Hypertension Artérielle Pulmonaire (HTAP)

N. Methia, S.Benkedda

Service de Cardiologie A2 - CHU Mustapha Alger

1er cours africain sclérodermie systémique 21 mai 2016, Alger

PLAN

- Définir l'hypertension pulmonaire (HTP)
- Définir l'hypertension artérielle pulmonaire (HTAP)
- HTP dans la sclérodermie :
  - HTAP
  - MVO
  - Pathologie du cœur gauche(dysfonction diastolique)
  - Post-embolique
  - PID

- HTAP/ScS : dépistage, DC, traitement, …

Introduction & Définitions

- L'hypertension pulmonaire (**HTP**) :

état hémodynamique et physiopathologique caractérisé par une élévation persistante des pressions pulmonaires dans le lit vasculaire pulmonaire, **conséquence de plusieurs états pathologiques** .

- HTP: définition hémodynamique

- **Probabilité** échographique de l'hypertension pulmonaire

- HTAP : Maladies à caractéristiques cliniques communes , des atteintes pathologiques de la **microcirculation** pulmonaire similaires.

European Heart Journal
doi:10.1093/eurheartj/ehv317

ESC/ERS GUIDELINES

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT)

Authors/Task Force Members: Nazzareno Galiè* (ESC Chairperson) (Italy), Marc Humbert*[a] (ERS Chairperson) (France), Jean-Luc Vachiery[c] (Belgium), Simon Gibbs (UK), Irene Lang (Austria), Adam Torbicki (Poland), Gérald Simonneau[a] (France), Andrew Peacock[a] (UK), Anton Vonk Noordegraaf[a] (The Netherlands), Maurice Beghetti[b] (Switzerland), Ardeschir Ghofrani[a] (Germany), Miguel Angel Gomez Sanchez (Spain), Georg Hansmann[b] (Germany), Walter Klepetko[c] (Austria), Patrizio Lancellotti (Belgium), Marco Matucci[d] (Italy), Theresa McDonagh (UK), Luc A. Pierard (Belgium), Pedro T. Trindade (Switzerland), Maurizio Zompatori[e] (Italy) and Marius Hoeper[a] (Germany)

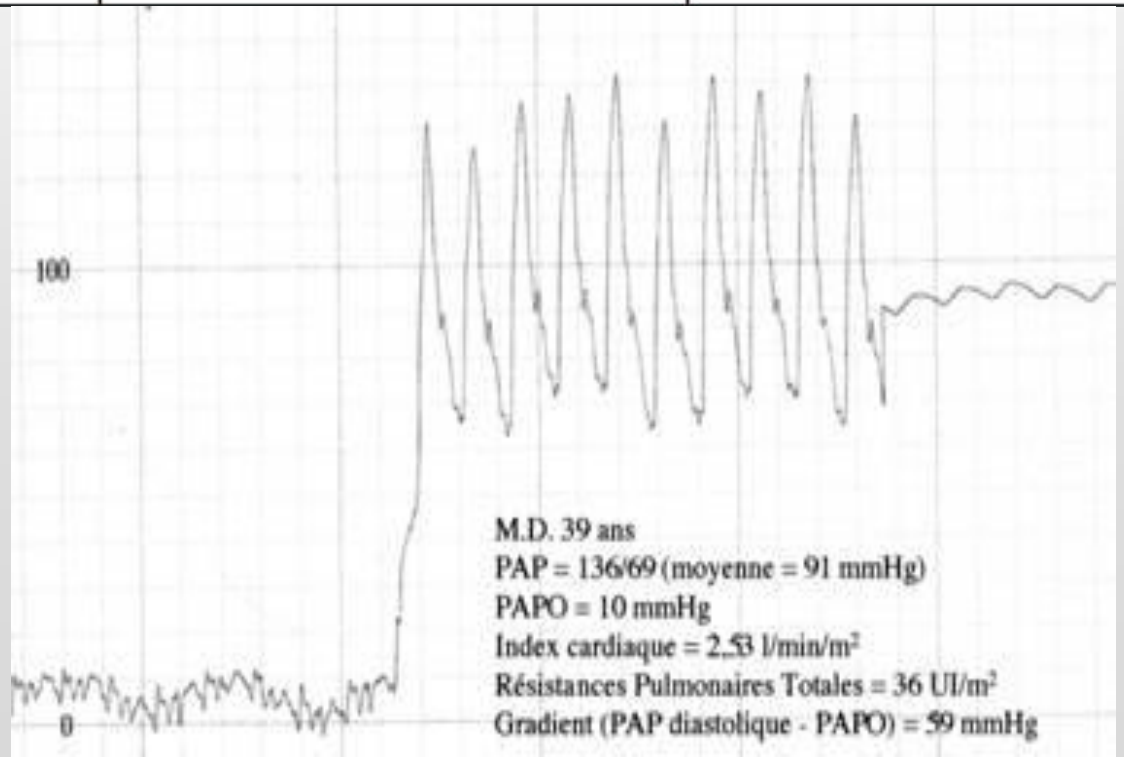
Définition de l'hypertension pulmonaire

Definition	Characteristics[a]	Clinical group(s)[b]
PH	PAPm ≥25 mmHg at rest	All

- Normale au repos
- PAPm = 14 ± 3 mmHg
- PAPm anormale : 14 + 2DS = 20 mmHg
- PAPm 21 à 24 mmHg : pas de valeur pathologique
- Pas de définition à l'effort

Définition de l'hypertension pulmonaire

Definition	Characteristics[a]	Clinical group(s)[b]
PH	PAPm ≥25 mmHg	All
Pre-capillary PH	PAPm ≥25 mmHg PAWP ≤15 mmHg	1. Pulmonary arterial hypertension 3. PH due to lung diseases 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial mechanisms



Définition de l'hypertension pulmonaire

Definition	Characteristics[a]	Clinical group(s)[b]
PH	PAPm ≥25 mmHg	All
Pre-capillary PH	PAPm ≥25 mmHg PAWP ≤15 mmHg	1. Pulmonary arterial hypertension 3. PH due to lung diseases 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial mechanisms
Post-capillary PH	PAPm ≥25 mmHg PAWP >15 mmHg	2. PH due to left heart disease 5. PH with unclear and/or multifactorial mechanisms
Isolated post-capillary PH (Ipc-PH)	DPG <7 mmHg and/or PVR ≤3 WU[c]	
Combined post-capillary and pre-capillary PH (Cpc-PH)	DPG ≥7 mmHg and/or PVR >3 WU[c]	

- **Cathétérisme cardiaque droit**
- **Conséquences**
  - **Hypertrophie ventriculaire droite**
  - **Insuffisance cardiaque droite**
  - **Dyspnée, syncope, décès**

Classification des Hypertensions Pulmonaires

1973 : OMS → HTAP primitive et HTAP secondaire à une affection identifiable

1998 : Symposium Mondial sur HTP de **EVIAN** → individualisation de groupes

2003 : Classification modifiée Symposium Mondial de **VENIS**

2009 : Classification de **DANA POINT** → 5 groupes +++/ESC/ERS reco

2013 : Classification de **NICE** : quelques modifications → ESC/ERS 2015

Classification des Hypertensions Pulmonaires

1. Pulmonary arterial hypertension

- 1.1 Idiopathic
- 1.2 Heritable
  - 1.2.1 BMPR2 mutation
  - 1.2.2 Other mutations
- 1.3 Drugs and toxins induced
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 Human immunodeficiency virus (HIV) infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart diseases (Table 5)
  - 1.4.5 Schistosomiasis

1'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

- 1'.1 Idiopathic
- 1'.2 Heritable
  - 1'.2.1 EIF2AK mutation
  - 1'.2.2 Other mutations
- 1'.3 Drugs, toxins and radiation induced
- 1'.4 Associated with:
  - 1'.4.1 Connective tissue disease
  - 1'.4.2 HIV infection

1''. Persistent pulmonary hypertension of the newborn

2. Pulmonary hypertension due to left heart disease

- 2.1 Left ventricular systolic dysfunction
- 2.2 Left ventricular diastolic dysfunction
- 2.3 Valvular disease
- 2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
- 2.5 Congenital/acquired pulmonary veins stenosis

3. Pulmonary hypertension due to lung diseases and/or hypoxia

- 3.1 Chronic obstructive pulmonary disease
- 3.2 Interstitial lung disease
- 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
- 3.4 Sleep-disordered breathing
- 3.5 Alveolar hypoventilation disorders
- 3.6 Chronic exposure to high altitude
- 3.7 Developmental lung diseases (Web Table III)[a]

4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions

- 4.1 Chronic thromboembolic pulmonary hypertension
- 4.2 Other pulmonary artery obstructions
  - 4.2.1 Angiosarcoma
  - 4.2.2 Other intravascular tumors
  - 4.2.3 Arteritis
  - 4.2.4 Congenital pulmonary arteries stenoses
  - 4.2.5 Parasites (hydatidosis)

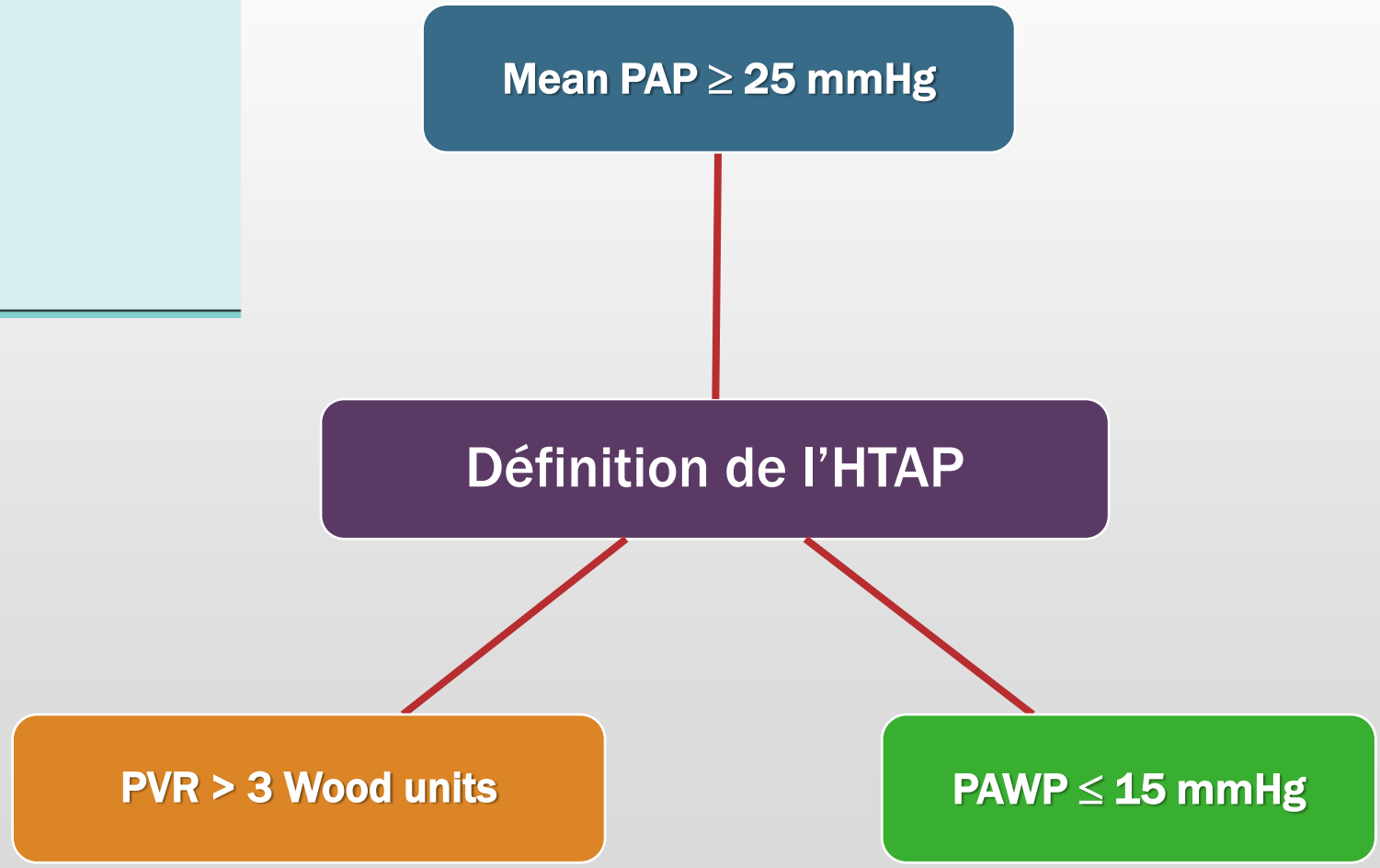
5. Pulmonary hypertension with unclear and/or multifactorial mechanisms

- 5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy.
- 5.2 Systemic disorders, sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
- 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
- 5.4 Others: pulmonary tumoral thrombothic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

Groupe 1 : Hypertensions Artérielle Pulmonaire

1. Pulmonary arterial hypertension

- 1.1 Idiopathic
- 1.2 Heritable
  - 1.2.1 BMPR2 mutation
  - 1.2.2 Other mutations
- 1.3 Drugs and toxins induced
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 Human immunodeficiency virus (HIV) infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart diseases (Table 5)
  - 1.4.5 Schistosomiasis



HTAP/ScS : Intérêt

→ Complication gravissime / Pc

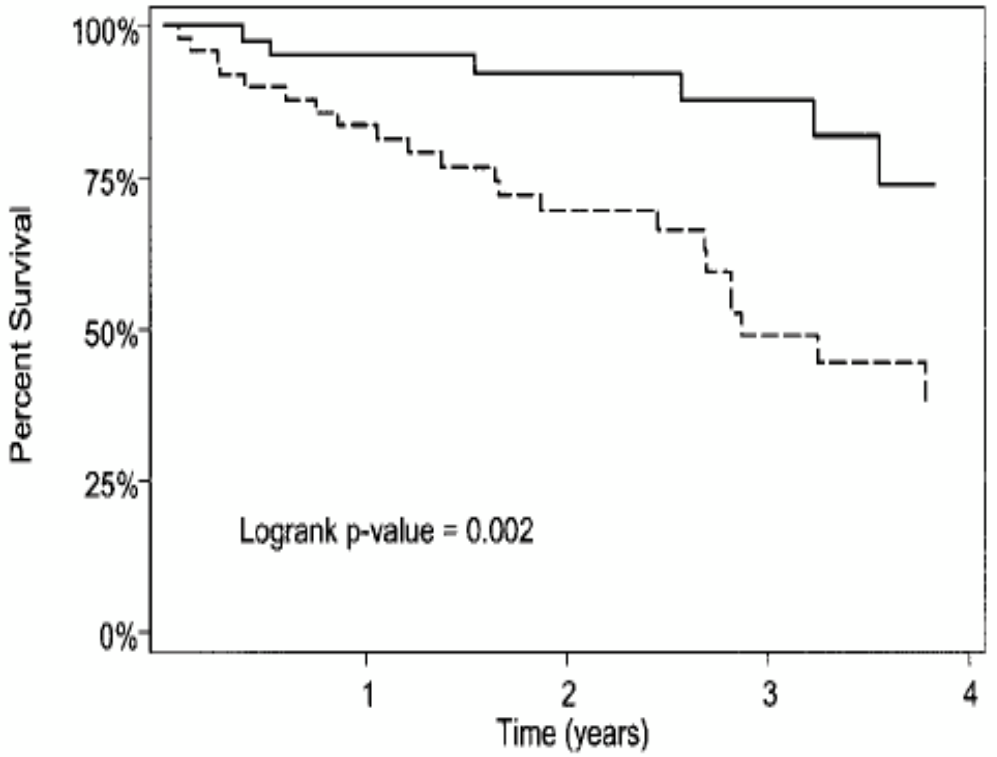
→ ScS : Connectivite qui se complique le plus d'HTAP

→ Dépistage → Améliore le pronostic

→ Traitement

Le Pronostic HTAP/ScS

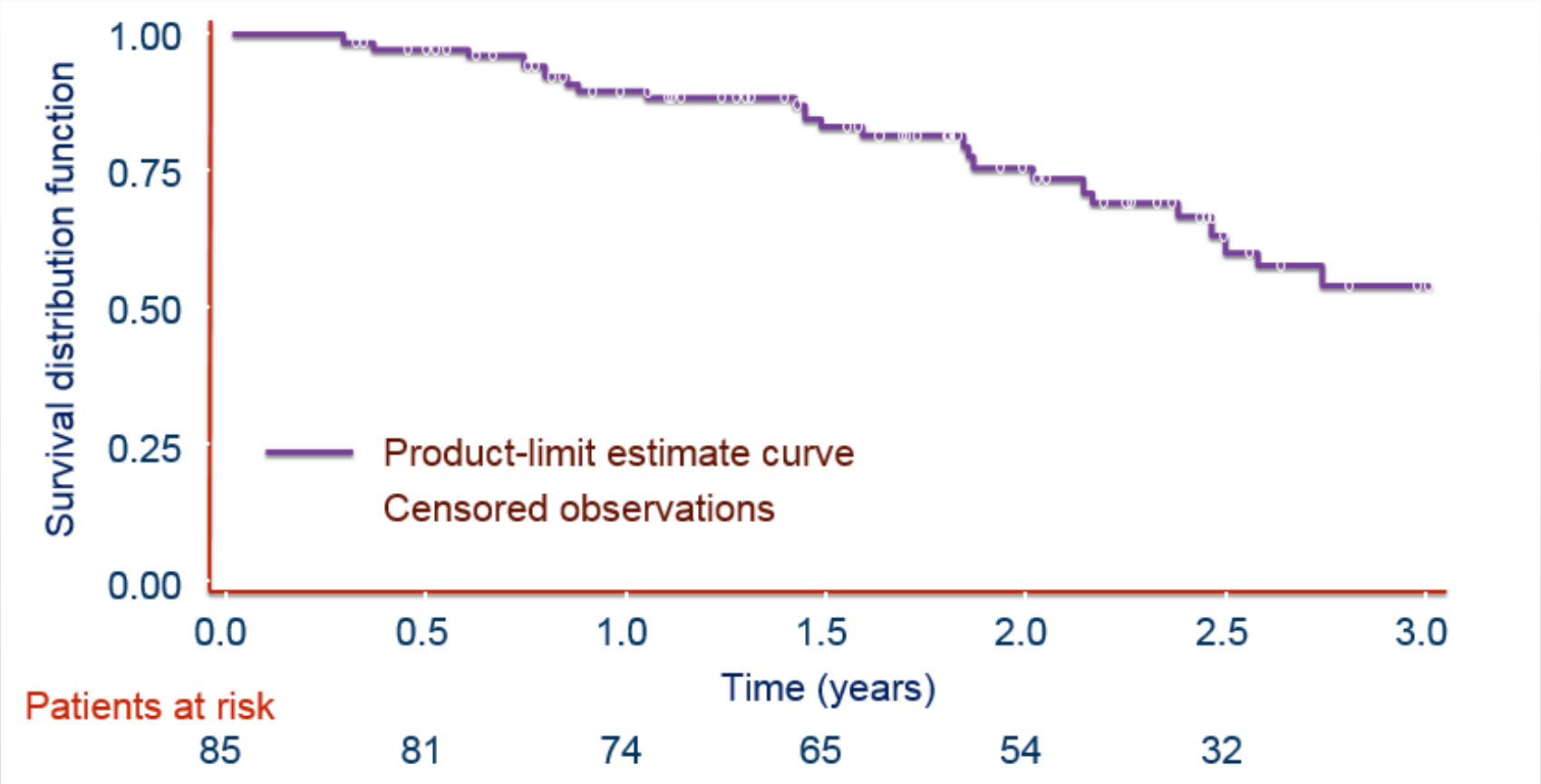
	IPAH (n = 41)	PAH-Scl (n = 50)	*P*
Right atrial pressure, mm Hg	10.1 ± 0.9	11.2 ± 0.7	0.36
Pulmonary artery systolic pressure, mm Hg	86.4 ± 2.9	75.6 ± 2.4	0.004
Pulmonary artery pressure, mm Hg	54.4 ± 1.9	46.6 ± 1.5	0.002
Pulmonary capillary wedge pressure, mm Hg	12.0 ± 0.8	11.4 ± 0.7	0.59
Cardiac index, liters/minute/m^2	2.1 ± 0.1	2.2 ± 0.1	0.19
Pulmonary vascular resistance index, Wood units	22.8 ± 1.8	17.5 ± 1.5	0.026



→ **Survie à 1 et 3 ans : 87,8% et 48,9% HTAP-SSc vs 95,1% et 83,6% HTAPi**

Fisher et al Arthritis Rheum 2006

PAH-SSc patients have a particularly poor prognosis



3-year survival in PAH-SSc patients was 56%[1] compared with 73.7%[2] in IPAH patients

IPAH: **I**diopathic **PAH**; SSc: **S**ystemic **Sc**lerosis

1. Launay D, *et al. Ann Rheum Dis* 2013; 72:1940-6.
2. Benza RL, *et al. Chest* 2012; 142:448-56.

HTAP/ScS : Intérêt

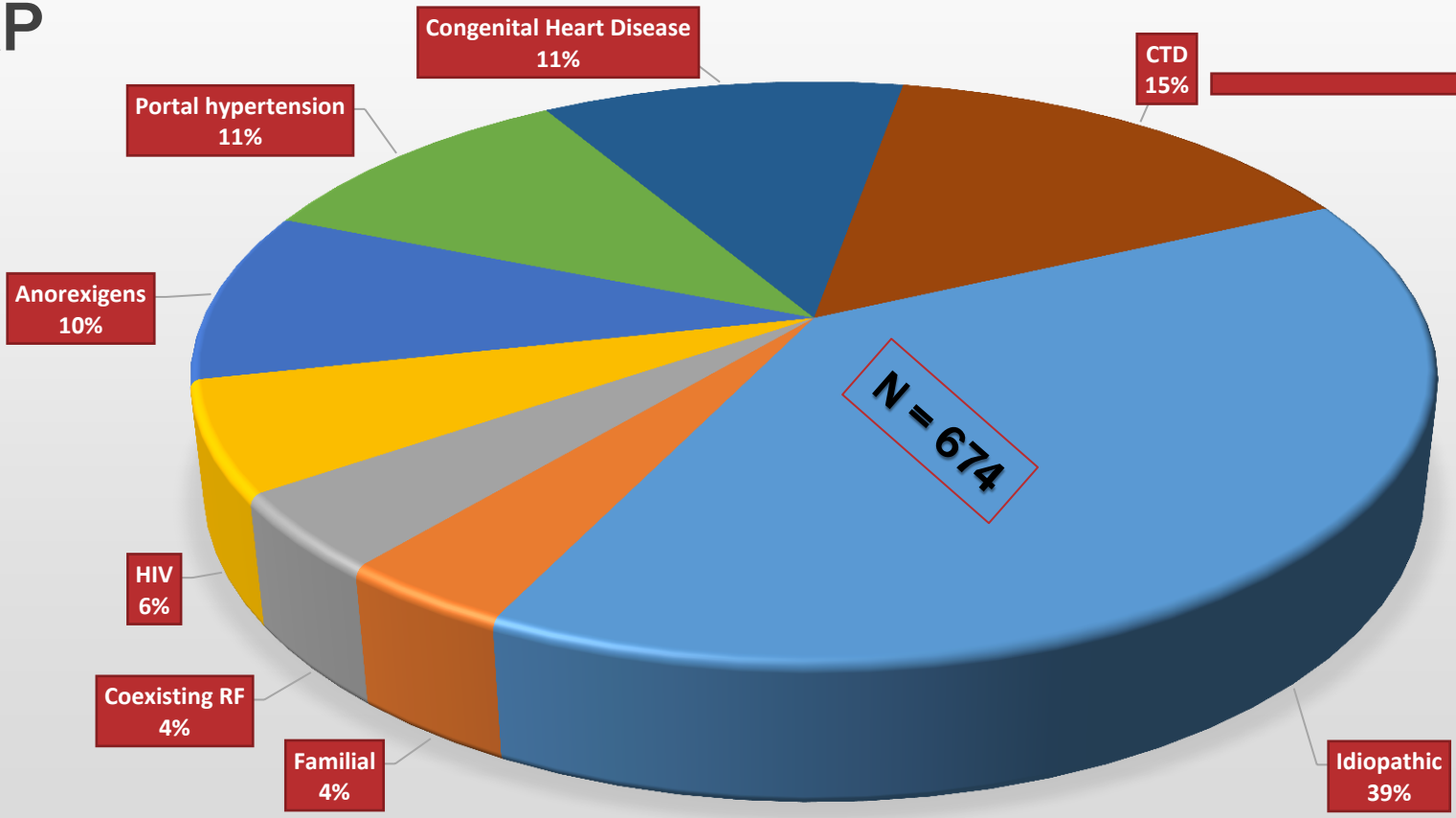
→ Complication gravissime / Pc

→ **ScS : Connectivite qui se complique le plus d'HTAP**

→ Dépistage → Améliore le pronostic

→ Traitement

Les connectivites représentent la 1ère condition associée à la survenue d'une HTAP



- 75 SSc
- 15 SLE
- 9 MCTD
- 1 UCTD
- 1 PR+UCTD
- 1 Sjögren
- 1 MPA

Humbert M et al. AJRCCM 2006

Epidémiologie de l'HTAP dans la ScS

- ScS est la connectivite qui se complique le plus d'HTAP :

Registre	HTAP/Connectivite	ScS
Français	15%	76%
American	25%	62%
Espagnole	15%	61%
Chinois	19%	9%

Epidémiologie de l'HTAP dans la ScS

Prévalence de l'HTAP au cours de la ScS : très variable

5 - 35 % : Populations étudiées / méthodes de diagnostic [écho/KT] / critère échographique retenu

5 - 12 % : études basées sur le KT droit

→ En Algérie **: 6 %** sur un dépistage échographique et confirmation par KT droit[1]

[1] *Thèse METHIA N.*

Epidémiologie de l'HTAP dans la ScS

Tableau Comparatif

Référence	Méthodologie	Nombre de Patients	Profil de ScS	Définition de l'HTAP	Prévalence
RG Ungerer 1983 États-Unis[78]	**Etude prospective monocentrique** 1973-1979	**49**	ScS proximale et CREST	PAPm ≥ 20 mm Hg et pression capillaire moyenne ≤ 12 mm Hg	**16%**
ET Koh 1996 Canada[81]	**Etude prospective monocentrique** 1978-1994	**344**	ScS diffuse ou limitée	PAPm ≥ 25mm Hg et pression capillaire moyenne ≤ 12 mm Hg au cathétérisme cardiaque droit, ou pression systolique VD > 35mm Hg à l'échodoppler cardiaque ou dilatation ventriculaire droite, fuite pulmonaire ou tricuspide ou mouvement paradoxal du septum à l'échodoppler cardiaque	**4,90%**
D Mukerjee 2003 Grande Bretagne[84]	**Etude prospective monocentrique** 1998-2002	**722**	ScS diffuse ou limitée	PAPm >2 5 mm Hg ou > 30 à l'effort Capillaire < 14 mm Hg	**12%**
E Hachulla 2005 France[87]	**Etude observationnelle transversale multicentrique**	**599**	ScS diffuse ou limitée	PAPm ≥ 25 mm Hg ou ≥ 30 mm Hg à l'effort, pression capillaire < 15mm Hg	**8%**
notre étude Algérie	**Etude transversale descriptive**	**202**	ScS diffuse ou limitée	PAPm ≥ 25 et pression capillaire moyenne < 15 mm Hg	**6%**

HTAP/ScS : Intérêt

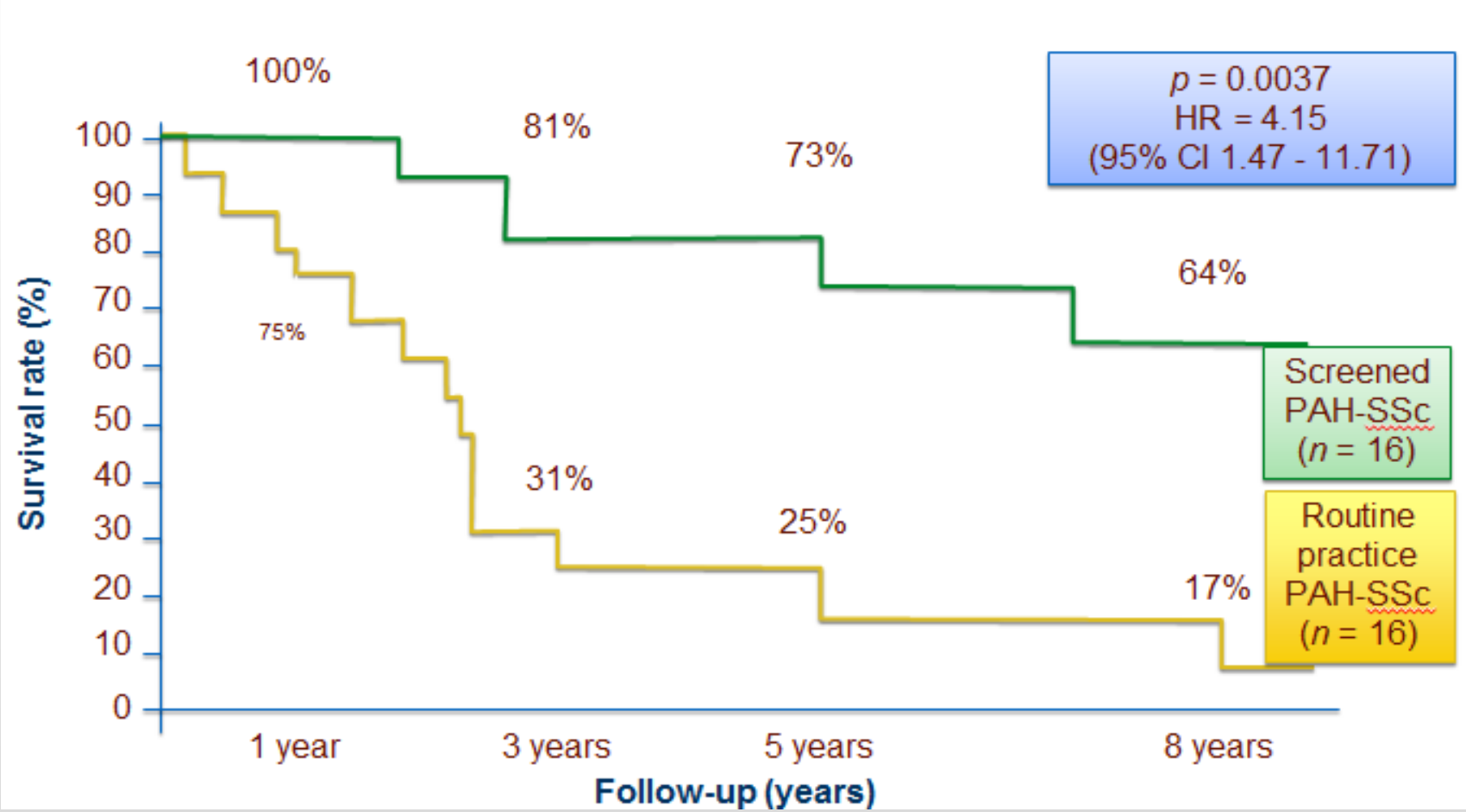
→ Complication gravissime / Pc

→ ScS : Connectivite qui se complique le plus d'HTAP

→ **Dépistage → Améliore le pronostic**

→ Traitement

Screening improves long-term outcomes in SSc patients



CI: Confidence interval; HR: Hazard ratio; SSc: Systemic Sclerosis

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

Impact sur la survie à long terme du dépistage de l'HTAP chez les patients sclérodermiques

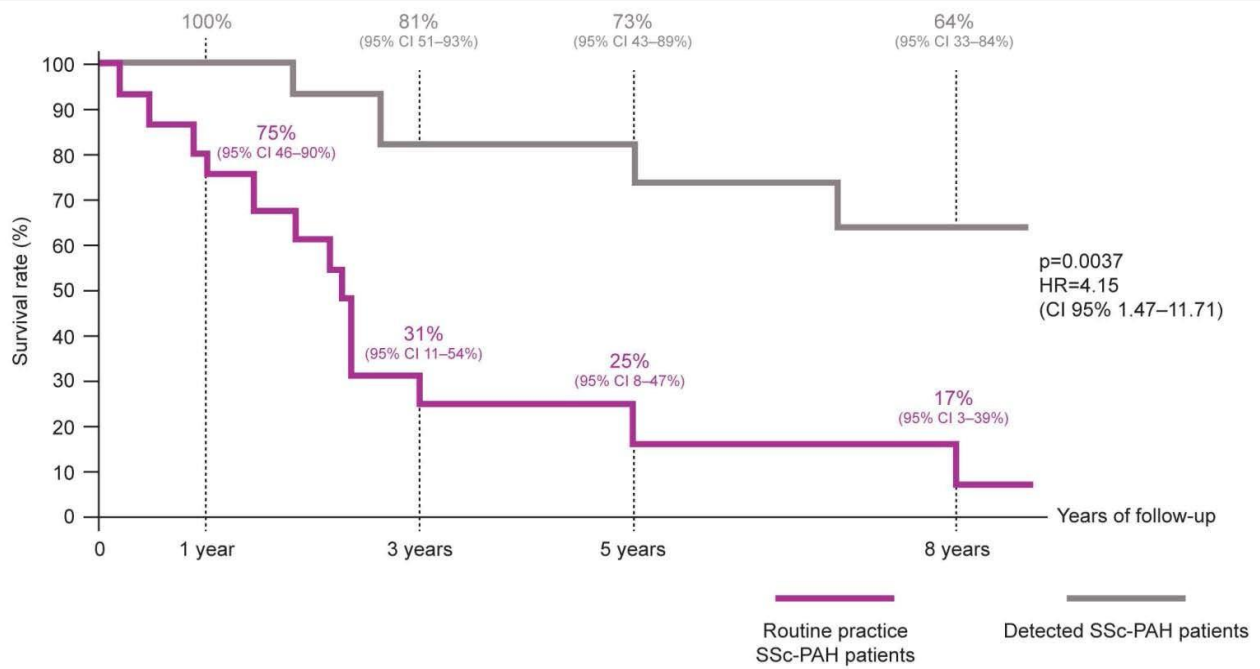


Figure 2: Eight-year survival from diagnosis of incident SSc-PAH patients diagnosed during routine clinical practice (n=16) and by a systematic detection program (n=16).

- Cohorte de patients sclérodermiques
- Dépistage par échocardiographie
- Confirmation par KT droit
- Prise en charge thérapeutique laissée à l'appréciation du clinicien
- Suivi prospectif pendant 8 ans

Humbert Arthritis Rheum 2011

HTAP/ScS : Intérêt

→ Complication gravissime / Pc

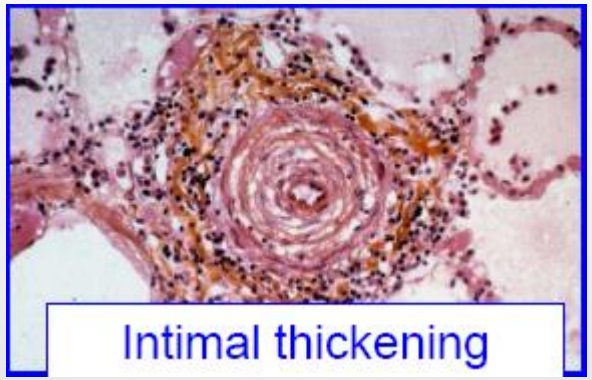
→ ScS : Connectivite qui se complique le plus d'HTAP

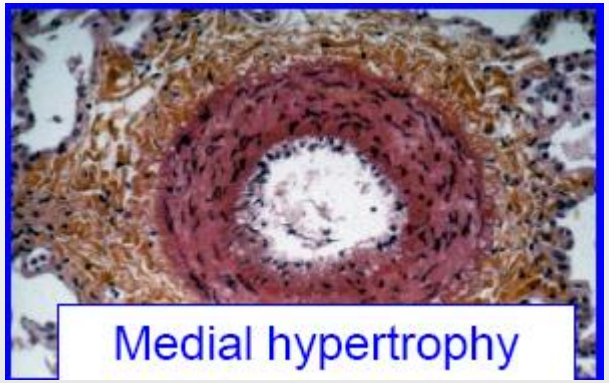
→ Dépistage → Améliore le pronostic

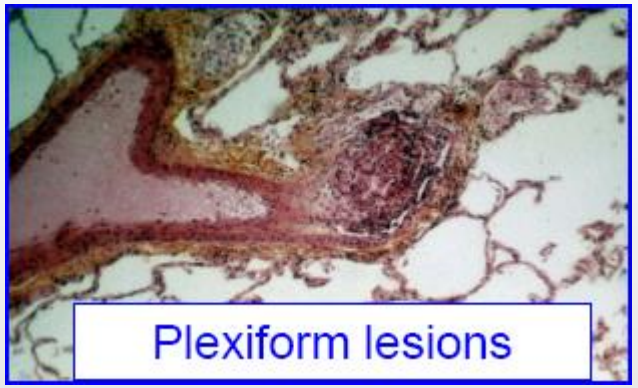
→ **Traitement**

Groupe 1: Hypertension artérielle pulmonaire

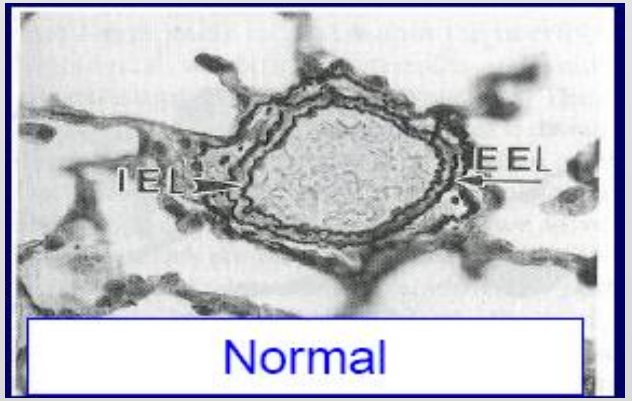
- Intense remodelage microvasculaire pulmonaire





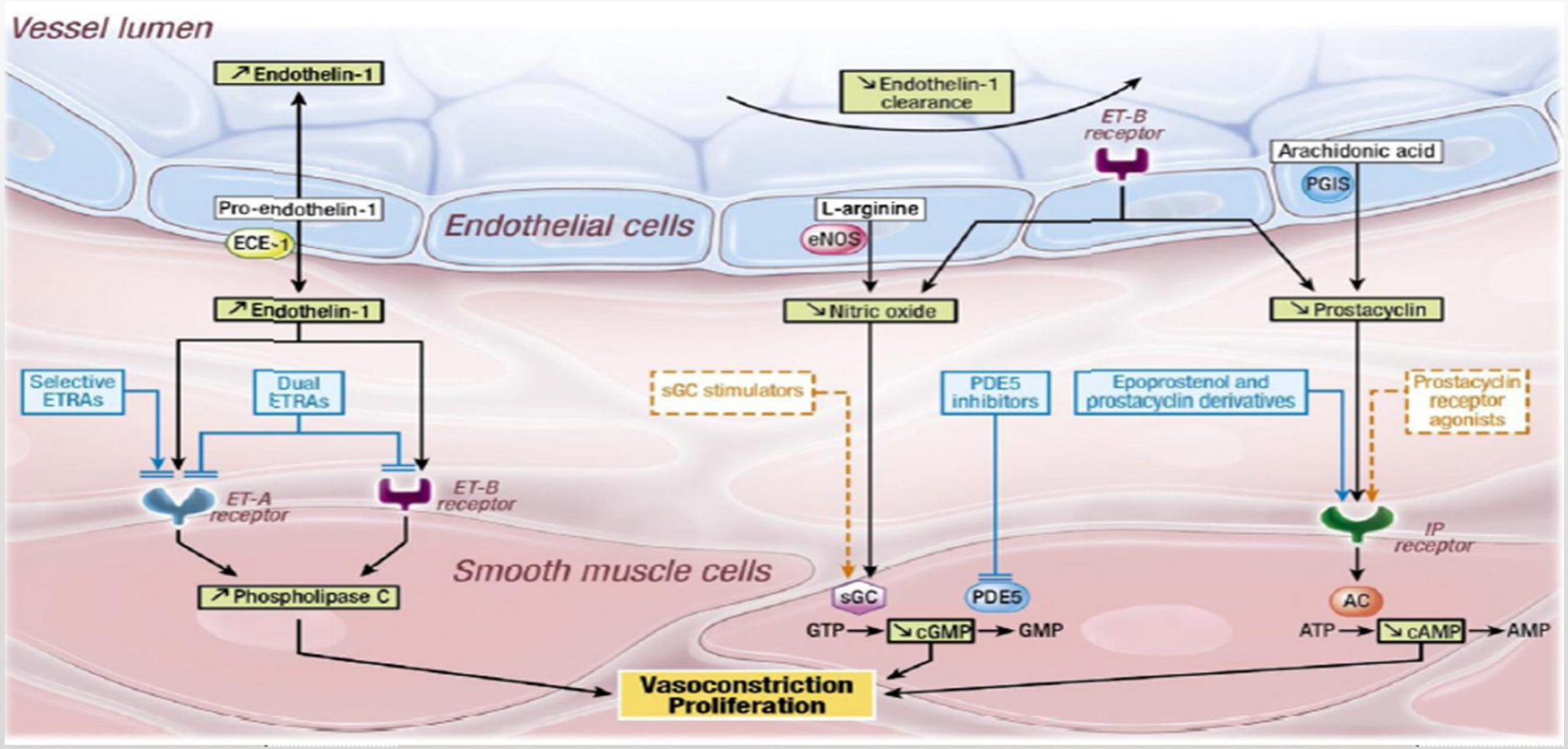


- Dysfonction endothéliale
- Trois mécanismes impliqués
  - Thrombose in situ
  - Prolifération musculaire lisse et endothéliale
  - Vasoconstriction



Physiopathologie de L'HTAP

- Physiopathologie de l'HTAP incertaine → 3 voies principales impliquées :

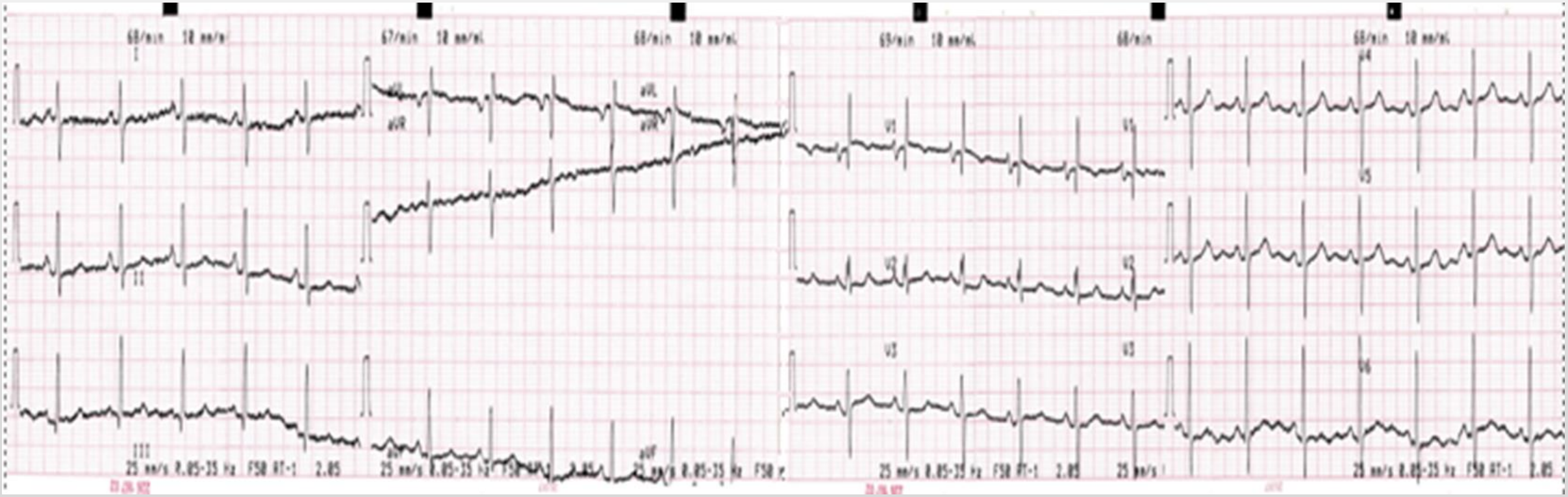


Dépistage et Diagnostic de l'HTAP dans la ScS

- Comment dépister l'HTAP/ScS ?
- Comment confirmer l'HTAP ?
- Eliminer les DC différentiels

Dépistage et Diagnostic de l'HTAP dans la ScS

- Clinique / Dyspnée NYHA
- Radiographie Thoracique, ECG : anomalies dans les formes évoluées (Dc tardif)



5th World Symposium on PH: Updated Recommendations on Screening for PAH in SSc

Recommendations on screening of high-risk populations for PAH
Annual screening for PAH is recommended in asymptomatic patients with the SSc spectrum of diseases
Screening should include a two-step approach using clinical assessment in the initial stage, followed by echocardiography and consideration of RHC in patients with abnormal findings* •
Screening programs for patients with SSc should be part of a scientific protocol, or a registry, whenever possible
Patients with SSc and other CTDs with clinical signs and symptoms of PH should be evaluated by RHC

* Based on the DETECT study

•There is a lack of data with DLCO ≥ 60%

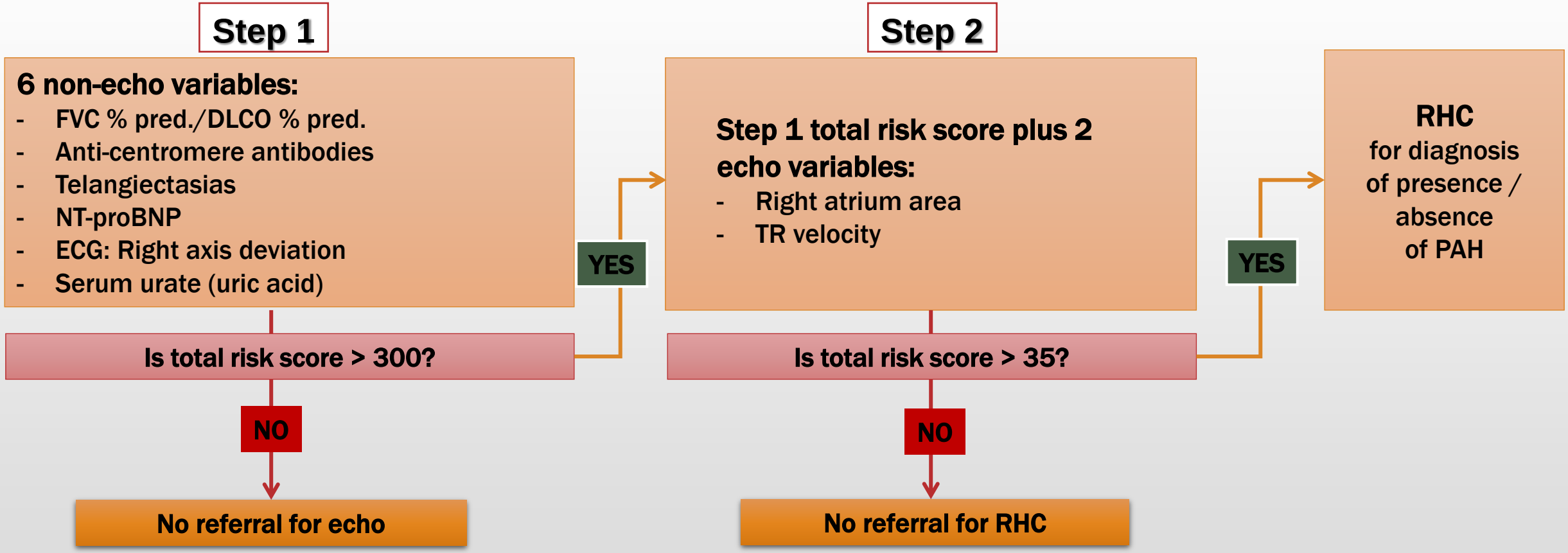
Table 26 Recommendations for pulmonary arterial hypertension associated with connective tissue disease

Recommendations	Class[a]	Level[b]	Ref.[c]
In patients with PAH associated with CTD, the same treatment algorithm as for patients with IPAH is recommended	I	C	46
Resting echocardiography is recommended as a screening test in asymptomatic patients with SSc, followed by annual screening with echocardiography, DLCO and biomarkers	I	C	46
RHC is recommended in all cases of suspected PAH associated with CTD	I	C	46,327
Oral anticoagulation may be considered on an individual basis and in the presence of thrombophilic predisposition	IIb	C	175,339

CTD = connective tissue disease; DLCO = diffusing capacity of the lung for carbon monoxide; IPAH = idiopathic pulmonary arterial hypertension; PAH = pulmonary arterial hypertension; RHC = right heart catheterization; SSc = systemic sclerosis.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Dépistage annuel
ECHO
DLCO
Biomarqueurs

DETECT two-step decision tree for screening SSc patients



DLCO: Diffusing capacity of the Lungs for Carbon monoxide; **ECG**: Electrocardiogram;
FVC: Forced vital capacity; **NT-proBNP**: N-terminal prohormone brain natriuretic peptide;
RHC: Right heart catheterisation; **SSc**: Systemic Sclerosis; **TR**: Tricuspid regurgitation

Coghlan JG, et al. Ann Rheum Dis 2014; 73:1340-9.

Dépistage et Diagnostic de l'HTAP dans la ScS

- **Echo-Doppler cardiaque est l'examen de dépistage de référence**

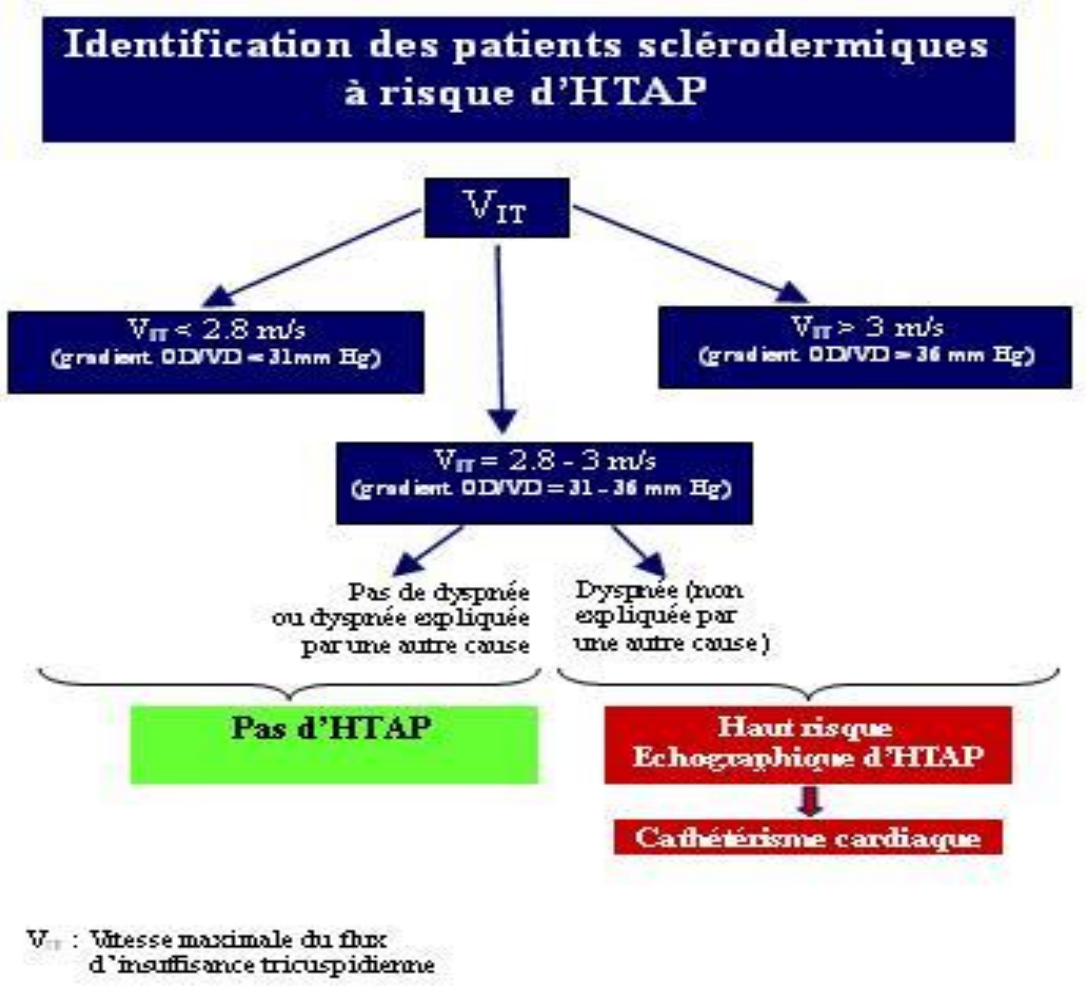


Table 26 Recommendations for pulmonary arterial hypertension associated with connective tissue disease

Recommendations	Class[a]	Level[b]	Ref.[c]
In patients with PAH associated with CTD, the same treatment algorithm as for patients with IPAH is recommended	I	C	46
Resting echocardiography is recommended as a screening test in asymptomatic patients with SSc, followed by annual screening with echocardiography, DLCO and biomarkers	I	C	46
RHC is recommended in all cases of suspected PAH associated with CTD	I	C	46,327
Oral anticoagulation may be considered on an individual basis and in the presence of thrombophilic predisposition	IIb	C	175,339

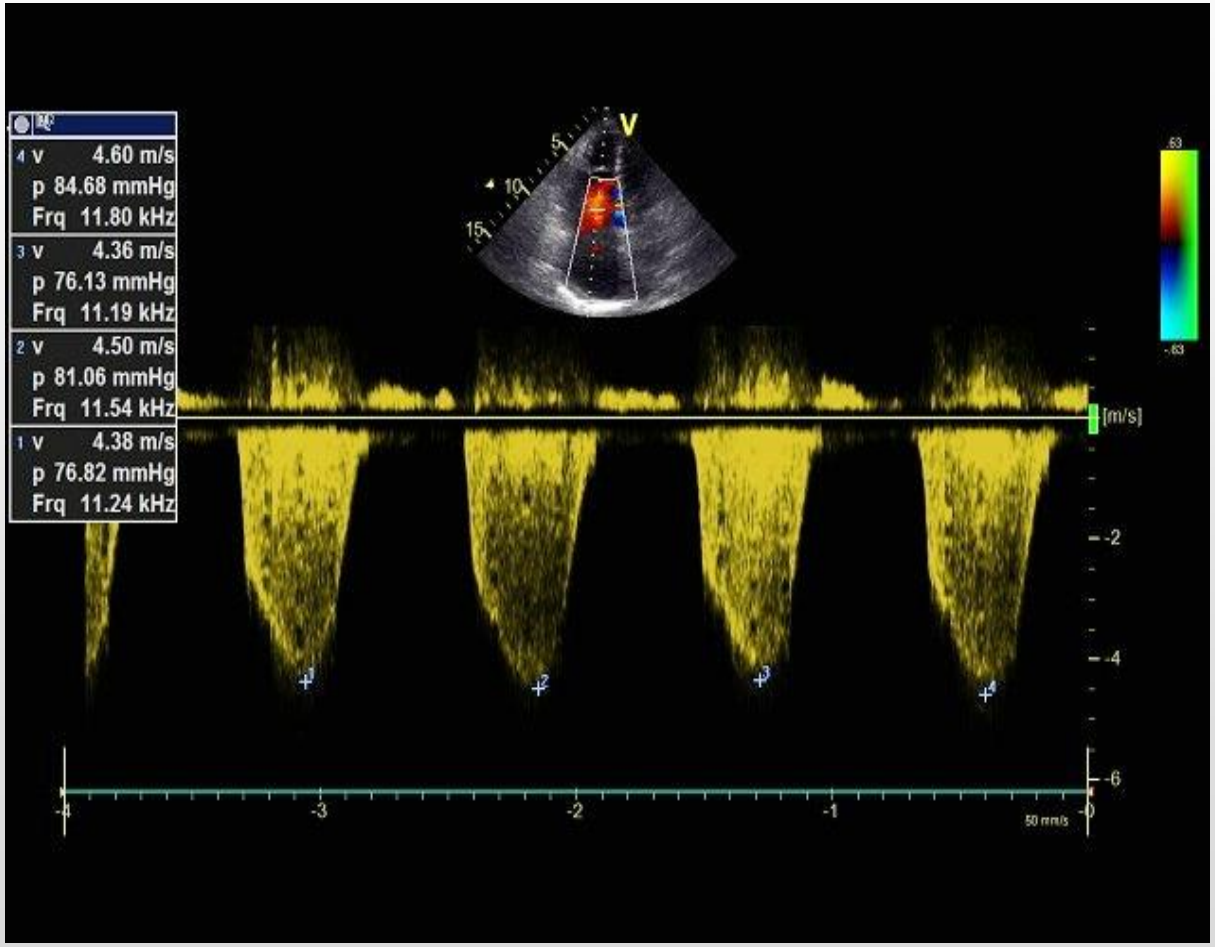
CTD = connective tissue disease; DLCO = diffusing capacity of the lung for carbon monoxide; IPAH = idiopathic pulmonary arterial hypertension; PAH = pulmonary arterial hypertension; RHC = right heart catheterization; SSc = systemic sclerosis.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Probabilité échocardiographique d'HTP

Peak tricuspid regurgitation velocity (m/s)	Presence of other echo "PH signs"[a]	Echocardiographic probability of pulmonary hypertension
≤2.8 or not measurable	No	Low
≤2.8 or not measurable	Yes	Intermediate
2.9–3.4	No	
2.9–3.4	Yes	High
>3.4	Not required	

A: The ventricles[a]	B: Pulmonary artery[a]	C: Inferior vena cava and right atrium[a]
Right ventricle/left ventricle basal diameter ratio >1.0	Right ventricular outflow Doppler acceleration time <105 m/sec and/or midsystolic notching	Inferior cava diameter >21 mm with decreased inspiratory collapse (<50 % with a sniff or <20 % with quiet inspiration)
Flattening of the interventricular septum (left ventricular eccentricity index >1.1 in systole and/or diastole).	Early diastolic pulmonary regurgitation velocity >2.2 m/sec	Right atrial area (end-systole) >18 cm^2
	PA diameter >25 mm	

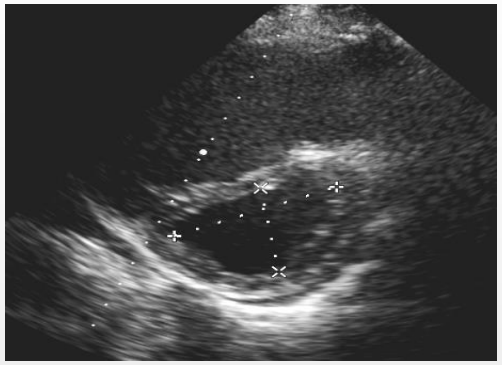
Estimation Des Pressions Pulmonaires sur le flux d'IT



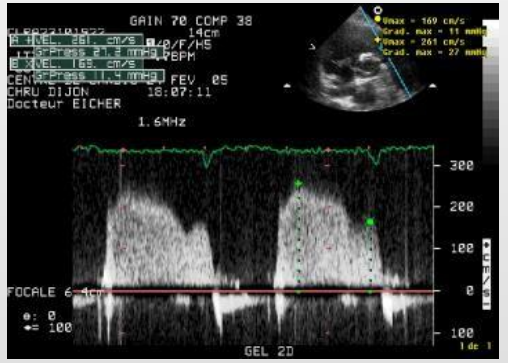
- Insuffisance tricuspide estime (en l'absence de sténose pulmonaire) la PAP systolique et non la PA moyenne
- PAPS = $4(VmaxIT)^2$ +POD
- Alignement sur le flux d'IT: multiplier les incidences ++
- V max de l'IT
- POD? 0-5-10-15 ou plus

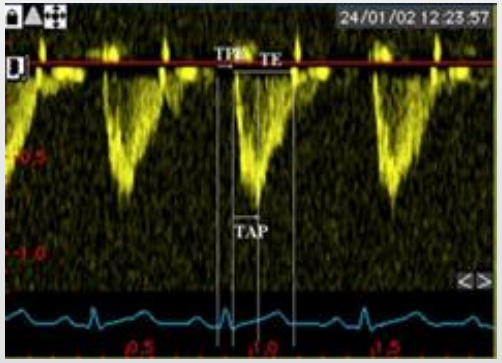
Signes échographiques augmentant la probabilité d'une HTP associés à la VIT

- **VD :** rapport **VD/VG >1**
  Index d'excentricité **IEx >1.1**



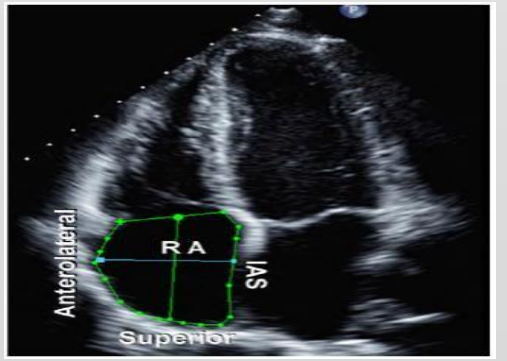
- **AP : TAccP < 105 m/s** et/ou encoche mésosystolique

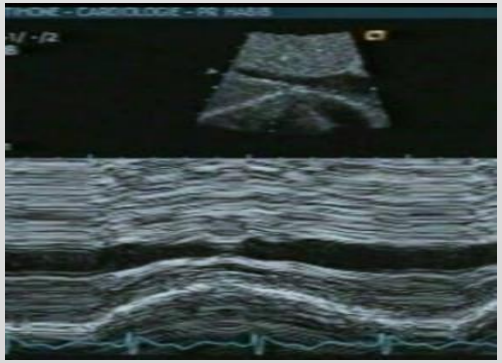




Velocité protodiastolique de **l'IP > 2.2 m/s**
TAP>25mm

- **VCI >21 mm**
  ICVCI < 50% insp, < 20 % resp nle





- SOD> 18 cm^2

Au moins 2 parametres de chacun des groupes (VD, AP, VCI & OD)

Probabilité écho d'HTP: chez qui faut-il faire un KT?

Echocardiographic probability of PH	Without risk factors or associated condition for PAH or CTEPH[d]	Class[a]	Level[b]
Low	Alternative diagnosis should be considered	IIa	C
Intermediate	Alternative diagnosis, echo follow-up, should be considered	IIa	C
	Further investigation of PH may be considered[e]	IIb	
High	Further investigation of PH (including RHC[c]) is recommended	I	C

KT droit

Echocardiographic probability of PH	With risk factors or associated conditions for PAH or CTEPH[c]	Class[a]	Level[b]
Low	Echo follow-up should be considered	IIa	C
Intermediate	Further assessment of PH including RHC should be considered[e]	IIa	B
High	Further investigation of PH[e] including RHC is recommended	I	C

KT droit

KT droit

- Analyse des seuils de VIT dans le dépistage de l'HTAP

References	Parameter cutoff	Number with suspected PH undergoin RHC	RHC-proven PAH N (%)
Phung *et al.* [318]	**VTR > 2,73** or 2,5-2,73 m/s with symptoms	**44**	**24** (55)
Jansa *et al.* [319]	**VTR > 2,73**	**17**	**6** (35)
Ciurzynski *et al.* [320]	**VTR > 2,8 m/s** at rest and/or > 1,58 m/s increase with exercise	**16**	**2** (12.5)
Hachulla *et al.* [87]	**VTR > 3 m/s** or 2,5-3 m/s with symptoms	**33**	**14** (42)
Hachulla *et al.* [88]	**VTR > 3 m/s** or 2,5-3 m/s with symptoms	**26**	**6** (23%)+ **2** additional with exercise PH
Launay *et al.* [189]	**VTR ≥ 3,16 m/s**	**32**	**12** (38)
Hinchcliff *et al.* [321]	**VTR > 2,5** and DLCO < 55% predicted, FVC/DLCO ≥ 1,6	**87**	**49** (57)
Avouac *et al.* [93]	**VTR > 2,73 m/s** or DLCO < 50% w/o ILD or unexplained dyspnea	**206**	**42** (20)
Allanore *et al.* [322]	**VTR > 2,73 m/s**, DLCO < 50% in absence of ILD. unexplained dyspnea and r/o thromboembolic	**19**	**8** (42)
Rajaram *et al.* [323]	**VTR ≥ 3,16**, VTR 2,73-3,16 with DLCO < 50% or unexplained dyspnea	**81**	**54** (67)
Ruiz-Irastorza *et al.* [324]	**VTR 2,95 m/s** (on two separate TTE) and VTR > 3 (RAP 5 mm Hg)	**3**	**0** (0)
Our Study	**VTR > 3 m/s** or 2,8-3 m/s with symptoms	**22**	**12** (55)

Dépistage échocardiographique

Littérature :

20 - 67% HTAP confirmée

- KT droit : Confirmation diagnostique

Table 11 Recommendations for right heart catheterization (A) and vasoreactivity testing (B)

	Class[a]	Level[b]
A		
RHC is indicated in all patients with PAH to confirm the diagnosis, to evaluate the severity, and when PAH specific drug therapy is considered	I	C
RHC should be performed for confirmation of efficacy of PAH-specific drug therapy	IIa	C
RHC should be performed for confirmation of clinical deterioration and as baseline for the evaluation of the effect of treatment escalation and/or combination therapy	IIa	C
B		
Vasoreactivity testing is indicated in patients with IPAH, heritable PAH, and PAH associated with anorexigen use to detect patients who can be treated with high doses of a CCB	I	C

Dépistage et Diagnostic de l'HTAP dans la ScS

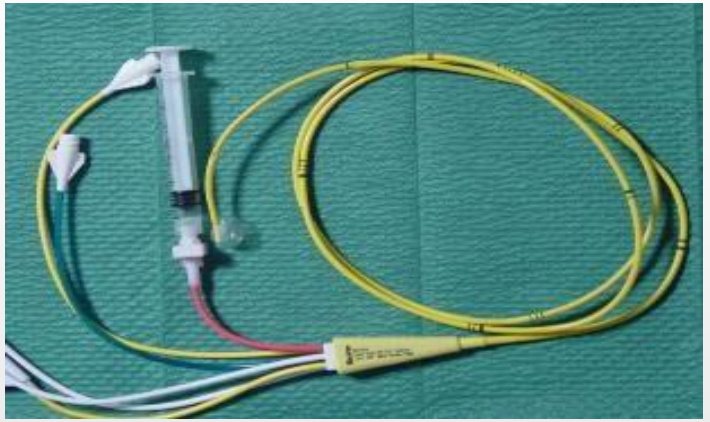
HTP = PAPm $\geq$ 25 mm Hg

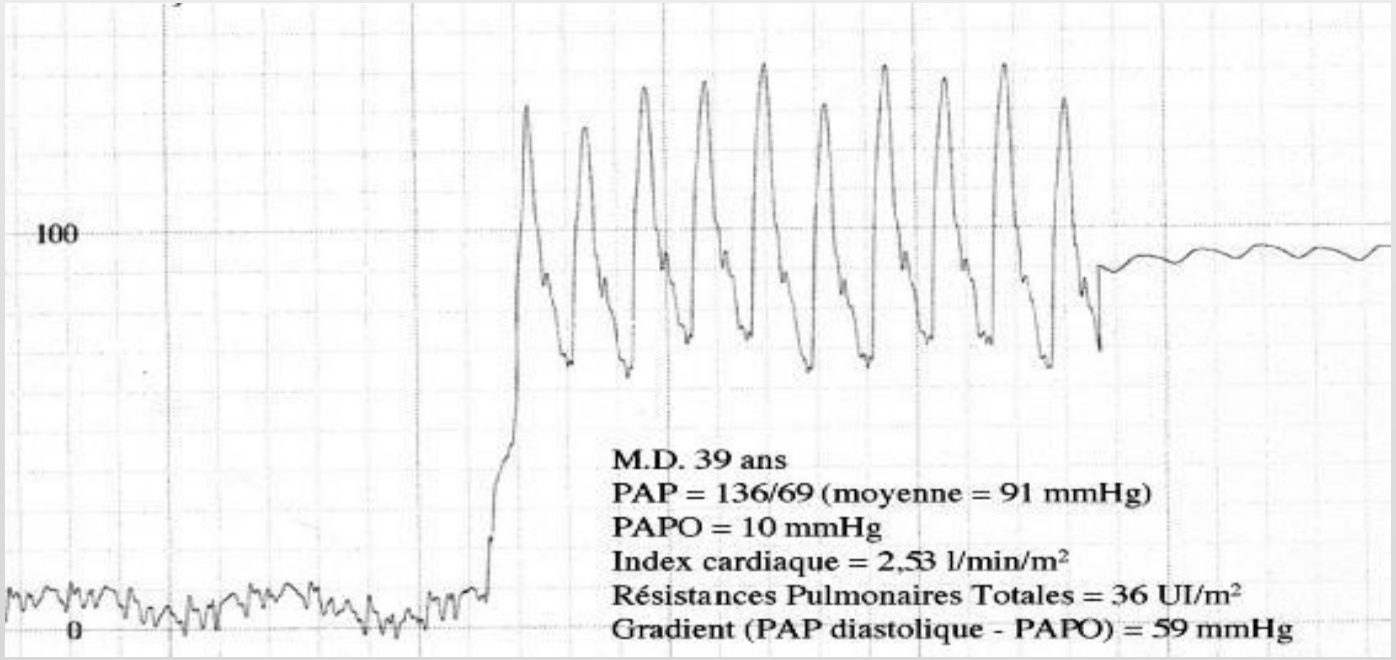
KT droit recommandé

- Confirmer le diagnostic d'une hypertension pulmonaire
- Evaluer la sévérité de l'hypertension pulmonaire
- Eliminer une cardiopathie du cœur gauche (dysfonction diastolique)

Diagnostic : cathétérisme cardiaque droit

- Demeure l'examen de référence +++
- Mesure à l'état de base POD
  - PAPs, PAPd, PAPm,
  - PAPO
  - IC
  - SvO2
  - Calcul des RPTI
- Test au NO +++





RHC must be performed in patients with suspected PH to establish diagnosis

33 patients with suspicion of PAH on cardiac echoDoppler

33 right heart catheterizations

PAH confirmed
18 (54%)

Post-capillary PH
(PAWP >15)
3 (10%) [Mukerjee[1] 13%]

No PAH
12* (36%)
[Mukerjee 24-35%]

*6 with mPAP ≥20 mmHg

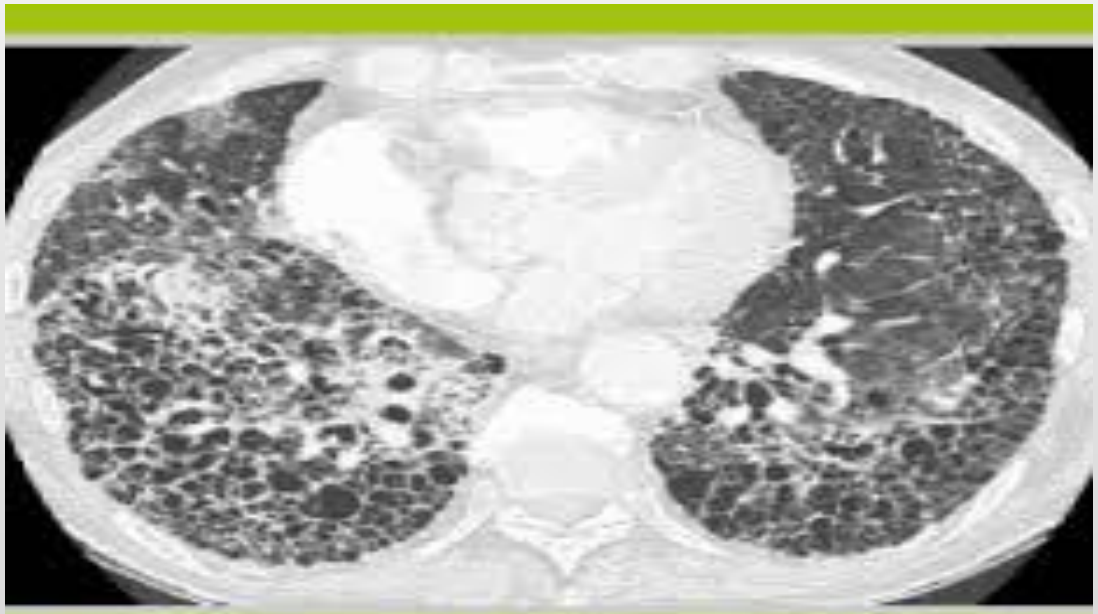
Hachulla E, et al. Arthritis Rheum 2005; 52:3792-800.
1. Mukerjee D, et al. Ann Rheum Dis 2003; 62:1088-93.

Confirmation de l'hypertension pulmonaire

Etudes	Série (N)	Patients sélectionnés	Seuils VIT	HTP non confirmée KT
Notre étude	202	22	2,8-3 m/s	**31,8%** (7/22)
Hachulla 2005	599	33	2,5-3 m/s	36% (12/33)
Hachulla 2009	384	26	2,8-3 m/s	**30%** (8/26)
Schmid 2007	51	12	> 3 m/s	41,6% (5/12)

Diagnostic différentiel de l'HTAP dans la ScS

- **TDM thoracique** / EFR : pneumopathie interstitille diffuse (PID) ⇨HTP-PID



CT-scanner en haute résolution (CTHR) des bases pulmonaires hautement évocateur d'une UIP avec nid d'abeille

PVOD: maladie veino-occlusive

Prise en Charge de l'HTAP

HTAP/ScS et HTAPi :

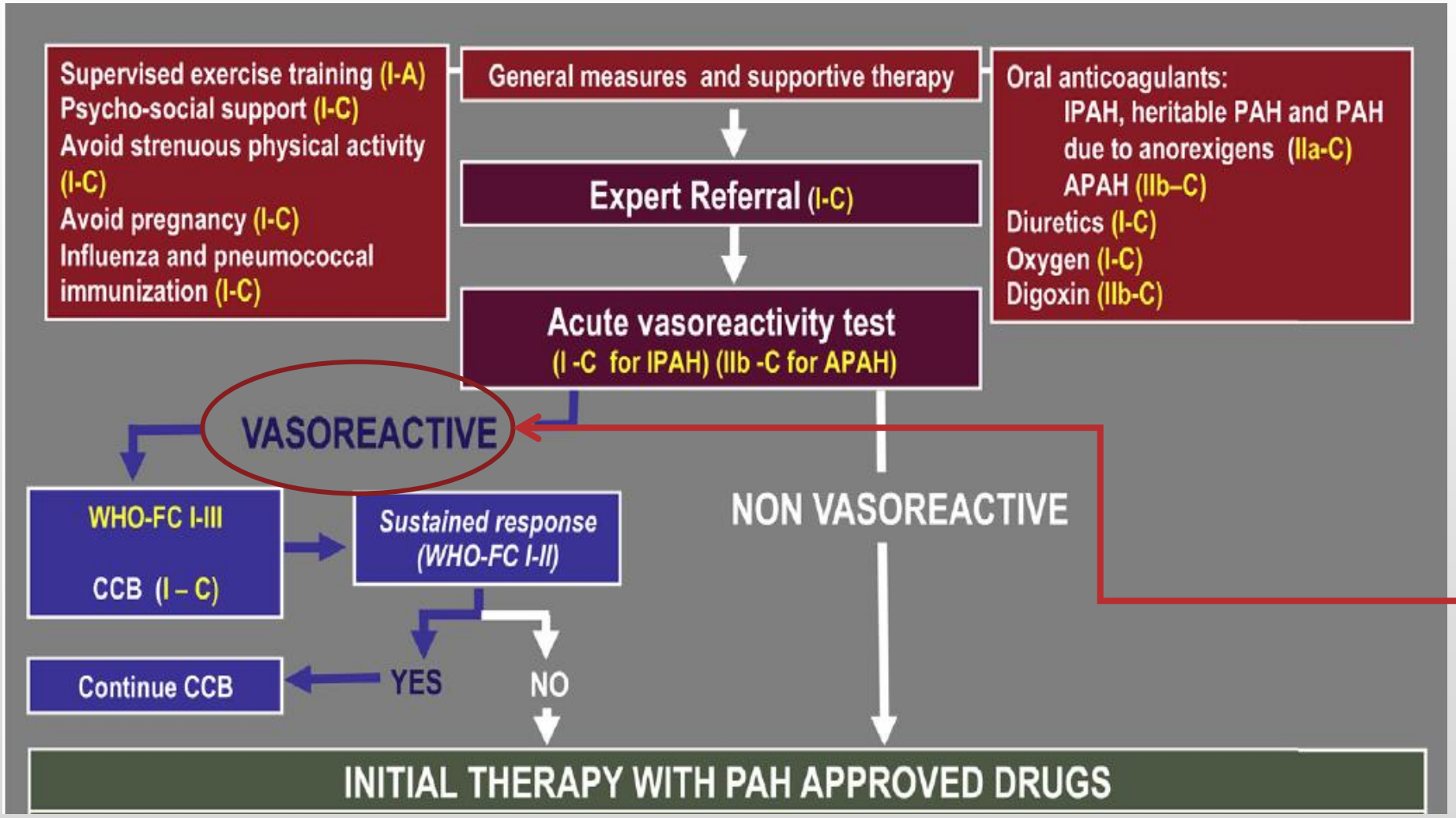
- Traitement Identique
- Plus complexe
- Bénéfice moindre p/p a l'HTAPi

Table 26 Recommendations for pulmonary arterial hypertension associated with connective tissue disease

Recommendations	Class[a]	Level[b]	Ref.[c]
In patients with PAH associated with CTD, the same treatment algorithm as for patients with IPAH is recommended	I	C	46
Resting echocardiography is recommended as a screening test in asymptomatic patients with SSc, followed by annual screening with echocardiography, DLCO and biomarkers	I	C	46
RHC is recommended in all cases of suspected PAH associated with CTD	I	C	46,327
Oral anticoagulation may be considered on an individual basis and in the presence of thrombophilic predisposition	IIb	C	175,339

CTD = connective tissue disease; DLCO = diffusing capacity of the lung for carbon monoxide; IPAH = idiopathic pulmonary arterial hypertension; PAH = pulmonary arterial hypertension; RHC = right heart catheterization; SSc = systemic sclerosis.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Prise en Charge de l'HTAP



Baisse PAPm > 10 mmHg
+ PAPm < 40 mmHg
+ IC stable ou augmenté

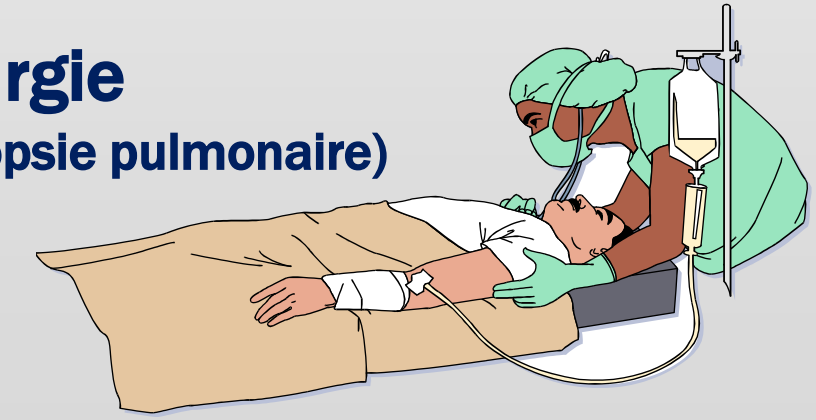
Les Mesures Générales

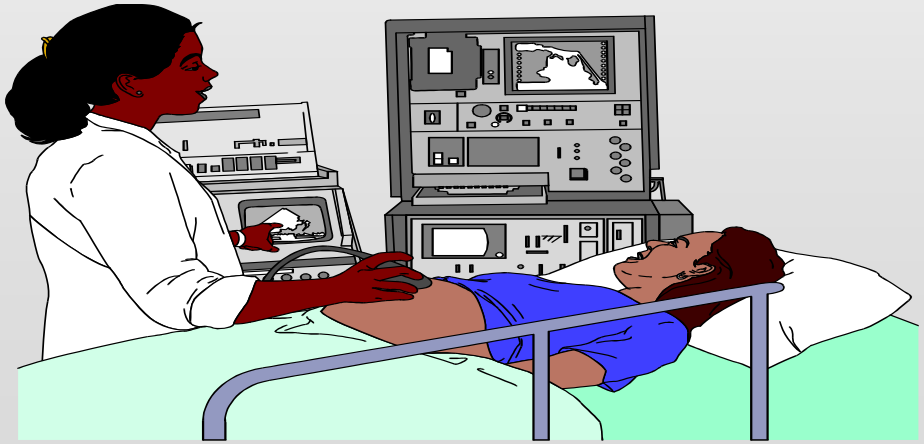
- **Les patients doivent éviter les situations aggravantes**

Activité physique excessive

Chirurgie

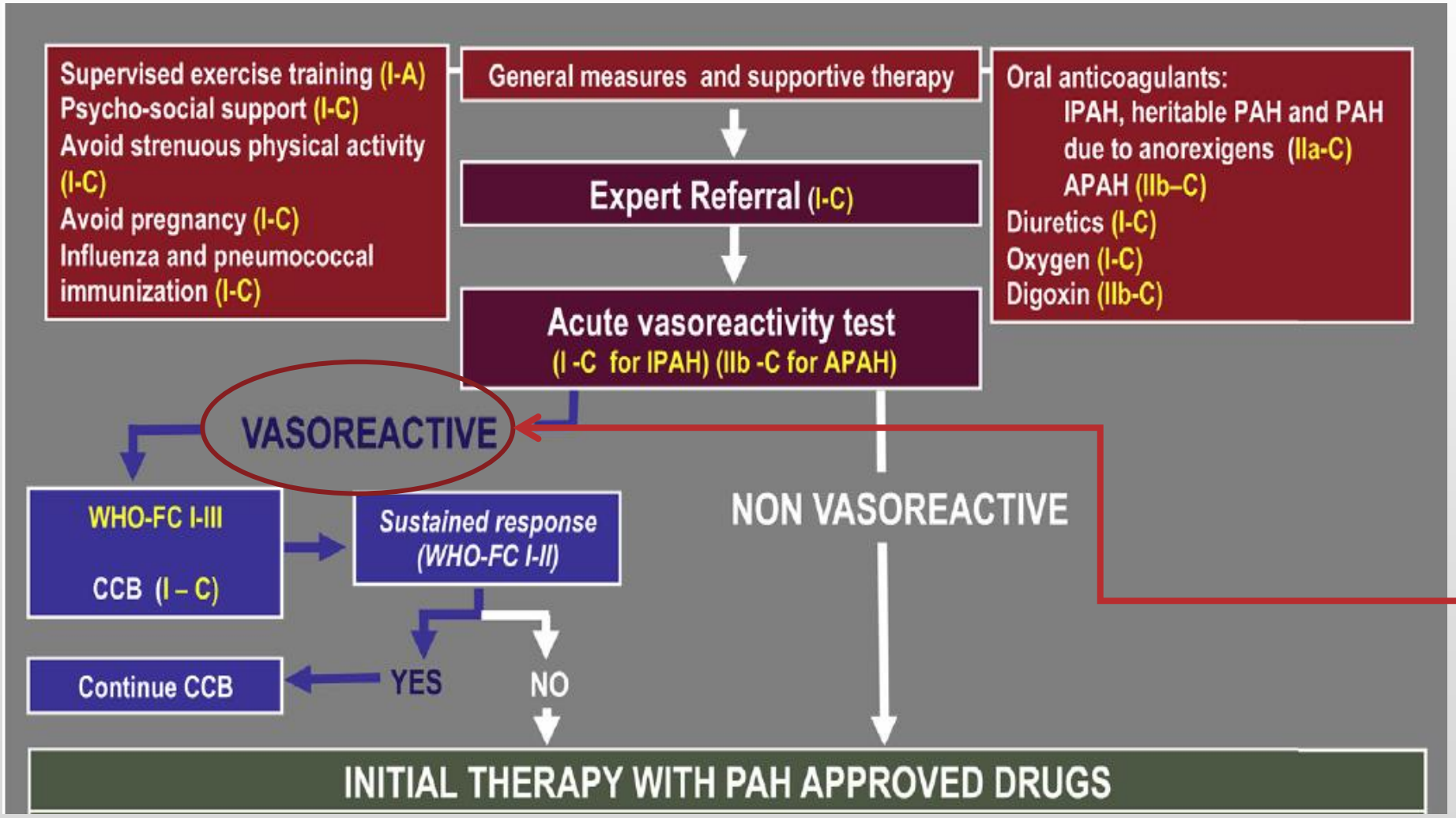
(en particulier : biopsie pulmonaire)





Grossesse

Prise en Charge de l'HTAP



Baisse PAPm > 10 mmHg
+ PAPm < 40 mmHg
+ IC stable ou augmenté

Recommandations:

www.escardio.org/guidelines

Recommendations for general measures

Statement	Class[a]	Level[b]
It is recommended to avoid pregnancy in patients with PAH	I	C
Immunization of PAH patients against influenza and pneumococcal infection is recommended	I	C
Physically deconditioned PAH patients should be considered for supervised exercise rehabilitation	IIa	B
Psychosocial support should be considered in patients with PAH	IIa	C
In-flight O_2 administration should be considered for patients in WHO-FC III and IV and those with arterial blood O_2 pressure consistently less than 8 kPa (60 mmHg)	IIa	C
Epidural anaesthesia instead of general anaesthesia should be utilised, if possible, for elective surgery	IIa	C
Excessive physical activity that leads to distressing symptoms is not recommended in patients with PAH	III	C

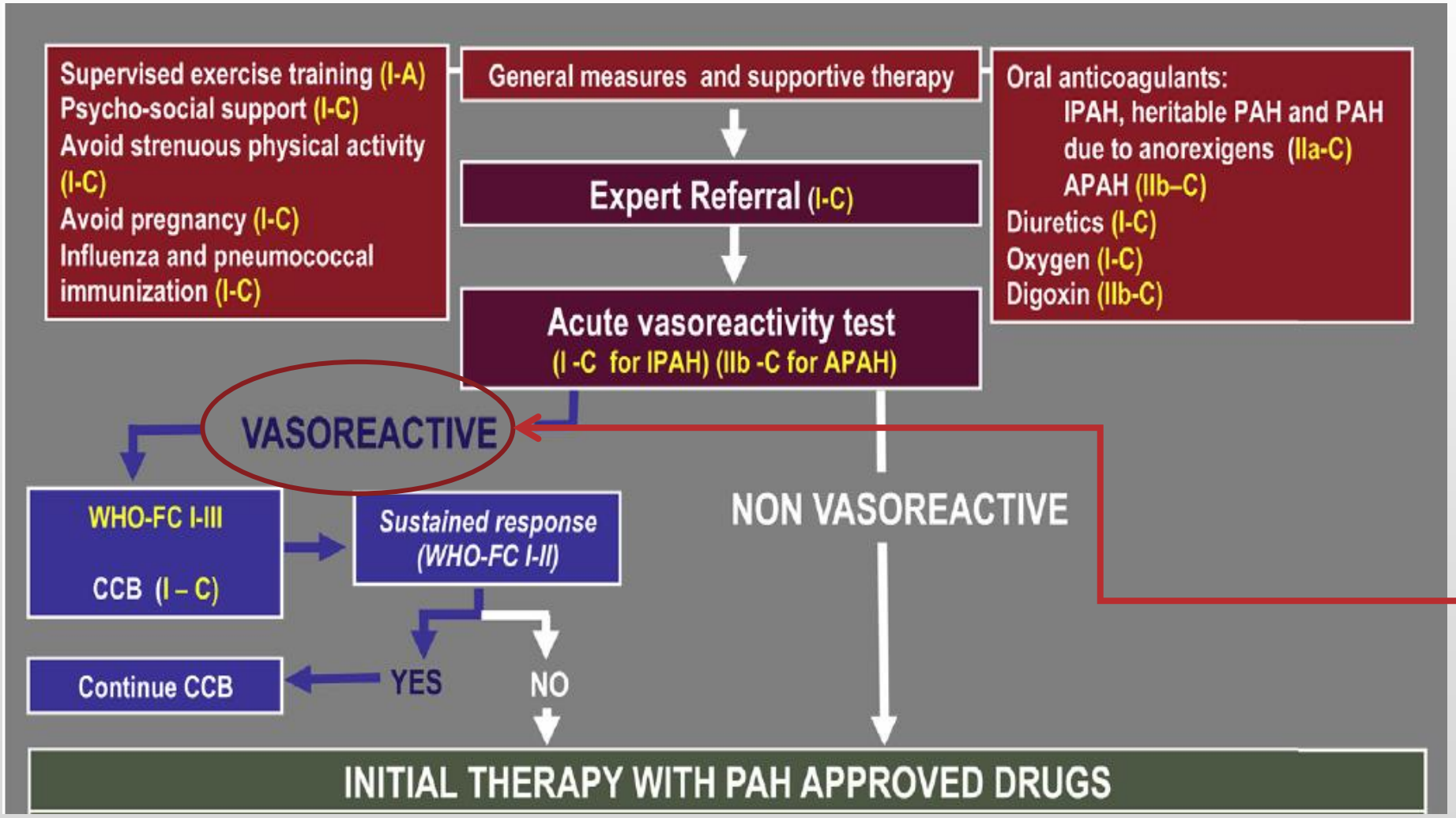
[a]Class of recommendation.
[b]Level of evidence.

Recommendations for supportive therapy

Statement	Class[a]	Level[b]
Diuretic treatment is indicated in PAH patients with signs of RV failure and fluid retention	I	C
Continuous long-term O_2 therapy is indicated in PAH patients when arterial blood O_2 pressure is consistently less than 8 kPa (60 mmHg)[c]	I	C
Oral anticoagulant treatment should be considered in patients with IPAH, heritable PAH, and PAH due to use of anorexigens	IIa	C
Oral anticoagulant treatment may be considered in patients with APAH	IIb	C
Digoxin may be considered in patients with PAH who develop atrial tachyarrhythmias to slow ventricular rate	IIb	C

[a]Class of recommendation.
[b]Level of evidence.
[c]See also recommendations for PAH associated with congenital cardiac shunts (*Table 25*).

Prise en Charge de l'HTAP



Réponse favorable < 1% HTAP/ScS

Baisse PAPm > 10 mmHg
+ PAPm < 40 mmHg
+ IC stable ou augmenté

TRAITEMENT

Table 11 Recommendations for vasoreactivity testing

Recommendations	Class[a]	Level[b]	Ref.[c]
Vasoreactivity testing is indicated only in expert centres	I	C	69
Vasoreactivity testing is recommended in patients with IPAH, HPAH and PAH associated with drugs use to detect patients who can be treated with high doses of a CCB	I	C	84,85
A positive response to vasoreactivity testing is defined as a reduction of mean PAP ≥10 mmHg to reach an absolute value of mean PAP ≤40 mmHg with an increased or unchanged cardiac output	I	C	85,86
Nitric oxide is recommended for performing vasoreactivity testing	I	C	85,86
Intravenous epoprostenol is recommended for performing vasoreactivity testing as an alternative	I	C	85,86
Adenosine should be considered for performing vasoreactivity testing as an alternative	IIa	C	87,88
Inhaled iloprost may be considered for performing vasoreactivity testing as an alternative	IIb	C	89,90
The use of oral or intravenous CCBs in acute vasoreactivity testing is not recommended	III	C	
Vasoreactivity testing to detect patients who can be safely treated with high doses of a CCB is not recommended in patients with PAH other than IPAH, HPAH and PAH associated with drugs use and is not recommended in PH groups 2, 3, 4 and 5	III	C	

CCB = calcium channel blocker; HPAH = heritable pulmonary arterial hypertension; IPAH = idiopathic pulmonary arterial hypertension; PAP = pulmonary arterial pressure; PAH = pulmonary arterial hypertension.

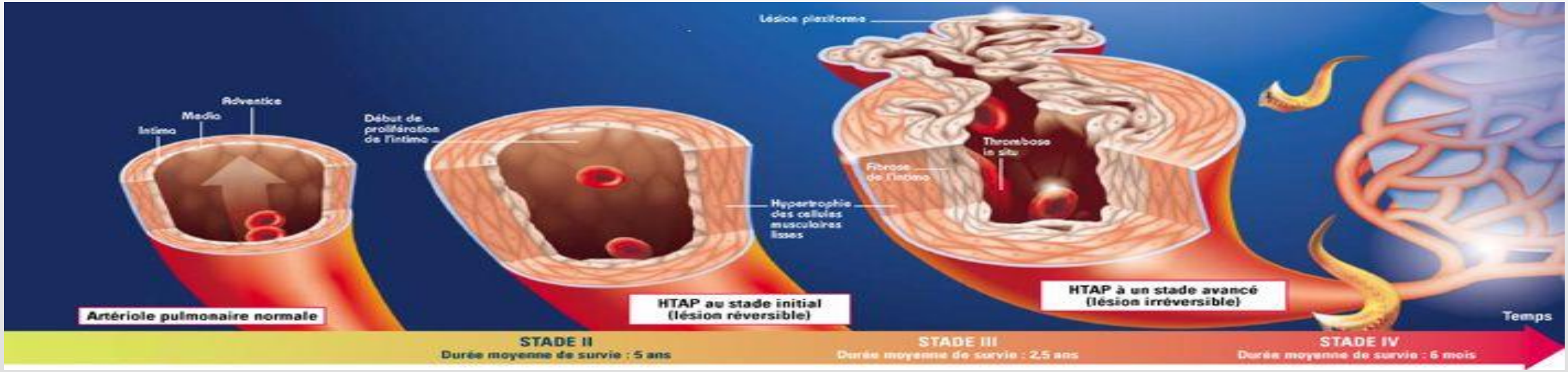
[a]Class of recommendation.

[b]Level of evidence.

[c]Reference(s) supporting recommendations.

Objectifs Thérapeutiques

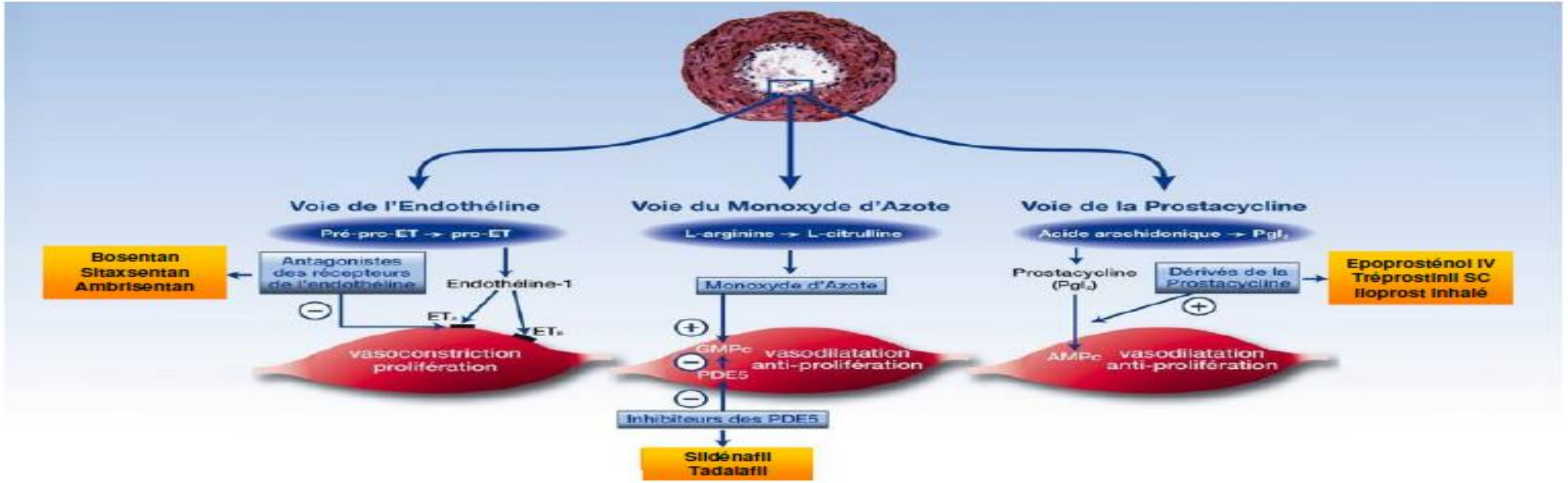
Maladie évolutive +/- rapidement fatale



- Améliorer les symptômes et les performances à l'effort
- Amélioration hémodynamique
- Allonger le délai d'aggravation clinique
- Améliorer la survie

TRT spécifique de l'HTAP

Cibles actuelles du traitement de l'HTAP
Correction de la dysfonction endothéliale



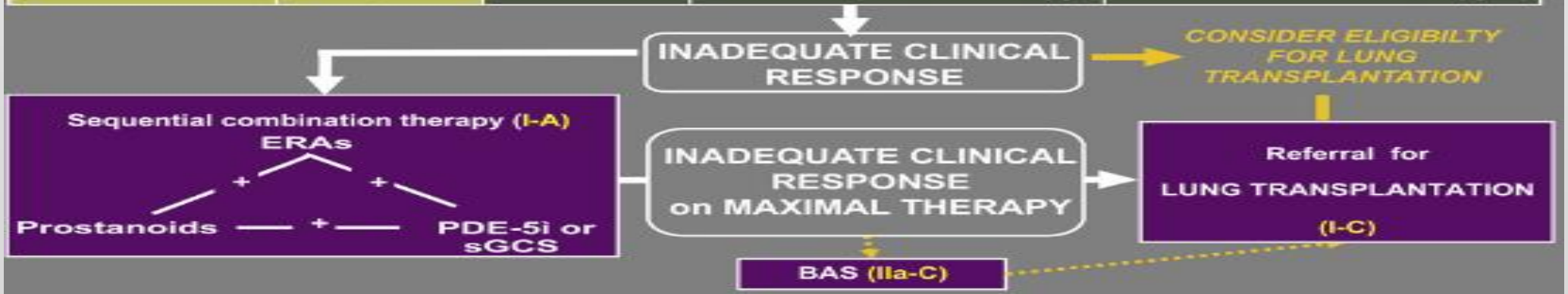
D'après Humbert M *et al.* N Engl J Med 2004

Prise en Charge de l'HTAP

INITIAL THERAPY WITH PAH APPROVED DRUGS

YELLOW: Morbidity and mortality as primary end-point in randomized controlled study or reduction in all-cause mortality (prospectively defined)
*Level of evidence is based on the WHO-FC of the majority of the patients of the studies.
†Approved only: by the FDA (macitentan, riociguat, treprostinil inhaled); in New Zealand (iloprost i.v); in Japan and S.Korea(beraprost).
‡ Positive opinion for approval of the CHMP of EMA

Recommendation	Evidence*	WHO-FC II	WHO-FC III	WHO-FC IV
I	A or B	Ambrisentan Bosentan Macitentan†‡ Riociguat† Sildenafil Tadalafil	Ambrisentan Bosentan Epoprostenol i.v. Iloprost inhaled Macitentan†‡ Riociguat† Sildenafil Tadalafil Treprostinil s.c., inhaled†	Epoprostenol i.v.
IIa	C		Iloprost i.v. † Treprostinil i.v.	Ambrisentan, Bosentan Iloprost inhaled and i.v† Macitentan†‡ Riociguat† Sildenafil, Tadalafil Treprostinil s.c., i.v., Inhaled†
IIb	B		Beraprost†	
	C		Initial Combination Therapy	Initial Combination Therapy



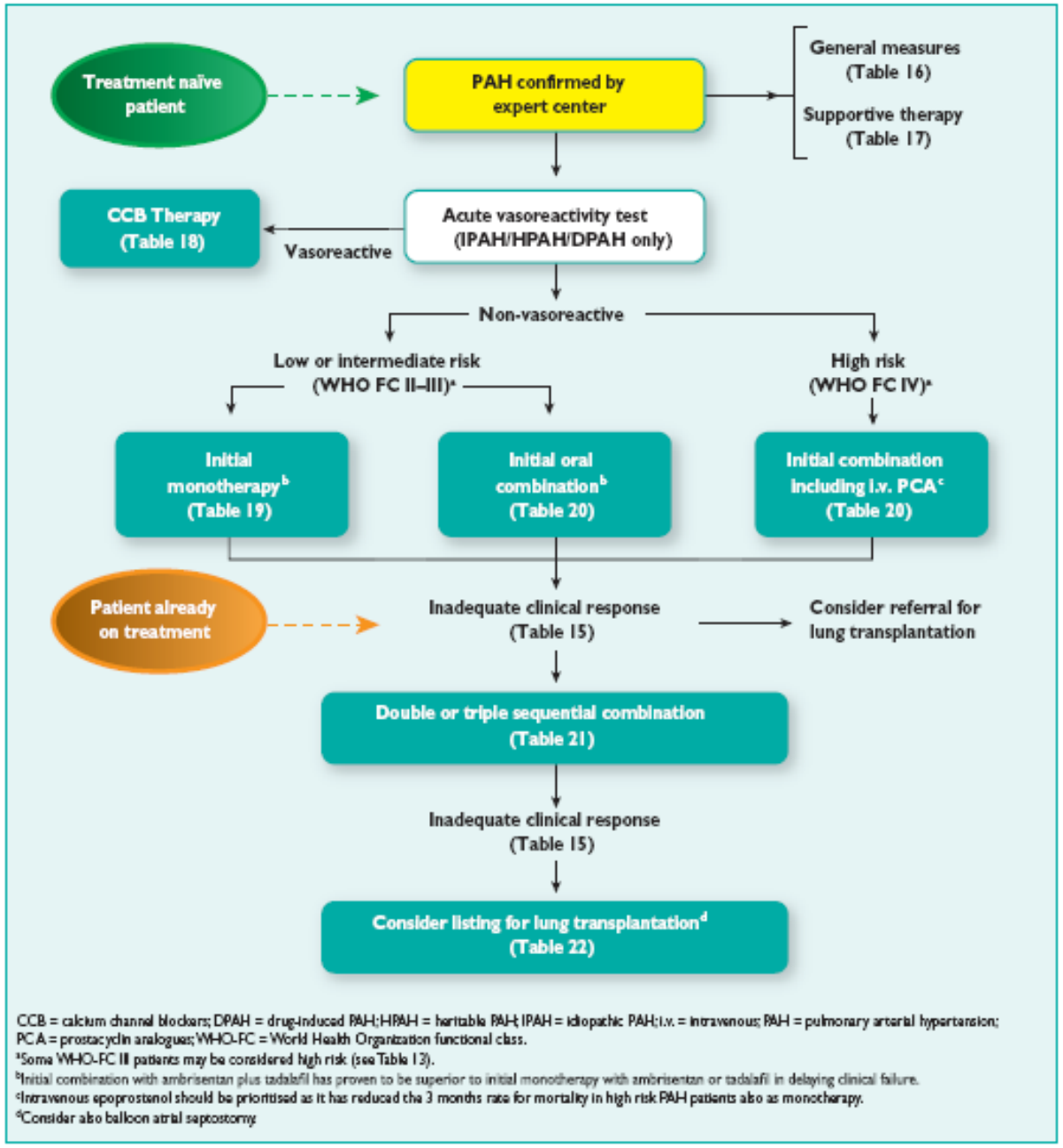


Figure 2 Evidence based treatment algorithm for pulmonary arterial hypertension patients (for group 1 patients only; see description in the text).

Choix du traitement initial dépend de la classe fonctionnelle(II-IV)

Efficacite des différentes molécules HTAP/ScS: bosentan,macitentan,sildenafil,riociguat,treprostinil, epoprostenol

Effets favorables moindre P/P HTAPi
Co-morbidités , microangiopathie…

Approche multidisciplinaire

conclusion

- Sclérodermie systémique est la connectivite qui se complique le plus d'HTAP
- Dépistage précoce (ECHO, DLCO, Biomarqueurs) amélioration du pronostic ++
- Diagnostic différentiel PID, MVO…
- Effficacite du traitement spécifique
- Prise en charge muti-disciplinaire

MERCI