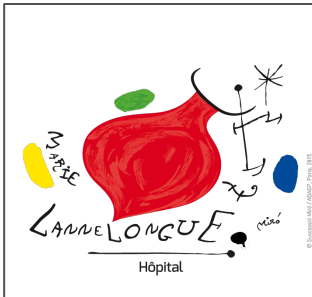


# Transplantation Pulmonaire pour SSc

## Jérôme Le Pavec

Unité de Transplantation Pulmonaire  
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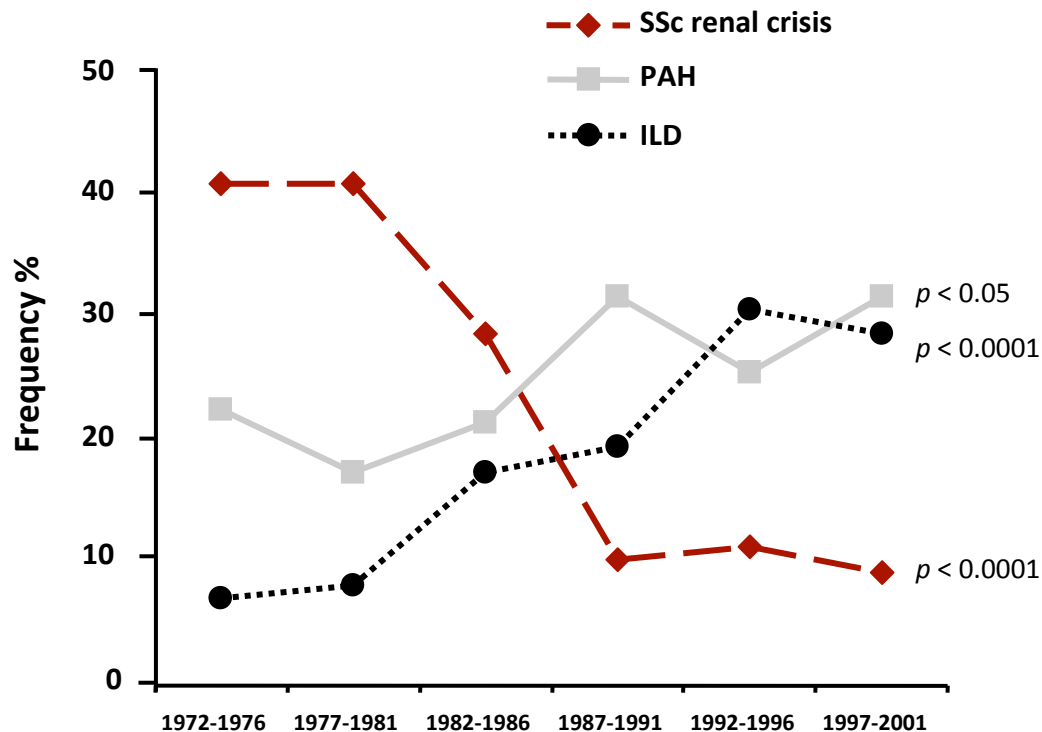


6<sup>ème</sup> journée SSc - Cochin  
Vendredi 29 novembre 2019

# Scleroderma Lung Disease

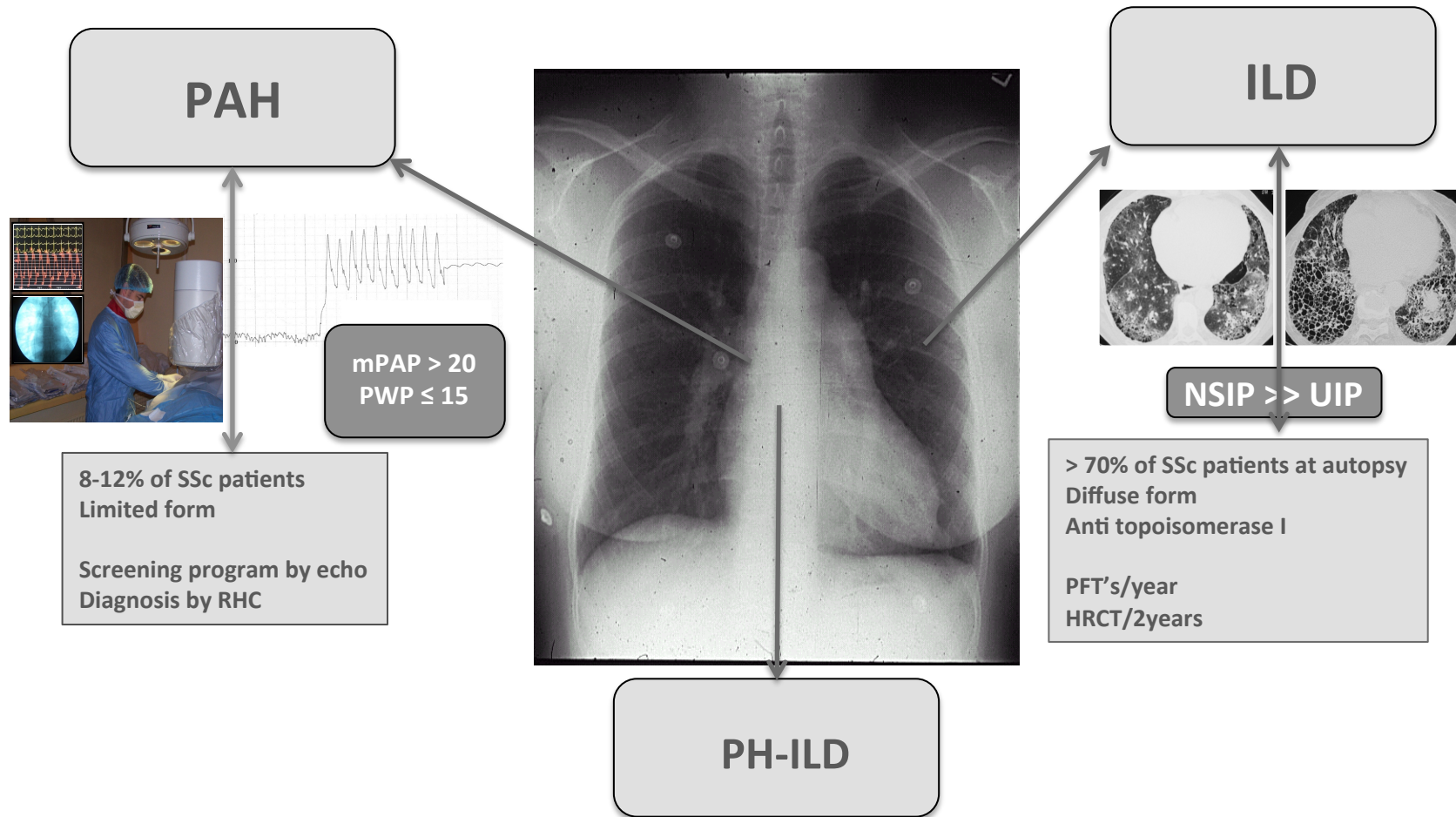
*Why considering  
transplantation ?*

# Pulmonary involvement is the major cause of death in SSc



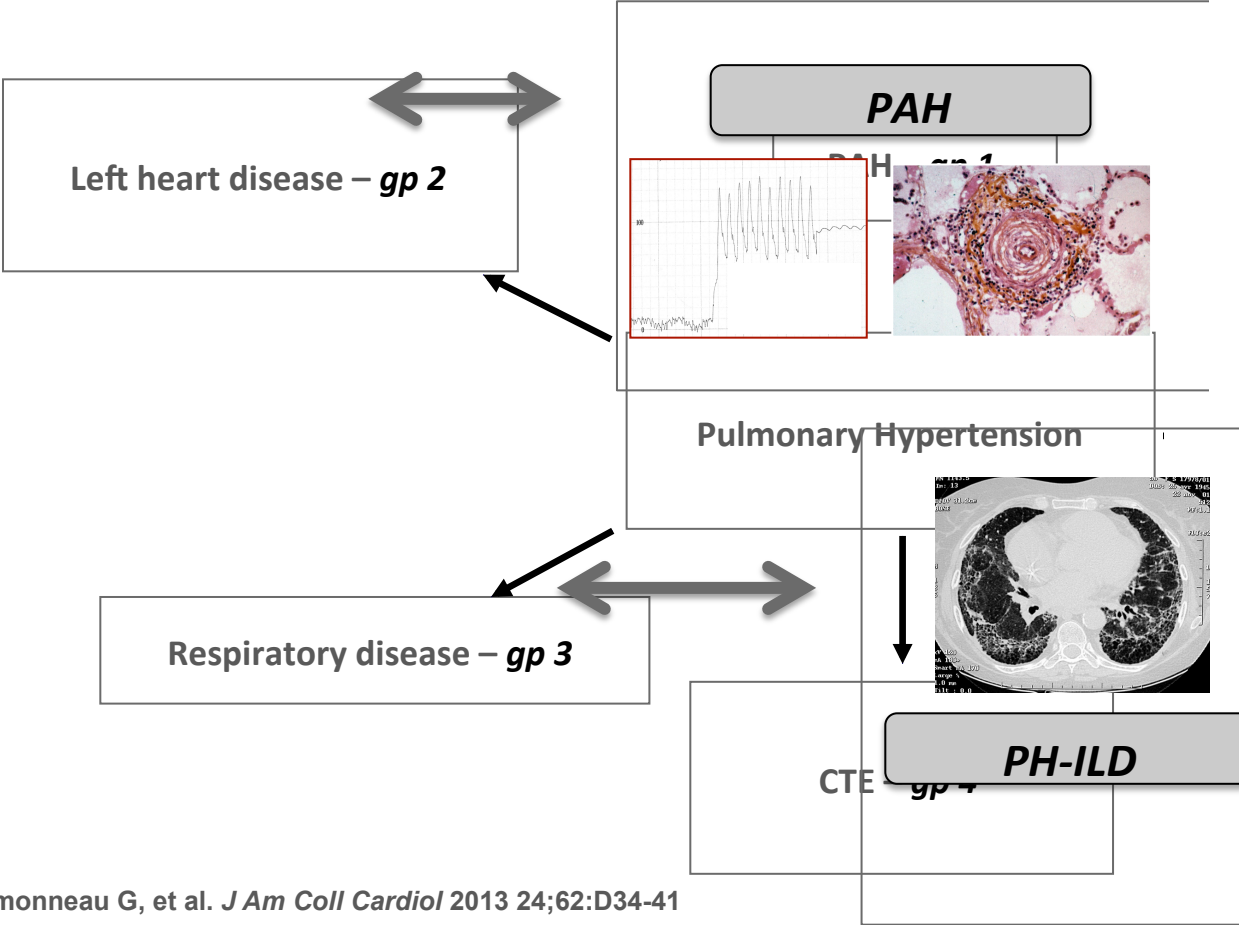
Steen VD and Medsger TA.  
*Ann Rheum Dis* 2007

# Pulmonary involvement in SSc





# Updated classification of Spectrum of pulmonary hypertension in SSc

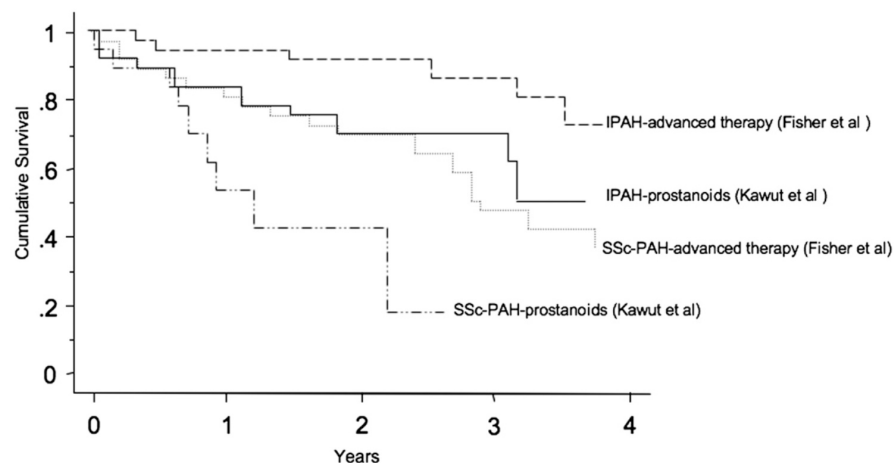
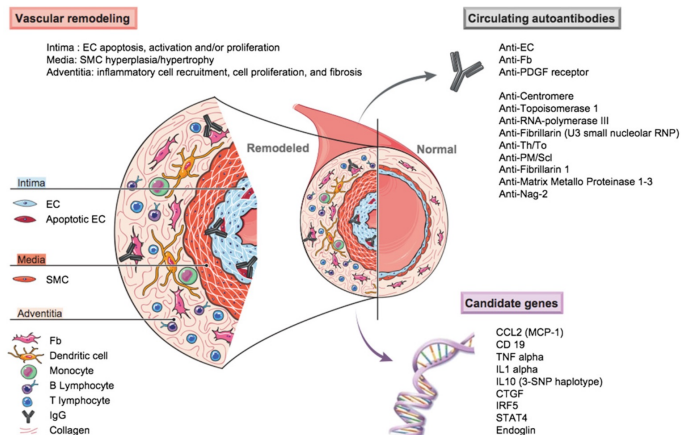


# Pulmonary Perspective

## Systemic Sclerosis-associated Pulmonary Arterial Hypertension

Jérôme Le Pavec<sup>1,2</sup>, Marc Humbert<sup>2</sup>, Luc Mouthon<sup>3</sup>, and Paul M. Hassoun<sup>1</sup>

<sup>1</sup>Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland; <sup>2</sup>Université Paris-Sud 11, Service de Pneumologie et Réanimation Respiratoire, Hôpital Antoine Bécélère, Assistance Publique Hôpitaux de Paris, Clamart, France; and the Université Paris-Descartes, Department of Internal Medicine, Hôpital Cochin, Assistance Publique Hôpitaux de Paris, Paris, France



- Pronounced inflammatory response
- Comorbidities (age, myocardial & musculoskeletal involvement, PVOD, ILD)
- Reliability of current evaluation tool (6-min WT)

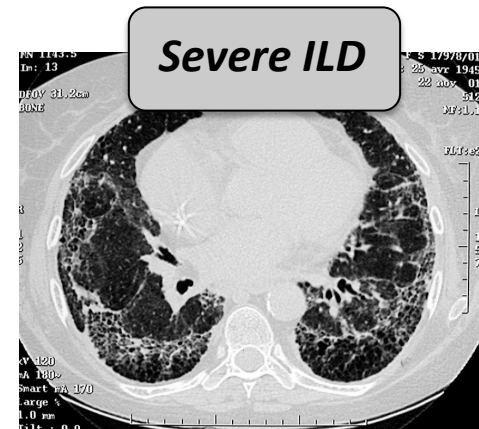
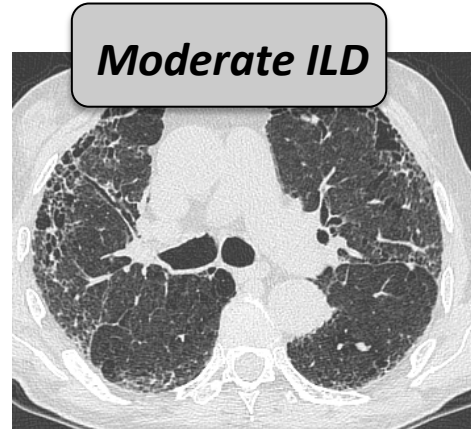
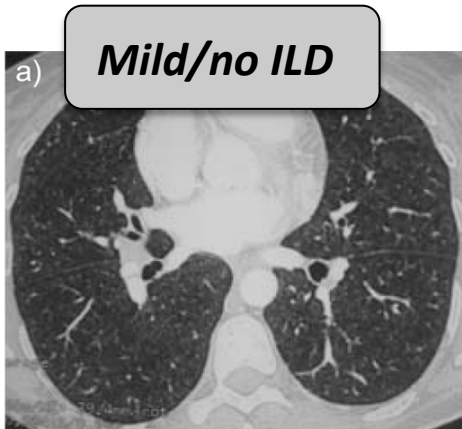
# Pulmonary Hypertension in SSc with ILD

## Criteria favouring group 1

- Normal or mildly impaired
  - FVC > 70% predicted
- Absence of or only modest (<20%) airway or parenchymal abnormalities on high-resolution CT scan


## Criteria favouring group 3

- Moderate to very severe impairment
  - FVC < 70% predicted
- Characteristic airway and / or parenchymal abnormalities (>20%) on high-resolution CT scan




# Frequency of PH-ILD in SSc


## ▪ Among SSc population of unselected patients


Steen et al, J Rheumatol 2007 (833 SSc) :  8% (*FVC<55%, RHC or echo*)

Launay et al, J Rheumatol 2007 (197 SSc) :  5% (*FVC<70%, RHC*)

Avouac et al, J Rheumatol 2010 (1165 SSc) :  2% (*FVC<70%, RHC*)

## ▪ Among SSc patients with ILD

Chang et al, J Rheumatol 2003 (619 SSc) :  22% (*65%<FVC<55%, echo*)

 30% (*50%≤FVC≤64%, echo*)

 47% (*FVC<50%,echo*)

## ▪ Among SSc patients with PH

Condliffe et al, AJRCCM 2009 (315 SSc) :  18% (*60%<FVC, RHC*)

# Impact of PH-ILD on prognosis (1)

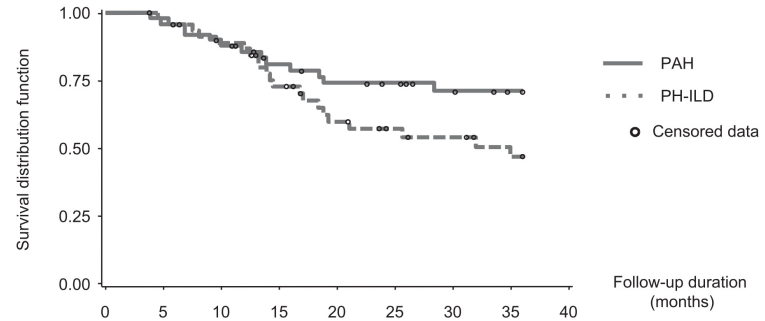
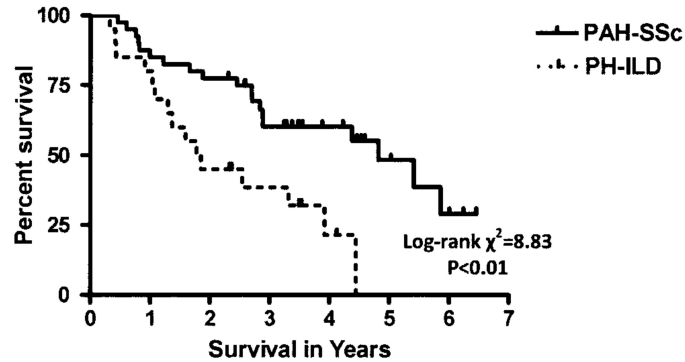


FIGURE 1. Survival in patients with systemic sclerosis (SSc) with PH-ILD or isolated PAH. Survival rates at 36 months were 47% and 71% in the PH-ILD and PAH groups, respectively (log-rank test  $P = .07$ ).

Mathai SC, et al. *Arthritis Rheum* 2009; 60:569-77.

Launay D, et al. *Chest* 2011; 140:1016-24.

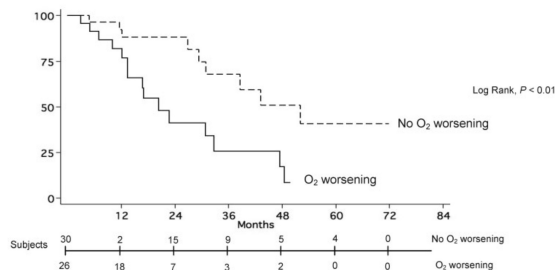
Author	recruitment period	Survival (95% confidence intervals)
Mukerjee et al. PH-ILD	1998-2002	0.50 [ 0.28 , 0.72 ]
Mathai et al. 2009 PH-ILD	2000-2005	0.39 [ 0.19 , 0.61 ]
Condliffe et al. PH-ILD	2001-2006	0.28 [ 0.15 , 0.43 ]
Launay et al. 2011 PH-ILD	2001-2006	0.47 [ 0.31 , 0.63 ]
Le Pavec et al.	2000-2009	0.21 [ 0.10 , 0.34 ]
PH-ILD I2: 57 % Phet: 0.0532		0.35 [ 0.24 , 0.47 ]

Lefevre G, et al. *Arthritis Rheum* 2013; 65:2012-23.

# Impact of PH-ILD on prognosis (2)

**Table 3.** Response to therapy for pulmonary arterial hypertension at followup evaluation, by mPAP group\*

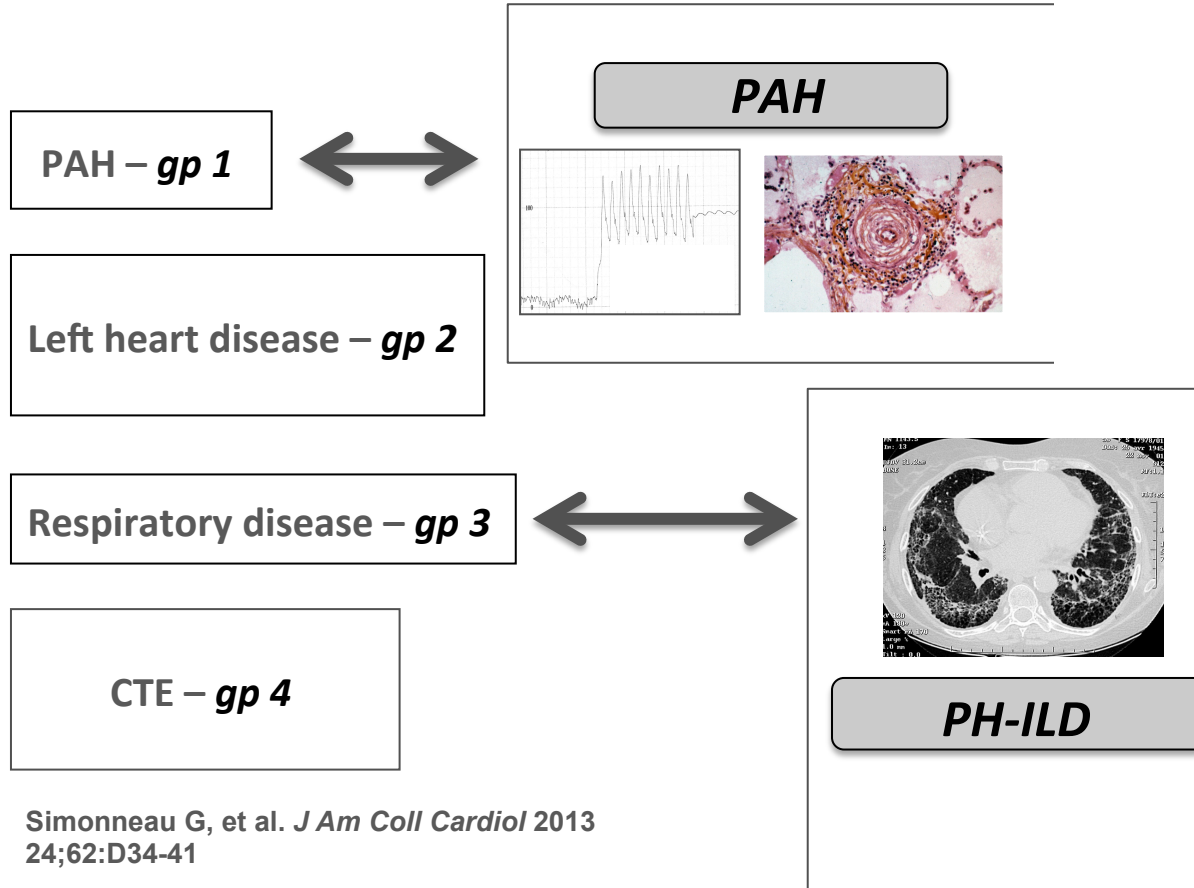
	Baseline	Followup	P
<b>mPAP &lt;40 mm Hg</b>			
No. in WHO functional class I-II/III-IV	8/20	8/20	1.00
6-minute walk distance, mean ± SD meters (n = 15)	316 ± 108	325 ± 90	0.75
Arterial oxygen saturation, mean ± SD % (n = 26)	96 ± 4	95 ± 4	0.25
<b>mPAP ≥40 mm Hg</b>			
No. in WHO functional class I-II/III-IV	4/35	8/31	0.34
6-minute walk distance, mean ± SD meters (n = 19)	274 ± 102	275 ± 115	0.96
Arterial oxygen saturation, mean ± SD % (n = 30)	94 ± 4	92 ± 5	0.04



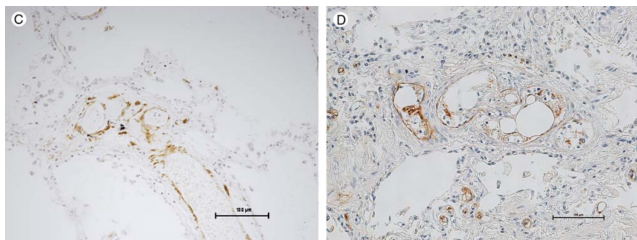
**Table 5.** Multivariate model of risk factors for death in patients with pulmonary hypertension complicating systemic sclerosis–related interstitial lung disease\*

	HR (95% CI)	P
Age	0.99 (0.96–1.04)	0.91
Estimated glomerular filtration rate†		
With imputation	0.54 (0.30–0.94)	0.03
Without imputation	0.47 (0.21–1.02)	0.06
Heart rate†		
With imputation	0.67 (0.42–1.07)	0.10
Without imputation	1.20 (0.57–2.52)	0.62
Oxygen use at baseline	1.38 (0.62–3.05)	0.43
Worsening oxygenation†		
With imputation	3.11 (1.08–8.92)	0.04
Without imputation	7.00 (1.53–32.08)	0.01

# Spectrum of pulmonary hypertension in SSc



# PVOD in SSc



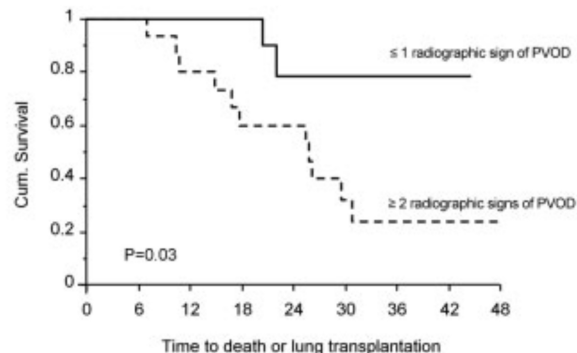
Dorfmueller P et al, *Hum Pathol* 2007; 38:893-902

75% CTD patients  
with veins involvement vs 17% in non CTD patients

**Table 2.** Radiographic characteristics on HRCT in SSc patients with precapillary PH and SSc patients without PAH or ILD\*

	SSc patients with precapillary PH (n = 26)	SSc patients without PAH or ILD (n = 28)	P
Lymph node enlargement	15 (57.7)	1 (3.6)	<0.0001
Tracheobronchial lymphadenopathy	7 (26.9)	0 (0)	<0.0112
Subcarinal	13 (50)	1 (3.6)	<0.0003
Right hilar side	2 (7.7)	0 (0)	0.4389
Left hilar side	3 (11.5)	0 (0)	0.2095
Hilar bilateral	4 (15.4)	0 (0)	0.1018
Other	4 (15.4)	0 (0)	0.1018
Parenchymal abnormalities			
Peribular ground-glass opacities	4 (15.4)	2 (7.1)	0.5968
Homogeneous	3 (11.5)	0 (0)	0.2095
Heterogeneous	1 (3.8)	2 (7.1)	0.9466
Centrilobular ground-glass opacities	12 (46.2)	3 (10.7)	<0.001
Superior	5 (19.2)	3 (10.7)	0.9697
Inferior	1 (3.8)	0 (0)	0.9697
Diffuse	6 (23.1)	0 (0)	<0.0236
Mosaic attenuation pattern	0 (0)	0 (0)	-
Septal lines	23 (88.5)	2 (7.1)	<0.0001
Nodes	11 (42.3)	14 (50)	0.7695
Other abnormalities			
Cardiomegaly	23 (88.5)	2 (7.1)	<0.0001
PA enlargement	22 (84.6)	6 (21.4)	<0.0001
PV enlargement	3 (11.5)	0 (0)	0.2095
Pericardial effusion	14 (53.8)	2 (7.1)	<0.0005
Pleural effusion	1 (3.8)	0 (0)	0.9697

\* Values are the number (%). HRCT = high-resolution computed tomography; PA = pulmonary artery; PV = pulmonary vein (see Table 1 for other definitions).



≥ 2 radiographic signs of PVOD	16	16	12	9	9	4	2	1	1
≤ 1 radiographic sign of PVOD	10	10	10	10	7	4	3	2	1

50% CTD patients with ≥ 2 PVOD signs had pulmonary edema under PAH-specific therapies



# Combined pulmonary fibrosis and emphysema: a distinct underrecognised entity

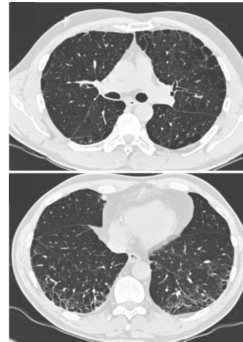
V. Cottin\*, H. Nunes<sup>#</sup>, P-Y. Brillet<sup>†</sup>, P. Delaval<sup>+</sup>, G. Devouassoux<sup>§</sup>, I. Tillie-Leblond<sup>f</sup>, D. Israel-Biet<sup>\*\*</sup>, I. Court-Fortune<sup>###</sup>, D. Valeyre<sup>#</sup>, J-F. Cordier\* and the Groupe d'Etude et de Recherche sur les Maladies "Orphelines" Pulmonaires (GERM"O" P)

Cottin V et al, *Eur Respir J* 2005;26:586-93

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

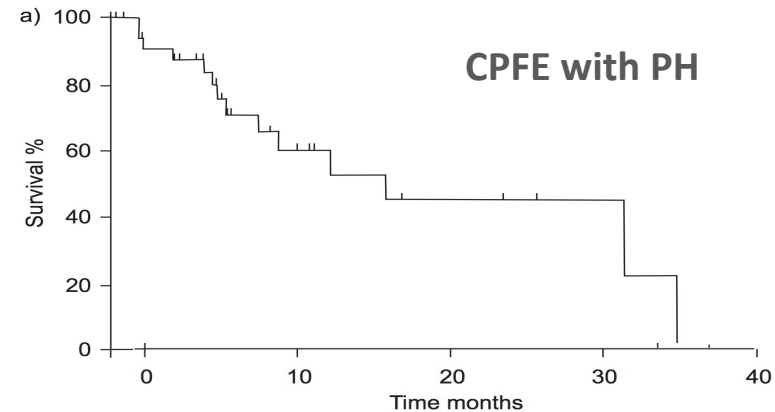
Rheumatoid arthritis	18 (53)
Systemic sclerosis	10 (29)
Diffuse cutaneous	3 (9)
Limited cutaneous	7 (20)
Mixed connective tissue disease	2 (6)
Overlapping connective tissue disease	2 (6)
Sjögren's syndrome	1 (3)
Polymyositis	1 (3)

\* Values are the number (%) of patients.



## All SSc patients who underwent RHC had PH

Cottin V et al, *Arthrit Rheum* 2011; 63:295-304

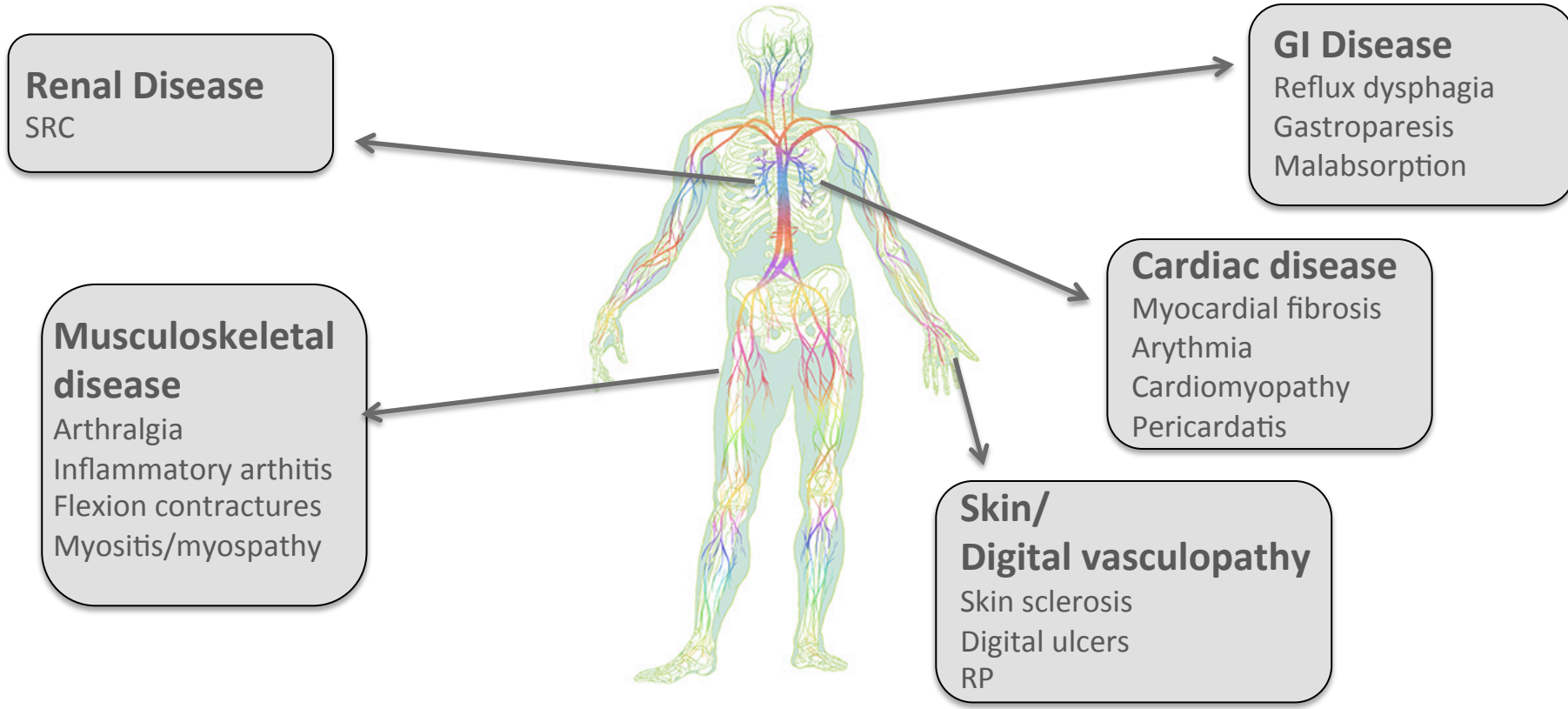


Cottin V, Le Pavec J et al, *Eur Respir J* 2010; 35:105-111

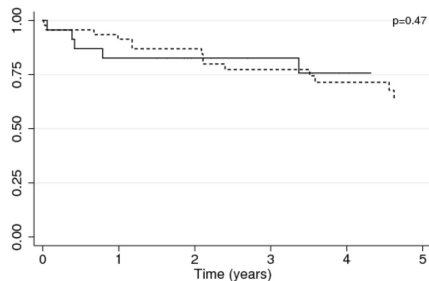
# **Scleroderma Lung Disease**

*Why NOT considering  
transplantation ?*

# Multisystemic disease

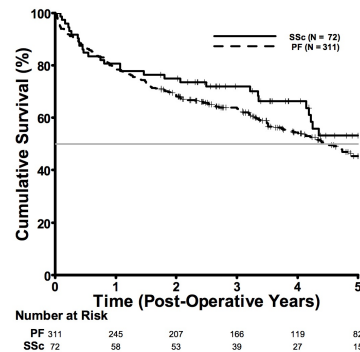


# Outcomes in lung transplantation in SSc



SSc, n = 23 (PVR 650)  
ILD, n = 46

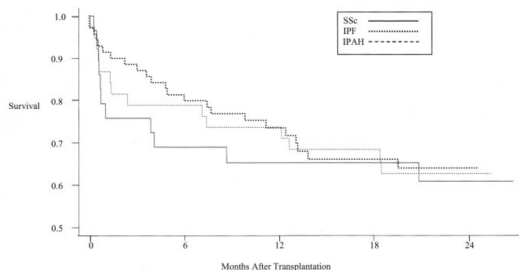
Sottile PD et al. *Transplantation* 2013.



SSc, n = 72  
(PH 31%)

ILD, n = 311

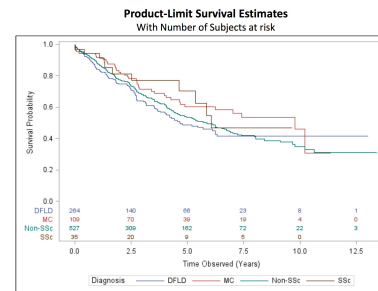
Crespo MM et al. *Ann Am Thorac Soc* 2016.



SSc, n = 11  
(mPAP 33)

ILD, n = 23  
IPAH, n = 14

Schachna L et al. *Arthritis Rheum* 2006.



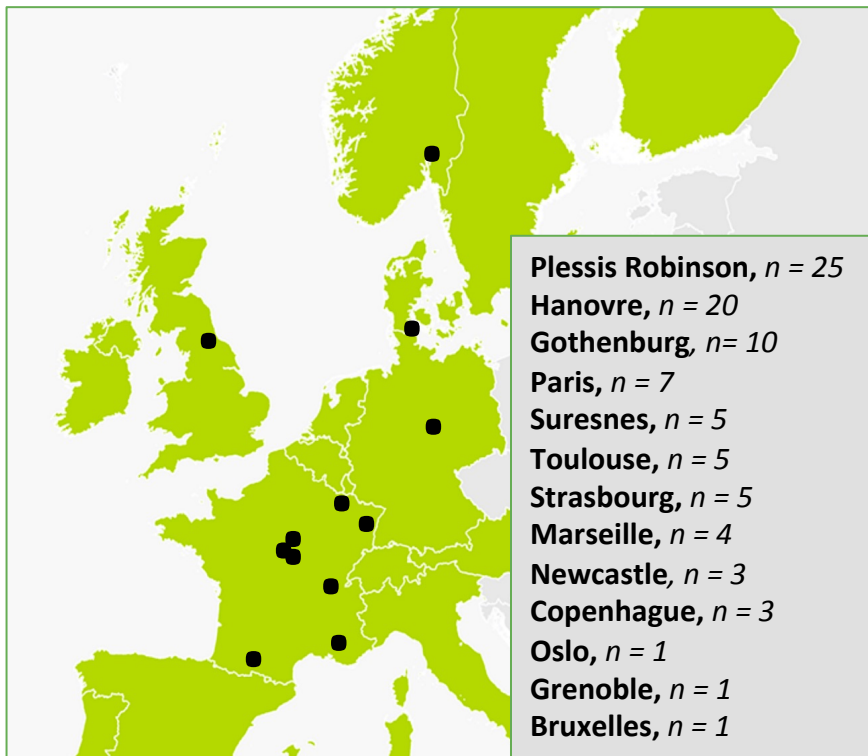
SSc, n = 35  
(PVR 380)

ILD, n = 264  
non SSc, n = 67  
Matched, n = 109

Figure 1. Kaplan-Meier curves for post-lung transplant survival for all cohorts. SSc=systemic sclerosis; DFLD=diffuse fibrotic lung disease; MC=matched group. Log-rank test SSc vs. the following: non-SSc (p=0.31), DFLD (p=0.20), and matched groups (MG) (p=0.95).

Miele CH et al. *Ann Am Thorac Soc* 2016.

# Lung transplantation for SSc Lung Disease: an International Multicenter Observational Cohort Study



- Multicenter retrospective
- Clinical phenotypes ILD / PAH / PH-ILD / PVOD / CPFE
- Comorbidities incl GER, Left Heart & renal diseases
- Prognostic factors / Survival
- Post transplant evolution : pulmonary & renal functions, digital injuries

# Lung transplantation for SSc Lung Disease: an International Multicenter Observational Cohort Study

**Table 1** Demographics and Clinical Characteristics

	Overall population (n = 90)	PH-ILD (n = 40)	ILD (n = 30)	PAH (n = 20)	p-value
Female gender	52 (58)	20 (50)	15 (50)	17 (85)	0.02
Recipient age (years)	49 ± 9	49 ± 9	49 ± 10	49 ± 9	0.84
BMI (kg/m <sup>2</sup> )	24 ± 4	24 ± 4	25 ± 5	23 ± 4	0.41
Cigarette smoke exposure	31 (34)	20 (50)	7 (23)	4 (20)	0.02
Induction therapy (n = 62) <sup>a</sup>	22 (35)	10 (25)	7 (23)	5 (20)	0.78
Lung transplant procedure, double L/HL/single L (n)	66 / 9 / 15	28 / 4 / 8	22 / 1 / 7	16 / 4 / 0	0.06
Pre-operative intensive care unit, (n = 54) <sup>a</sup>	10 (11)	6 (15)	0 (0)	4 (20)	0.03
High-emergency transplantation program (n = 69) <sup>a,b</sup>	15 (17)	5 (12)	2 (7)	8 (40)	0.01
Cardiopulmonary bypass (n = 77) <sup>a</sup>	27 (39)	12 (30)	6 (20)	9 (45)	0.25
Intra-operative ECMO (n = 76) <sup>a</sup>	26 (29)	8 (20)	9 (30)	9 (45)	0.18
Post-operative ECMO (n = 72) <sup>a</sup>	16 (18)	8 (20)	5 (17)	3 (15)	1.00
Ischemic time (minutes)					
Right	277 ± 95	286 ± 78	304 ± 117	224 ± 67	0.13
Left	281 ± 117	254 ± 91	289 ± 164	310 ± 70	0.34
Heart-lung	164 ± 126	150 ± 102		169 ± 155	0.82
Dialysis during ICU stay (n = 51) <sup>a</sup>	11 (12)	3 (7)	4 (14)	4 (20)	0.57
PGD score Grade 3 at 72 hours (n = 34) <sup>a</sup>	10 (11)	6 (15)	2 (7)	2 (10)	0.28
Ventilation time during ICU stay (days)	14 ± 10	19 ± 12	8 ± 5	15 ± 8	0.08
In-hospital mortality	8 (9)	5 (12)	0 (0)	3 (15)	0.07
CLAD (n = 57) <sup>a</sup>	16 (18)	7 (17)	7 (23)	2 (10)	0.54

- Higher severity in PAH patients according to
  - Number of HLT
  - High emergency transplant
  - In-hospital mortality

Pradere P et al. *JHLT* 2018;**37**: 903-11.

# Lung transplantation for SSc Lung Disease: an International Multicenter Observational Cohort Study

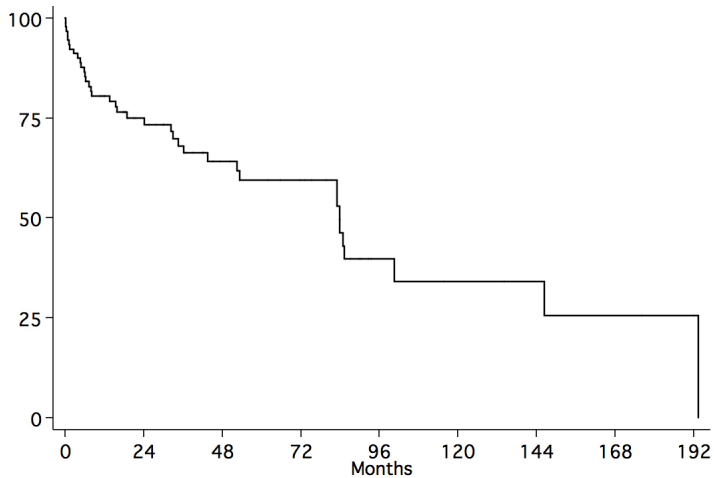
**Table 2** Functional, Hemodynamic, and Radiographic Characteristics

	Overall population (n = 90)	PH-ILD (n = 40)	ILD (n = 30)	PAH (n = 20)	p-value
6-minute walking distance (m)	260 ± 121	244 ± 123	264 ± 131	288 ± 106	0.49
Lung function test results					
FVC (% predicted)	54 ± 22	50 ± 18	47 ± 14	77 ± 29	0.01
FEV <sub>1</sub> (% predicted)	54 ± 18	51 ± 16	49 ± 15	69 ± 21	0.01
FEV <sub>1</sub> /FVC	88 ± 9	87 ± 8	89 ± 11	87 ± 4	0.95
TLC (% predicted)	55 ± 15	51 ± 13	51 ± 9	72 ± 19	0.01
DLCO (% predicted)	25 ± 10	20 ± 7	27 ± 11	29 ± 12	0.12
KCO (% predicted)	46 ± 23	41 ± 20	50 ± 26	43 ± 32	0.68
PaO <sub>2</sub> (mm Hg)	62 ± 21	56 ± 22	69 ± 23	62 ± 9	0.17
PaCO <sub>2</sub> (mm Hg)	38 ± 8	38 ± 7	38 ± 5	35 ± 15	0.17
Right heart catheterization					
Right atrial pressure (mm Hg)	8 ± 5	7 ± 3	5 ± 4	11 ± 7	0.01
Mean pulmonary arterial pressure (mm Hg)	37 ± 16	38 ± 10	21 ± 2	51 ± 15	0.01
Capillary wedge pressure (mm Hg)	9 ± 4	9 ± 5	9 ± 3	7 ± 3	0.15
Cardiac index (liters/min/m <sup>2</sup> )	2.9 ± 0.8	3.0 ± 0.9	3.0 ± 0.5	2.4 ± 0.8	0.01
Pulmonary vascular resistance (dyn/s/cm <sup>5</sup> )	502 ± 351	461 ± 226	215 ± 110	824 ± 394	0.01
Thoracic HRCT findings (n = 46) <sup>b</sup>					
UIP	16 (34)	8 (44)	8 (50)		
NSIP	12 (25)	7 (39)	5 (31)		
Unclassified ILD	3 (7)	0 (0)	3 (19)		
CPFE	3 (7)	3 (17)	0 (0)		
PVOD <sup>b</sup>	9 (20)			9 (75)	
No significant changes	3 (7)			3 (25)	

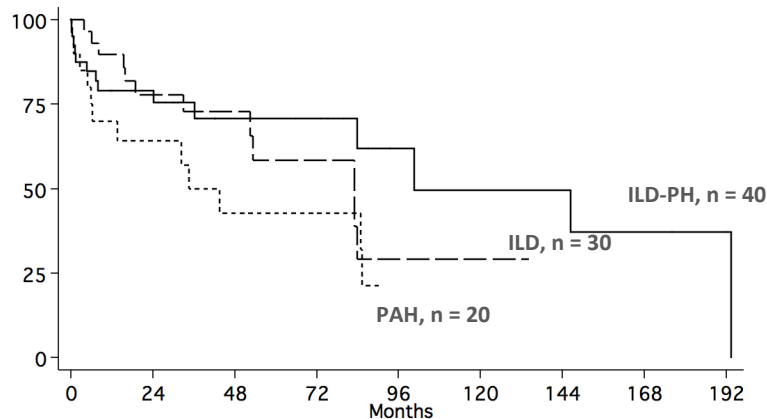
- Higher severity in PAH (RVP)
- UIP most frequent CT pattern
- PVOD in 75% of PAH patients

Pradere P et al. *JHLT* 2018;37: 903-11.

# Lung transplantation for SSc Lung Disease: an International Multicenter Observational Cohort Study



Survival rates were 80%, 68%, and 59% at 1, 3, and 5 years, respectively.



Survival rates were 70, 50, and 43% in PAH, 93%, 76%, and 60% in ILD and 79, 75 and 71 % in ILD-PH patients at 1, 3 and 5 years respectively, Logrank  $P = 0.14$

- Mean follow-up 42 months (0.1 – 194 months)
- Nearly half the deaths (16 of 39 patients [41%]) were attributed to respiratory failure due to CLAD (n=8), pneumonia (n=7), or primary graft dysfunction (n=1)
- Other causes included septic shock (n=4), multiple organ failure (n=3), cancer (n=3), stroke (n=2), colon perforation (n=1), left heart failure (n=1), bronchial complications (n=1), and sudden death (n=1)

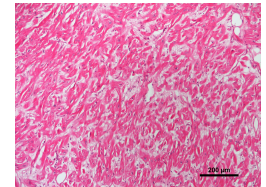
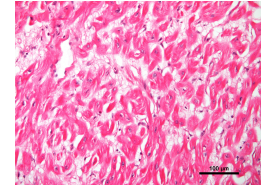


# Univariate analysis

Sex/PAH	Hazard Ratio	95 Confidence Interval	<i>p</i> value
Male without PAH*	1.00	0.50 – 3.38	0.59
Male with PAH	0.00	0.00 – 0.00	0.01
Female without PAH	1.51	0.66 – 3.45	0.33
Female with PAH	3.01	1.27 – 7.15	0.01

# Myocardial lesions from HLT

	Coronary atherosclerosis	Myocardial Fibrosis	Myocardial inflammation	Other <sup>##</sup>	Female
Patient 1	+++	+			1
Patient 2	+		++		1
Patient 3	++	++	+		1
Patient 4				+++	1
Patient 5	+	+++			0
Patient 6	+	+++			1
Patient 7	+	+			1
Patient 8 <sup>#</sup>	+				0
Patient 9 <sup>#</sup>					0



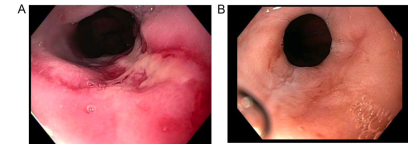
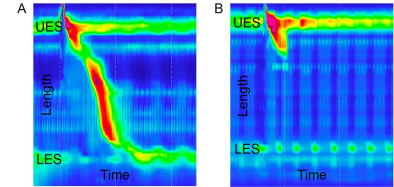
<sup>#</sup>: no data available  
<sup>##</sup>: lipid inclusion

# Oesophagus (& Stomach) in SSc

- 70 to 90% patients
- Oesophagus > ano-rectum > small bowel
- Distal 2/3 of oesophagus including muscle atrophy, fibrosis and dilatation
- 50% patients are asymptomatic

**Table 1**  
Common investigation for gastrointestinal involvement in SSC

Organ	Abnormality	Investigations
Esophagus	Esophagitis, stricture, Barrett esophagus	EGD
	Dysmotility, GER	Esophageal transit (nuclear medicine)
	Stricture, dysmotility	Barium swallow
	Dysmotility	Manometry
Stomach	Dysmotility	Gastric emptying study (nuclear medicine)
	GAVE, gastritis, ulcers, adenocarcinoma	EGD

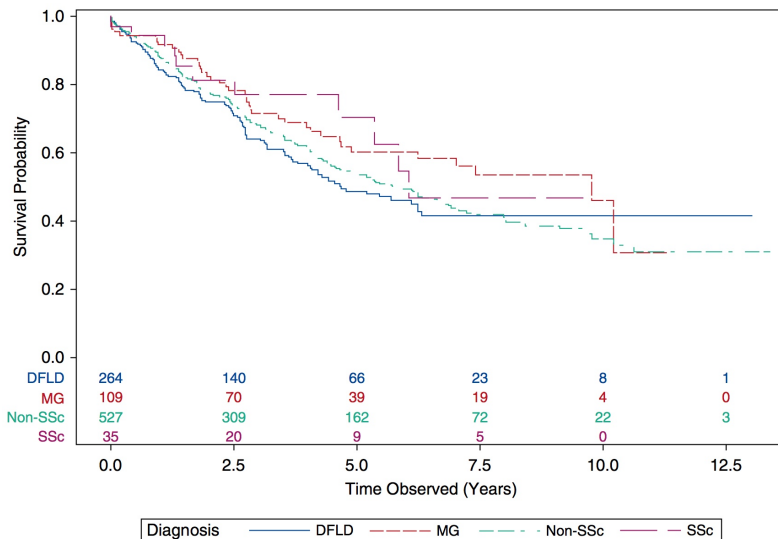


# Lung Transplant Outcomes in Systemic Sclerosis with Significant Esophageal Dysfunction

## A Comprehensive Single-Center Experience

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Miele CH, *Ann Am Thorac Soc* 2016



**Table 6.** Prevalence of severe esophageal dysfunction

	SSc (%)	Matched Cohort w/DFLD (%)	P Value
Severe esophageal dysfunction*	54	8	<0.0001
MED <sup>†</sup> ≥ 20 mm	69	17	<0.0001
Esophageal AFL <sup>†</sup>	57	10	<0.0001
Both MED ≥ 20 mm and AFL	54	8	<0.0001
Aperistalsis on manometry	17	—	—

Reasons for Denial: SSc patients evaluated for LT but without subsequent LT (n=36)

### Gastrointestinal Concerns

- Multifactorial<sup>1</sup> with gastrointestinal<sup>2</sup> concerns (n=4)
- Isolated gastrointestinal concerns<sup>3</sup> (n=1)

### Non-Medical Reasons For Denial

- LT evaluation completed but patient did not follow through (n=1)
- Patient did not complete LT evaluation (n=3)
- Insurance dictated referral to another LT center (n=1)

### No Gastrointestinal Concerns

- Multifactorial<sup>1</sup> without gastrointestinal concerns (n=6)
- Unacceptable renal insufficiency (n=1)

### Clinical Course in Evolution or Modifiable Risk Factor(s)

- Patient deemed too early for LT and/or notable response to medical therapy
- *i) not formally presented to committee (n=8) or ii) accepted by committee (n=7)*
- Accepted by committee pending resolution of modifiable risk factor(s) (n=4)

75% oesophageal pHmetry, 63% endoscopy, 40% manometry, 29% all three

# Lung transplantation for SSc Lung Disease: an International Multicenter Observational Cohort Study

**Table 3** Scleroderma Characteristics

	Overall population (n = 90)	PH-ILD (n = 40)	ILD (n = 30)	PAH (n = 20)	p-value
Scleroderma duration at transplantation (years)	9.7 ± 7.4	7.9 ± 5.8	12.4 ± 8.6	9.1 ± 7.8	0.13
Percent with localized cutaneous scleroderma (n = 62) <sup>a</sup>	43%	19%	8%	18%	0.01
Antibody positivity					
ANAs	38%	20%	9%	9%	0.24
Anti-Scl70	39%	20%	18%	0%	0.07
ACA	14%	3%	5%	7%	0.04
Gastrointestinal involvement					
Severe gastroesophageal reflux	16%	4%	7%	5%	0.41
Active gastrointestinal ulceration (n = 23) <sup>a</sup>	30%	17%	3%	10%	0.17
Esophageal hypoperistalsis (n = 19) <sup>a</sup>	30%	22%	4%	4%	0.82
Esophageal aperistalsis (n = 19) <sup>a</sup>	35%	17%	18%	0%	0.14
Lower esophageal sphincter hypotonia (n = 19) <sup>a</sup>	55%	36%	19%	0%	0.05
Maximum esophageal diameter on HRCT (n = 38 cm) <sup>a</sup>	20 ± 10	21 ± 9	19 ± 13	20 ± 10	0.81
Skin involvement					
History of digital ulcerations	21%	10%	9%	3%	0.86
History of digital ulcerations requiring IV treatment	7%	2%	4%	1%	0.42
Active digital ulcerations at transplantation	4%	1%	3%	0%	0.59
Renal involvement					
History of SRC (n = 41)	2%	2	0	0	1.00
Estimated GFR (ml/min/1.73 m <sup>2</sup> )	87 ± 28	94 ± 29	92 ± 26	72 ± 25	0.03

Pradere P et al. *JHLT* 2018;**37**: 903-11.

- Too many missing data to conclude

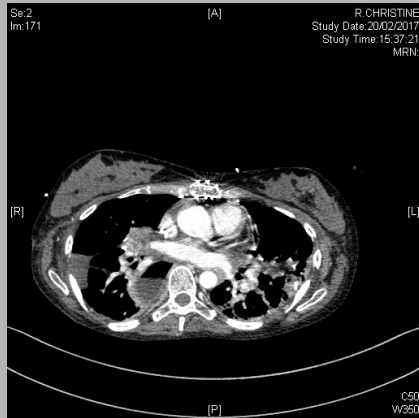
# Upper digestive tract involvement

	Mrs S, 33 yo	Mrs R, 34 yo
<b>Manometry</b>	Peristaltism = 0	Peristaltism = 0
<b>GES</b>	Normal	Normal
<b>CT</b>	Dilatation ++	Dilatation ++
<b>Endoscopy</b>	Normal	Normal

# Upper digestive tract involvement

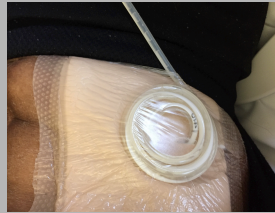
Mrs R, 34 yo

**BLT Nov 16**



*4-month USI stay*

**Jejunostomy**



**Gastric PM**

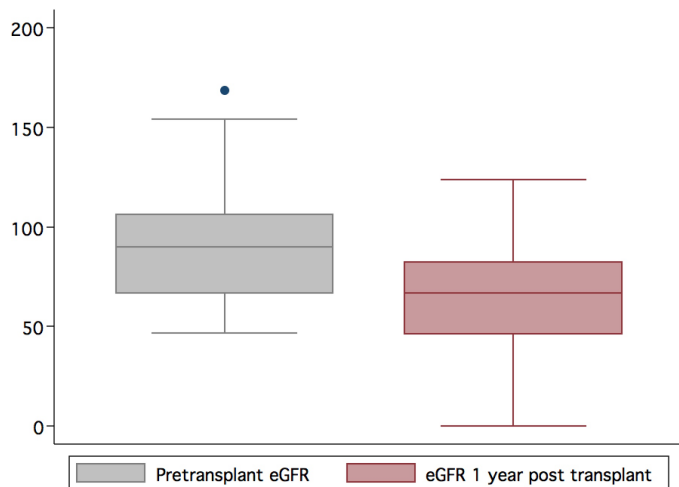


EVITER LES CHAMPS MAGNÉTIQUES  
Avoid magnetic fields

Date d'implantation 16.10.2017  
(j / mn / année)  
Type du dispositif médical implanté / Type of implanted medical device  
cuberra

Medtronic France S.A.S. - 77 Quai Alphonse Le Gall - CS 30001 - 92513 Boulogne Billancourt Cedex  
www.medtronic.fr - +33 (0) 1 55 38 17 00 - Fax: +33 (0) 1 55 38 18 00 - c2000402-0001 - Med - www.medtronic.fr

# Post transplant SSc manifestations



- Worsening of GERD in 15 patients, including 3 with clinically relevant symptoms requiring surgery (n=2) or gastro-intestinal pacemaker implantation (n=1)
- Gastro-intestinal bleeding requiring blood transfusion occurred in 5 patients.
- Post-transplant renal crisis occurred in 8 patients.
- Digital ulcers developed in 6 patients, including 3 who required intravenous vasodilator therapy.

eGFR was  $97 \pm 5$  mL/min at transplantation and  $67 \pm 5$  mL/min 1 year later;  $P < 0.01$  by paired  $t$  test

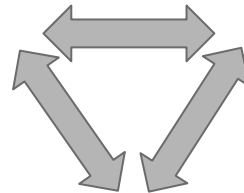


# A consensus document for the selection of lung transplant candidates: 2014—An update from the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation

Weill D et al, *JHLT* 2015

- Déclin  $\geq 10\%$  CVF 6 derniers mois
- Saturation  $< 88\%$  ou distance  $< 250$  m ou déclin  $> 50$  m 6 derniers mois au T6
- Déclin de la DLCO  $\geq 15\%$  au cours des 6 derniers mois
- Hypertension pulmonaire
- Hospitalisation pour évènement respiratoire

*Référencement précoce*  
*PVOD ++*  
*PH-ILD*  
*CPFE*



- NYHA FC III or IV despite a trial of at least 3 months of combination therapy, including prostanoids
- Cardiac index of  $< 2$  L/min/m<sup>2</sup>
- Mean right atrial pressure of  $> 15$  mm Hg
- 6-min walk test of  $< 350$  m
- Hemoptysis, pericardial effusion, or signs of progressive right heart failure

***Fibrosis***

***Scleroderma***

***PAH***

# Pre transplant work-up

## *GI tract*

- **Esophageal Manometry**
- **Gastric emptying study**
- **Esophagogastroduodenoscopy**
  
- **Esophagogram and barium swallow study**
- **CT chest to assess the esophageal diameter**

## *LV*

- **Echocardiography**
- **Cardiac MRI**
  
- **Myocardial biopsy may be recommended to confirm active inflammation**

## *Other*

- **Raynaud's severity / DU**
- **UA / protien**
- **Hematological work-up**
- **Immunoglobulin quantitation**
  
- **Eustar activity index score**

# Proposed specific SSc contraindications

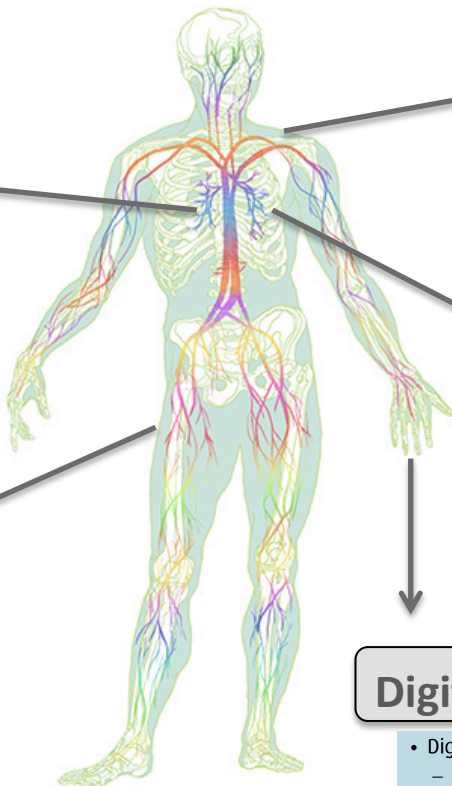
Launay D, et al. Press Med 2014; 43:e345-63

## Renal Disease

- kidney:
  - renal function should have been stable for 3 months except in the case of acute functional renal failure related to right ventricle dysfunction;
  - interval < 3 years between SRC and HLT/LT;
  - increased risk of scleroderma renal crisis:
    - a. diffuse systemic sclerosis evolving for less than 3 years since the first non-Raynaud sign/symptom;
    - b. rapidly progressive and severe cutaneous involvement: progression of the cutaneous involvement characterised by an increase of more than 25% in Rodnan score within 6 to 12 months;
    - c. corticosteroids > 15 mg prednisone (or equivalent)/day.

## Musculoskeletal disease

- Uncontrolled active inflammatory myopathy; progressive myopathy; myopathy with diaphragm involvement;



## GI Disease

- gastrointestinal:
  - oesophageal stricture;
  - active and severe upper gastrointestinal ulcerations despite optimal treatment with proton pump inhibitors and prokinetics;
  - high grade dysplasia;
  - gastroparesis (abnormal gastric emptying) at 90 min post-injection of a radiolabelled meal;
  - chronic gastrointestinal bleeding with or without anaemia;

**Caution with**  
**oesophageal aperistalsis**  
**LES hypotonia (CI)**  
**gastroparesis (CI)**

## Cardiac disease

- heart:
  - conduction abnormalities and/or rhythm disturbances (symptomatic bradycardia, ventricular and atrial tachycardia); the presence of a pacemaker (implantation of a pacemaker is not a contraindication)

**Caution in female with PAH**  
**HLT, ECMO...**

## Digital vasculopathy

- Digital ulcers:
  - > 1 severe episode/year despite optimal treatment;
  - active digital ulcer: temporary contraindication.

# CTD : ISHLT working consensus

## Co-chairs

- Maria Crespo, Philadelphia USA
- Jérôme Le Pavec, Le Plessis Robinson, France



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- Dr Steve Mathai



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- Pr Olivier Sitbon / Dr Savale



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- Pr David Launay



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**Merci**



# Lung transplantation for SSc Lung Disease: an International Multicenter Observational Cohort Study

**Table 4** Univariate analysis to identify variables associated with survival

Variables*	Hazard Ratio	95 Confidence Interval	P value
Female gender	2.11	0.99 – 4.50	0.05
Recipient age	1.26	0.90 – 1.76	0.16
Transplantation date ≥ 2008	1.64	0.73 – 3.69	0.23
Cigarette smoke exposure	0.66	0.32 – 1.35	0.26
Body mass index	0.99	0.71 – 1.37	0.94
Group O	0.87	0.43 – 1.76	0.69
Group A	1.61	0.82 – 3.17	0.16
Estimated GFR (n = 53)	0.82	0.56 – 1.19	0.31
Transplantation for PH-ILD	0.68	0.34 – 1.36	0.28
Transplantation for ILD	0.91	0.46 – 1.80	0.79
Transplantation for PAH	1.90	0.96 – 3.92	0.06
Double-lung transplant	0.83	0.42 – 1.66	0.62
Heart-lung transplant	0.71	0.25 – 2.05	0.53
Single-lung transplant	1.57	0.74 – 3.34	0.24
Six-minute walking distance (n = 58)	1.39	0.85 – 2.29	0.19
Right atrial pressure	1.07	0.71 – 1.60	0.24
Pulmonary wedge pressure	0.82	0.55 – 1.25	0.38
Mean pulmonary arterial pressure	0.99	0.67 – 1.43	0.96
Cardiac index	0.84	0.67 – 1.43	0.40
Pulmonary vascular resistance	1.02	0.71 – 1.47	0.90
Forced vital capacity	1.20	0.87 – 1.66	0.26
Forced expiratory volume in one second	1.25	0.90 – 1.74	0.18
Total lung capacity	1.32	0.93 – 1.88	0.12
Diffusing capacity for carbon monoxide	0.69	0.53 – 1.53	0.69
ANA positivity (n = 45)	0.45	0.18 – 1.13	0.09
Anti-Scl70 positivity (n = 44)	1.99	0.78 – 5.05	0.14
ACA positivity (n = 44)	0.62	0.18 – 2.15	0.46
Cardiopulmonary bypass (n = 77)	1.33	0.64 – 2.63	0.47
Intraoperative-ECMO (n = 76)	0.69	0.29 – 1.61	0.39
Postoperative ECMO (n = 72)	1.05	0.42 – 2.62	0.91
Ischemic time right (n = 65)	1.39	0.79 – 2.43	0.25
Ischemic time left (n = 65)	1.24	0.79 – 1.96	0.34
Dialysis during ICU stay (n = 51)	0.93	0.34 – 2.53	0.89
PGD grade 3 at 72 hours (n = 34)	0.62	0.17 – 2.25	0.47
Ventilation time in ICU	1.01	0.90 – 1.14	0.74
CLAD (n = 57)	1.48	0.54 – 4.11	0.44



# Introduction



*Hardy JD. The first lung transplant in man*

- 1: Borel JF, *Agents Actions* 1976
- 2: Burke CM, *Chest* 1984
- 3: Cooper JD, *J Thorac Cardiovasc Surg* 1987
- 4: ISHLT 2019

1<sup>ère</sup> TP

40 procédures  
Survie < 2 mois

Ciclosporine <sup>1</sup>

CP <sup>2</sup>

Mono Poumon <sup>3</sup>

4452 procédures  
ISHLT <sup>4</sup>

1963

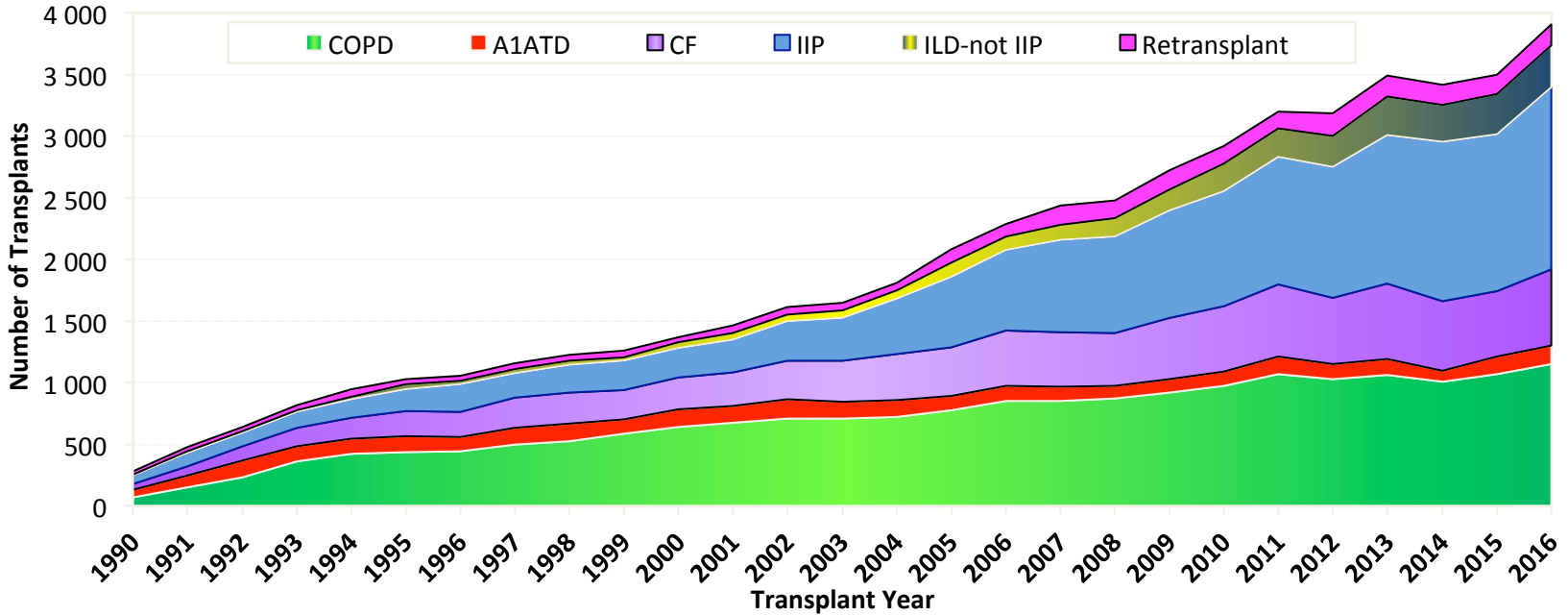
1976

1981

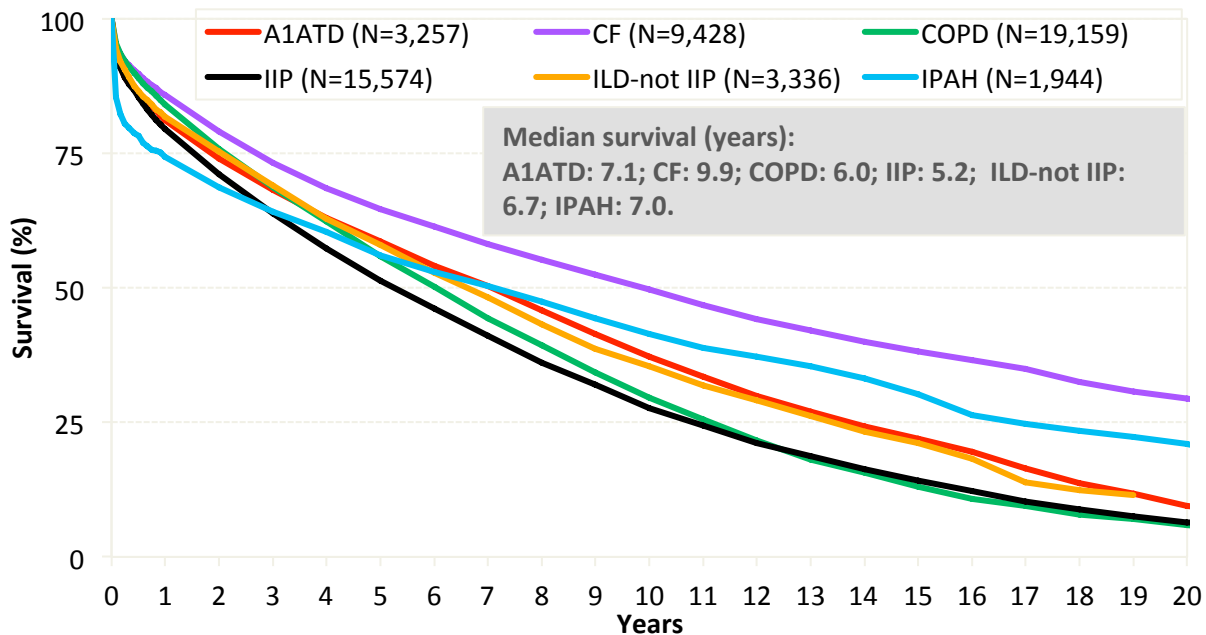
1983

2017

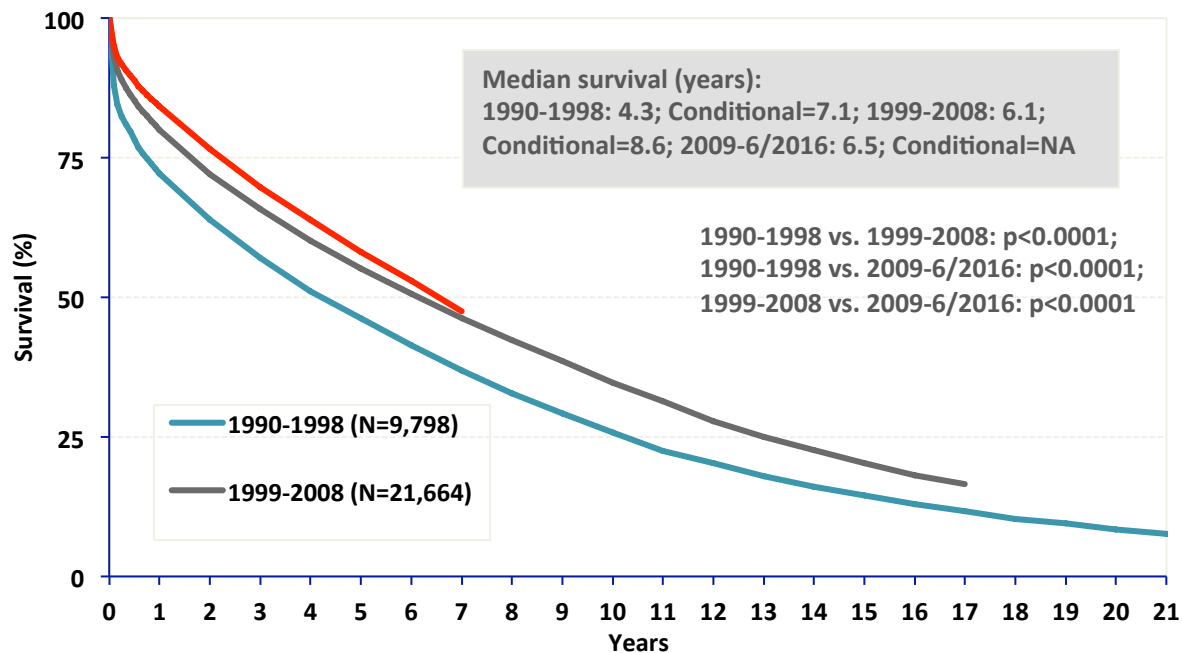
# Indications



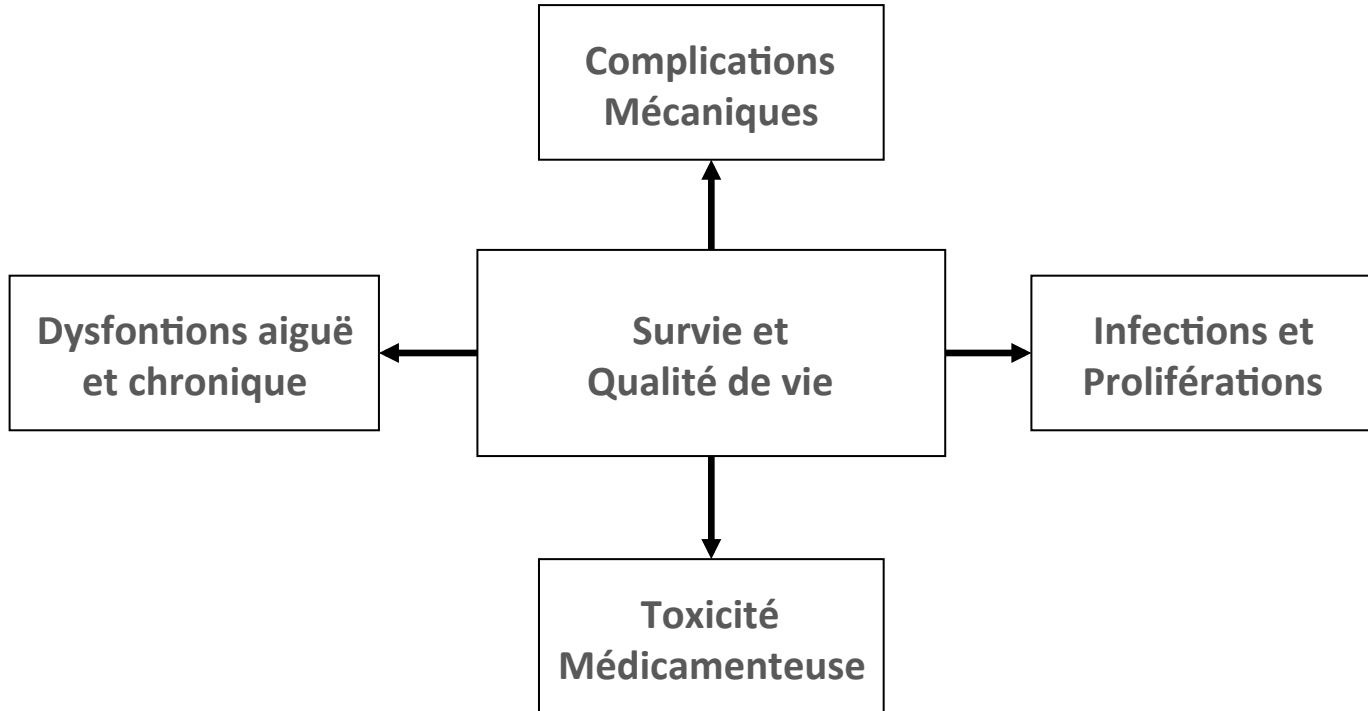
# Survival



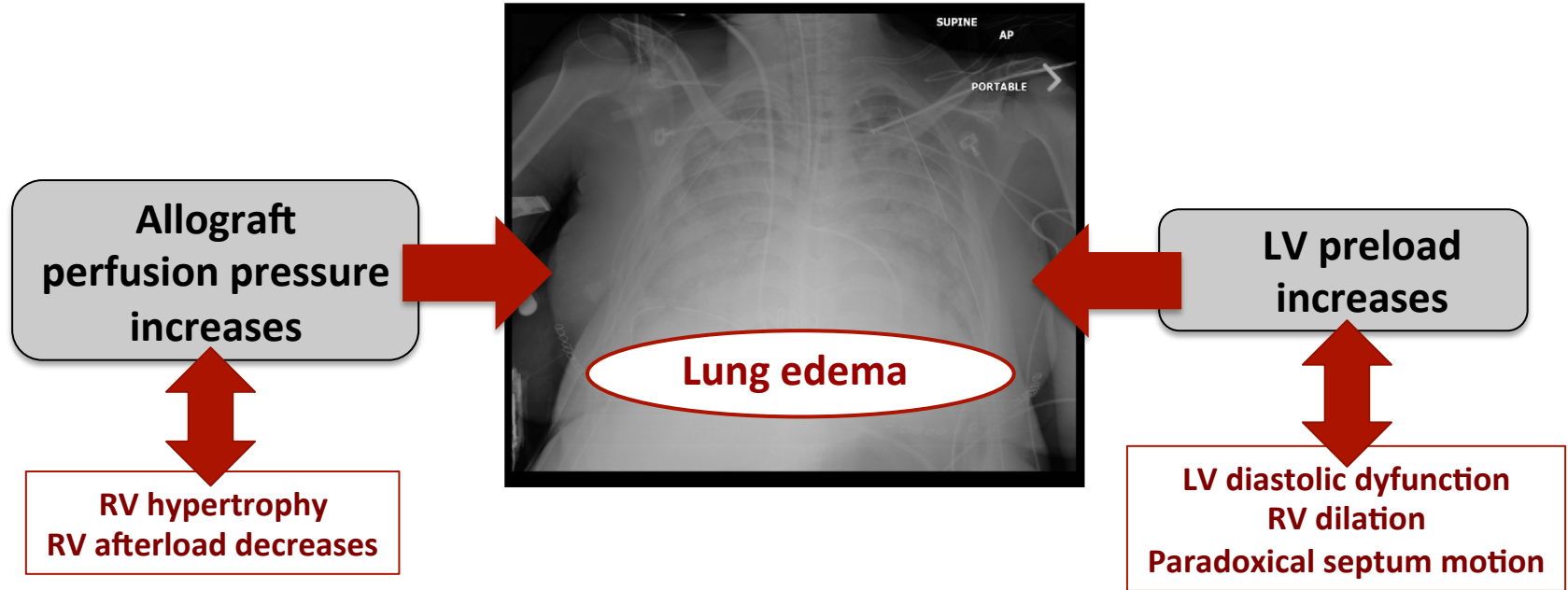
# Survival by era

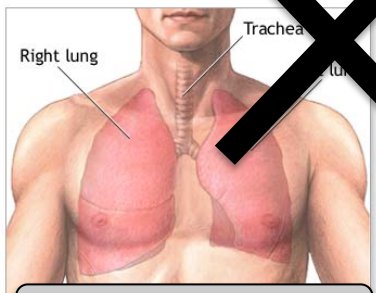
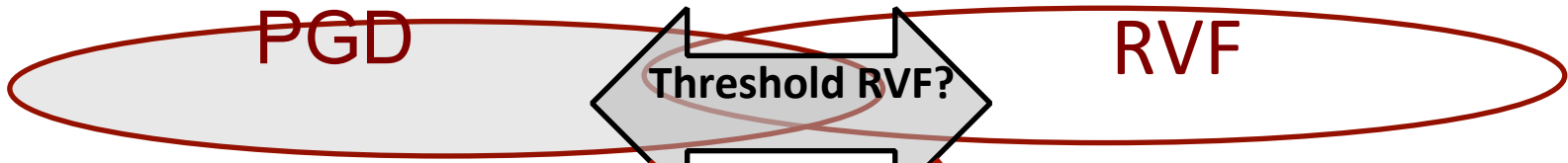


# Paradigme

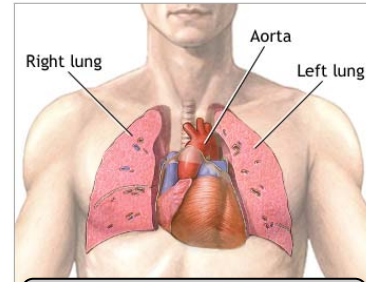


# Dysfonction primaire du greffon et HTAP





**DLT**



**HLT**

# Identify reversible cause of RVF

## Optimization of RV function

**Preload  
optimization**

Low volume loading  
Avoid RV overload  
Wedge pressure  
CVP  
Echo  
! Extubation ++

**Adequate  
perfusion**

Norepinephrine  
Consider Inotropic  
support

**Decrease  
RV afterload**

Avoid Hypoxemia  
and hypercarbia  
Inhaled NO

**Ventilatory  
support**

Protective Strategy  
Low tidal volume  
Optimized PEEP



**ECLS**



# ECLS timing in PAH w inotropic sup

Elevated creatinine

Low systemic blood pressure

Hyponatremia  
elevated BNP

Increasing inotropic requirement

## Modes of ECLS

### PA-LA Novalung

#### Strengths

Pumpless  
Long term bridge  
Easy to change  
Allow mobilization

#### Weaknesses

General anesthesia  
Sternotomy  
Normal LV function needed

### VA-ECMO

#### Strengths

Local anesthesia  
Safe and fast  
Awake patient  
Low heparin dose

#### Weaknesses

Arterial complication  
No mobilization  
*except upper body cannulation*

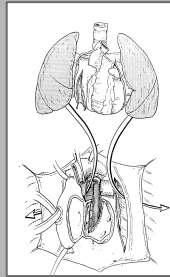
# Comment progresser ? Poser l'indication

**Programme  
de  
*Super  
Urgence***

**Infections  
DPG  
Rejets aigus**

**Réhabilitation  
du  
Greffon (EVLP)**

**Contre  
Indications**



**Bronchiolite  
Oblitérante**

**Atteinte  
infiltrante**

**Critères par  
pathologies**

**Complications  
mécaniques**

**IS  
AZM  
*Photophérèse  
Retransplantation***

**Assistance**

# Disclosures

**None**