

Sclérodermie systémique: introduction, quels examens réaliser ?

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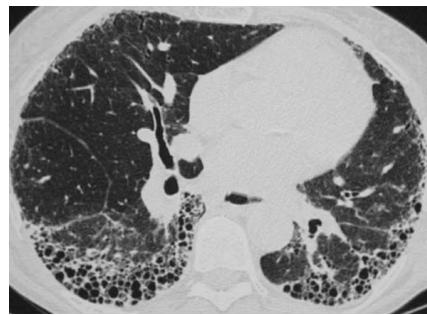
Conflicts of interest

- **Consultant:** Actelion, CSL Behring, Cytheris, GSK, LFB Biotechnologies, Lilly, Pfizer
 - Financial support to ARMIIC
- **Investigator:** Actelion, CSL Behring, Pfizer
- **Financial support (grants):** Actelion, CSL Behring, GSK, LFB Biotechnologies, Pfizer

Sclérodermie systémique

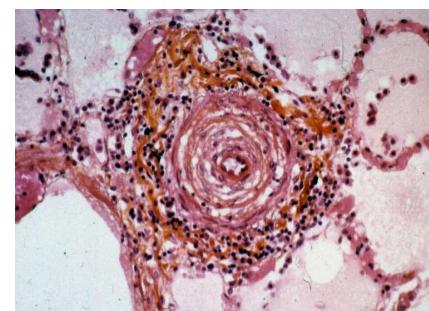
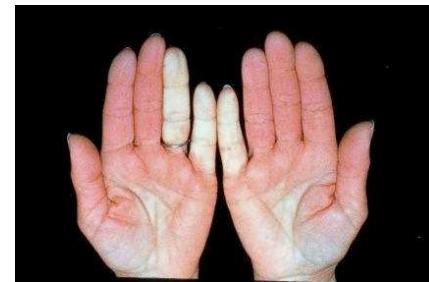
Fibrose

Peau
Poumon
Appareil digestif
Cœur



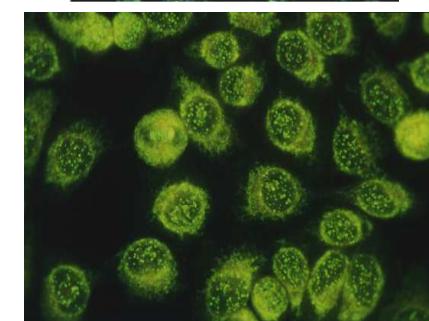
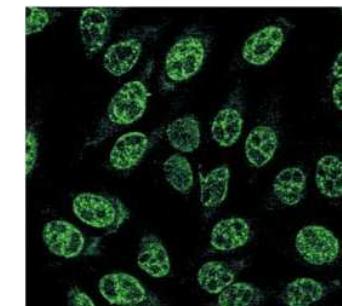
Atteintes vasculaires

Phénomène de Raynaud
Crise Rénale
Hypertension artérielle
pulmonaire (HTAP)

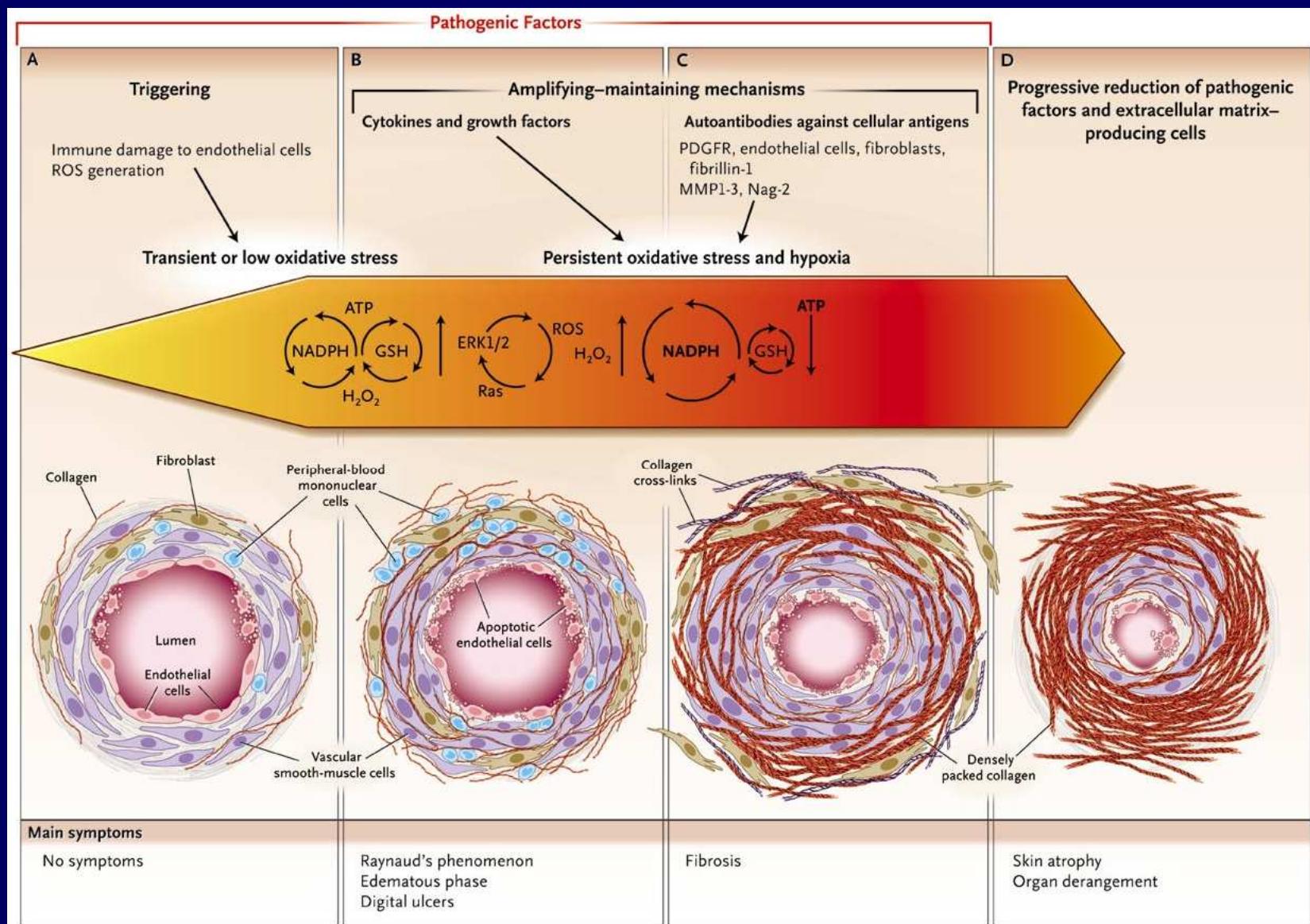


Autoimmunité

Autoanticorps spécifiques
Anti-Scl70
Anti-centromère
Anti-ARNPolIII
Autoanticorps non spécifiques



Systemic sclerosis: lesions at different stages



Gabrielli A. NEJM 2009

Prévalence

Auteurs	Régions	technique	Prévalence /million
Etats Unis			
Michet	Rochester	Hôpital	138
Mayes	Detroit	Sources multiples	242
Maricq	Caroline du sud	Population	190-750
Océanie			
Chandran	Australie du sud		147-208
Roberts-Thomson	Australie du sud	Sources multiples	233
Asie			
Shinkai	Japon	Santé publique	7
Tamaki	Tokyo	Santé publique	21-53
Europe			
Silman	West midland	Sources multiples	31
Asboe-Hansen	Danemark	Source hôpital	126
Le Guern	Seine Saint Denis	Sources multiples	158

Critères diagnostiques de sclérodermie systémique

Arthritis Rheum, 1980

Critère majeur

Sclérose cutanée proximale

Critères mineurs

Sclérodactylie

Cicatrices digitales, pertes de substance

Fibrose pulmonaire des bases

Sclérodermie systémique si un critère majeur ou deux critères mineurs

Criteres de classification des formes débutantes de SSc

Sclérodermie systémique limitée

➤ Phénomène de Raynaud

+

➤ Soit anomalie capillaroscopique

➤ Soit Ac spécifique de la Sclérodermie systémique
(anti-centromere, anti-topoisomérase 1, anti-fibrillarine,
anti-PMScl, anti-fibrilline, anti-RNA pol I ou III à un titre
1/100)

Sclérodermie systémique cutanée limitée

En plus des critères précédents, infiltration distale, en aval des coudes et des genoux

2013 classification criteria for SSc: an ACR/EULAR collaborative initiative (I)

- Skin thickening of the fingers extending proximal to the metacarpophalangeal joints: SSc;
- If that is not present, 7 additive items apply:
 - skin thickening of the fingers,
 - fingertip lesions,
 - telangiectasia,
 - abnormal nailfold capillaries,
 - interstitial lung disease or pulmonary arterial hypertension,
 - Raynaud's phenomenon,
 - SSc-related autoantibodies.

Skin thickening of the fingers (I)



Score = 2

Only count higher score

Puffy fingers

Skin thickening of the fingers (II)



Sclerodactily

Score = 4

Only count higher score



fingertip lesions

Digital ulcers

Score = 2



Fingertip pitting scars

Score = 3



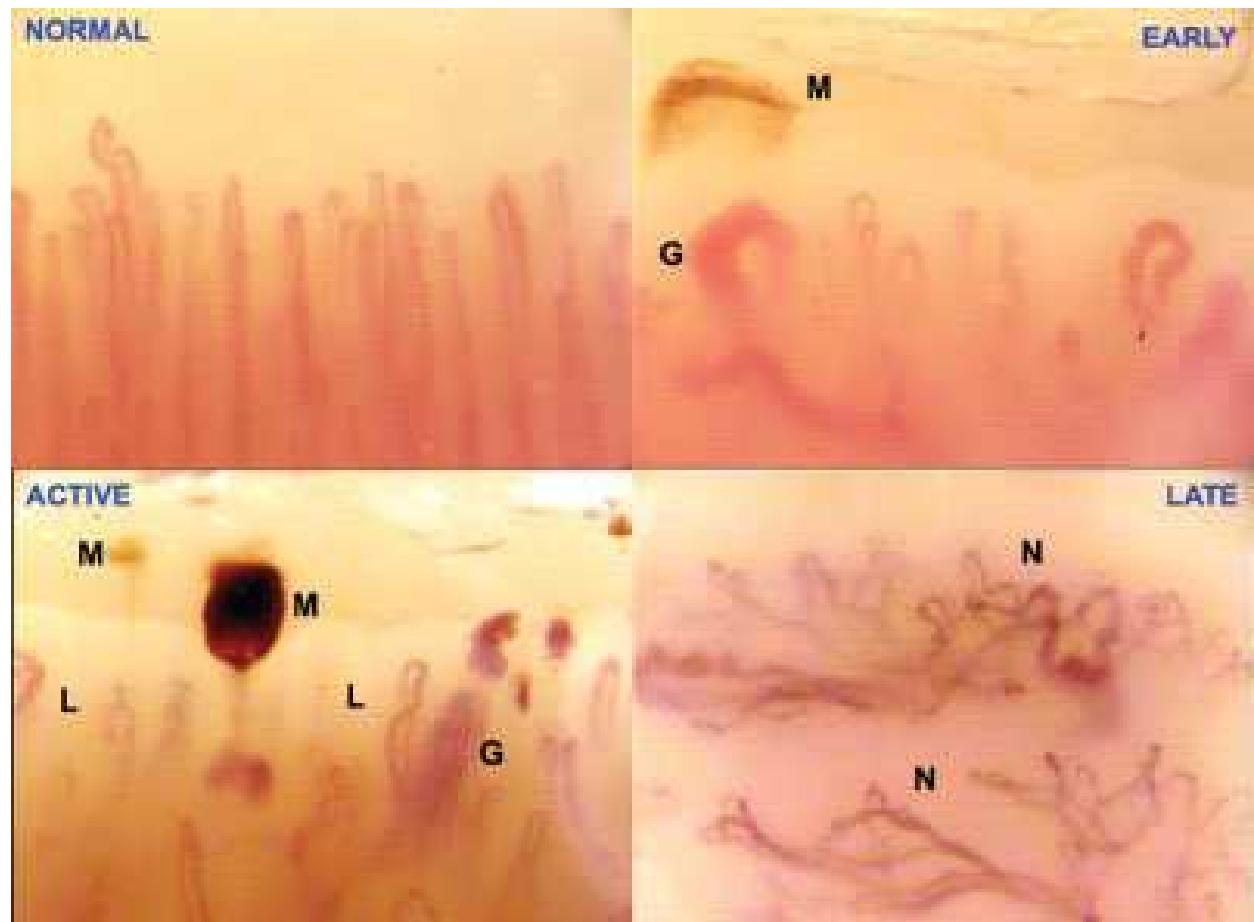
Only count higher score

telangiectasia



Score = 2

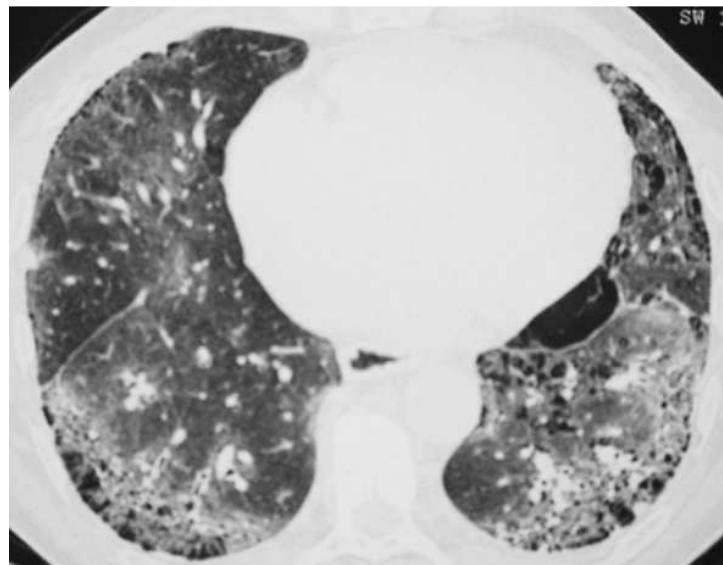
Abnormal nailfold capillaries



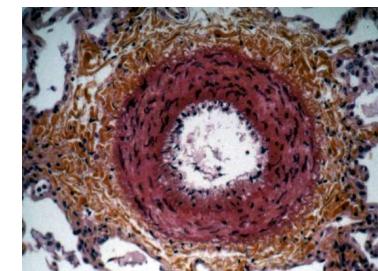
Score = 2

Interstitial lung disease/pulmonary arterial hypertension

Score = 2



Score = 2



Maximum score = 2



Raynaud's phenomenon



Score = 3

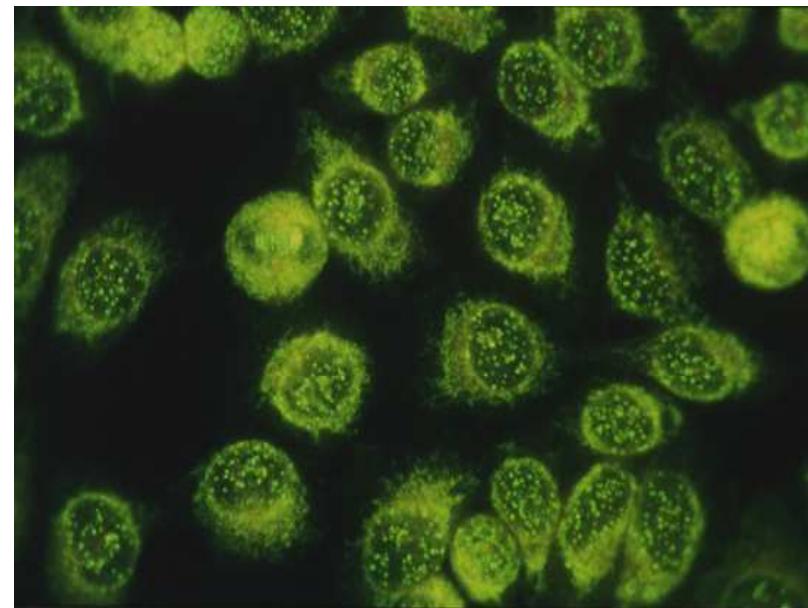
SSc-related autoantibodies

Anti-centromere

Anti-topoisomerase I

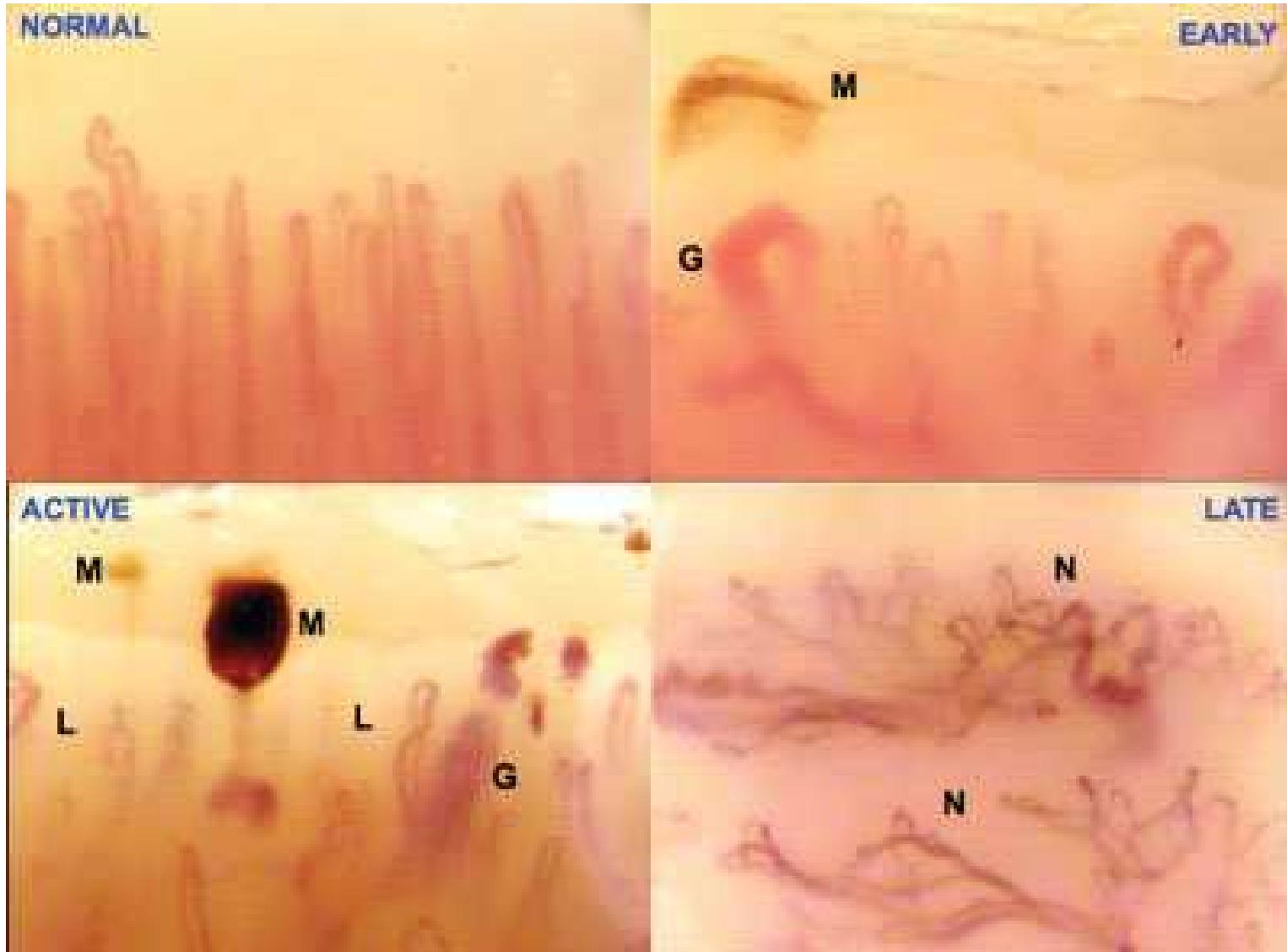
Anti-RNA polymerase III

Score = 3



Maximum score = 3

Specific microvascular changes that characterize the different nailfold videocapillaroscopic SSc patterns



Herrick A & Cutolo M A&R 2010

Clinical classification of SSc

Diffuse cutaneous SSc

- Skin sclerosis proximal to elbows and knees
- Inflammatory features prominent in 1st 3 years
- Anti-Scl-70 or anti-RNA polymerase
- Increased frequency of interstitial lung disease, renal crisis, bowel & cardiac involvement

Scleroderma sine Scleroderma

- No skin sclerosis

Limited cutaneous SSc

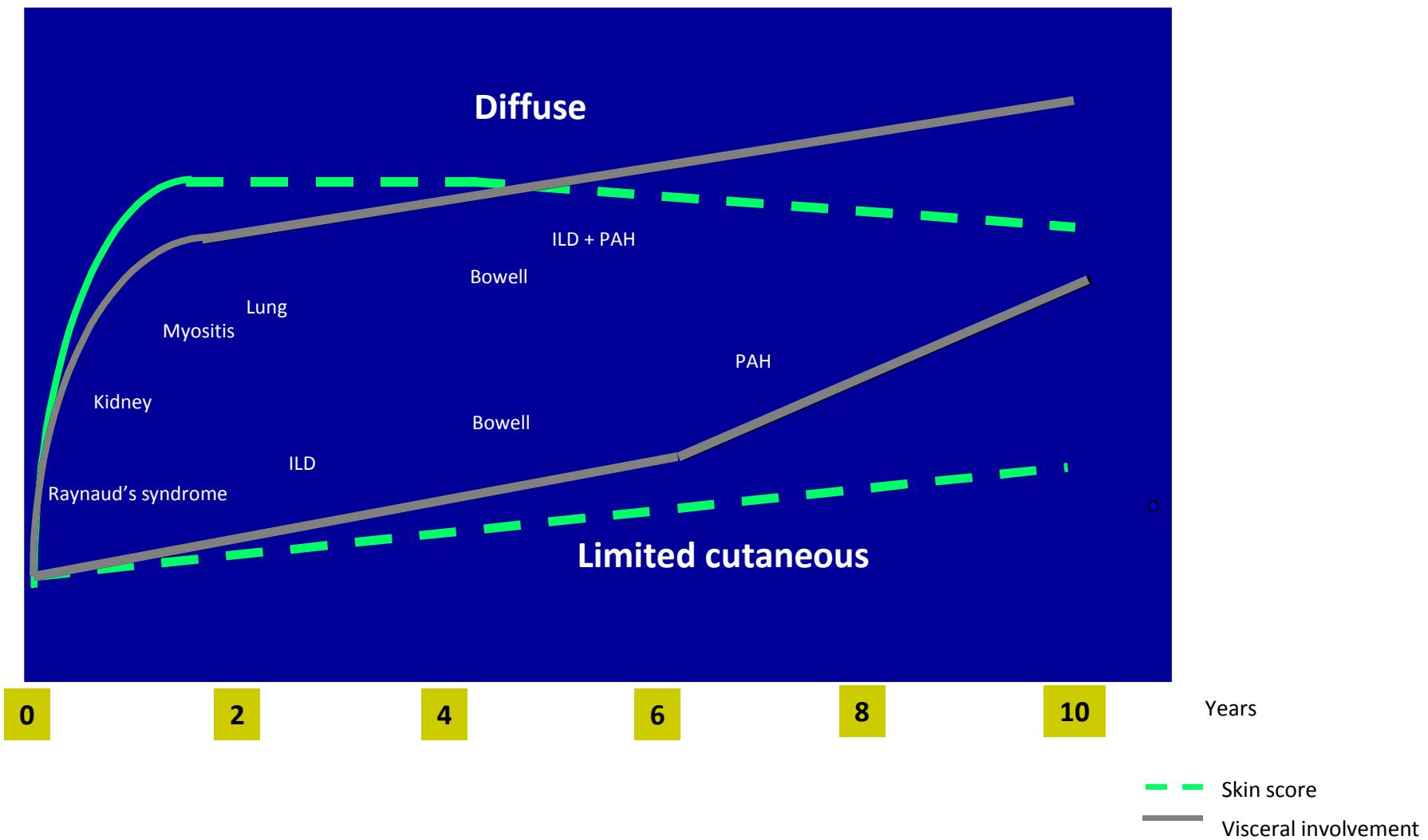
- No skin sclerosis proximal to elbows and knees
- Anti-centromere antibody (ACA)
- CREST subgroup
- Lung fibrosis, renal crisis & cardiac involvement less common than in dcSSc

Overlap syndrome

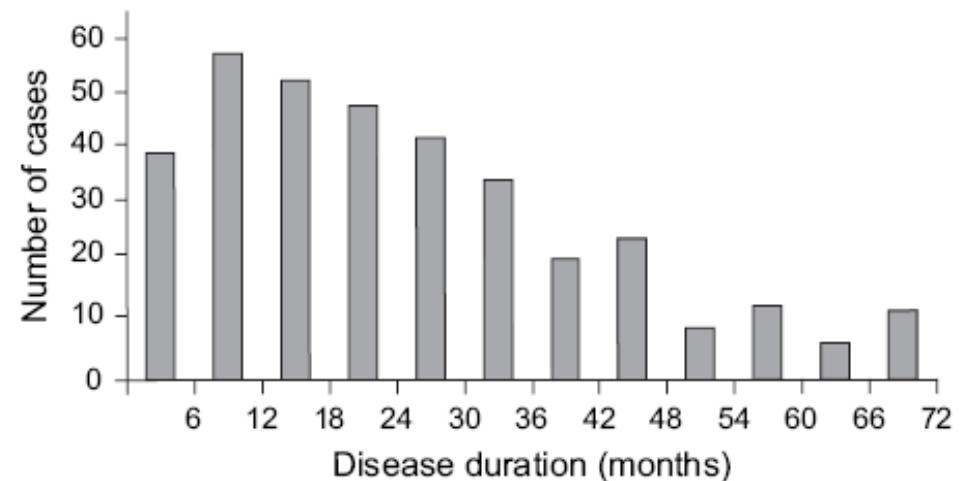
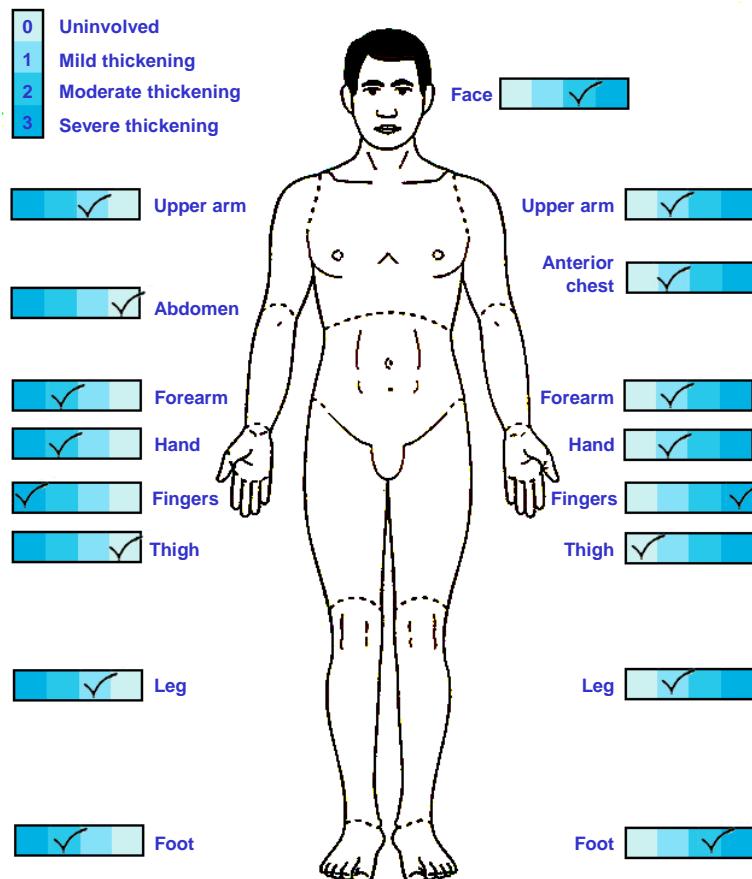
- Features include those of lcSSc or dcSSc with those of other autoimmune disease(s)

Poormoghim H, et al. *Arthritis Rheum* 2000; 43:444-51,
Denton CP and Black CM, *Trends Immunol* 2005; 26:596-602.

SYSTEMIC SCLEROSIS : EVOLUTION



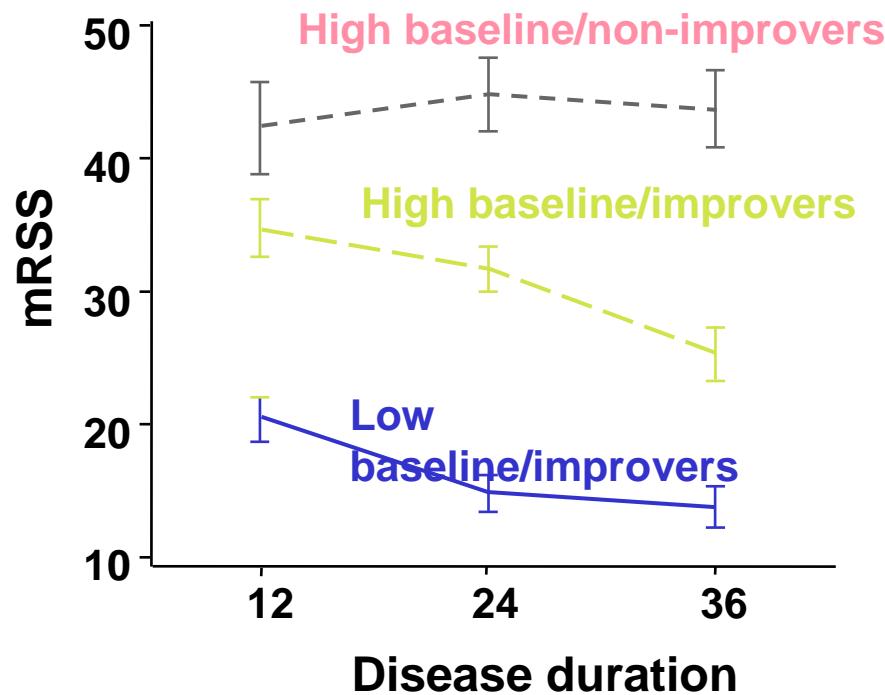
The modified Rodnan skin score (MRSS)



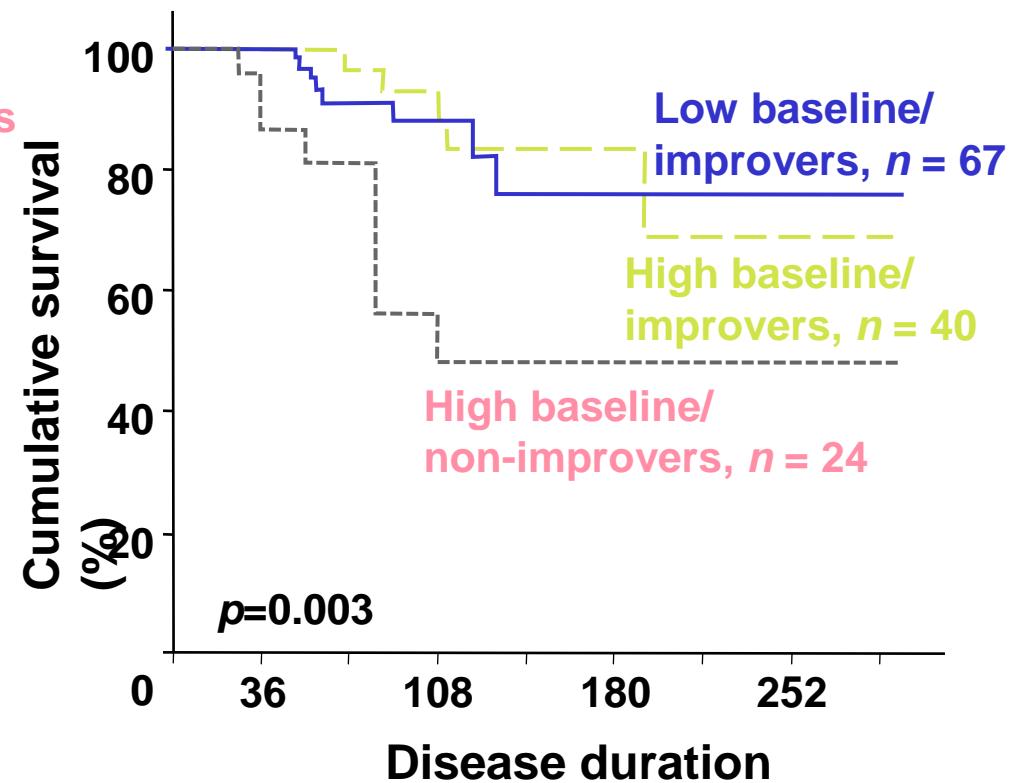
Disease duration at peak skin score of the patients who had dcSSc from the Royal Free Hospital scleroderma database.

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.

Prevalence of visceral involvement in SSc

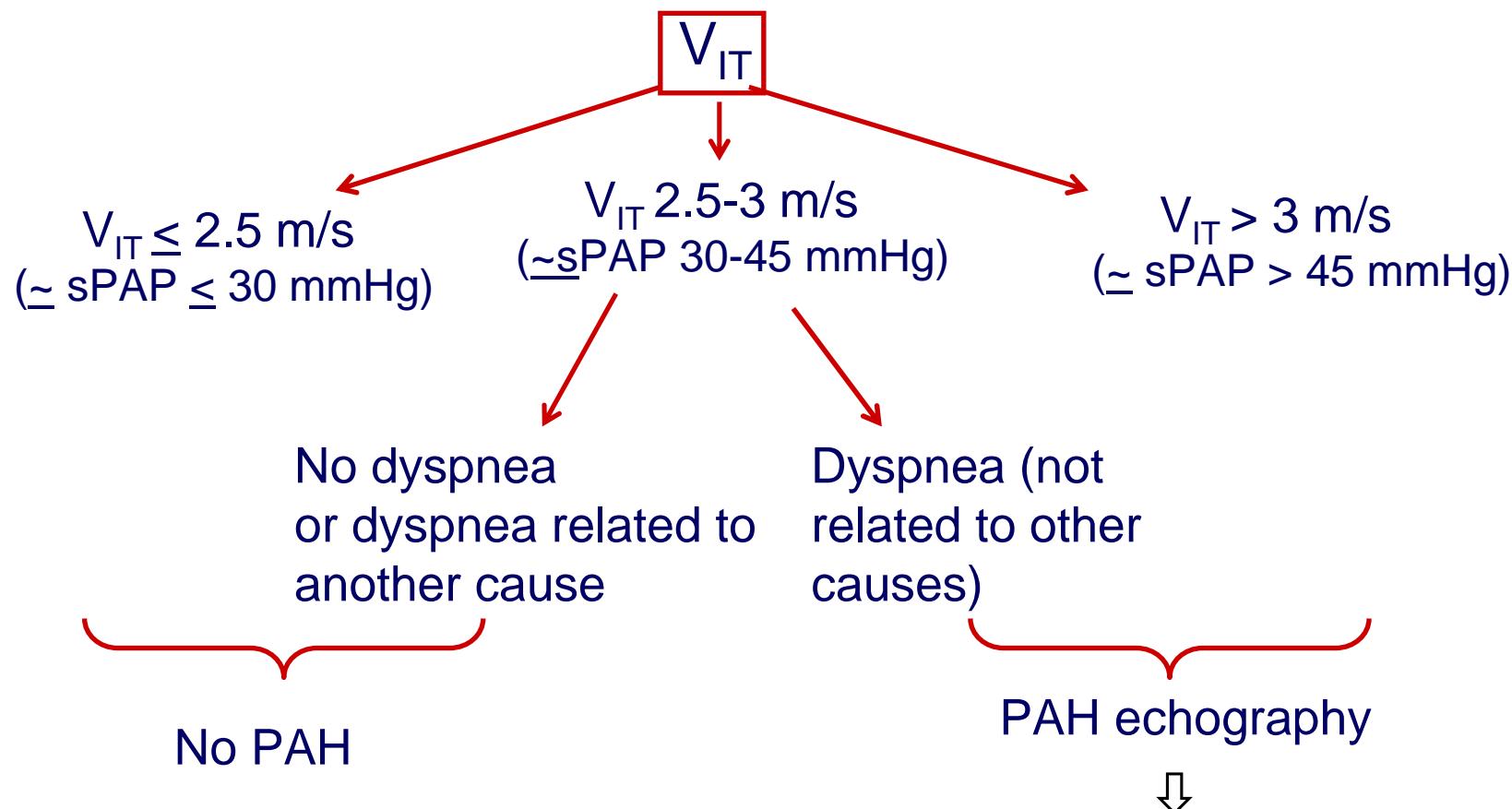
	Total	Missing data	IcSSc	dcSSc
Number of patients, n (%)	1483 (100)	0 (0)	674 (45.5)	484 (32.7)
Percentage of organ involvement by SSc subsets				
RP	94.4	0.1	96.3	94.2
Skin involvement	87.8	0.3	91.5	97.6
PAH	15.8	0.1	14.9	18.5
Pulmonary fibrosis	34.5	0.1	20.8	56.1
Oesophagus	60	0.1	59.2	69.3
Stomach	14.2	0.2	15.3	15.6
Intestine	5.7	0.2	6.1	5.3
Kidney	10.5	0.2	9.1	15.9
Heart	14.6	0.2	12	23
Musculoskeletal system	47.5	1.4	44.9	56.6
Nervous system	6.4	2.2	4.1	7.1
Sicca-symptoms	39.5	2.5	43.5	39.7
Masticatory organ	24.1	7.2	23.7	34.1

Hunzelmann N, et al. *Rheumatology* 2008; 47:1185-92.

Sclérodermie systémique: examens complémentaires

- Capillaroscopie: au diagnostic
- ECG chaque année
- Radiographie des mains au diagnostic puis selon évolution
- Echographie cardiaque avec mesure PAPs chaque année
- EFR avec mesure DLCO chaque année
- Scanner thoracique coupes fines haute résolution au diagnostic puis fonction de la présence PID
- Fibroscopie oeso-gastro-duodenale: dans les 5 premières années

Cardiac EchoDoppler PAH definition

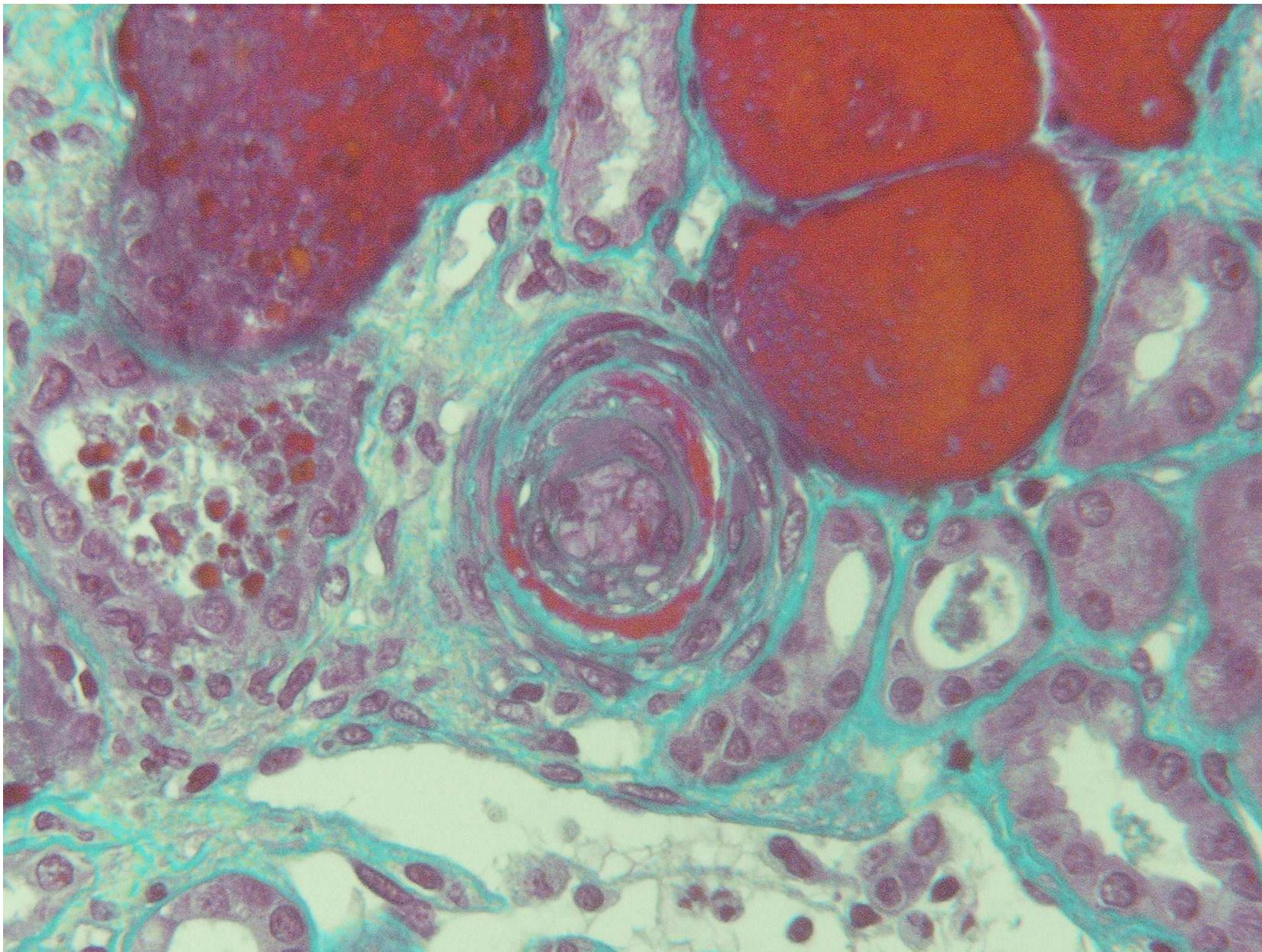


Right cardiac catheterisation
Hachulla et al. Arthritis Rheum 2005

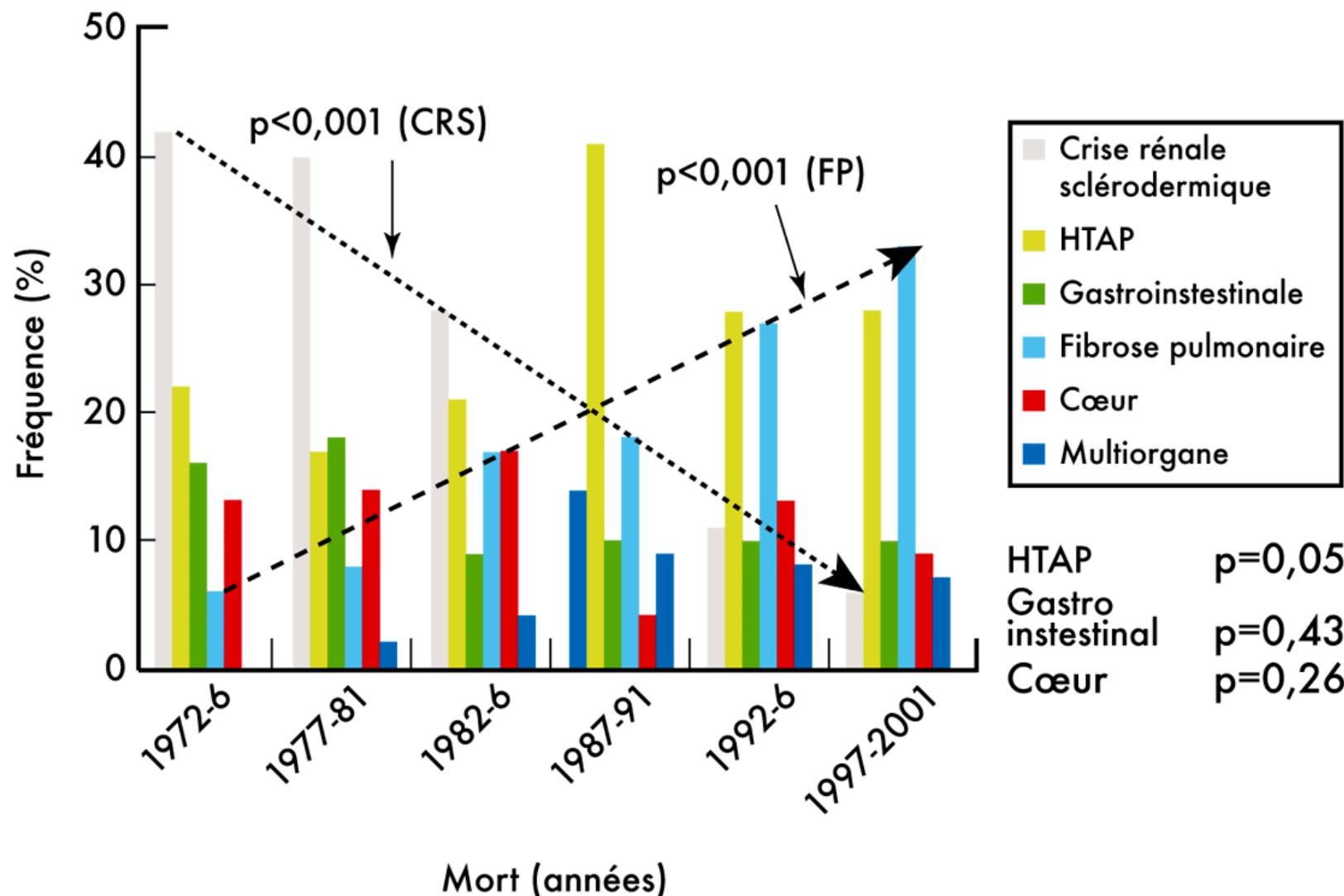
PAH: Detect study

- Six simple assessments in Step 1 of the algorithm determined referral to echocardiography.
- In Step 2, the Step 1 prediction score and two echocardiographic variables determined referral to RHC.
 - FVC % predicted/DLCO %predicted
 - Current/past telangiectasia
 - Anti-centromere Abs
 - Serum NT-pro-BNP
 - Serum urate
 - ECG: right axis deviation
 - Right atrium area
 - TR velocity

Interlobular artery with mucoid changes and concentric intimal fibroplasia with so-called « onion-skinning changes ».



Changes in causes of Systemic Sclerosis related deaths between 1972 and 2001



Disease modifying agents in systemic sclerosis

(adapted from Mounthon L et al. Presse Med, 2006)

Immunosuppressants

- *Corticosteroids*
- *Methotrexate #*
- *Cyclosporine A #*
- *Cyclophosphamide #*
- *Azathioprine*
- *Mycophenolate mofetyl*
- *Stem cell transplantation*
- *Photochemotherapy #*

Vasodilators

- *Epoprostenol*
- *Prostacycline*
- *Bosentan #*
- *Ambrisentan*
- *Sildenafil*
- *Tadalafil*

Anti-fibrotic agents

- *D-penicillamine #*
- *Colchicine*
- *Relaxine #*
- *Interferons #*
- *Calcitriol*
- *Pentoxifylline*
- *Factor XIII #*
- *Retinoids*

Other treatments

- *ACE inhibitors*
- *Octréotide*
- *Ketotifen #*
- *Plasmapheresis #*
- *Minocycline*

Biologics

- *Anti-TNF α*
- *Rituximab*

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