

Cardiology Update® 2013

Screening and diagnosing PH – still a challenge

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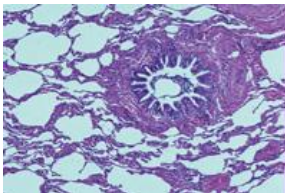
Haemodynamic definition of PH

Definition	Characteristics	Clinical group(s)
PH	Mean PAP $\geq$ 25 mmHg	All
Pre-capillary PH	Mean PAP $\geq$ 25 mmHg PWP $\leq$ 15 mmHg CO normal or reduced	1. PAH 3. PH due to lung disease 4. CTEPH 5. PH with unclear and/or multifactorial mechanism
Post-capillary PH	Mean PAP $\geq$ 25 mmHg PWP $>$ 15 mmHg CO normal or reduced	2. PH due to LHD
Passive	TPG $\leq$ 12 mmHg	
Reactive (out of proportion)	TPG $>$ 12mmHg	

CO: cardiac output

PAP: pulmonary arterial pressure

PCWP: pulmonary capillary wedge pressure



Pulmonary Hypertension

Diagnostic Classification Dana Point 2008

1. Pulmonary Arterial Hypertension

- Idiopathic PAH
- Heritable PAH
 - BMPR-2 mutations
 - Alk-1/endoglin
 - undefined
- Drug/toxin induced
- Related to:
 - Connective tissue diseases
 - schistosomiasis
 - HIV
 - Portal hypertension
 - systemic - to - pulmonary shunts
 - Hemolysis (SCD, thalassemia, PNH, spherocytosis, stomatocytosis)
- PPHN

1'. PVOD-PCH

2. PH with Left Heart Disease

- systolic
- diastolic
- valvular

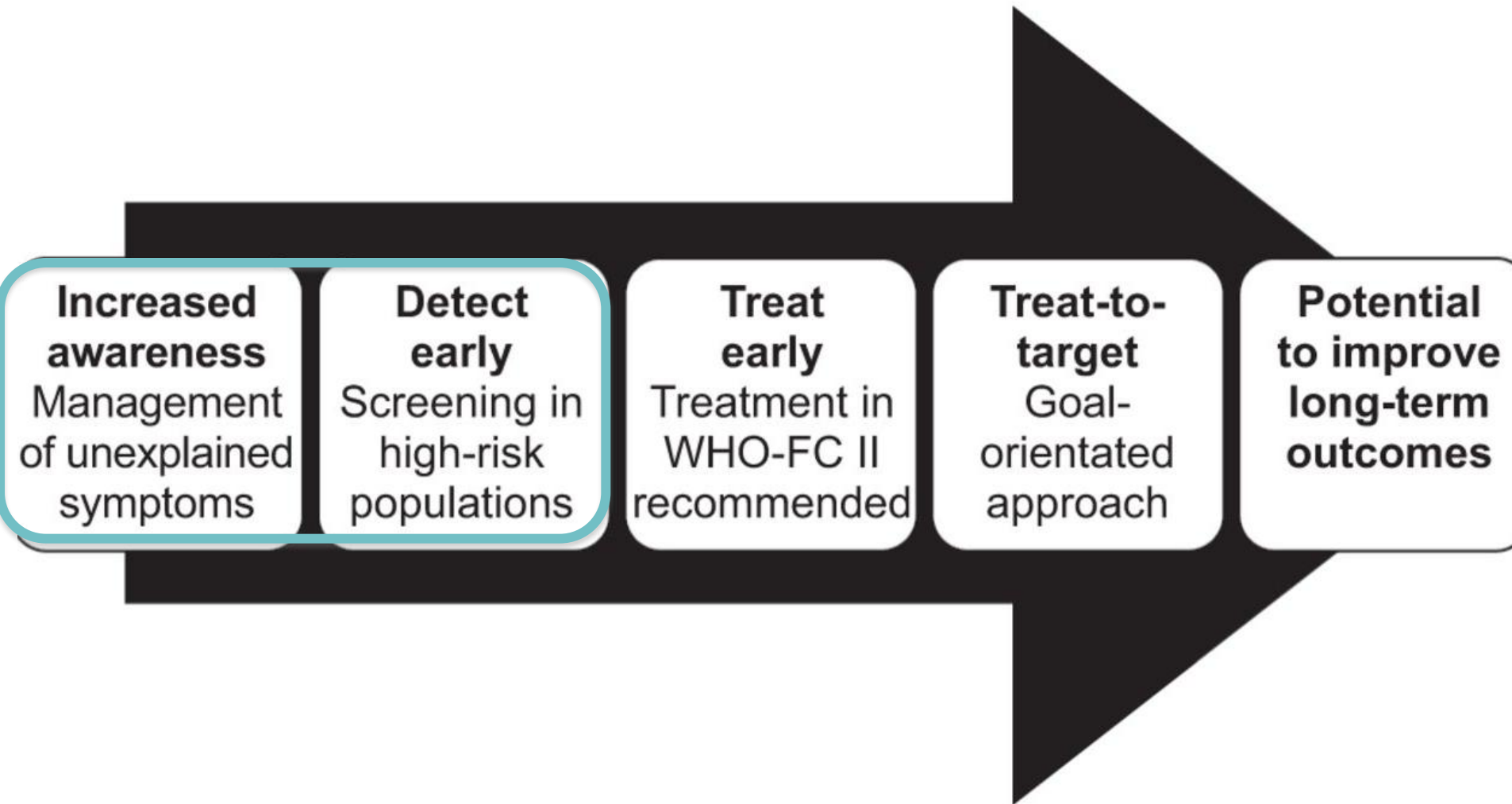
3. PH with Lung Diseases/Hypoxemia

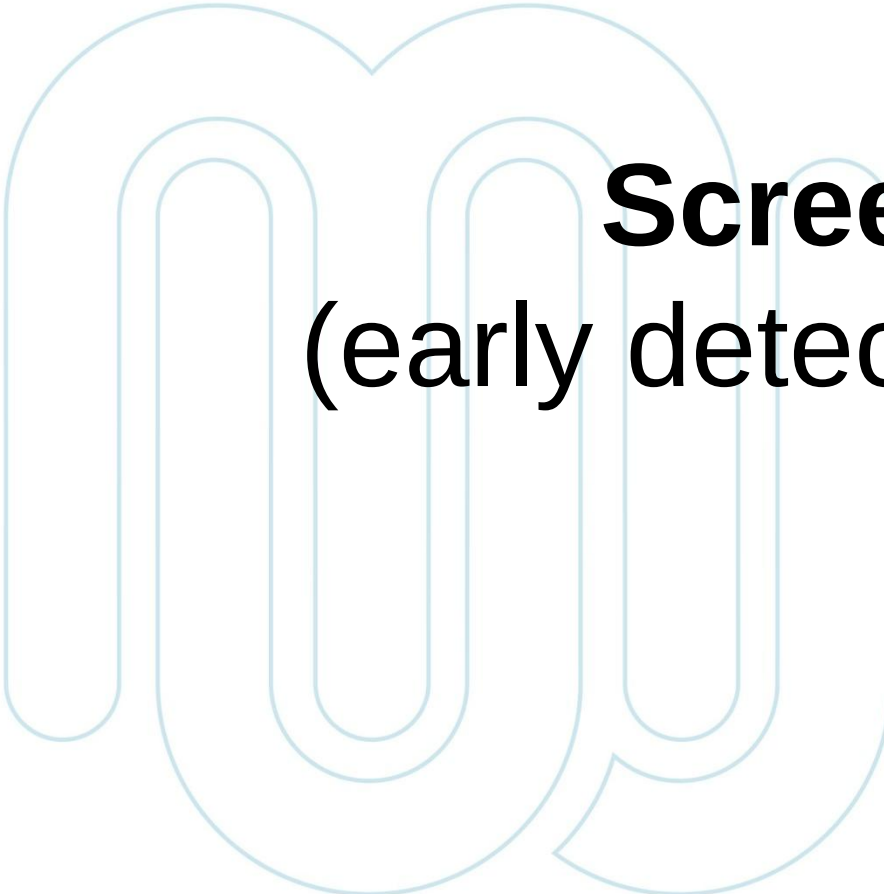
- COPD
- Interstitial Lung Diseases
- Sleep-disordered breathing
- Hypoxia

4. CTEPH

5. Unclear or multifactorial mechanisms

- Hematologic
- Systemic
- Metabolic
- CHD other than systemic-to-pulmonary shunt
- others





Screening (early detection of PH)

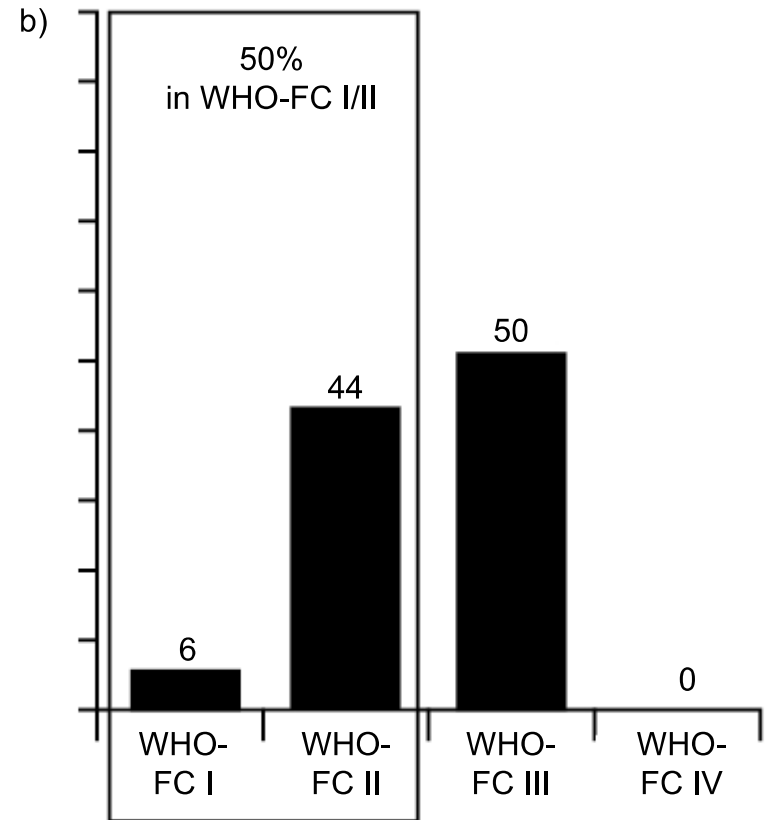
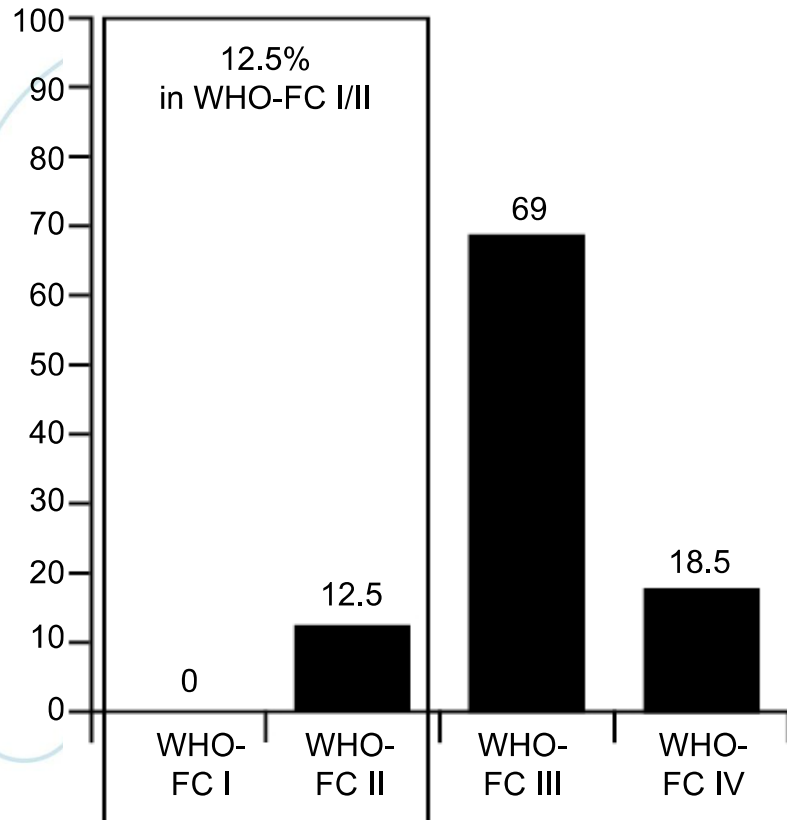
Who to screen?-1

- Prevalence of PAH in the general population
15–50 cases per million (0.0015–0.0050%)
- Prevalence of PAH in at risk populations
 - CHD: 4–15%
 - Systemic sclerosis: 8–10%
 - Portal hypertension: 0.5–10%
 - HIV: 0.5%
 - Sickle cell disease: 2%
 - BMPR2 mutation carriers: 20%
 - Prior appetite suppressant use (9.5%)

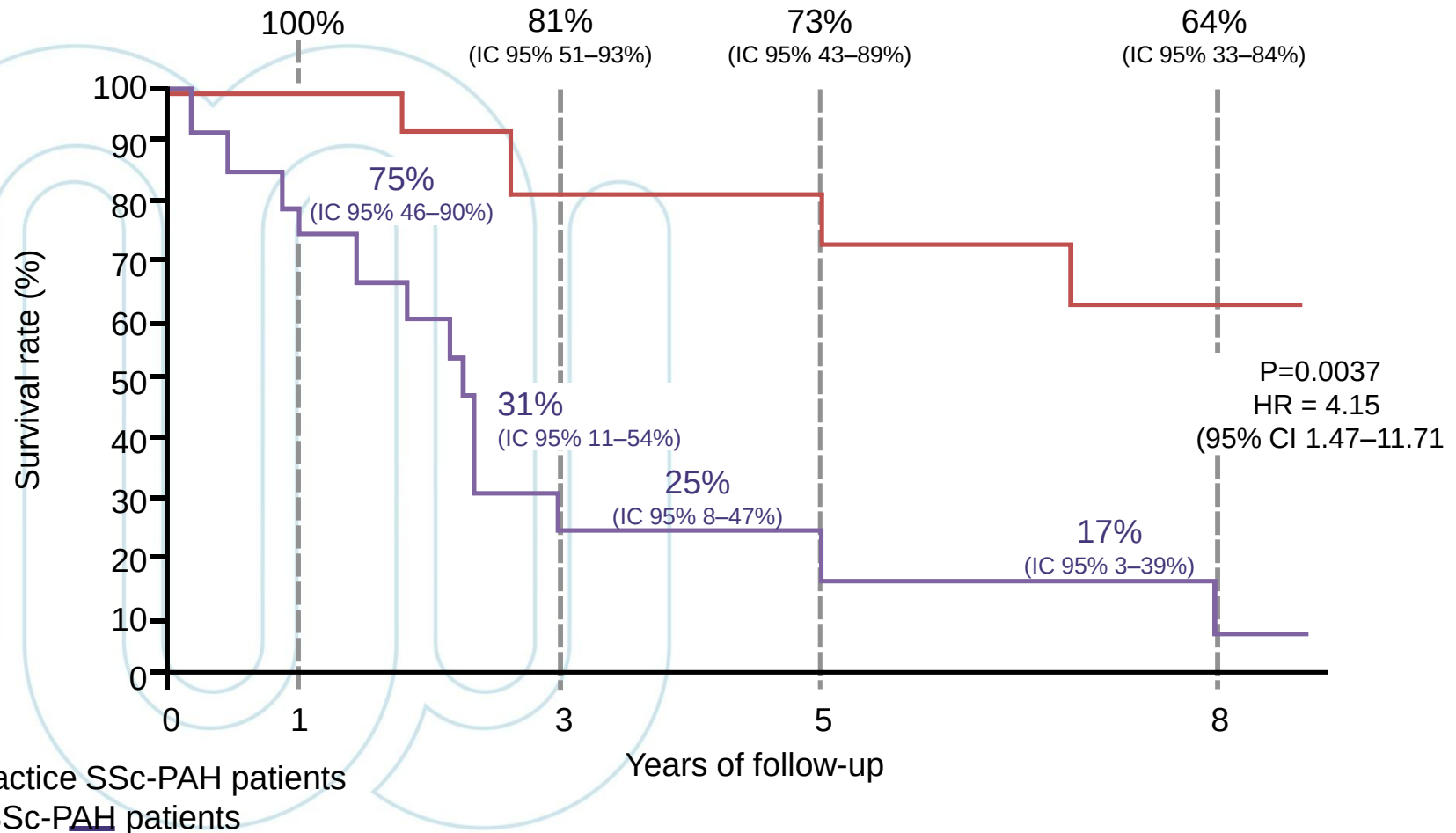
Who to screen?-2

- Prevalence of CTEPH in the general population
3–30 cases per million (0.0003–0.0030%)
- Prevalence of CTEPH in at risk populations
after major symptomatic PE: 0.1–9.1%
after splenectomy: ~2.0%
in carriers of APL/LAK: ~2.0%

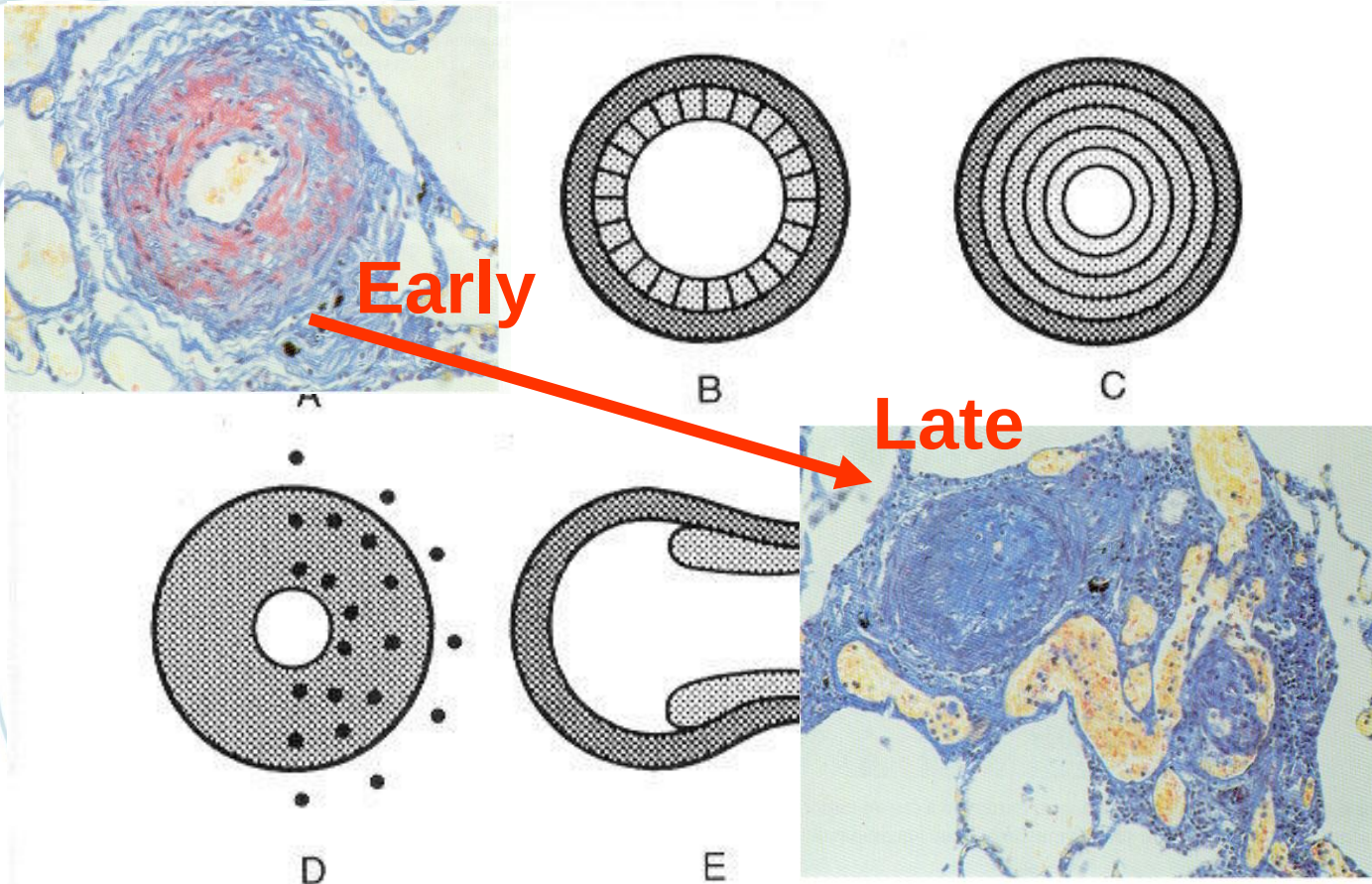
Screened patients are different from diagnosed patients



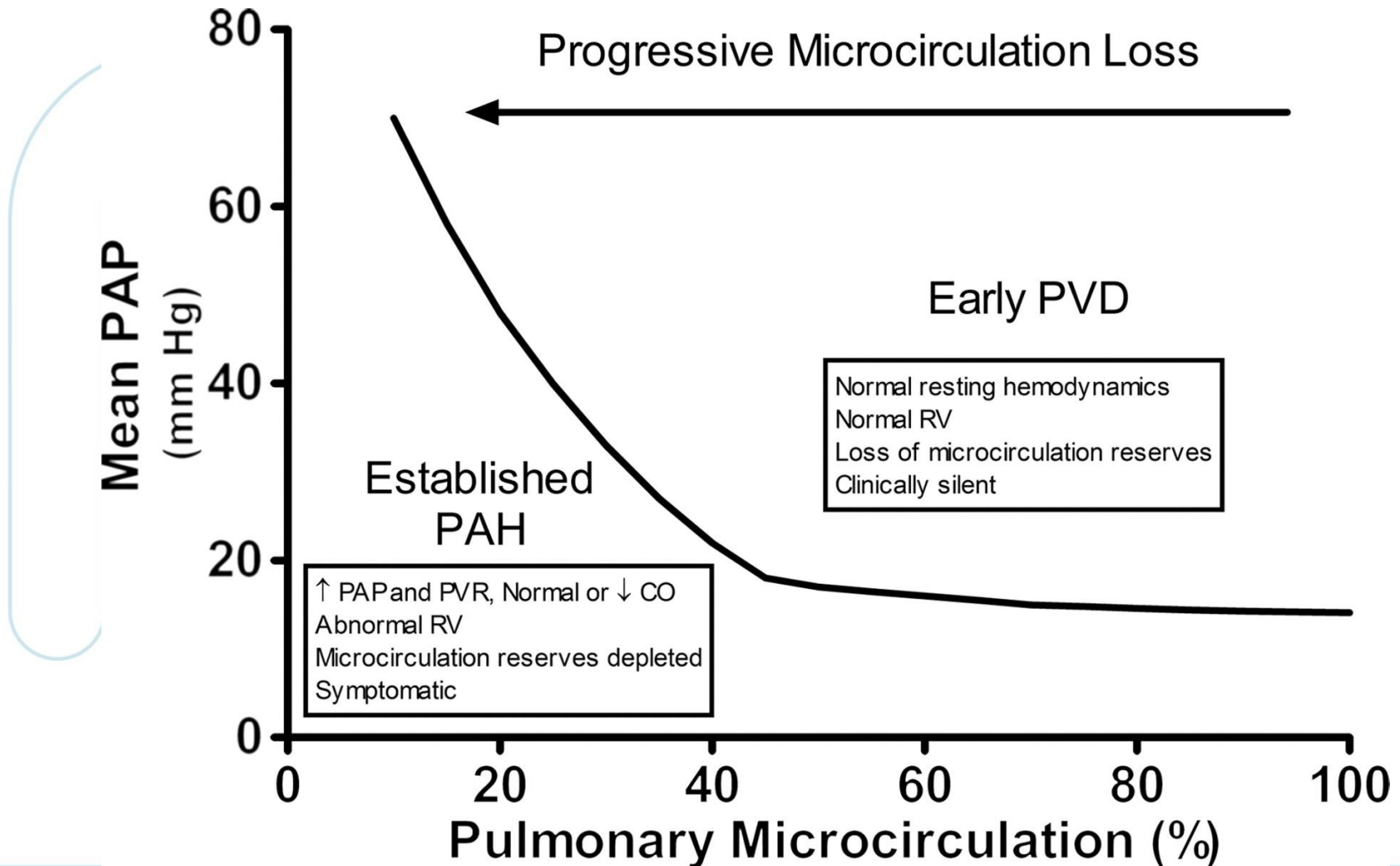
Early identification confers a benefit



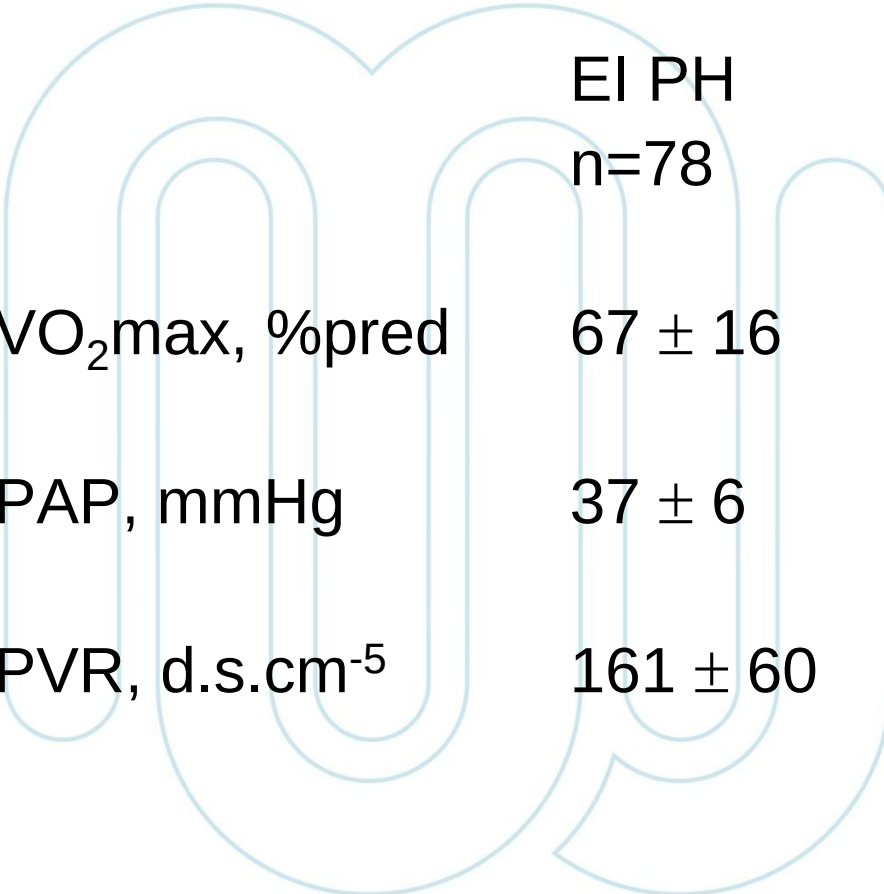
Histopathology of PAH (PPH): plexogenic arteriopathy



Pulmonary artery pressure rise is a late event

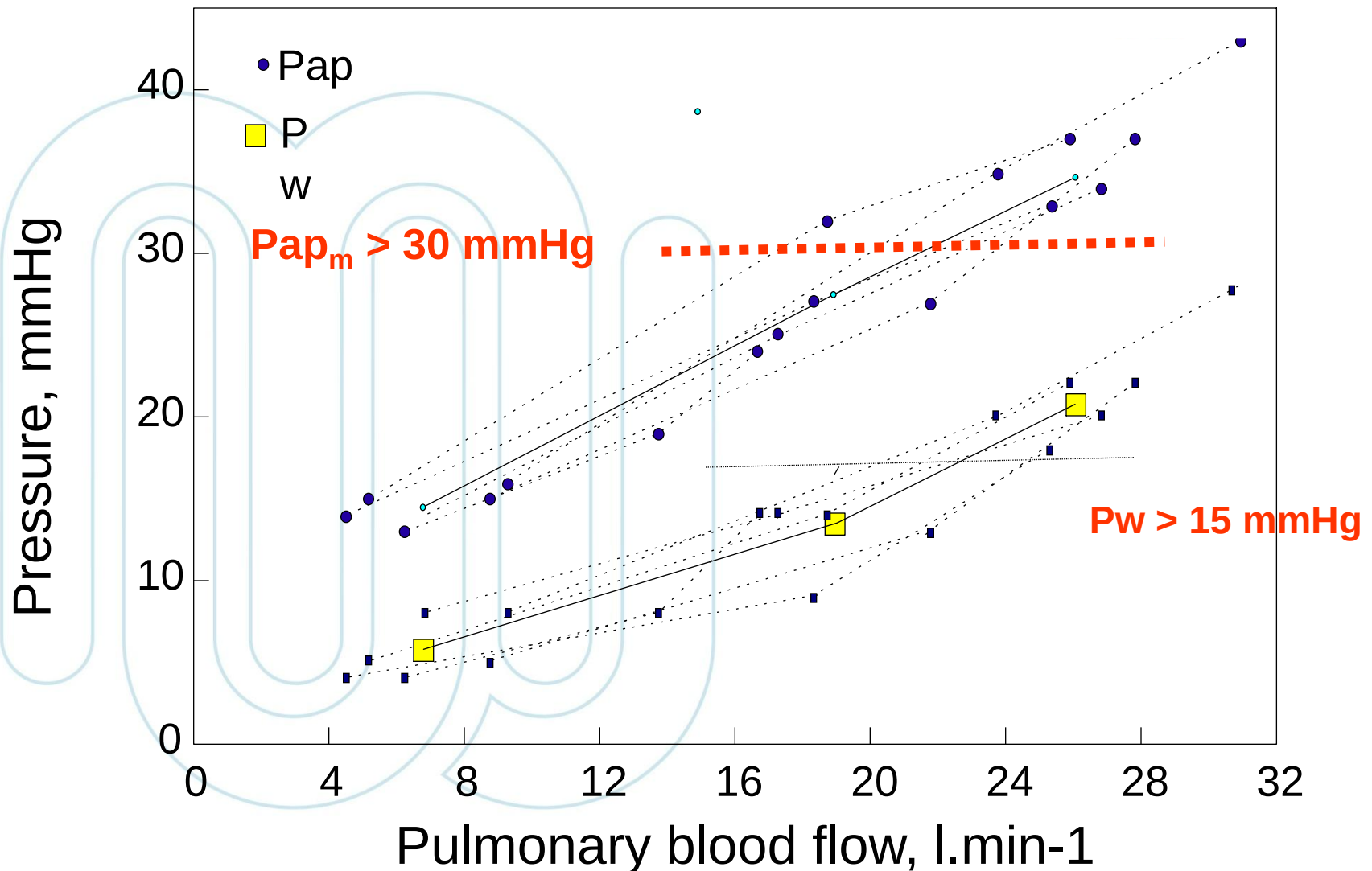


Exercise-induced pulmonary hypertension

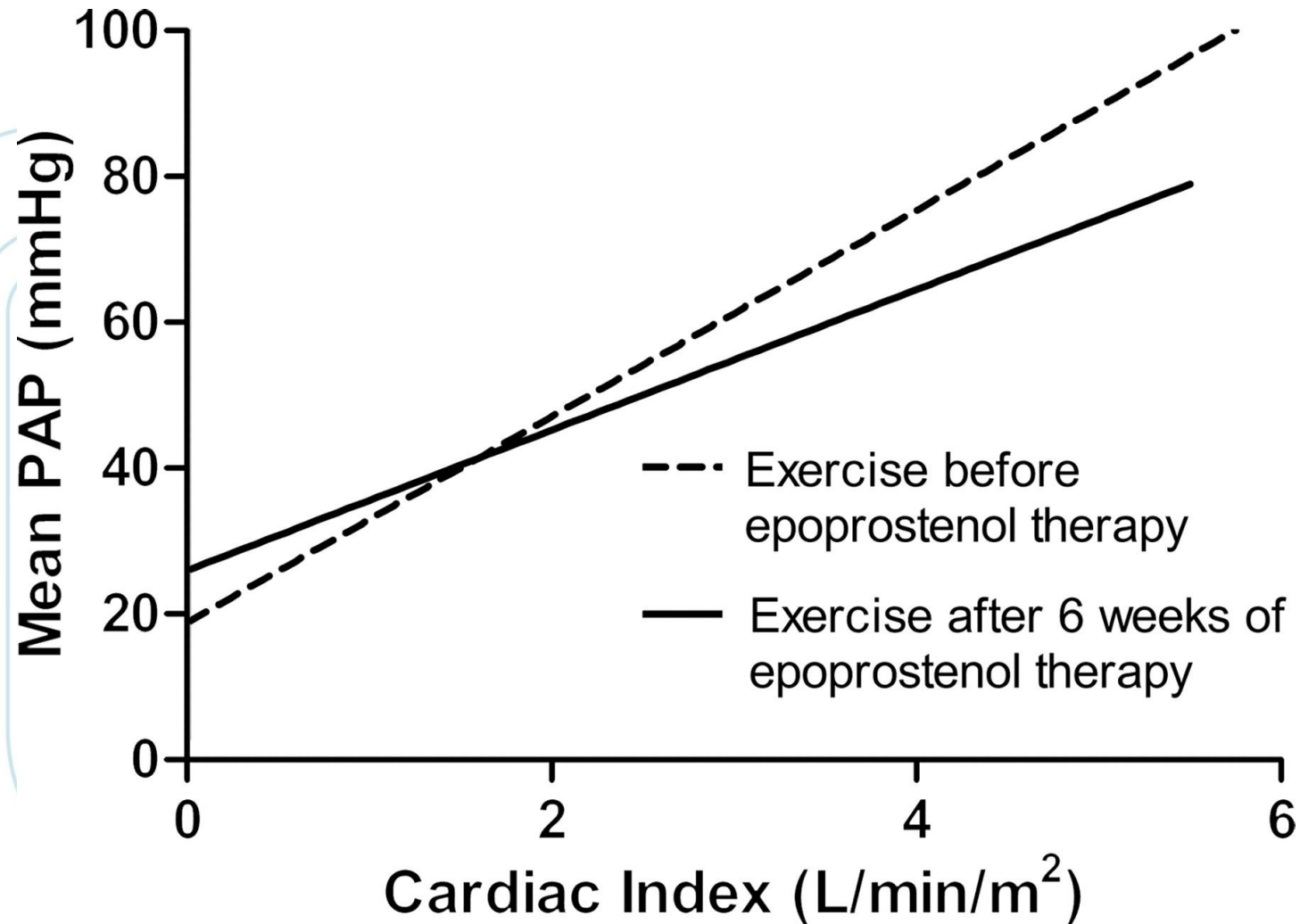


	EI PH n=78	PAH n=15	normals n=16
VO ₂ max, %pred	67 ± 16	56 ± 20	92 ± 14
PAP, mmHg	37 ± 6	48 ± 11	27 ± 4
PVR, d.s.cm ⁻⁵	161 ± 60	294 ± 258	62 ± 20

Levels of exercise in normal subjects



Exercise haemodynamics in PAH



Ideal screening test

- Sensitive
- Specific
- Non-invasive
- Widely available
- Inexpensive
- Able to detect disease at an early stage

Established screening tools

- Resting echocardiography
- Pulmonary Function test
- Biomarkers
- V/Q

Neural networks
CART

Arbitrary criteria for detecting the presence of PH based on tricuspid regurgitation peak velocity and Doppler-calculated PA systolic pressure at rest*

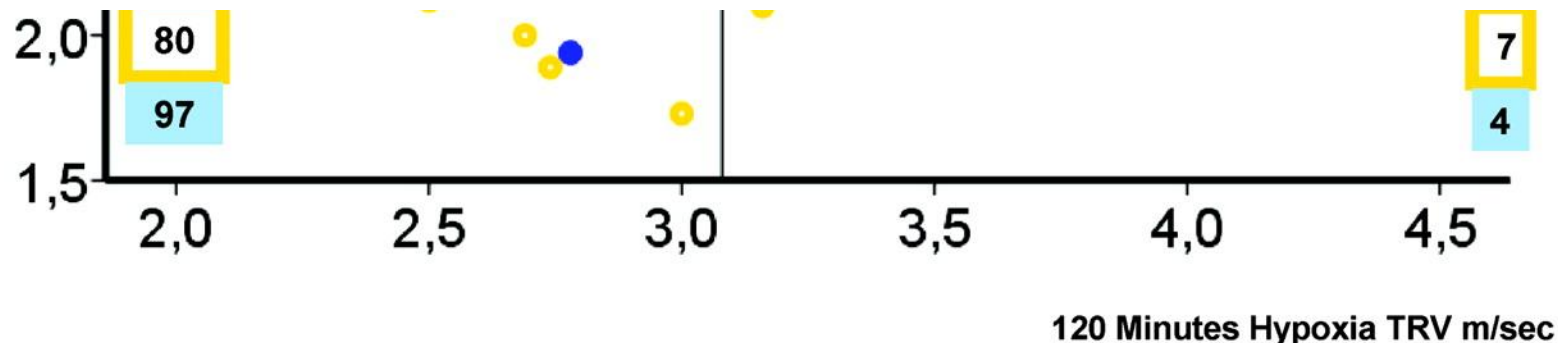
- **Echocardiographic diagnosis: PH unlikely**
 - Tricuspid regurgitation velocity ≤ 2.8 m/sec, PA systolic pressure ≤ 36 mmHg and no additional echocardiographic variables suggestive of PH.
- **Echocardiographic diagnosis: PH possible**
 - Tricuspid regurgitation velocity ≤ 2.8 m/sec, PA systolic pressure ≤ 36 mmHg but presence of additional echocardiographic variables suggestive of PH.
 - Tricuspid regurgitation velocity 2.9-3.4 m/sec, PA systolic pressure 37-50 mmHg with/without additional echocardiographic variables suggestive of PH.
- **Echocardiographic diagnosis: PH likely**
 - Tricuspid regurgitation velocity >3.4 m/sec, PA systolic pressure > 50 mmHg with/without additional echocardiographic variables suggestive of PH.
- **Exercise Doppler echocardiography is not recommended for screening of PH**

* Assuming a normal right atrial pressure of 5 mmHg and on additional echocardiographic variables suggestive of PH

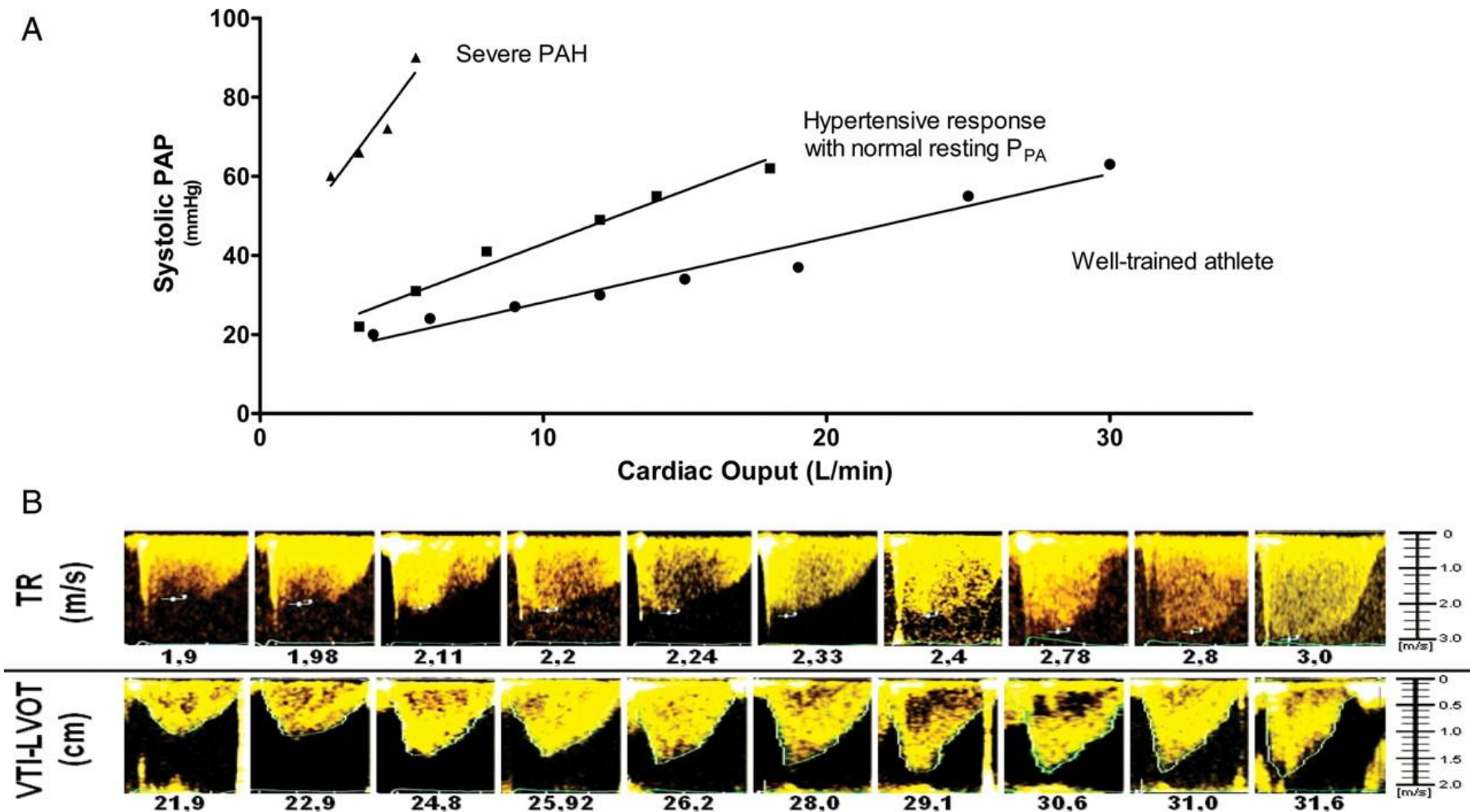
Maximum TRV values during hypoxia vs exercise in relatives (yellow) and control subjects (blue)

Exercise

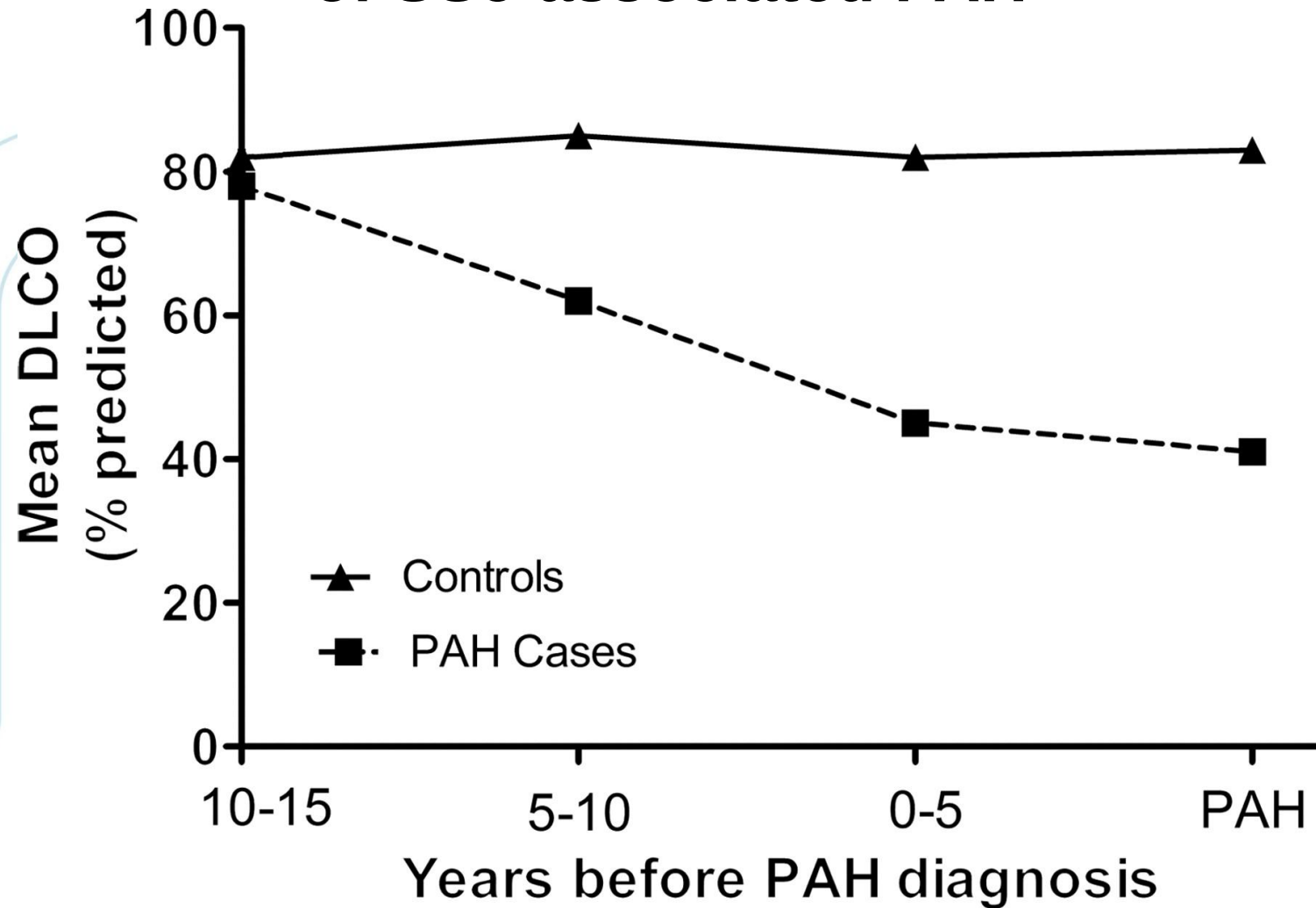
During exercise, 32% of relatives but only 10% of controls had TRV values >3.08 m/s; and during hypoxia, 26% of relatives had TRV values >3.08 m/s compared with 10% of controls.

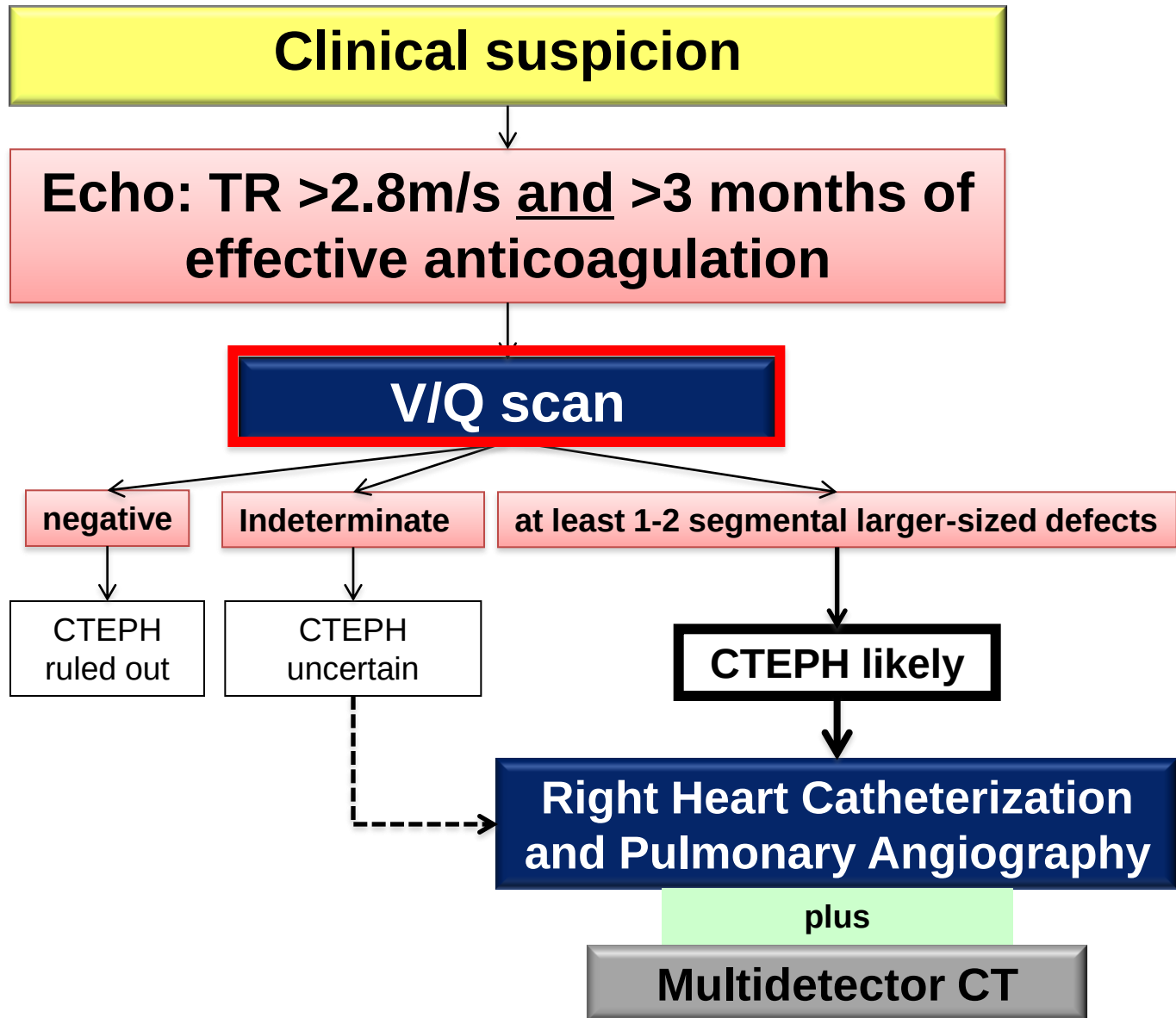


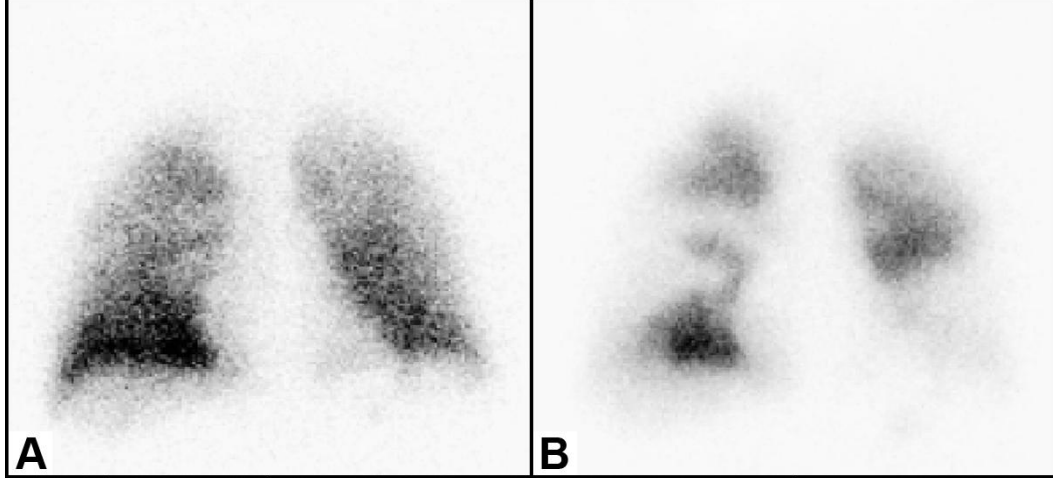
Exercise echocardiography data represented as multipoint pressure–flow relationship

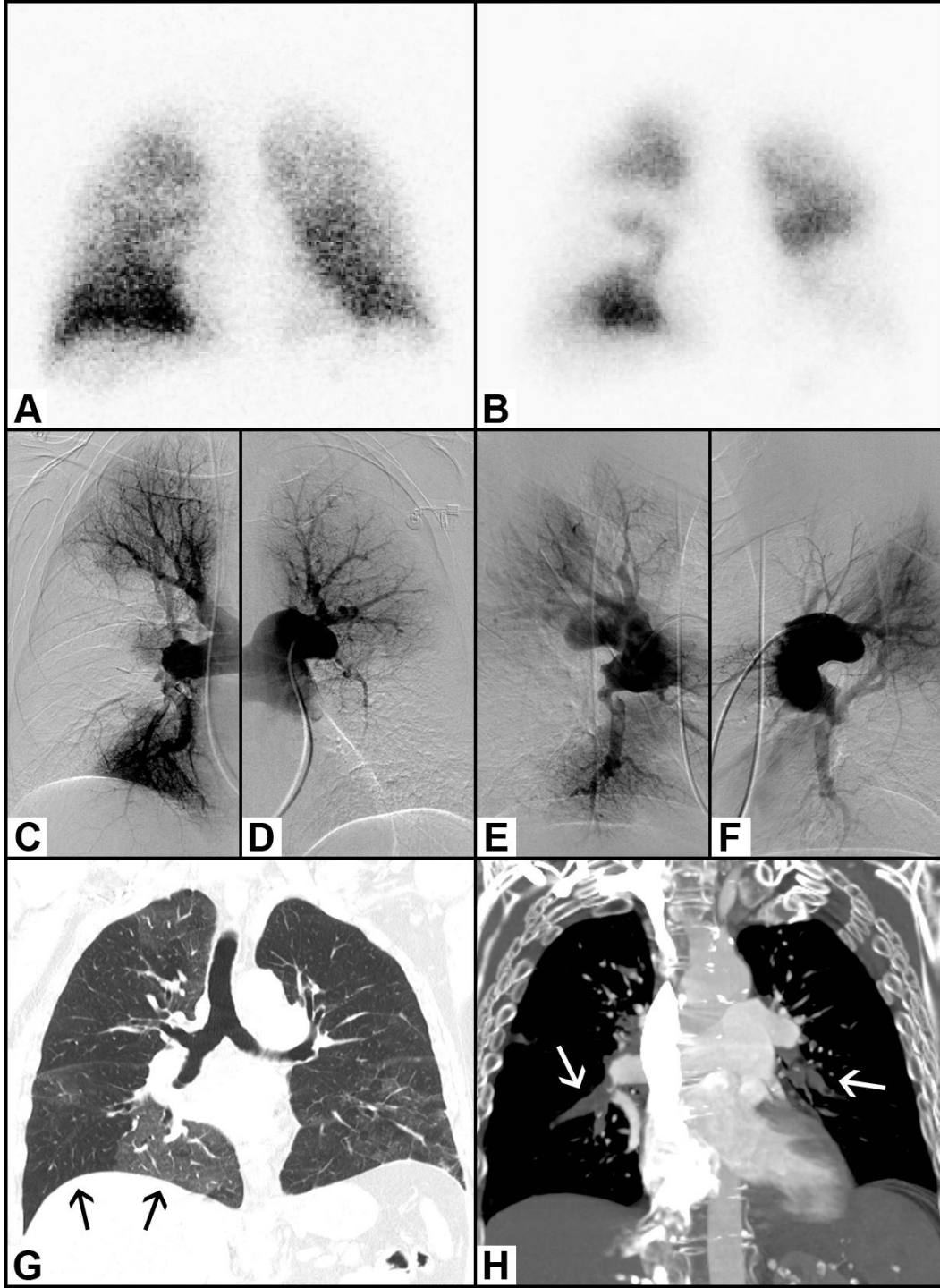


The relationship between DLCO and the development of SSc-associated PAH

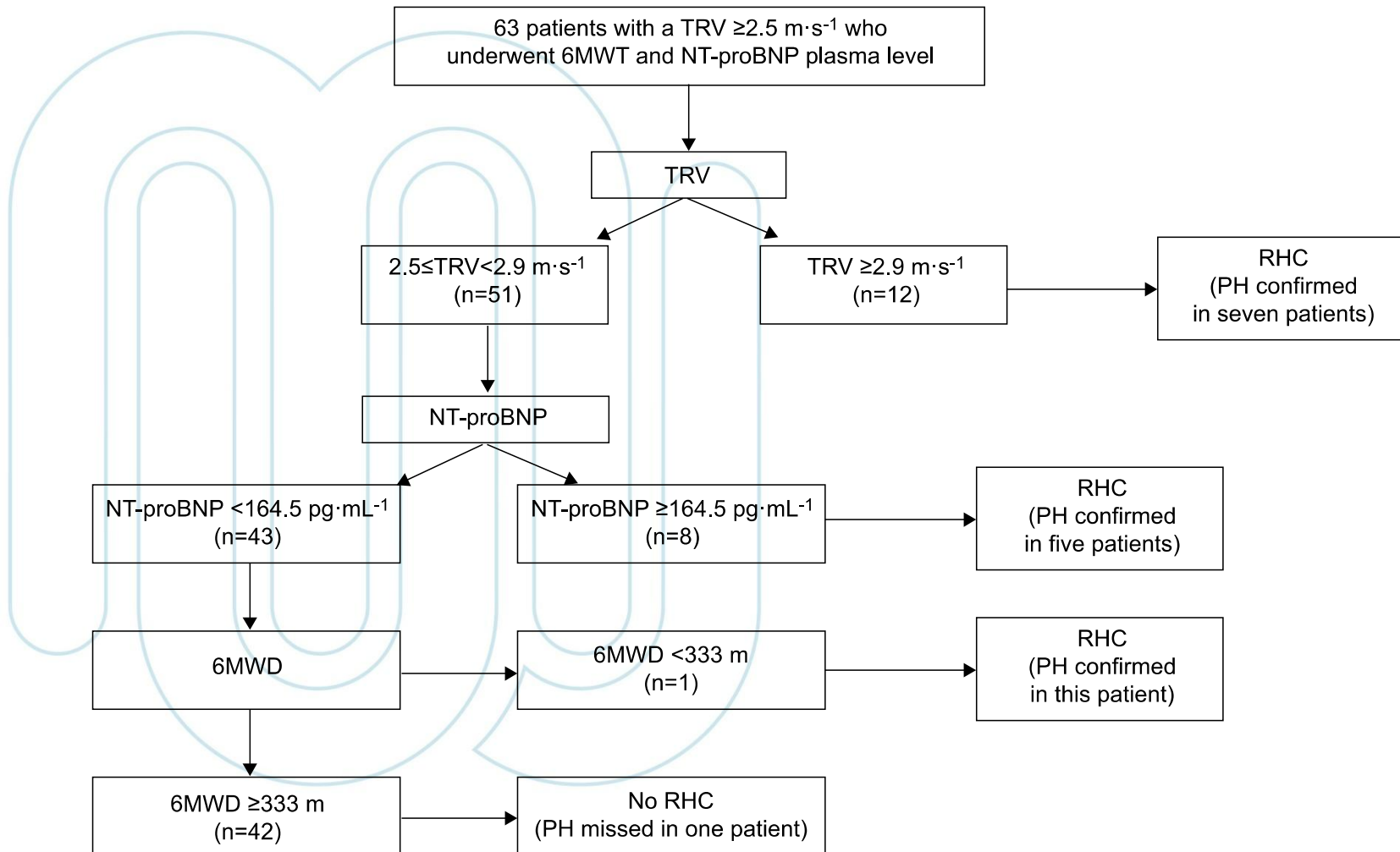




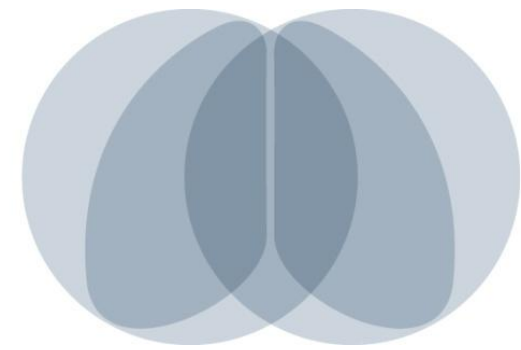




Classification and Regression Tree



DETECT



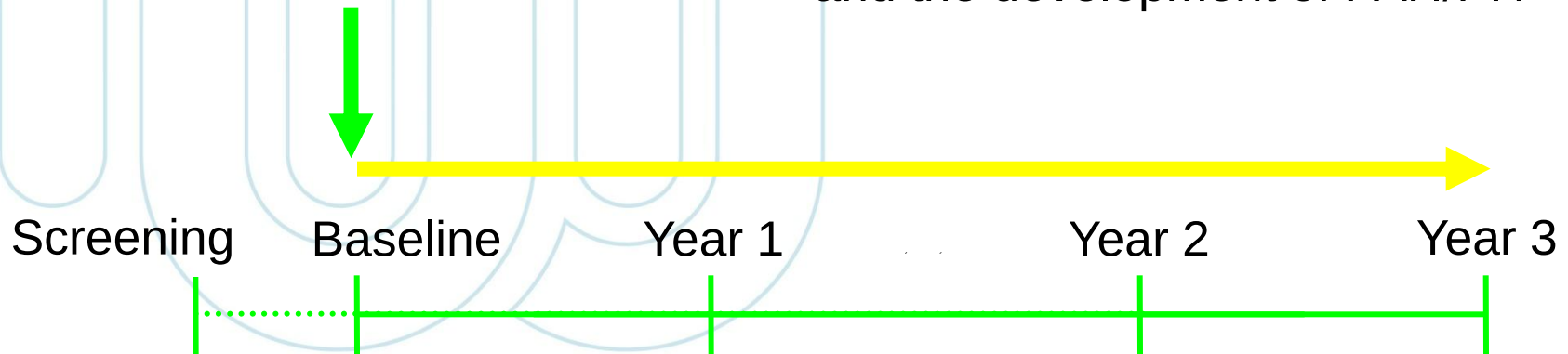
DETECTION of PAH in SSc

Cross-sectional phase

- To evaluate different screening tests (individually and combined) vs RHC for PAH (primary objective) and PH in SSc patients

Longitudinal cohort (follow-up)

- To evaluate the incidence of PAH and PH in a cohort of SSc patients
- To determine the association of potential prognostic or risk factors (eg, biomarkers, 6MWD, PFTs etc) and the development of PAH/PH



Performance of an optimal screening tool (96% sensitivity, 80% specificity)

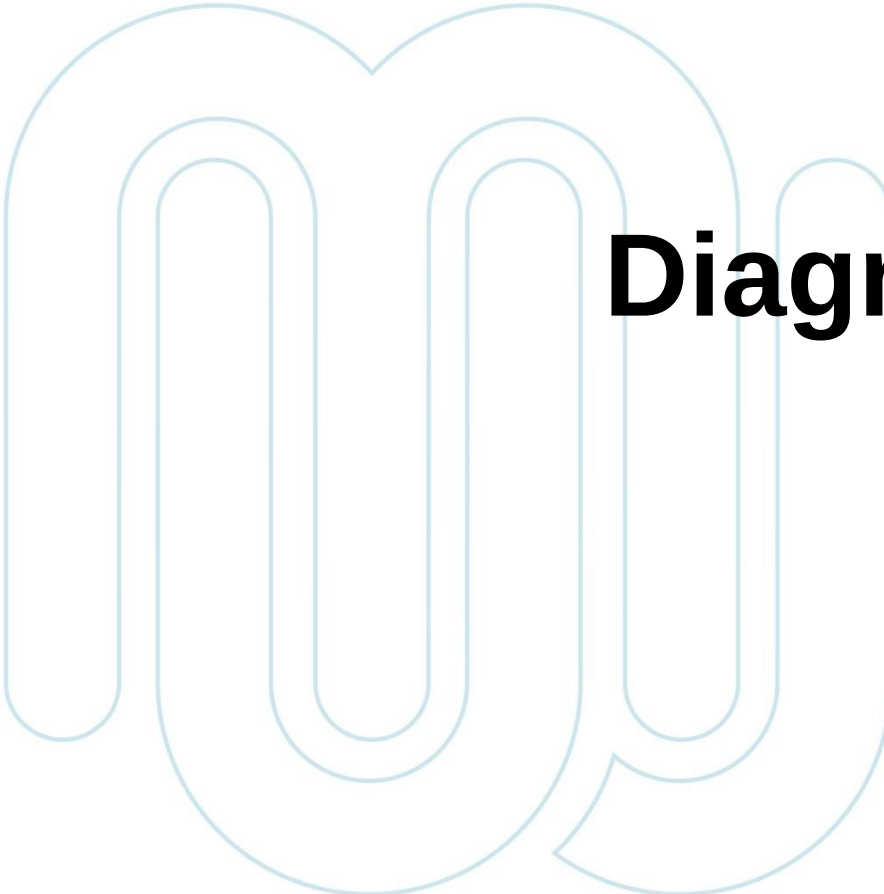


To detect one case of PAH-SCD: number needed to cath: 2.5

To detect one case of PAH-SLE: number needed to cath: 41

To detect one case of iPAH: number needed to cath: 101

To detect one case of CTEPH: number needed to cath: 50-500



Diagnosis

Diagnostic algorithm

Symptoms / signs / history suggestive of PH

Non invasive assessment compatible with PH?

Search for
Other causes
And/or
Re-check

Yes

No

Consider common causes of PAH

Group 2
Left heart disease?

Group 3
Lung diseases and/or hypoxia

History, Symptoms,
Signs ECG, Chest X Ray
TTE,PHT,HRCT

Group 2 or 3: diagnosis confirmed

Yes
PH 'proportionate' to severity

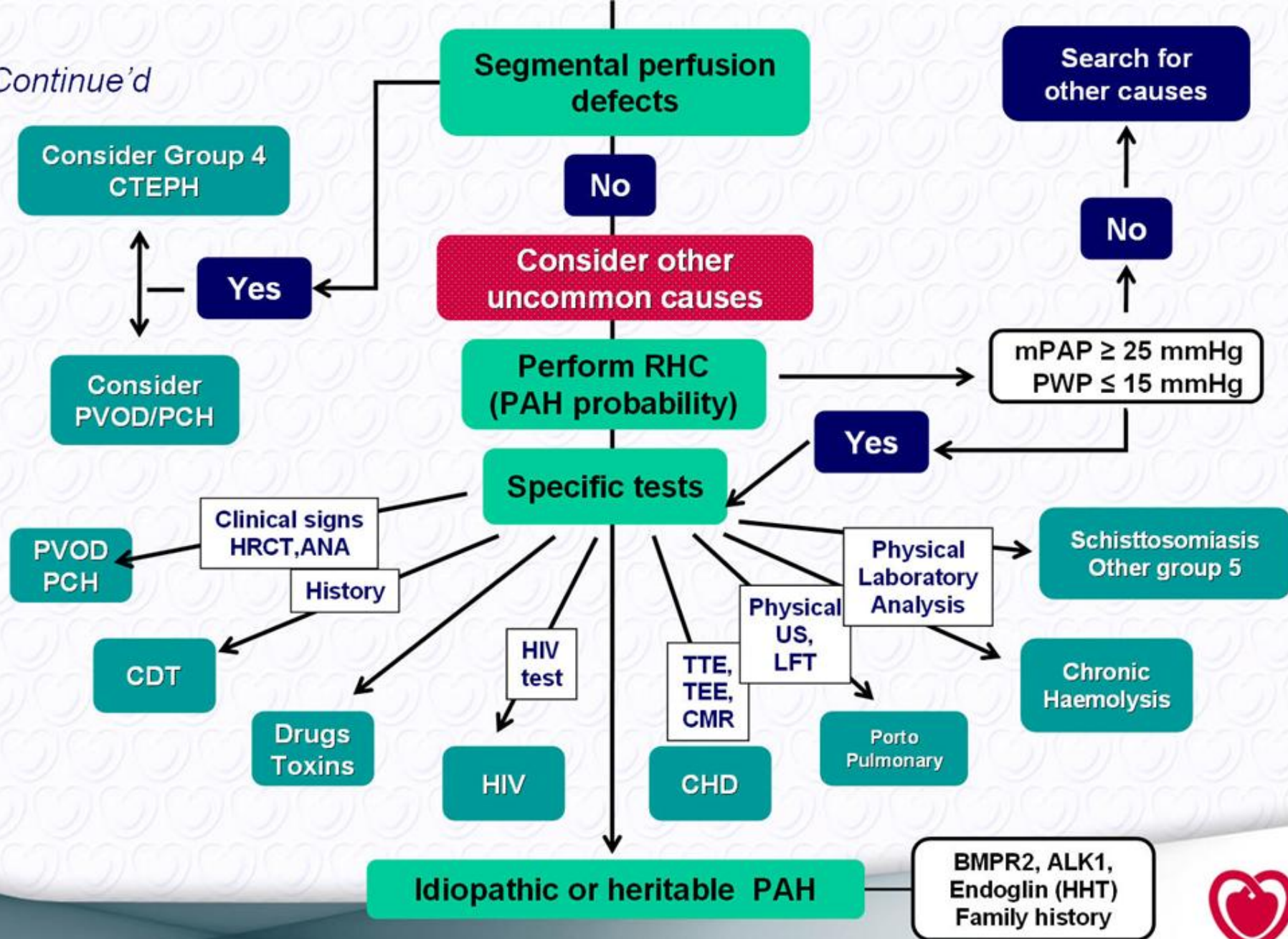
No

Yes 'out of proportion'
PH

Treat underlying disease
& check for progression

Perform V/Q scan

Continue'd



- L-S, 73-year old female
- SA: married, 1 daughter, retired,
- 162cm, 84kg
- Medical Hx: surgically corrected large ASD 1993
ablation of atrial fibrillation, pacemaker
implantation for Sick-Sinus-Syndrome, systemic
hypertension, hyperlipidemia, coronary disease
- Current medication: Phenprocoumon, Nicorandil
10mg bid, Bisoprolol 5mg, Allopurinol 100mg,
Escitalopram 10mg

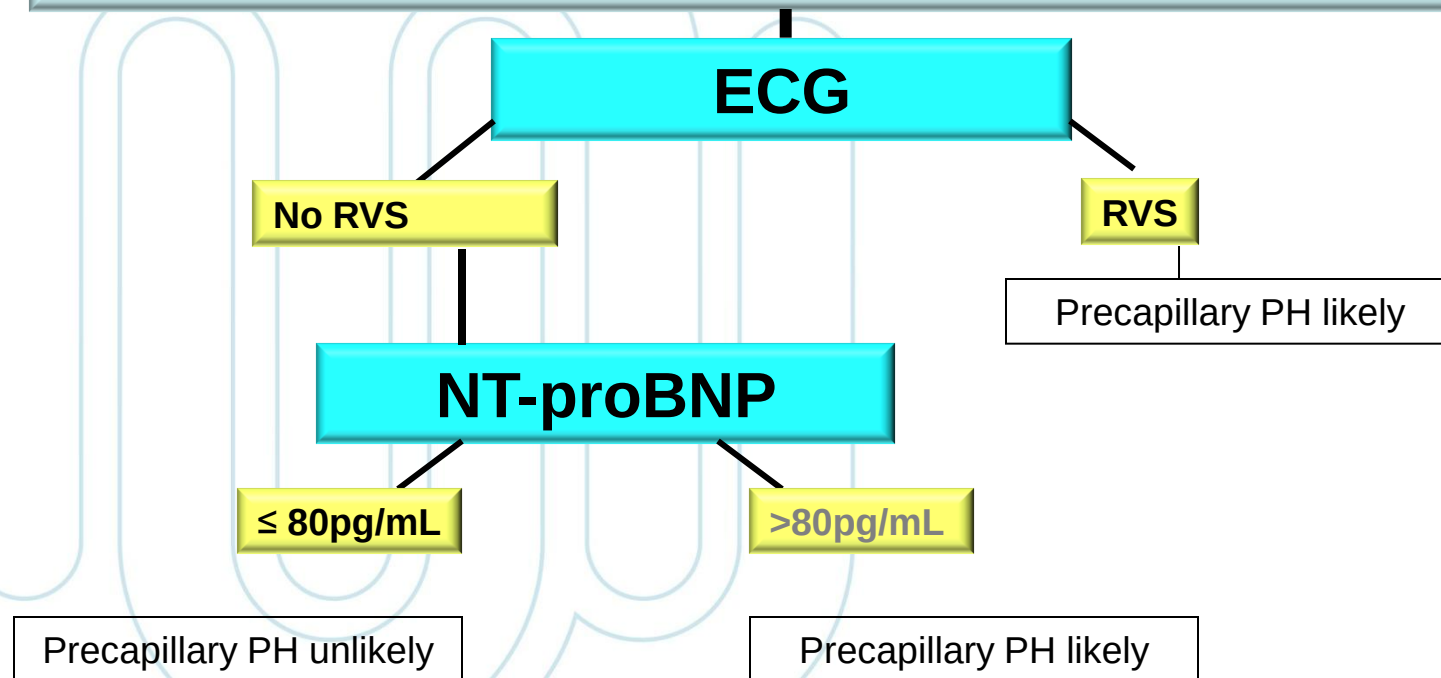
- NYHA III
- NT-BNP 3097pg/mL
- Echo sPAP 95mmHg

Hemodynamic parameters

	precapillary PH?
RAP, mm Hg	32
PAPs/d-m, mmHg	110/44-73
PCWP, mmHg	40
TPG, mmHg	33
CO, L.min	6,1
CI, L.min.m ²	2,5
PVR, WU (dyn.s.cm ⁻⁵)	5,9 (472)
SvO ₂ , %	53

Diagnosis tree based on echo, ECG and NT-BNP

Patients with a clinical suspicion of precapillary PH
and TRV>2.8m/s



Factors increasing the likelihood of HF with preserved EF (diastolic HF)

Clinical features

Age >65
Elevated systolic blood pressure
Elevated pulse pressure
Obesity, metabolic syndrome
Hypertension
Coronary artery disease
Diabetes mellitus
Atrial fibrillation

Echocardiography

Left atrial enlargement
Concentric remodelling of the LV (relative wall thickness >0.45)
LV hypertrophy
Presence of echocardiographic indicators of elevated LV filling pressure^{64,226}

Interim evaluation (after echocardiography)

Symptomatic response to diuretics
Exaggerated increase in systolic blood pressure with exercise
Re-evaluation of chest radiograph consistent with heart failure²²⁶

- L-S, 73-year old female
- SA: married, 1 daughter, retired,
- 162cm, 84kg
- Medical Hx: surgically corrected large ASD 1993 ablation of atrial fibrillation, pacemaker implantation for Sick-Sinus-Syndrome, systemic hypertension, hyperlipidemia, coronary disease
- Current medication: Phenprocoumon, Nicorandil 10mg bid, Bisoprolol 5mg, Allopurinol 100mg, Escitalopram 10mg

Hemodynamic parameters

	HFPEF, Post-capillary PH
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PAPs/d-m, mmHg	110/44-73
PCWP, mmHg	40
TPG, mmHg	33
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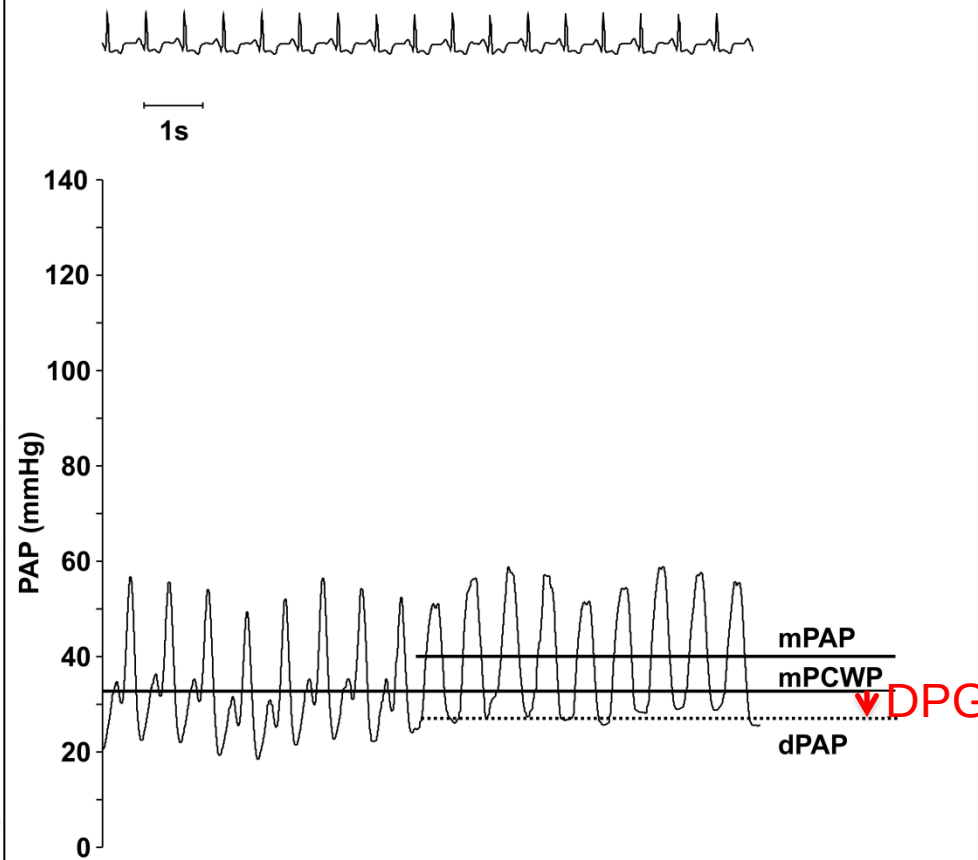
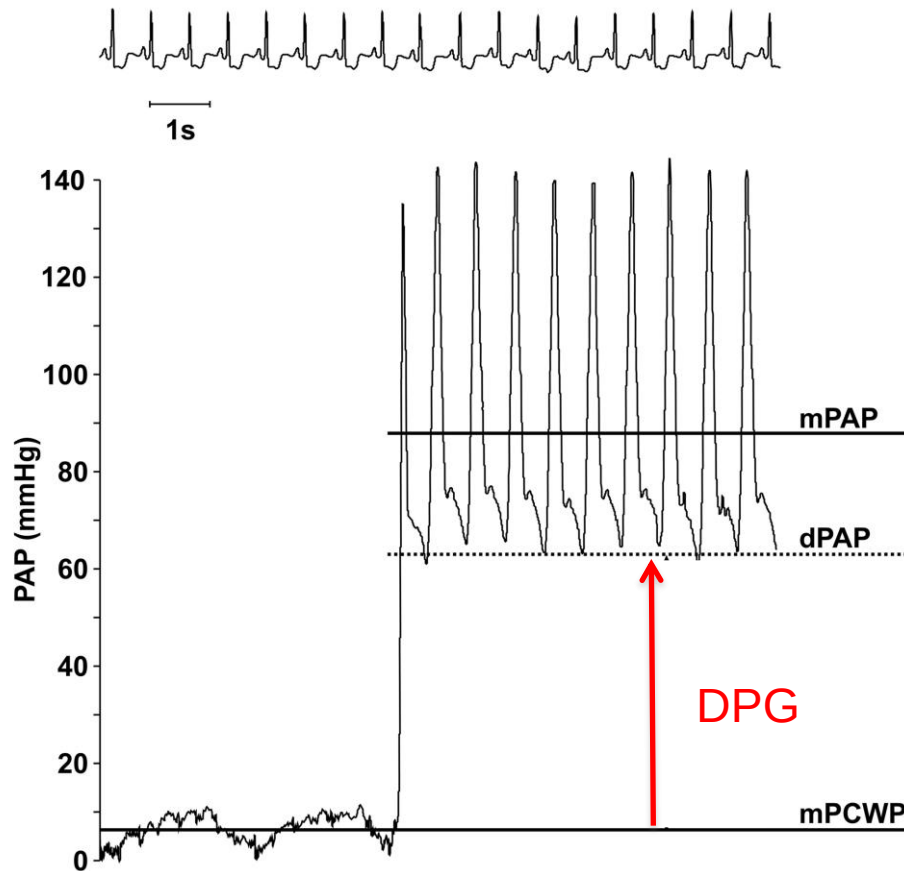
CO: cardiac output

PAP: pulmonary arterial pressure

PCWP: pulmonary capillary wedge pressure

Diastolic Pressure Gradient

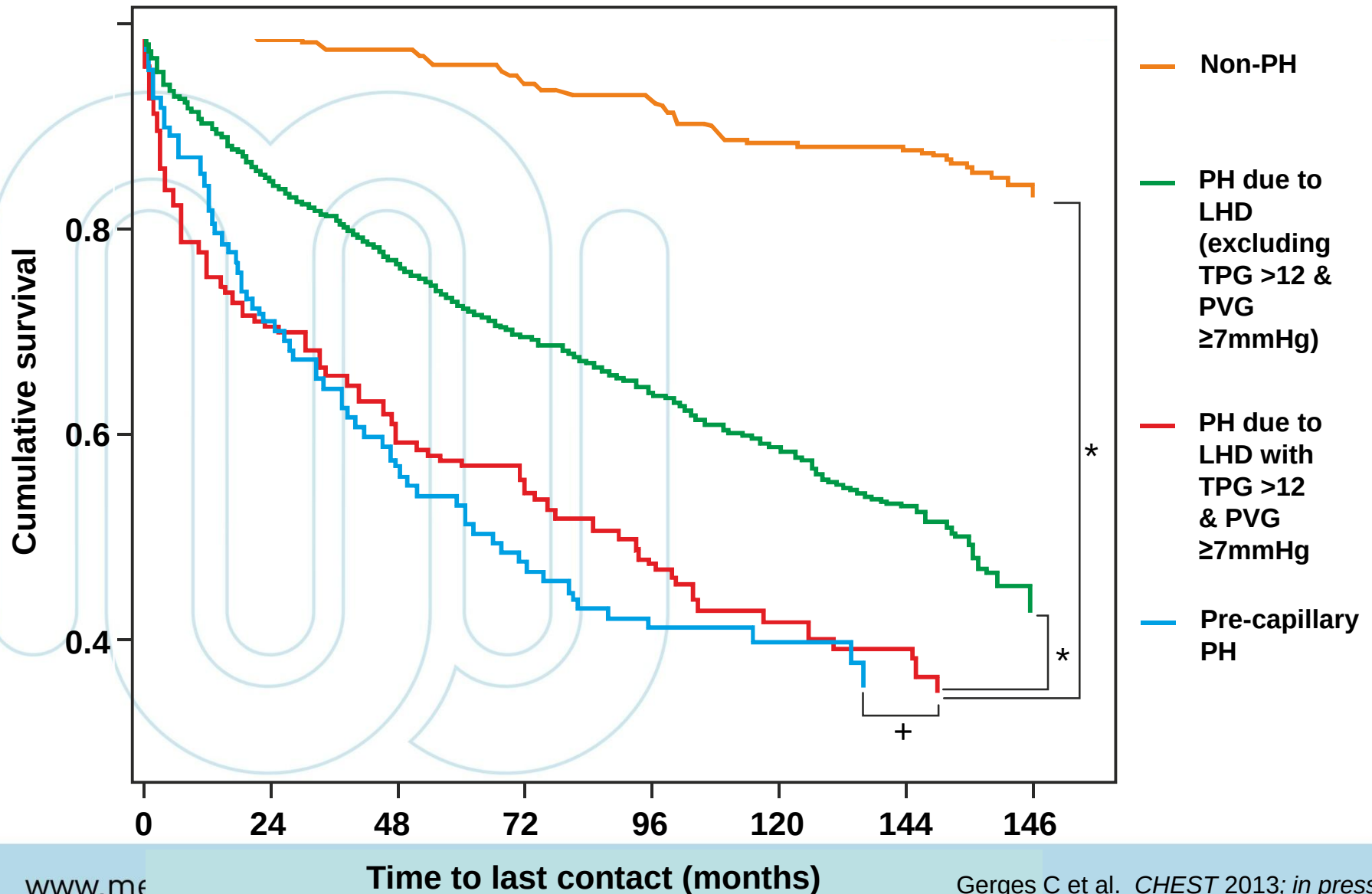
- $DPG = dPAP - mPCWP$



normal values ≤ 5 mmHg
DPG > 5 mmHg denotes pulmonary vascular disease

Buchbinder N and Ganz W. *Anesthesiology* 1976; 45(2): 146-55
Harvey RM, Enson Y and Ferrer MI. *Chest* 1971; 59(1): 82-94

DPG AND SURVIVAL



A low DPG is a marker for a favorable prognosis

	OOPPH in HFPEF, low DPG
RAP, mm Hg	32
PAPs/d-m, mmHg	110/44-73
PCWP, mmHg	40
TPG, mmHg	33
DPG, mmHg	4
CI, L.min.m ²	2,5
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Screening and diagnosing PH

- ▶ Rise of resting PA pressures (and symptoms) are late sequelae of the pathobiological processes that begin in the distal pulmonary arteries
- ▶ Resting echocardiography is currently the recommended screening modality for high-risk population groups
- ▶ Exercise stress may unmask early pulmonary vascular dysfunction but the definition, clinical significance, and natural history of 'exercise PAH' remain undefined.

Screening and diagnosing PH

– still a challenge

- ▶ Early diagnosis of PAH is currently not possible
- ▶ A major contemporary diagnostic challenge is the distinction between pre- and postcapillary PH

Thank you for your attention

