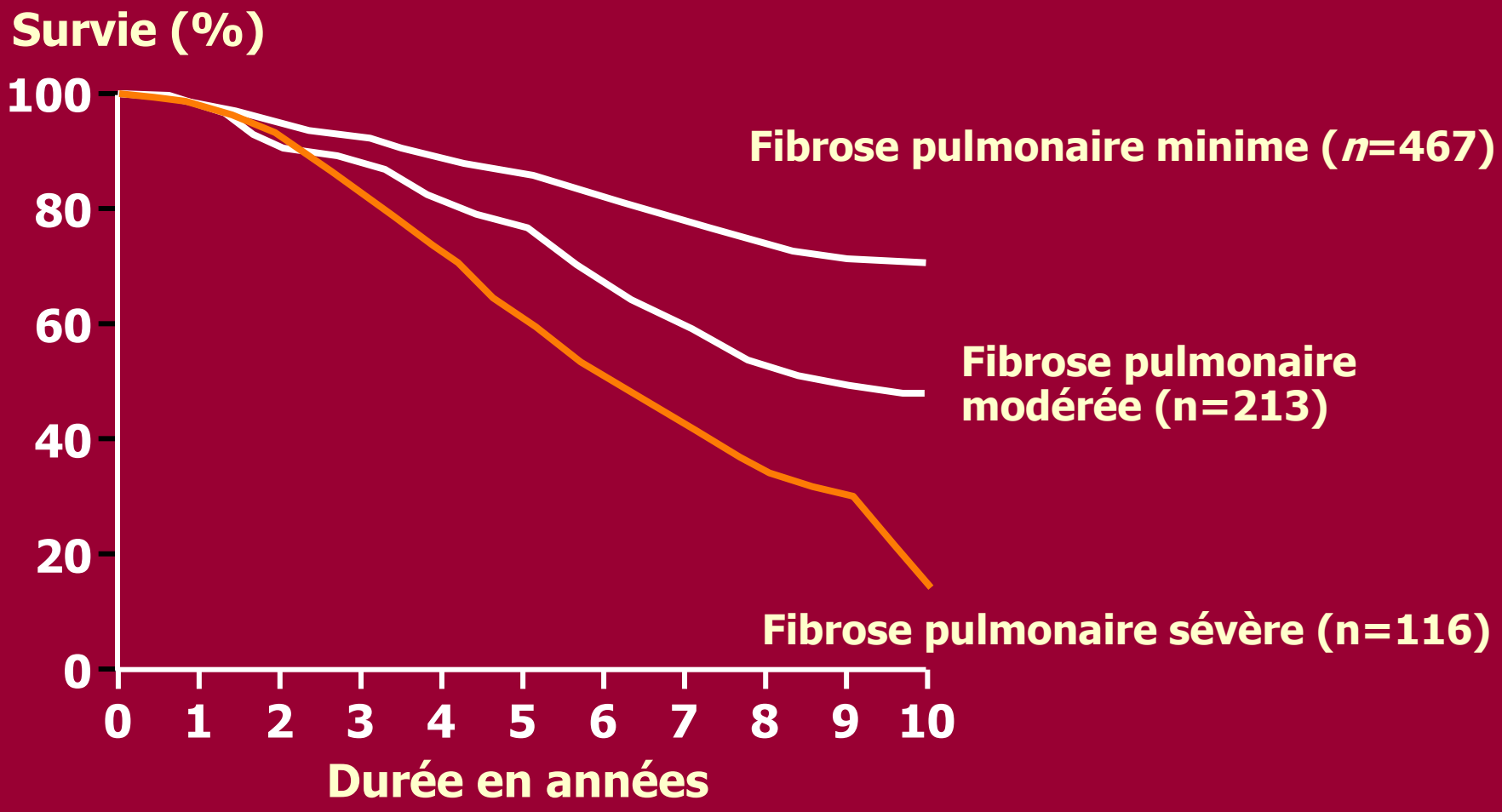
Shand L, *et al. Arthritis Rheum* 2007; 56:2422-31.

SURVIE DES PATIENTS ATTEINTS DE SCLÉRODERMIE



Koh et al. Br J Rheumatol 1996;35:989-93.

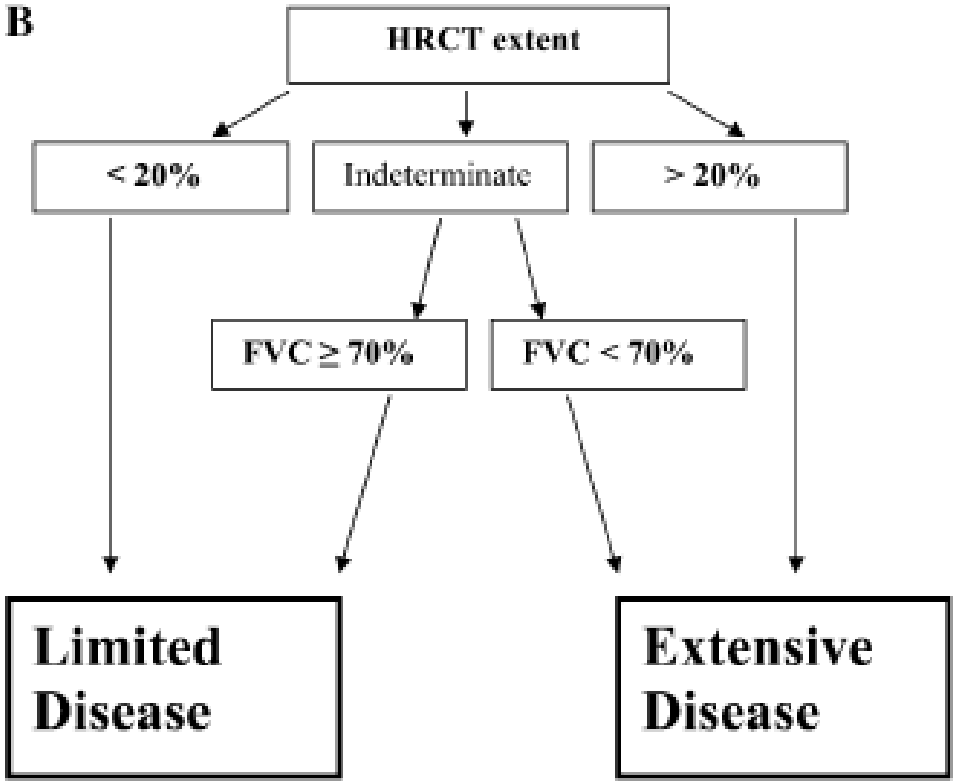
PRONOSTIC DE LA FIBROSE PULMONAIRE

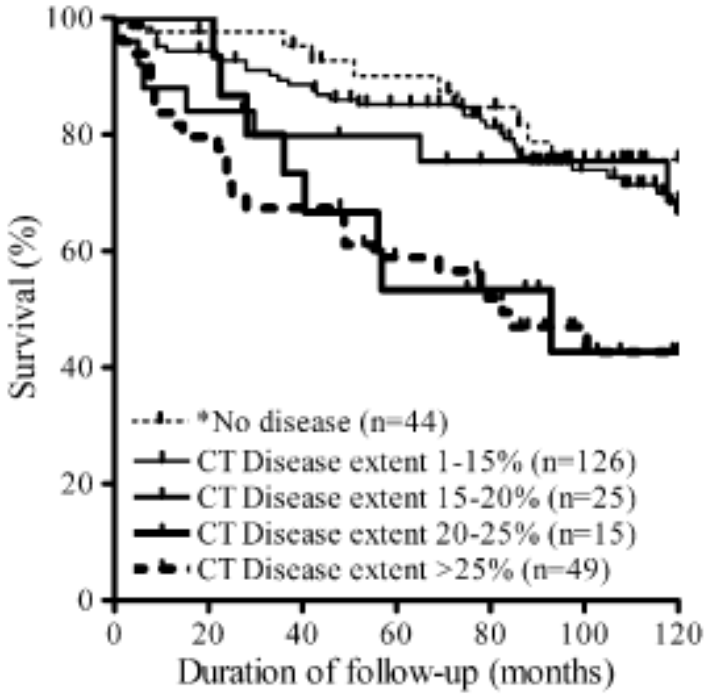


$p < 0.01$

Steen V, *Arthritis Rheum* 1994. 37:1283.

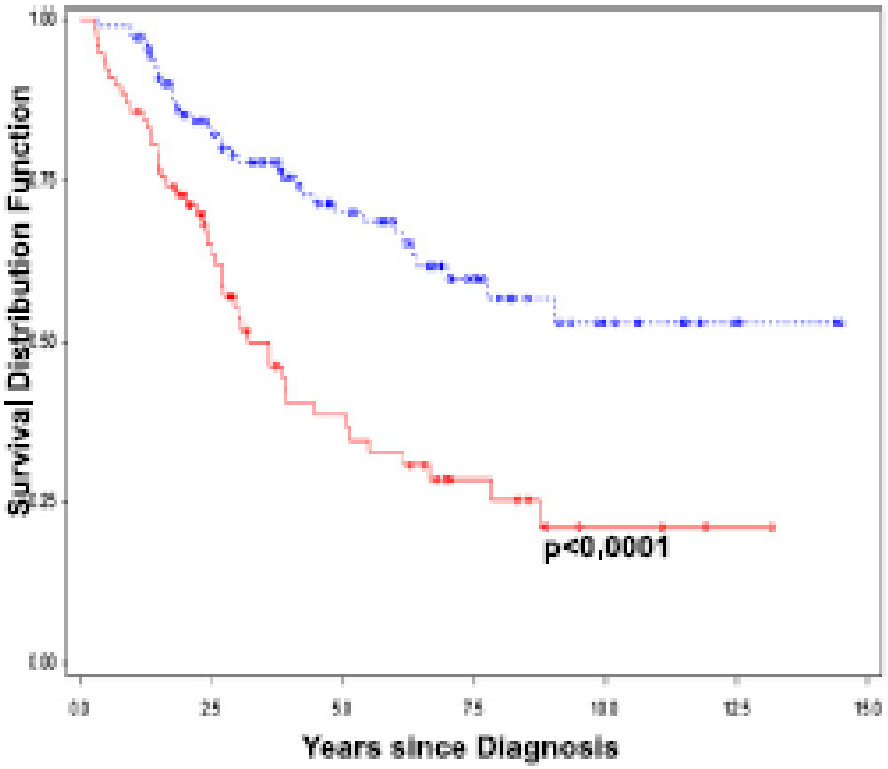
Interstitial Lung Disease in Systemic Sclerosis
A Simple Staging System
Goh NSL, AJRCCM 2008



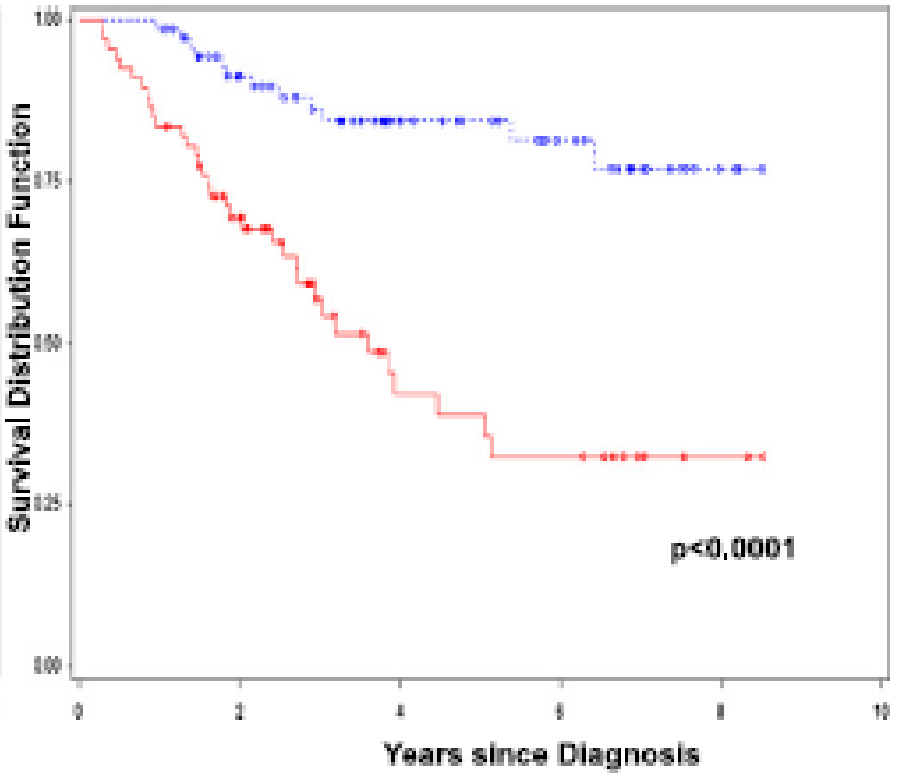


Comparison of survival in SSc-PAH and iPAH

All patients ('96-'10)



Patients diagnosed between ('02-'10)

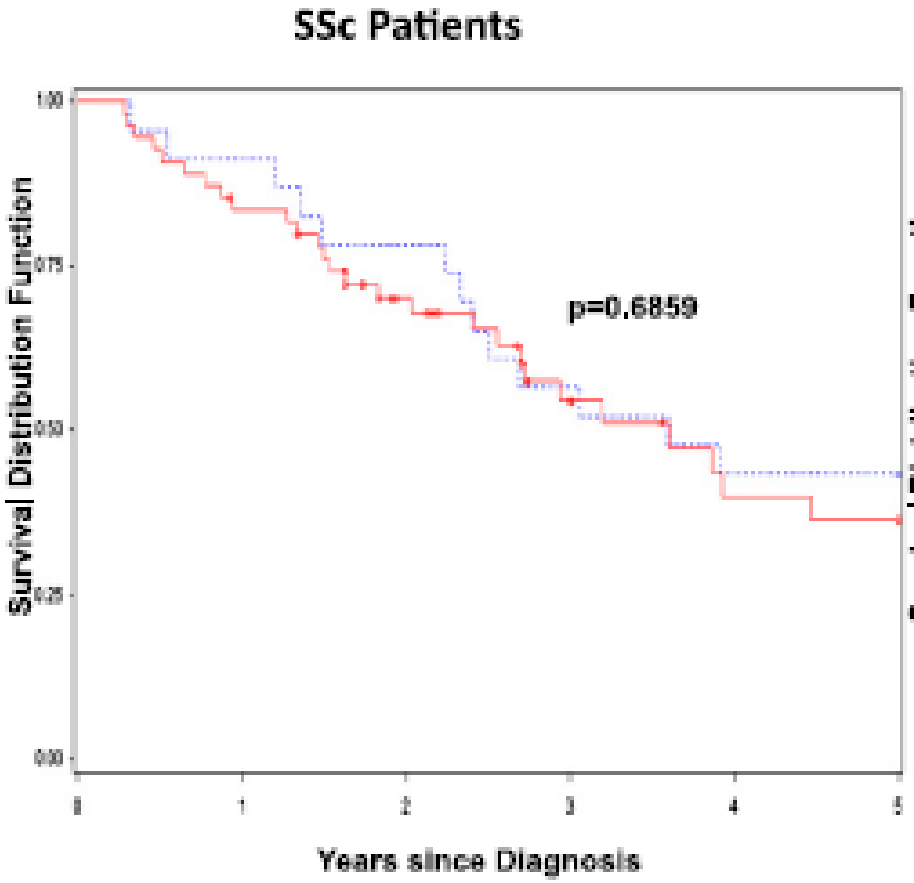


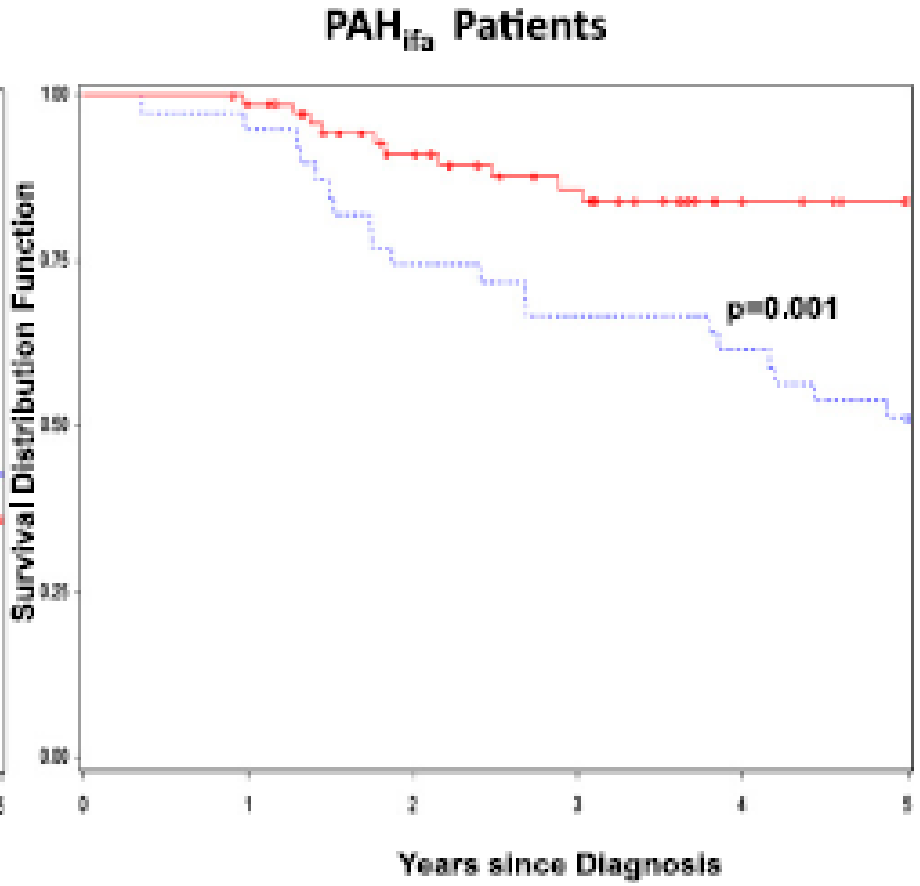
PAH$_{ifa}$
SSc

Diagnosis	1996-2010 (n=192)		2002-2010 (n=130)	
	Total	*Events*	*Total*	*Events*
PAH$_{ifa}$	114	37	75	12
SSc	78	48	55	30

Rubenfire M et al. Chest 2013

Comparison of survival in patients diagnosed prior to 2002 and after 2002





Pre-2002
Post -2002

Diagnosis	SSc (n=78)		PAH ifa (n=114)	
	Total	*Events*	*Total*	*Events*
Pre-2002	23	13	39	19
Post 2002	55	27	75	10

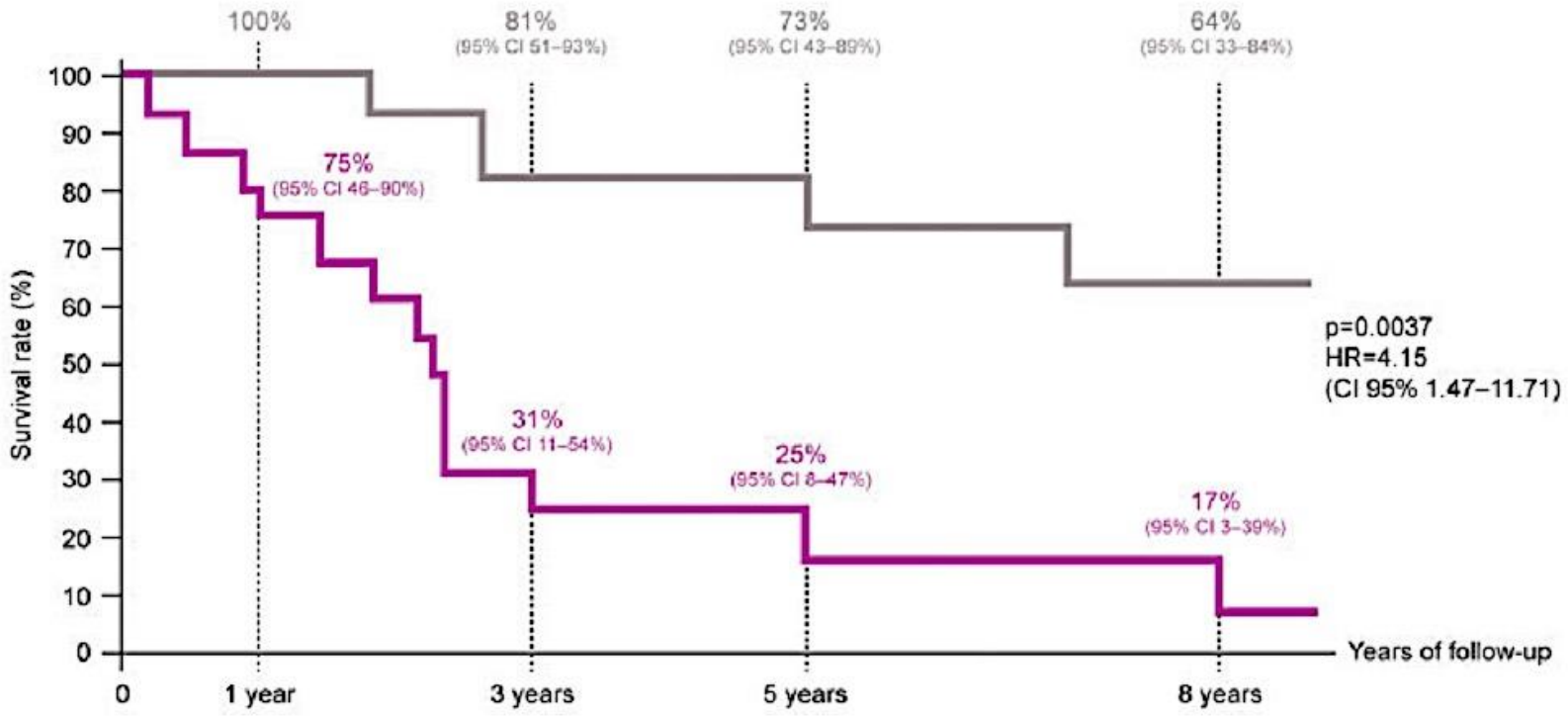
Rubenfire M et al. Chest 2013

Long-term outcomes in detected *vs* routine SSc-PAH

Screening for Pulmonary Arterial Hypertension in Patients With Systemic Sclerosis

Clinical Characteristics at Diagnosis and Long-Term Survival

Marc Humbert,[1] Azzedine Yaici,[1] Pascal de Groote,[2] David Montani,[1] Olivier Sitbon,[1] David Launay,[3] Virginie Gressin,[4] Loïc Guillevin,[5] Pierre Clerson,[6] Gérald Simonneau,[1] and Eric Hachulla[3]

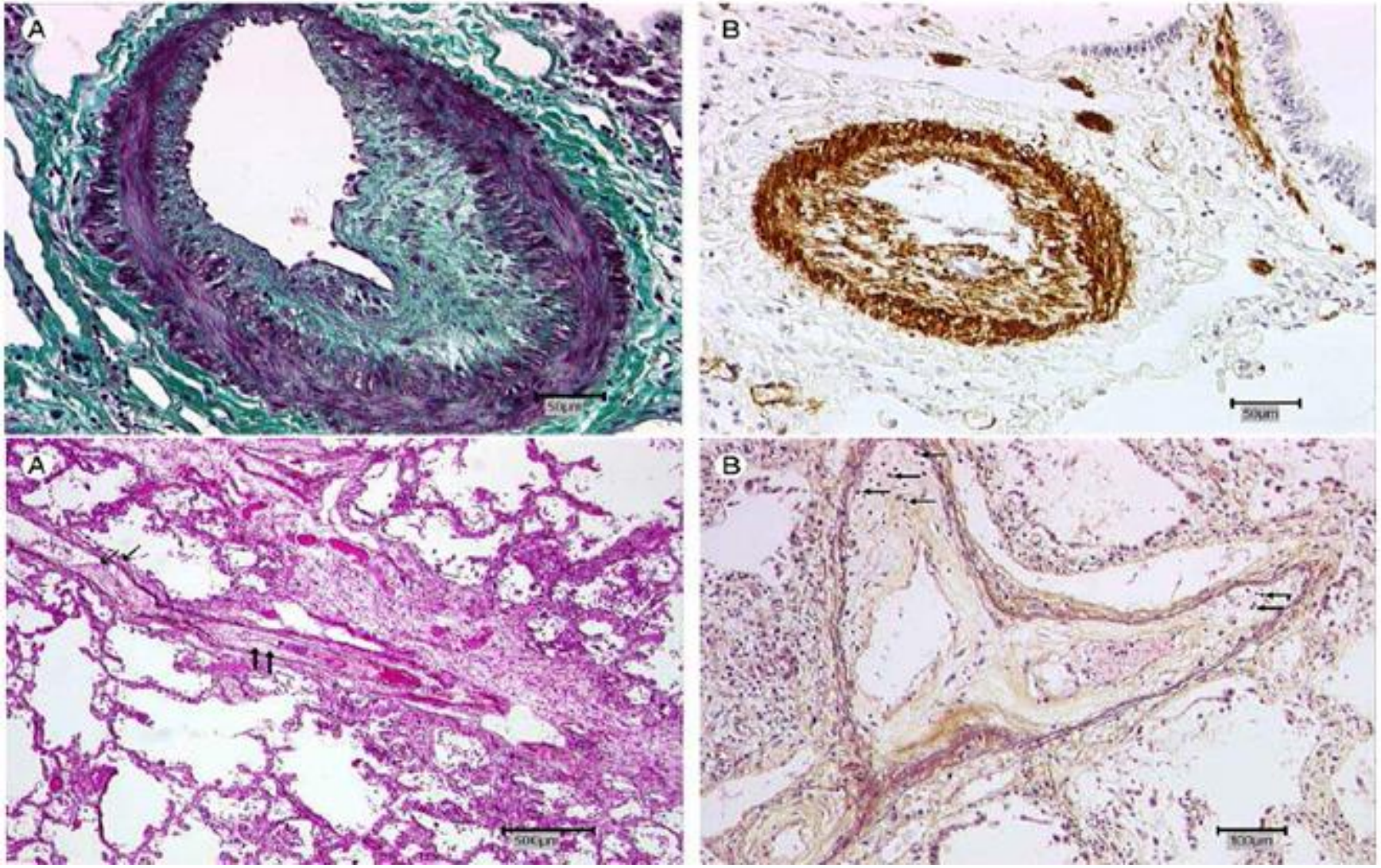


Humbert M, *et al. Arthritis Rheum* 2011; 63:3522-30.

PAH-SSc: The impact of comorbidities

- Age
- Myocardial involvement
- Musculoskeletal involvement
- Pulmonary fibrosis
- Pulmonary Veno-Occlusive Disease

Fibrous remodeling of the pulmonary venous system in PAH associated with CTD



Combined Pulmonary Fibrosis and Emphysema Syndrome in Connective Tissue Disease

Table 1. Classification of connective tissue diseases in the 34 study patients*

Rheumatoid arthritis	18 (53)
Systemic sclerosis	10 (29)
Diffuse cutaneous	3 (9)
Limited cutaneous	7 (20)
Mixed connective tissue disease	2 (6)
Overlapping connective tissue disease	2 (6)
Sjögren's syndrome	1 (3)
Polymyositis	1 (3)

* Values are the number (%) of patients.

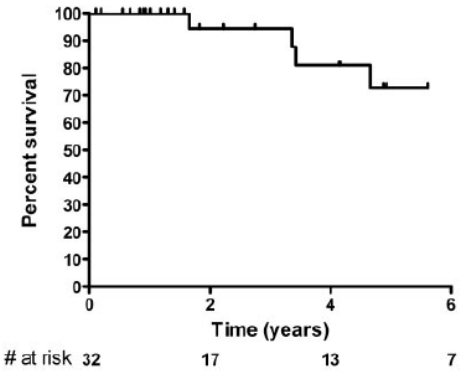
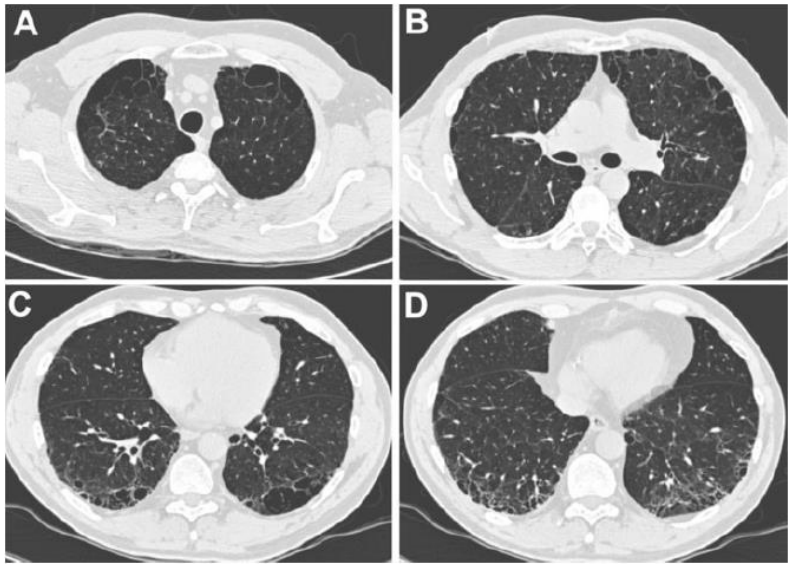
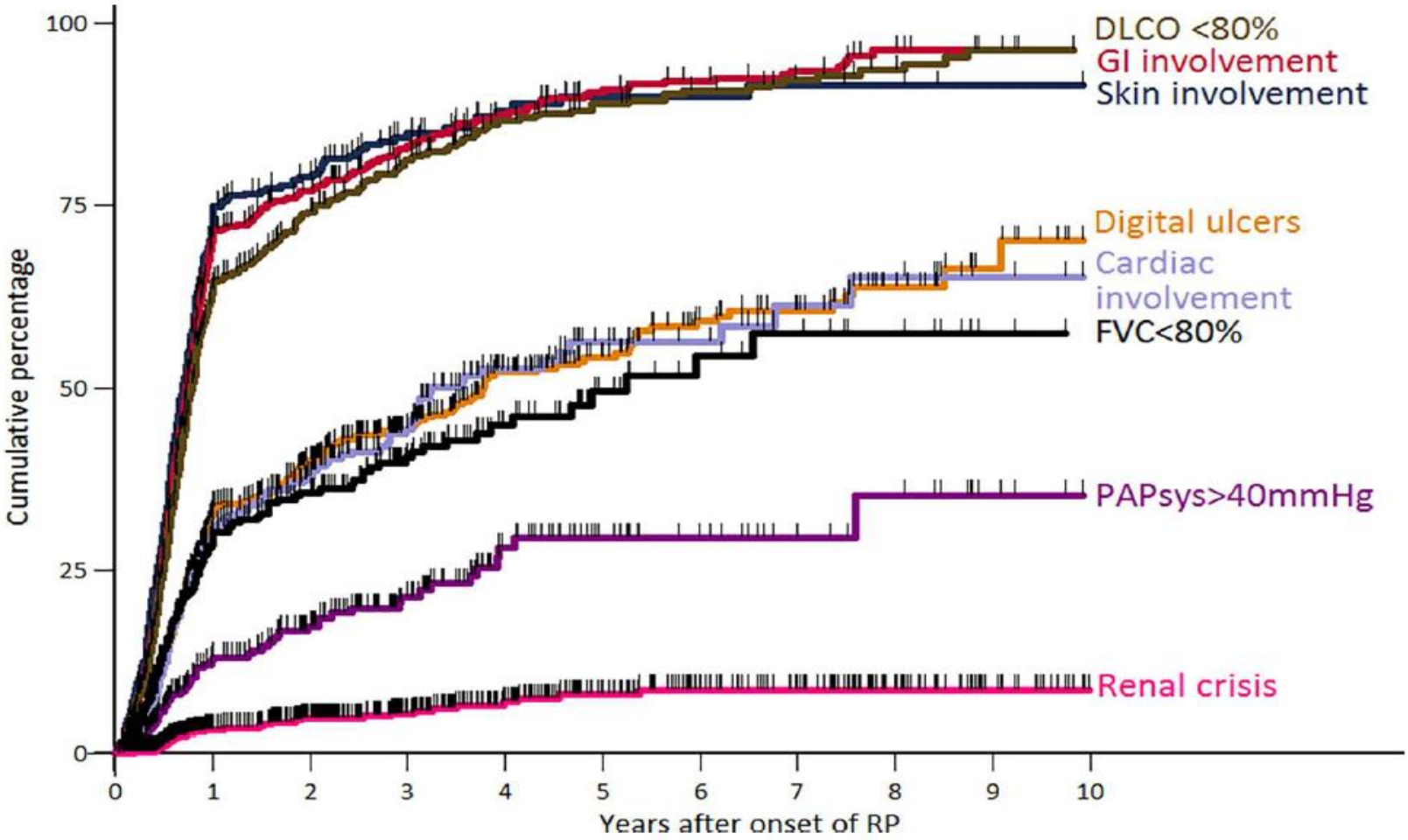


Figure 2. Kaplan-Meier estimates of survival in patients with combined pulmonary fibrosis and emphysema syndrome and connective tissue disease.



Incident organ involvement in SSc patients

695 SSc patients from the EUSTAR database
who had a baseline visit within 1 year after RP onset



Jaeger VK et al. Plos one 2016

Scleroderma renal crisis

Definition

- Rapidly progressive oliguric renal insufficiency with no other explanation
- and/or rapidly progressive hypertension occurring during the course of SSc

Risk factors for scleroderma renal crisis

Rapid progression of skin involvement

Disease duration < 4 years

Recent cardiac event:

- **pericarditis**
- **Left ventricular insufficiency**

Recent-onset anemia

Anti-RNA polymerase III antibodies

Treatment with > 15 mg/d prednisone within the preceding 3 months

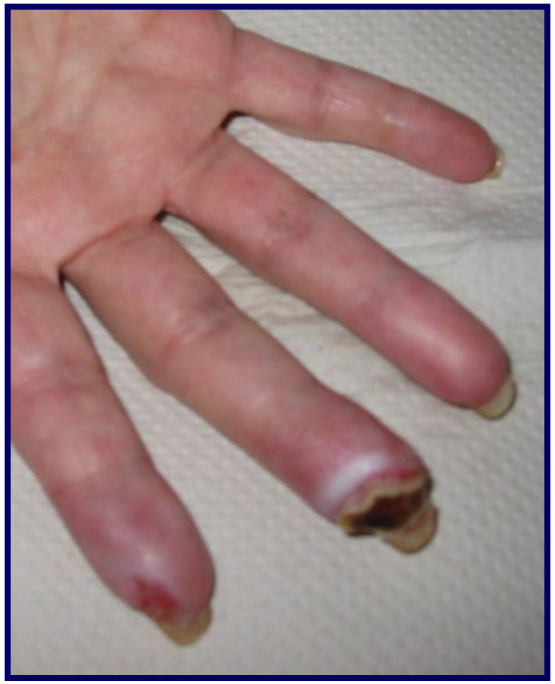
Exposure to ACEi prior to the onset of SRC*

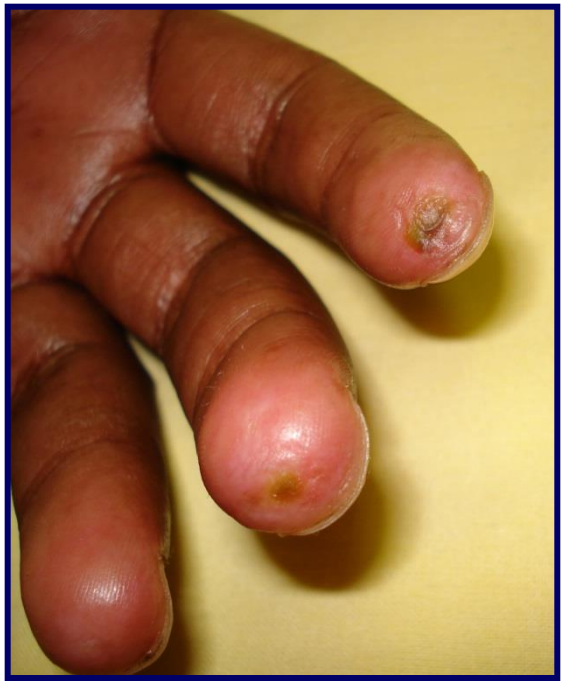
Steen VD. *Am J Med* 1984; 76:779-86.
Steen VD. *Rheum Dis Clin North Am* 2003; 29:315-33.
Hudson M et al. Sem Arthr Rheum 2013.

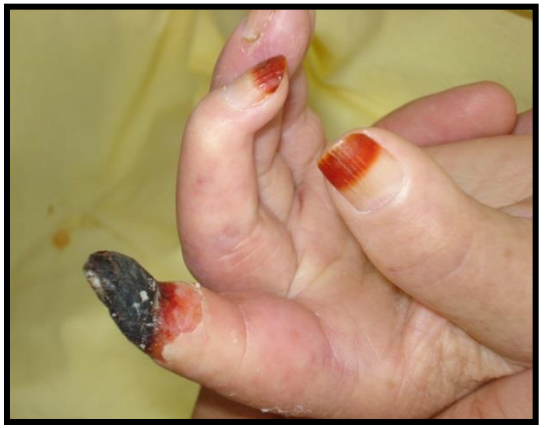
Pronostic des crises rénales sclérodermiques

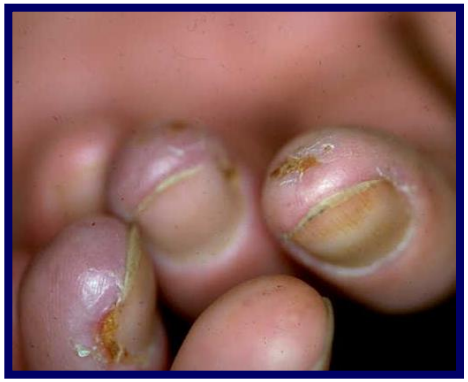
	Steen et al. (2)	Walker et al. (6)	DeMarco et al. (5)	Penn et al. (8)	Teixeira et al. (7)	Guillevin et al. (67)	Hudson et al. (65).
No. of patients	195	16	18	110	50	91	75
Dialysed patients, %	43	31	ND	64	56	54	53
Temporarily, %	23	6	ND	23	16	14	ND
Permanently, %	19	25	ND	42	22	39	25 (at one year)
Died while on dialysis, %	ND	ND	ND	18	18	26	ND
Deceased at 5 years, %	19*	31	50	41	31	40	36**

IMPACT OF DIGITAL ULCERS IN SYSTEMIC SCLEROSIS







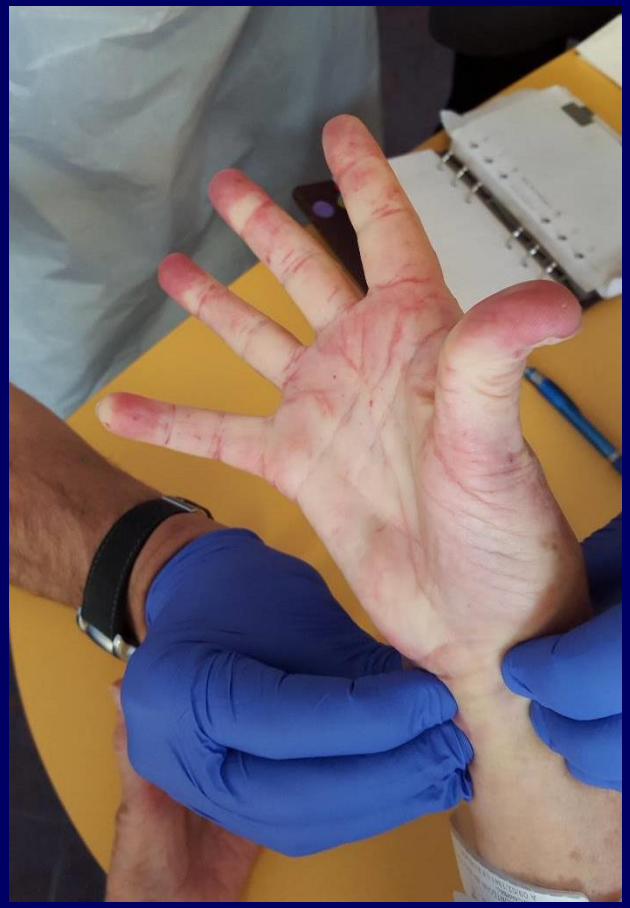


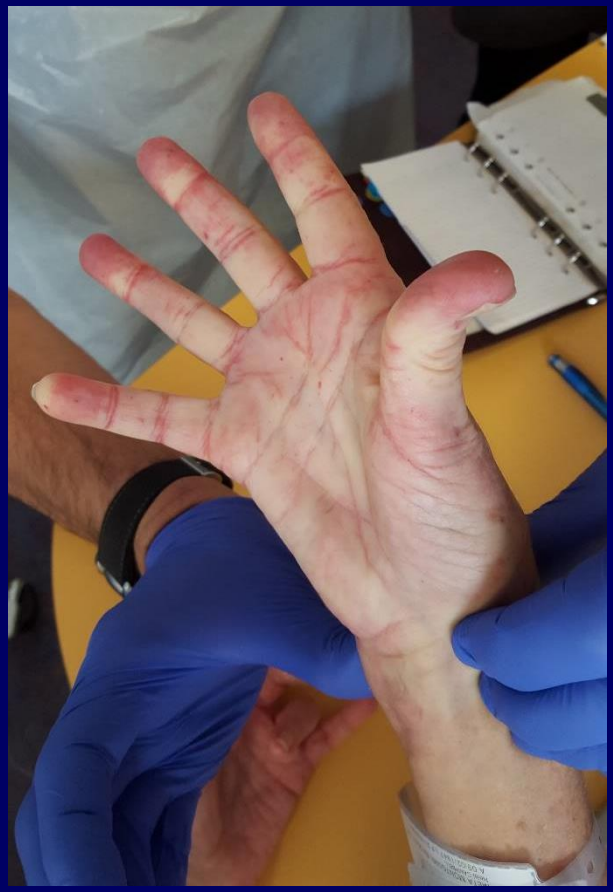
Infection
Gangrene
Amputation

→

Disability
Pain
Loss of function

Ulnar artery stenosis





Conclusion

- Diagnose early SSc
- Differentiate diffuse from limited
- Early complete evaluation
- Autoantibodies: anti-RNA pol III
- Follow up is mandatory: repeat Echo, PFTs

French Vasculitis Study Group

GFRS Groupe Francophone de Recherche sur la Sclérodermie

CMR CENTRE MALADIES RARES
VASCULARITES | SCLÉRODERMIES
GOUGEROT-SJÖGREN | LUPUS

Hôpital Cochin Paris

www.vascularites.org

Luc.mouthon@aphp.fr

Referral Center for
Rare Systemic and
Autoimmune Diseases