Sclérodermie systémique: quel suivi évolutif ?

Luc Mouthon

Service de Médecine Interne, hôpital Cochin,

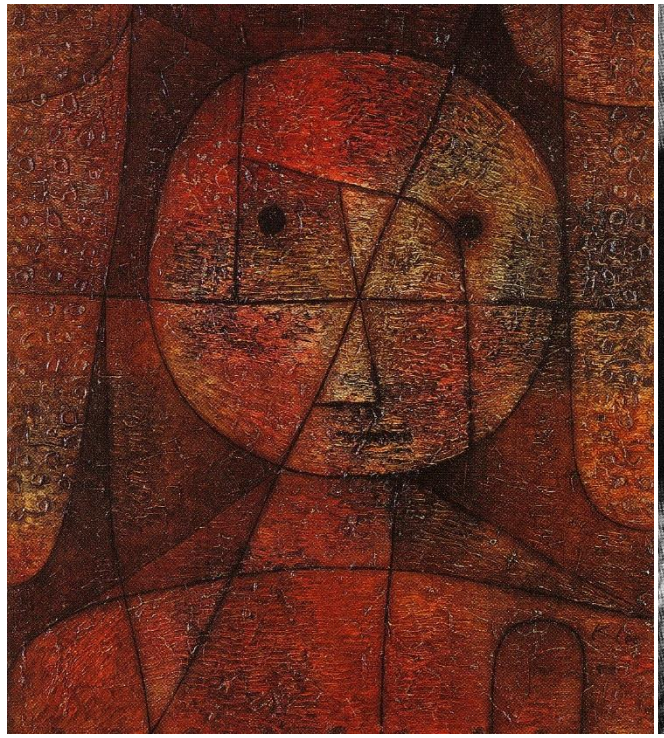
Centre de Référence Vascularites nécrosantes et sclérodermie systémique

Assistance publique-Hôpitaux de Paris, Paris

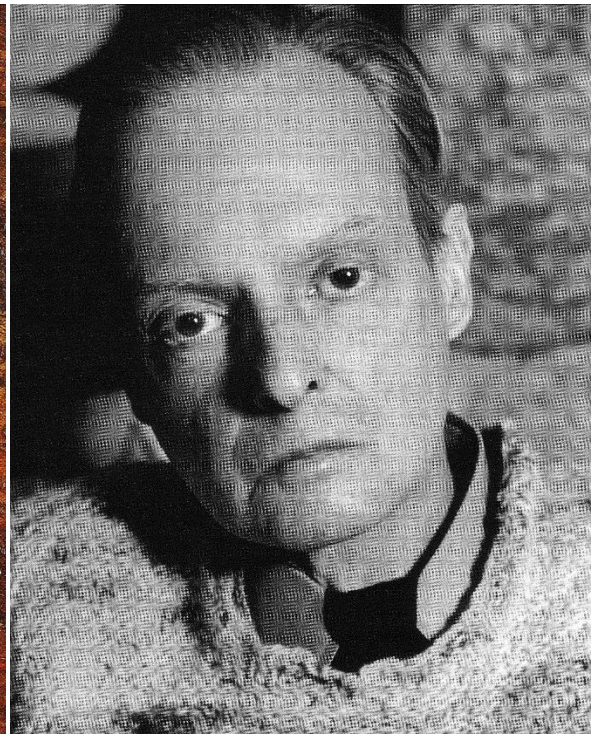
Université Paris Descartes, Inserm U1016, Institut Cochin, Paris

DHU *Authors*

Paul Klee : 1879-1940 (I)



Gezeichneter 1935
„portant la marque de la mort“

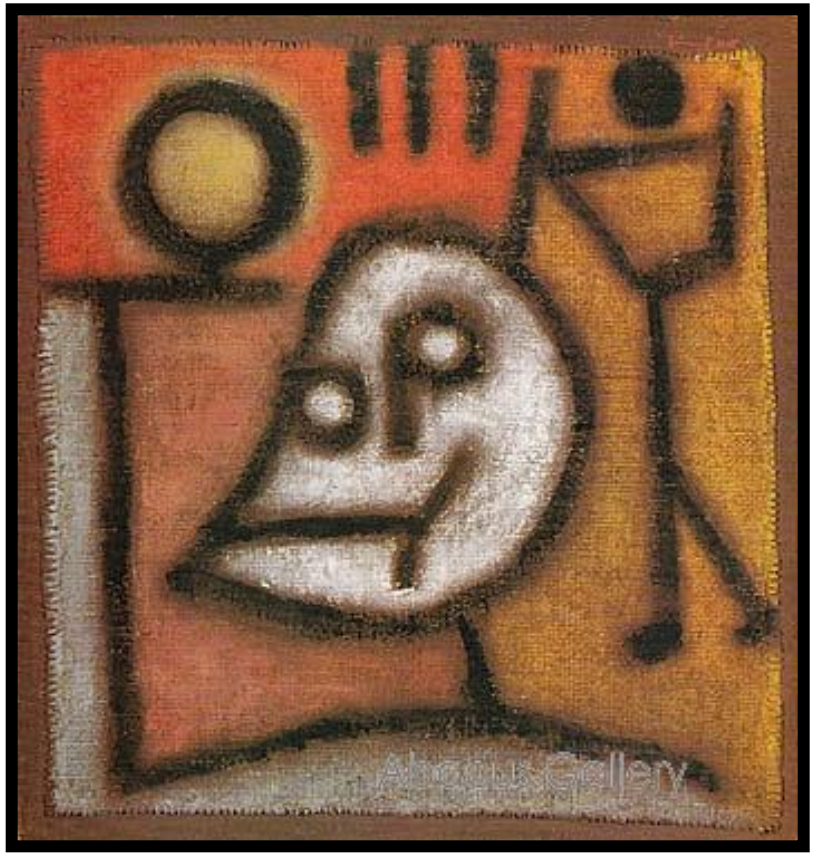


1933	Raynaud‘s phenomenon
1934	Fatigue, dyspnea, thickened skin
1936	Extension of skin fibrosis
1940	Hospitalisation at Sant‘ Agnes, Locarno (worsening of dyspnea)

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

Suivi évolutif d’un malade sclérodermique

- Diffus vs limité
- Examen clinique
- Examens complémentaires
- Atteintes viscérales
- Handicap/qualité de vie

Fréquence suivi

Diffuse:

- Consultation trimestrielle ou plus fréquente
- Bilan annuel ou plus fréquent

Limitée:

- Consultation semestrielle ou plus fréquente
- Bilan annuel

Evaluation clinique

Lésions cutanées
- Score de Rodnan modifié
- Télangiectasies
- Ulcérations/calcinoses
- Hyperpigmentation/dépigmentation

Pouls périphériques
- Pouls cubitaux
- Manœuvre d'Allen

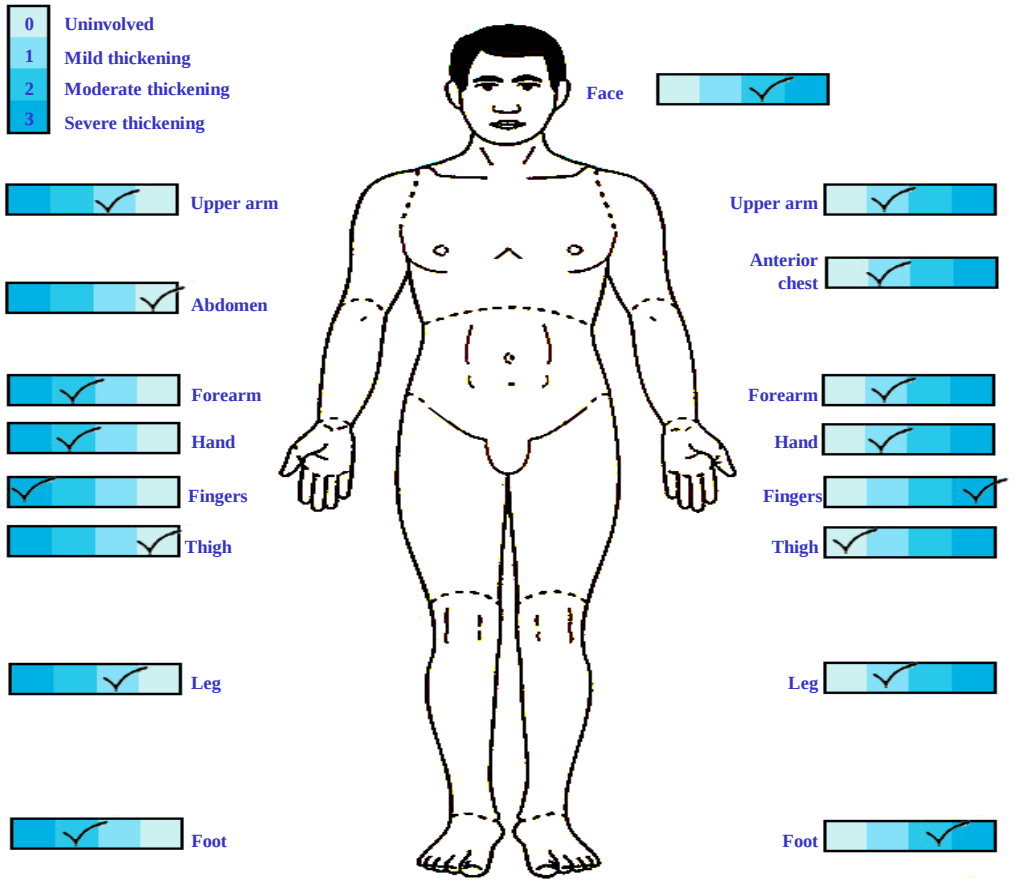
Articulations/muscles
- Douleurs
- Déformations
- Synovites
- Force musculaire
- Frictions tendineuses

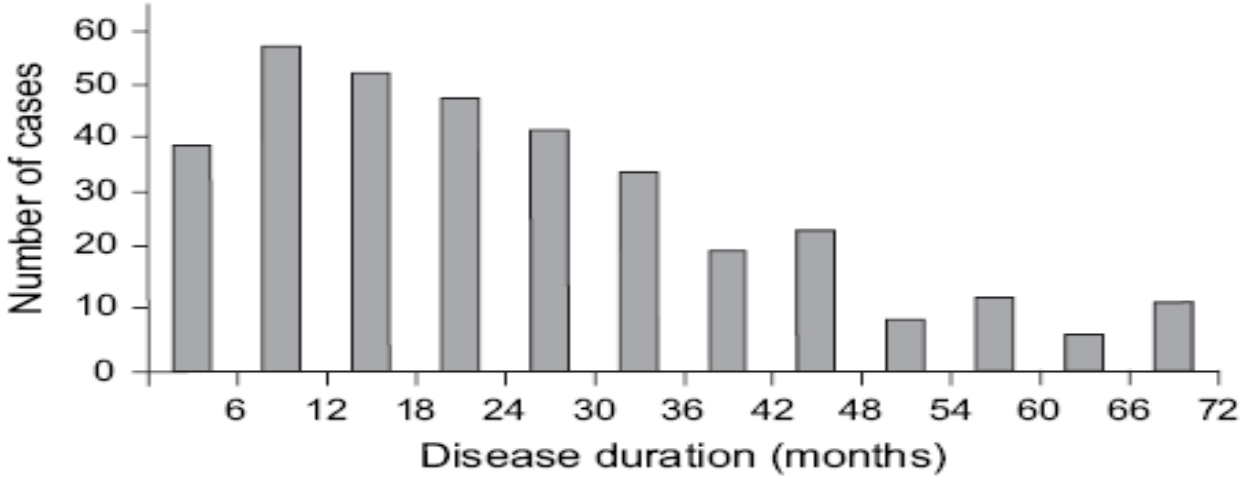
Les poumons
- Dyspnée
- Crépitants velcro des bases

Le cœur
- Palpitations
- Fréquence cardiaque/bruit/souffle

Tube digestif
- reflux/dysphagie
- Vomissements
- Distention abdominale
- Constipation / diarrhée
- Incontinence anale

The modified Rodnan skin score (MRSS)



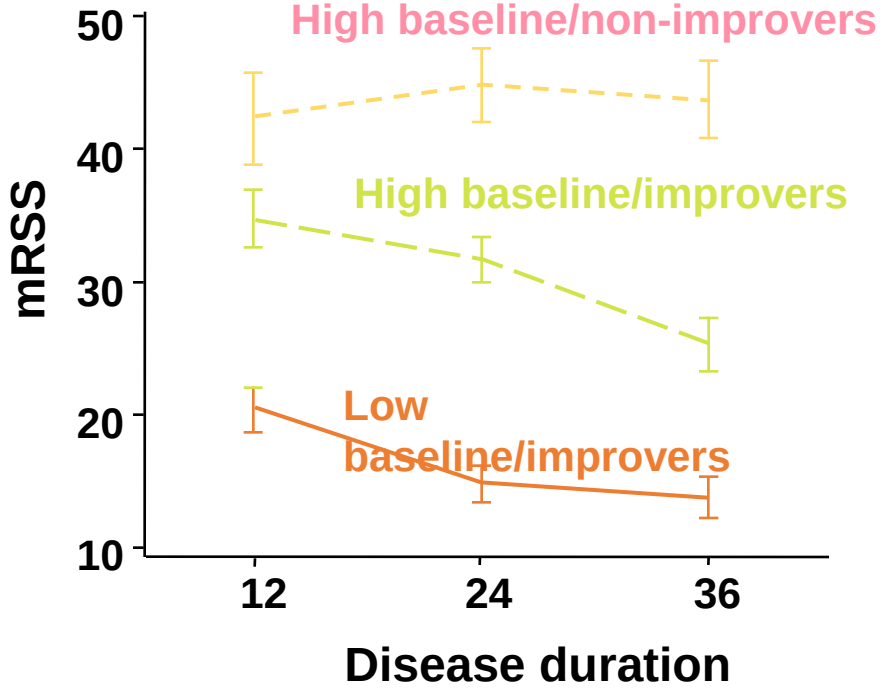


Disease duration at peak skin score of the patients who had dcSSc from the Royal Free Hospital scleroderma database.

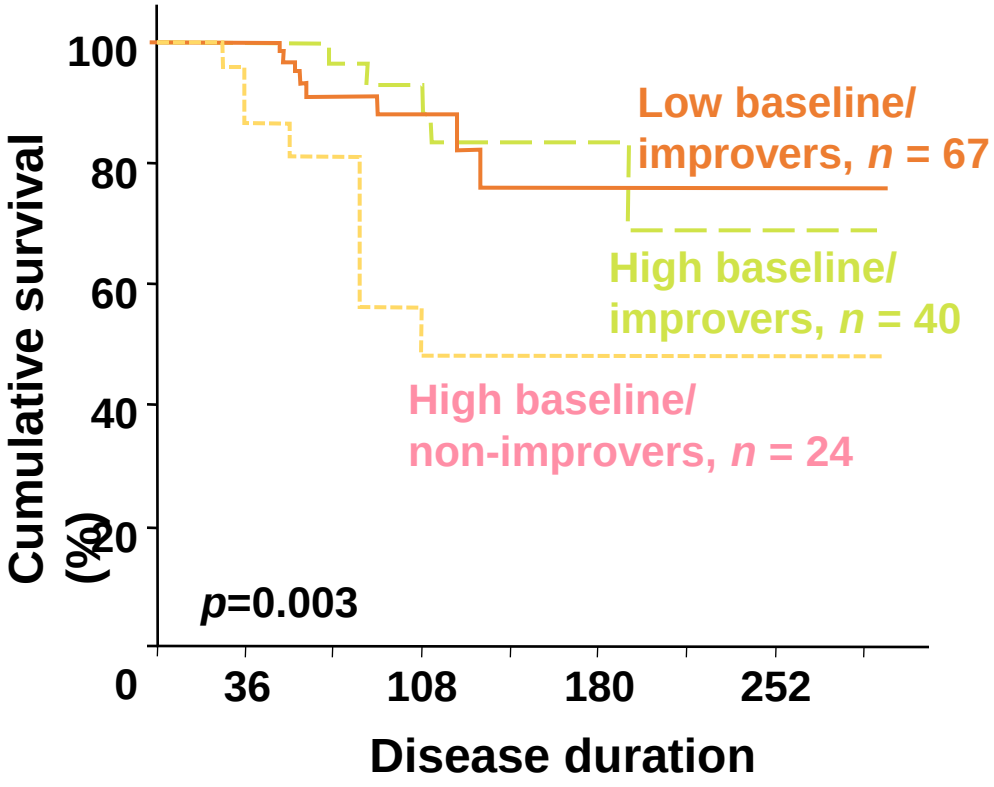
Nihtyanova SI, Denton CP. Rheum Dis Clin N Am 34 (2008) 161–179

Disease duration and skin score in dcSSc

Change in skin score over 3 years in the subgroups



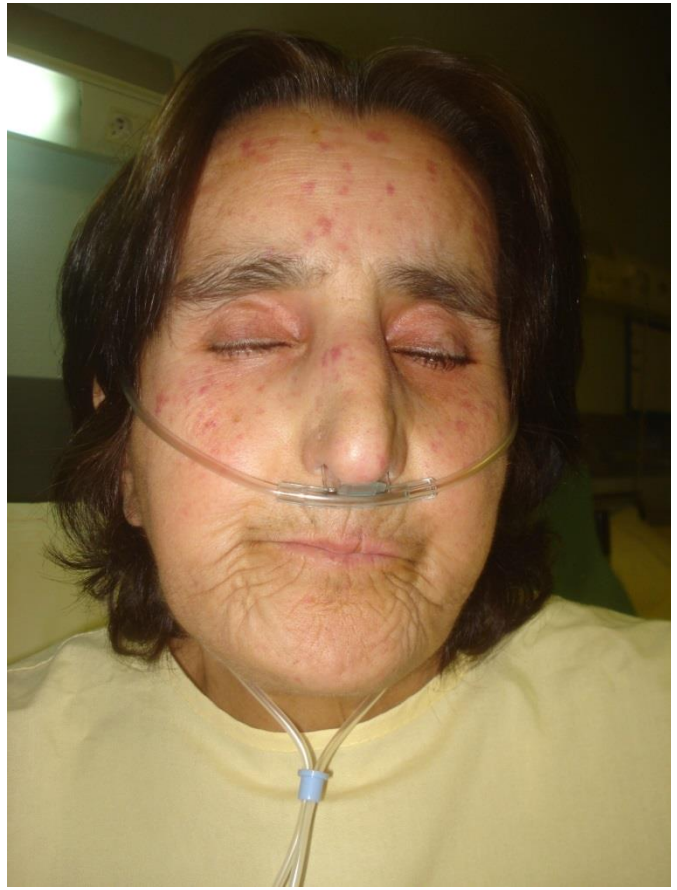
Survival in the subgroups



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

Telangiectases in Scleroderma: A Potential Clinical Marker of Pulmonary Arterial Hypertension

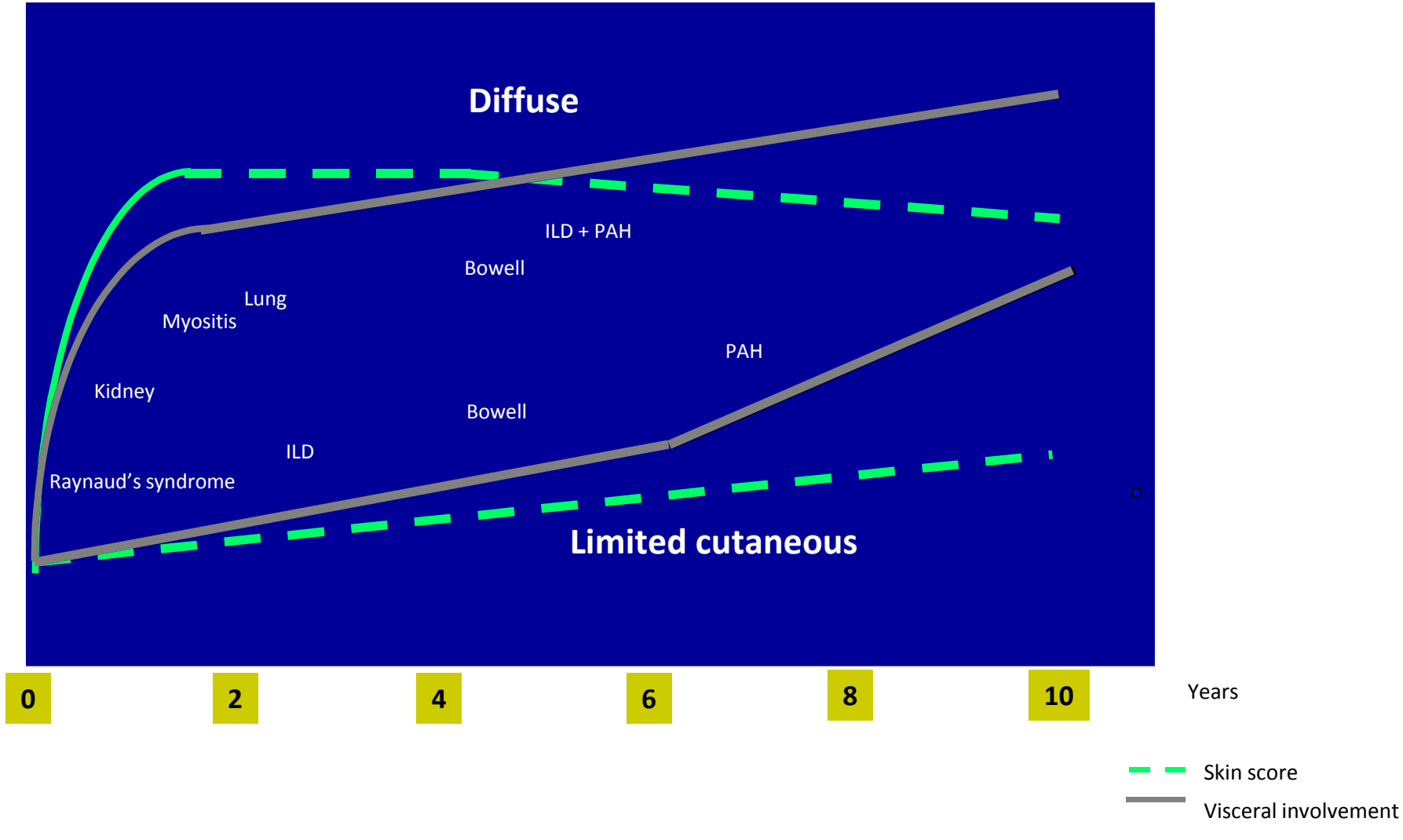
Shah et al. J Rheumatol 2010



Sclérodermie systémique: bilan initial (examens biologiques)

- **NFS plaquettes**
- **Ionogram, creatinin**
- **CRP**
- **Liver enzymes**
- **uricemia**
- **CK**
- **Serum protein electrophoresis**
- **NT pro-BNP**
- **ANA**
- **Anti-ECT**
- **Anti-RNA polymerase III**
- **Anti-fibrillarine**

SYSTEMIC SCLEROSIS : EVOLUTION



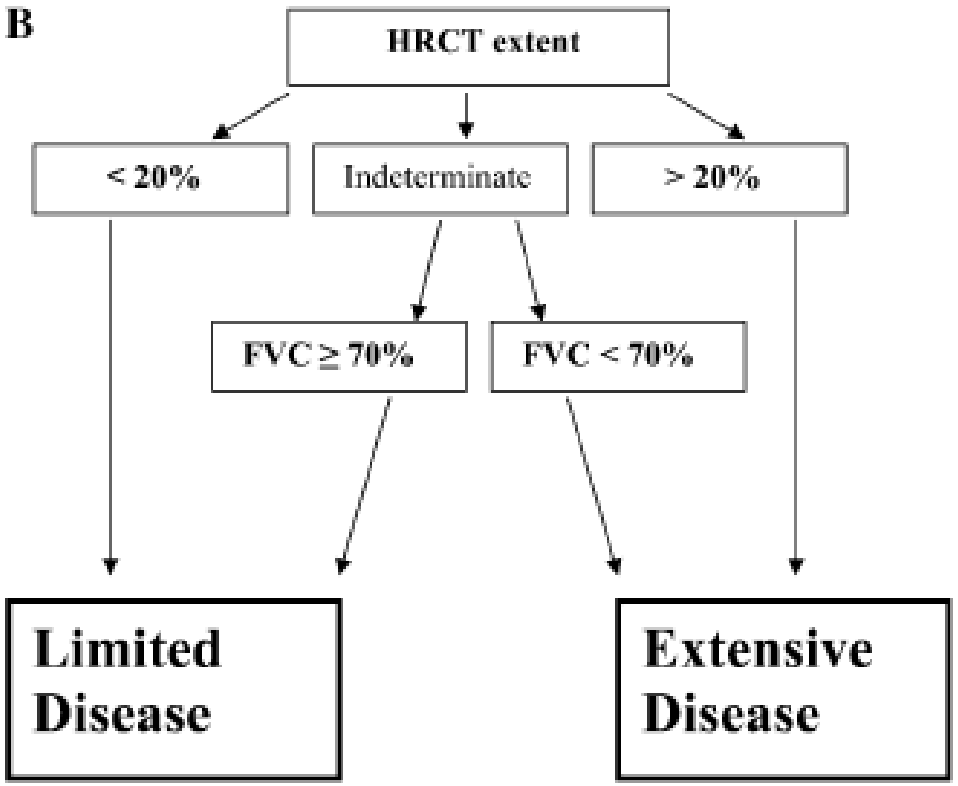
Sclérodermie systémique: examens complémentaires

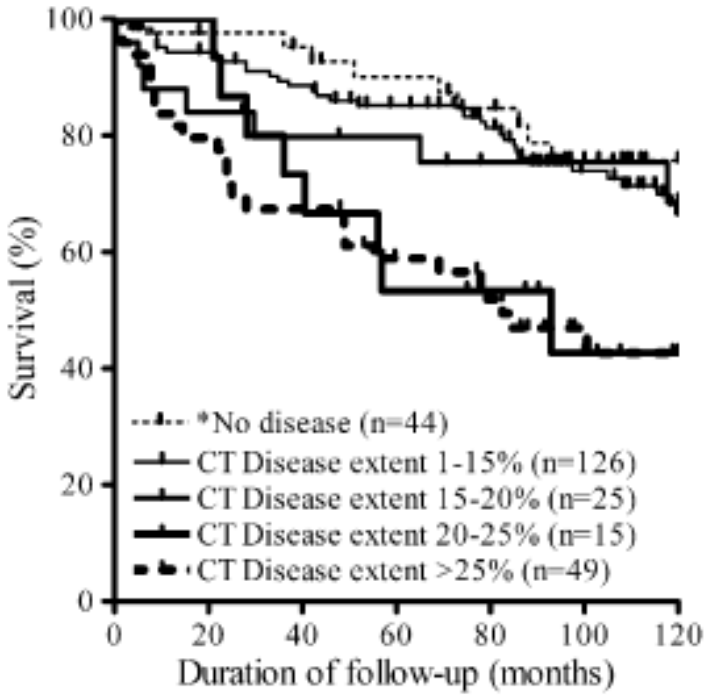
- Capillaroscopie: au diagnostic
- ECG chaque année (Holter ECG)
- Radiographie des mains au diagnostic puis selon évolution
- Echographie cardiaque avec mesure PAPs chaque année (IRM cardiaque)
- EFR avec mesure DLCO chaque année
- Scanner thoracique coupes fines haute résolution au diagnostic puis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

Anomalies du Holter ECG des 24 heures au cours de la sclérodermie systémique

Anomalie	Incidence
Extra-systole auriculaire	61%
Tachycardie supra-ventriculaire	21-32%
Extra-systole ventriculaire	67%
Tachycardie ventriculaire	10-13%
Anomalies de conduction	8-14%

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





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.

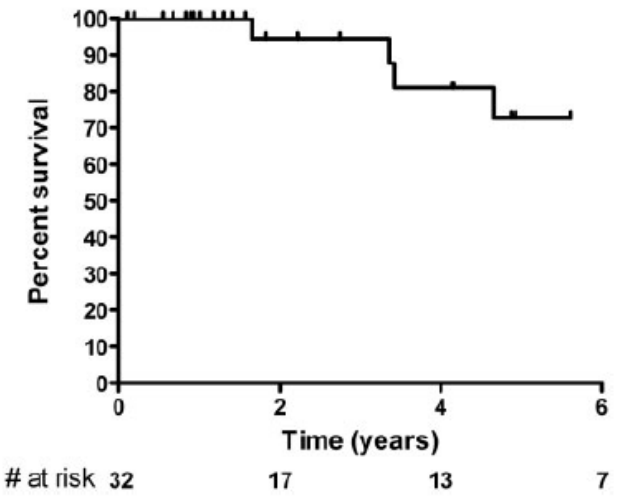
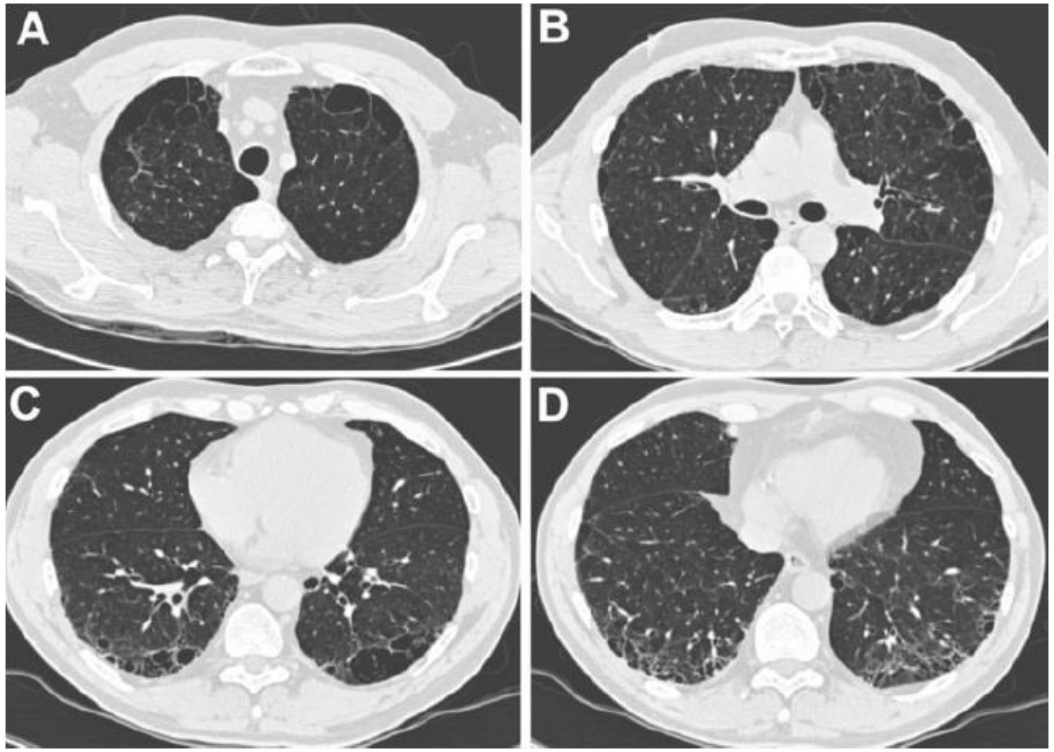


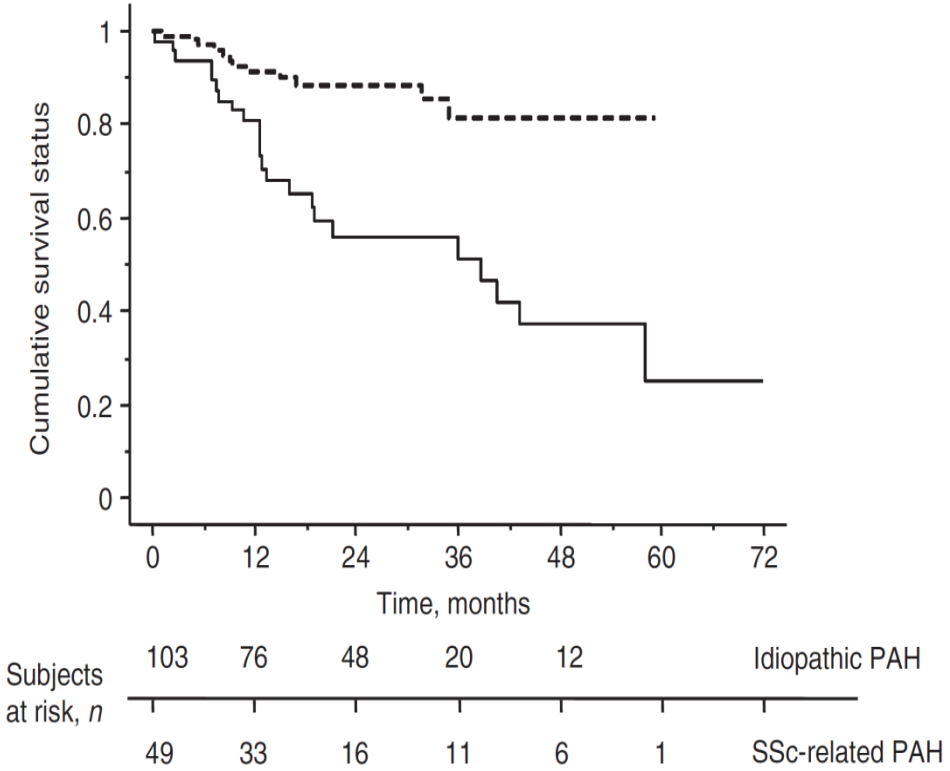
Figure 2. Kaplan-Meier estimates of survival in patients with combined pulmonary fibrosis and emphysema syndrome and connective tissue disease.



HTAP-SSc : un pronostic sombre…

Long-term outcome of systemic sclerosis-associated pulmonary arterial hypertension treated with bosentan as first-line monotherapy followed or not by the addition of prostanoids or sildenafil

David Launay[1,2,3,4], Olivier Sitbon[1,2,3], Jérôme Le Pavec[1,2,3], Laurent Savale[1,2,3], Colas Tchérakian[1,2,3], Azzedine Yaïci[1,2,3], Lara Achouh[1,2,3], Florence Parent[1,2,3], Xavier Jais[1,2,3], Gérald Simonneau[1,2,3] and Marc Humbert[1,2,3]



Launay D, *et al*. *Rheumatology* 2010;49:490-500.

Hôpitaux universitaires Paris-Sud
Antoine-Béclère Bicêtre Paul-Brousse

PAH-SSc: Prevalence

Author	Year of publication	Country	PAH definition (RHC)	PAH prevalence
Mukerjee et al.	2003	UK	mPAP > 25 mmHg at rest or > 30 at exercise pulmonary capillary < 14 mmHg	12% (86/722)
Hachulla E, et al.	2005	France	mPAP > 25 mmHg at rest or > 30 at exercise pulmonary capillary < 14 mmHg	7,85% (47/599)
Vonk, et al.	2009	Netherlands	PAPm ≥25mmHg at rest and normal pulmonary capillary pressure	9,9% (113/1,148)
Phung, et al.	2009	Australia	PAPm ≥25mmHg at rest, or ≥30mmHg at exercise pulmonary capillary < 15 mmHg and PVR> 240 dyn/s/cm²	13% (24/184)
Avouac, et al.	2010	France and Italy	PAPm ≥25mmHg at rest, or ≥30mmHg at exercise pulmonary capillary < 15 mmHg absence of pulmonary fibrosis	3,6% (42/1,165)
Hsu et al.	2014	North America	PAPm ≥25mmHg au repos, ou ≥30mmHg à l'effort et PCP < 15mmHg	13,9% (35/251)

Legendre P, Mouthon L. Presse Med 2014

Cardiac EchoDoppler
PAH definition

V_{IT}

$V_{IT} \leq 2.5$ m/s
(~ sPAP ≤ 30 mmHg)

V_{IT} 2.5-3 m/s
(~sPAP 30-45 mmHg)

$V_{IT} > 3$ m/s
(~ sPAP > 45 mmHg)

No dyspnea
or dyspnea related to
another cause

Dyspnea (not
related to other
causes)

No PAH

PAH echography

⇩

Right cardiac catheterisation

Hachulla et al. Arthritis Rheum 2005

Cardiac catheterisation (n=33)

- PAH : 18
- [mPAP > 25 mmHg at rest or > 30 mmHg at exercise with PAwP < 15 mmHg]
  - 25-35 mmHg: 14
  - 35-45 mmHg: 3
  - 45 mmHg: 1
- Post-capillary “venous”pulmonary hypertension: 3 (10%)
- No PAH : 12 => 6 with mPAP > 20 mmHg

Hachulla et al. Arthritis Rheum 2005

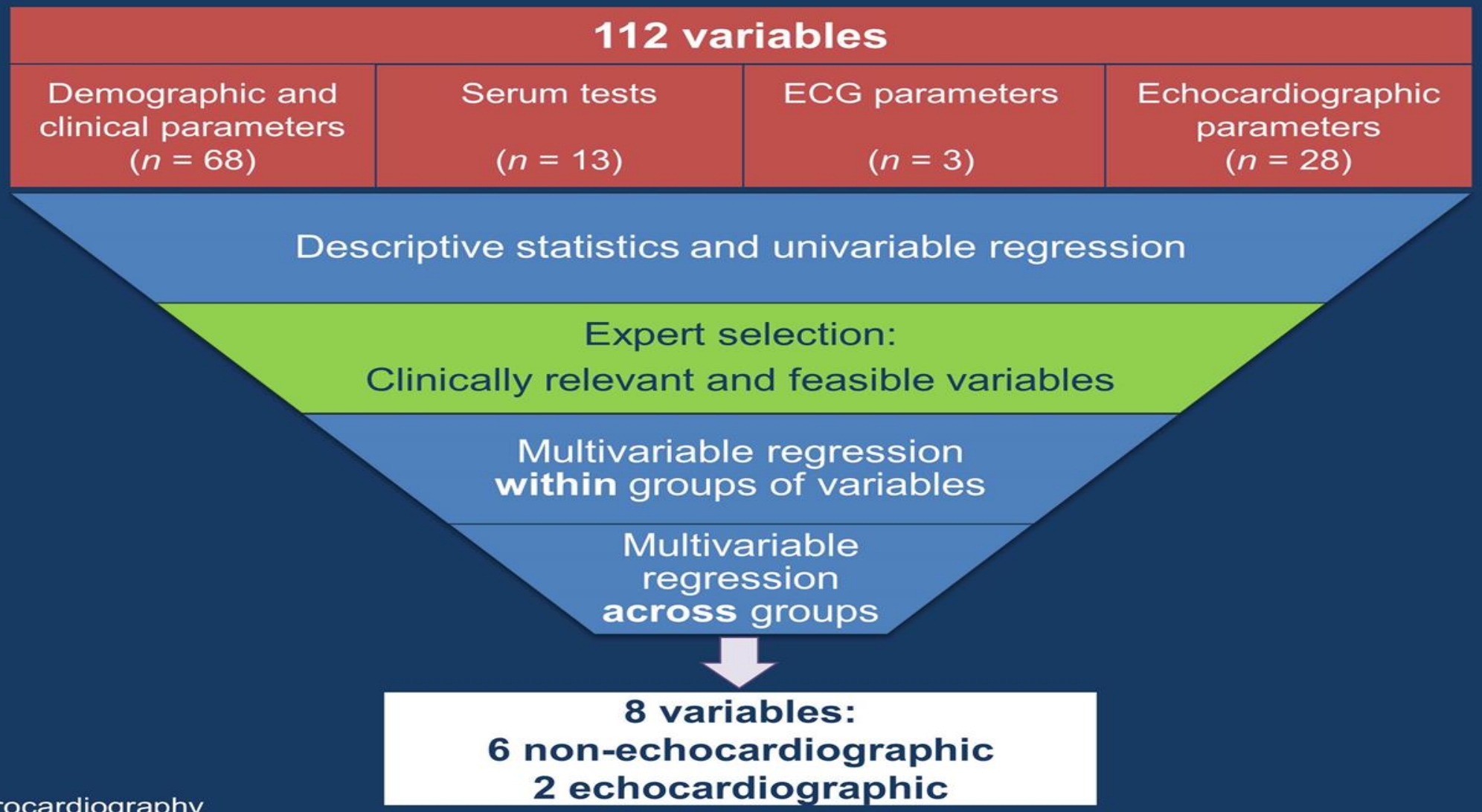
Estimated incidence of pulmonary hypertension during the 3-year followup period*

	Estimated incidence (no. of cases per 100 patient-years)	95% CI
All forms of pulmonary hypertension	1.37	0.74–2.00
Pulmonary arterial hypertension	0.61	0.26–1.20
Among patients with lcSSc	0.40	0.11–1.03
Among patients with dcSSc	1.25	0.34–3.20
Postcapillary pulmonary hypertension	0.61	0.26–1.20
Pulmonary hypertension secondary to pulmonary fibrosis	0.15	0.02–0.55

* 95% CI = 95% confidence interval; lcSSc = limited cutaneous systemic sclerosis; dcSSc = diffuse cutaneous systemic sclerosis.

Hachulla et al. Arthritis Rheum 2009

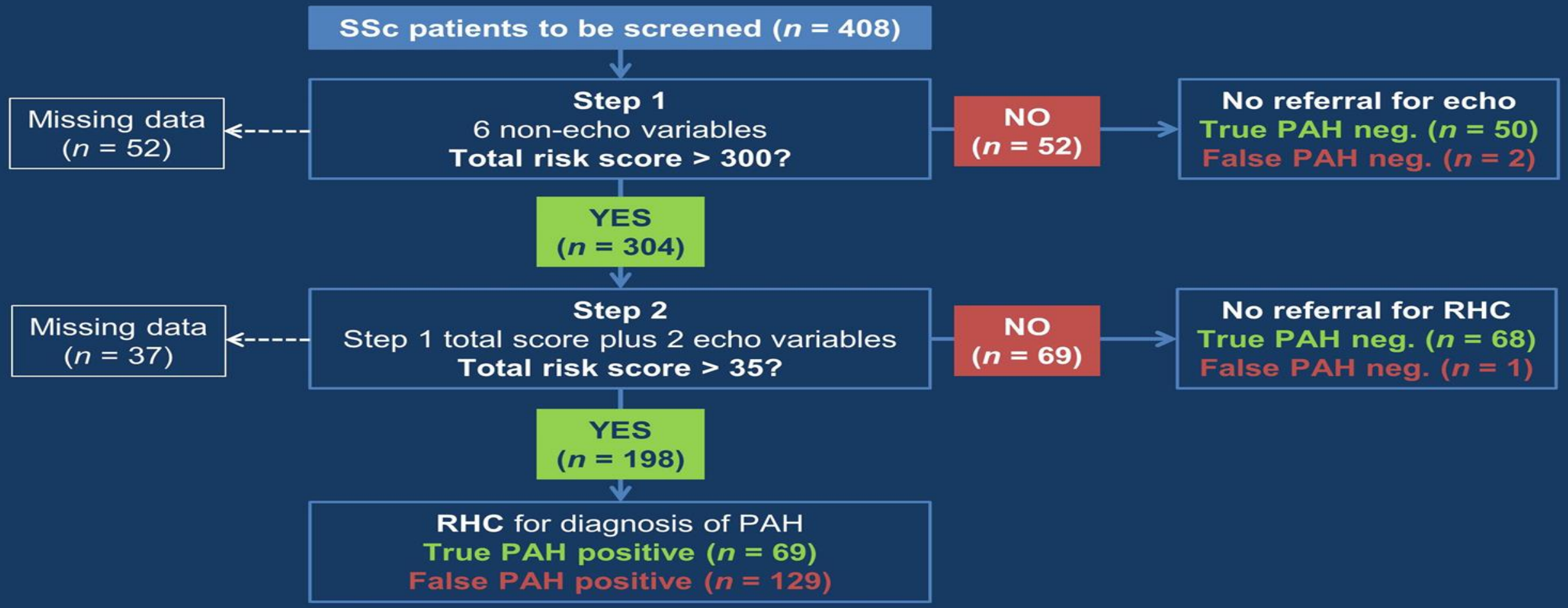
Selection of screening variables in the DETECT study



ECG: electrocardiography

Coghlan JG, *et al. Ann Rheum Dis* 2013; Epub ahead of print.

DETECT: Two-step decision tree performance



For step 1: ROC AUC = 0.844 (95% CI, 0.795, 0.898)
For step 2: ROC AUC = 0.881 (95% CI, 0.824, 0.923)

ROC: receiver operating characteristic; AUC: area under the curve

39; 20 October 2013

Coghlan JG, *et al. Ann Rheum Dis* 2013; Epub ahead of print.

Detect: results

- Six simple assessments in Step 1 of the algorithm determined referral to echocardiography.

- FVC % predicted/DLCO %predicted
- Current/past telangiectasia
- Anti-centromere Abs
- Serum NT-pro-BNP
- Serum urate
- ECG: right axis deviation

- In Step 2, the Step 1 prediction score and two echocardiographic variables determined referral to RHC.

- Right atrium area
- TR velocity

Coghlan G, ARD, 2013

DETECT online PAH risk calculator

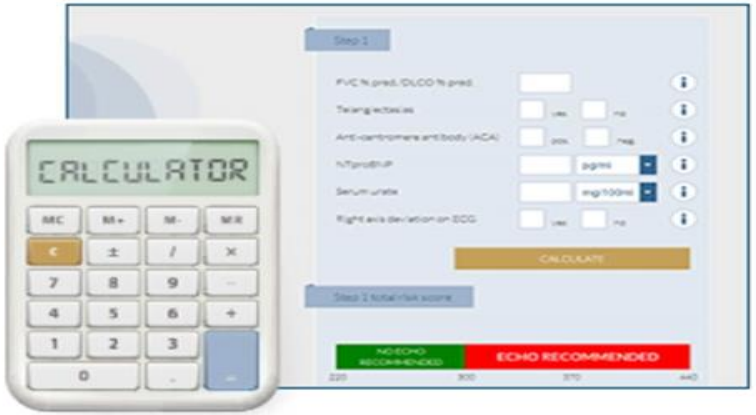
DETECT
DETECTion of PAH in SSc

HOME | WHAT IS DETECT? | PAH RISK CALCULATOR | ABOUT SSC AND PAH | SUPPORTING INFORMATION

WELCOME TO THE PAH RISK CALCULATOR

The PAH risk calculator is a tool for all physicians dealing with systemic sclerosis (SSc). The calculator was developed and validated in the DETECT study. The DETECT study was designed and carried out by a group of experts, all of whom are physicians practising in different countries, and was supported by Actelion Pharmaceuticals Ltd.

The calculator was developed for your daily clinical practise. It will help you to identify and diagnose SSc patients with pulmonary arterial hypertension (PAH), which is a serious condition that develops in 8-13% of SSc patients and is the leading cause of death in patients with this disease. The calculator is based on an algorithm with a high sensitivity and specificity and can help you to decide which of your SSc patients should be evaluated using echocardiography, and of those patients who should be referred for right heart catheterization.



START CALCULATOR

http://detect-pah.com

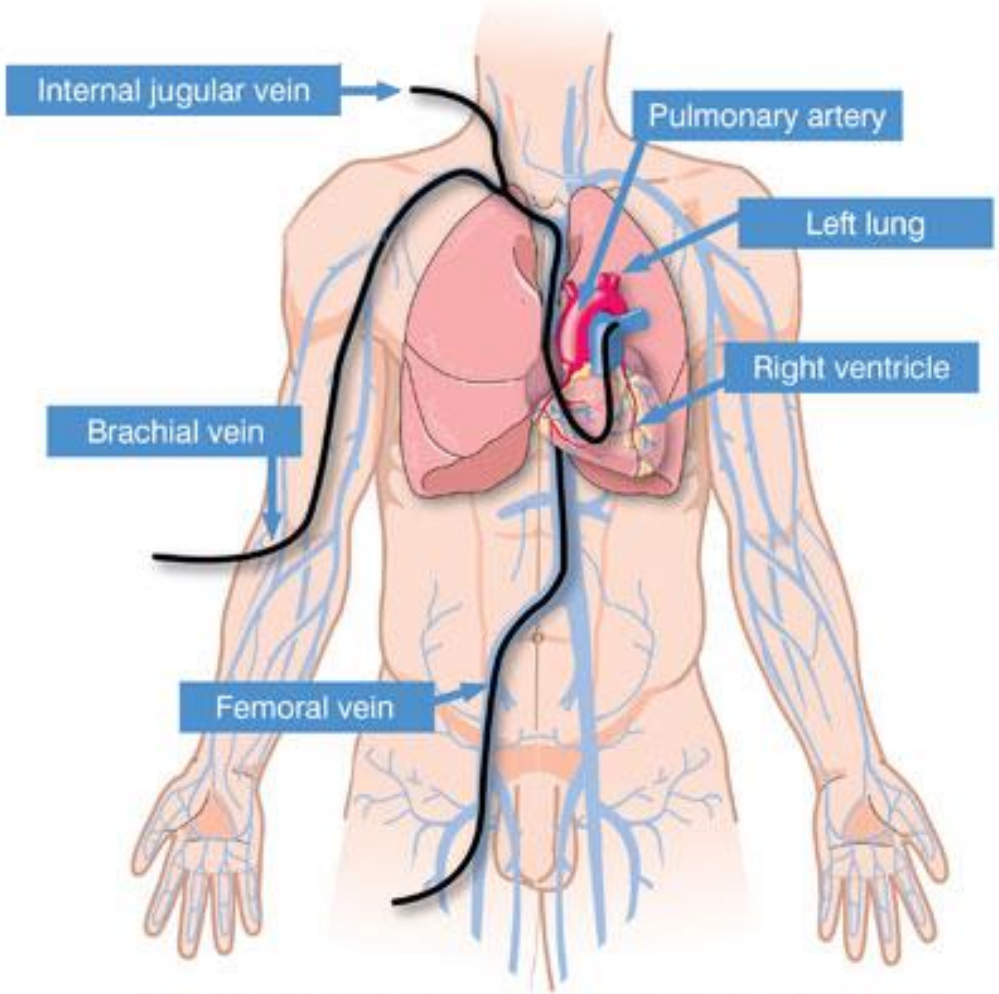
Pulmonary arterial hypertension: definition

Right heart catheterization

Right heart catheterization is required to confirm the diagnosis of PAH.

PAH is defined by

- mPAP ≥25 mmHg at rest
- PCWP ≤15mmHg



Standard approaches for catheter access

Galié et al. *Eur Heart J* 2009.