Pulmonary Hypertension

due to Left Heart Disease

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This slides is courtesy of Working Group on Heart Failure and Pulmonary Hypertension

Different entity…..?

Just comorbid…..?

“Cause and effect”…..?

PH Definition

The current hemodynamic definition of PAH is:

Mean Pulmonary Artery Pressure (mPAP) greater than 25 mm Hg;

Pulmonary Capillary Wedge Pressure (PCWP), Left Atrial Pressure, or Left Ventricular end-diastolic Pressure (LVEDP) less than or equal to 15 mm Hg;

Pulmonary Vascular Resistance (PVR) greater than 3 Wood units

ACCF/AHA Expert Consensus Document on PH, 2009

Haemodynamic definitions of pulmonary hypertension

Definition	Characteristics*	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]	

CO = cardiac output; DPG = diastolic pressure gradient (diastolic PAP - mean PAWP); mPAP = mean pulmonary arterial pressure; PAWP = pulmonary arterial wedge pressure; PH = pulmonary hypertension; PVR = pulmonary vascular resistance; WU = Wood units.

[a]All values measured at rest; see also section 7.
[b]According to Table 4.
[c]Wood Units are preferred to dynes.s.cm^{-5}.

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European Respiratory Journal 2015 46: 903-975;

WHY IT IS IMPORTANT ??

→ Prognosis

PROGNOSIS

Predictors of a poor prognosis include:
advanced functional class
poor exercise capa ity a
ar
high right atrial (RA) pressure
significant right ventricular (RV) dysfunction
e
low cardiac index
elevated brain natriuretic peptide (BNP)
and underlying diagnosis of scleroderma spectrum of diseases

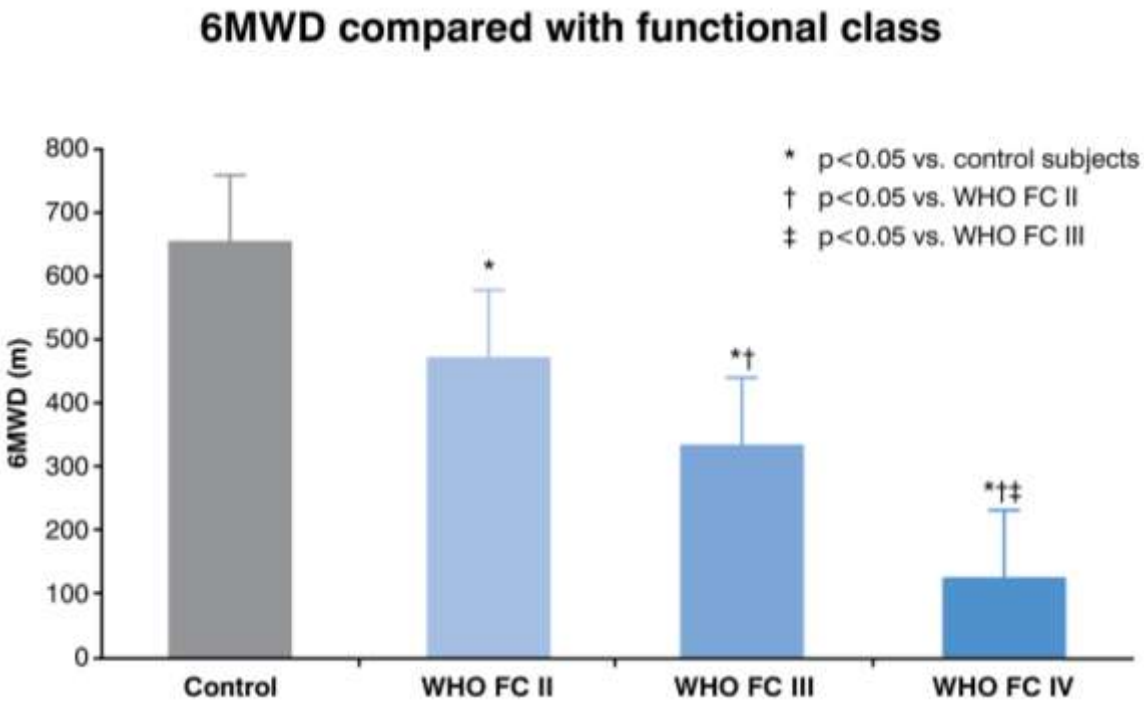
↑ MORBIDITAS

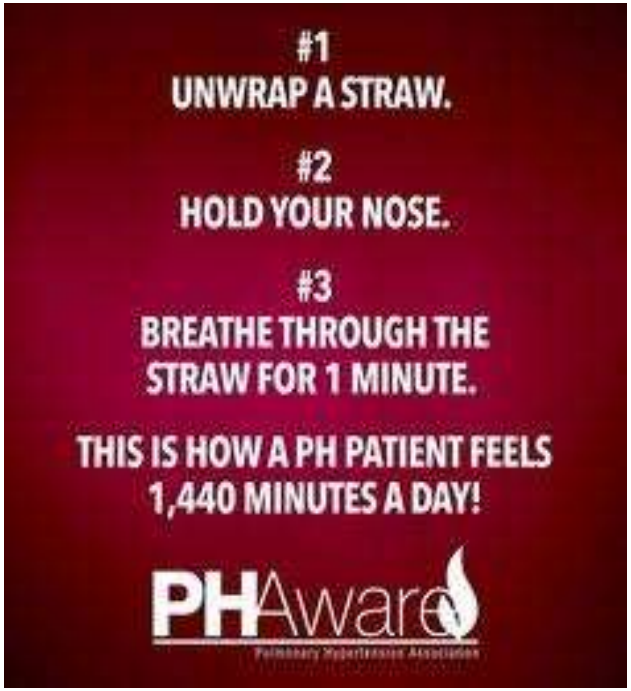
↑ MORTALITAS

ACCF/AHA Expert Consensus Document on PH, 2009

6 minute walk test (6-MWT)

- Measure of patients' functional limitations
- Simple, inexpensive, convenient
- Correlate with WHO FC

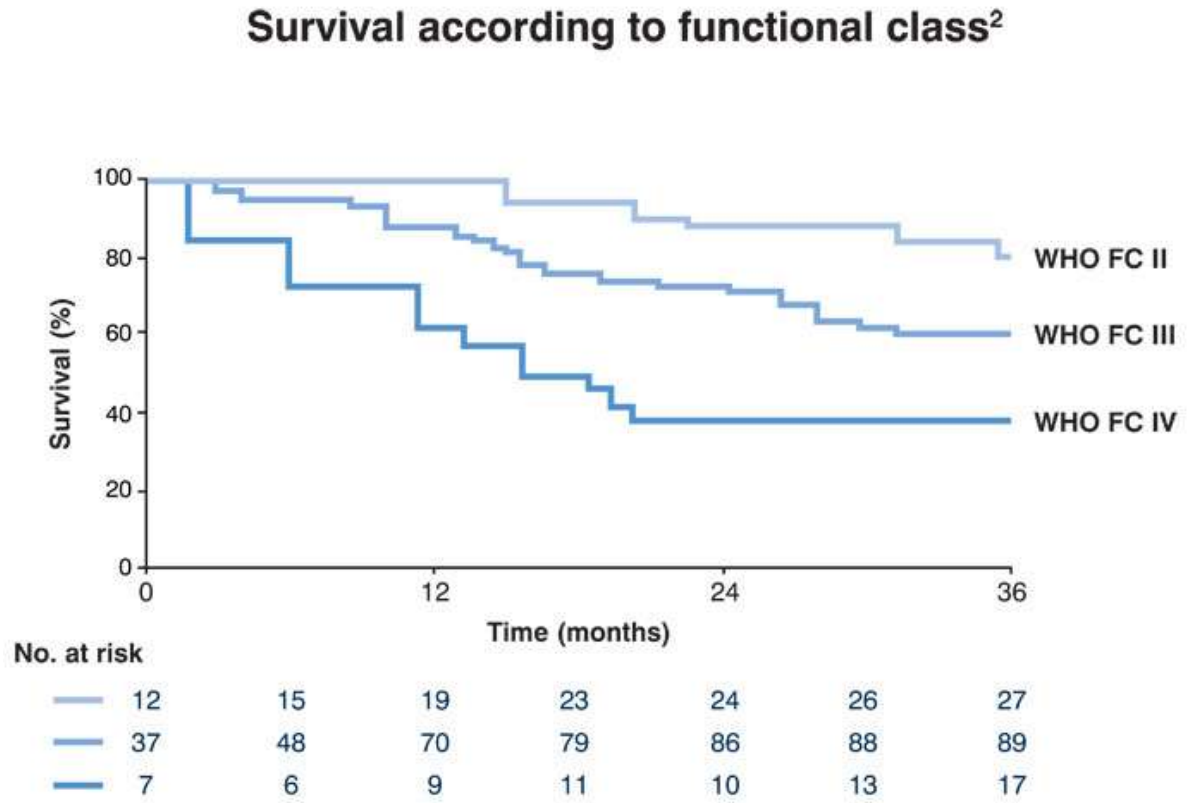




Miyamoto S et al. *Am J Respir Crit Care Med* 2000

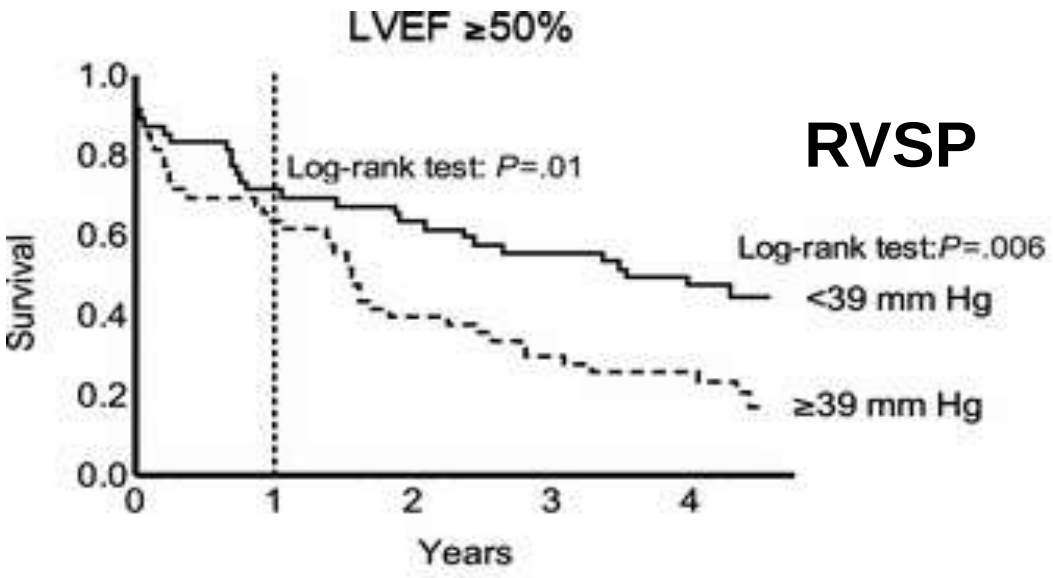
Functional class and survival

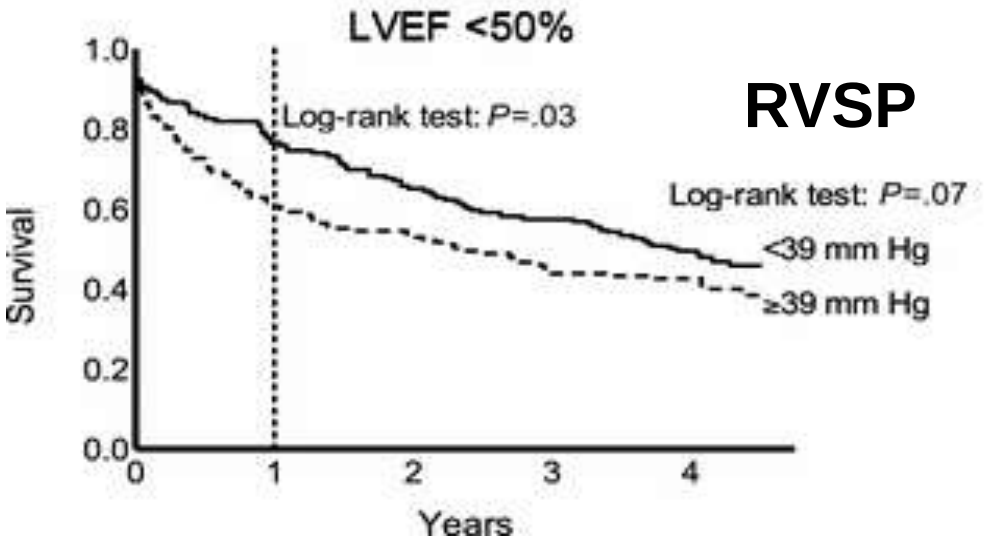
Even with advanced medical therapy, patients in WHO FC IV continue to have extremely poor survival rates.



Humbert M et al. *Circulation* 2010

Independent Predictor of mortality





Congestive Heart Failure
Volume 17, Issue 4, pages 189-198, 21 JUL 2011 DOI: 10.1111/j.1751-7133.2011.00234.x

Comprehensive clinical classification of pulmonary hypertension

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 disease (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 EIF2AK4 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)

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 thrombotic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

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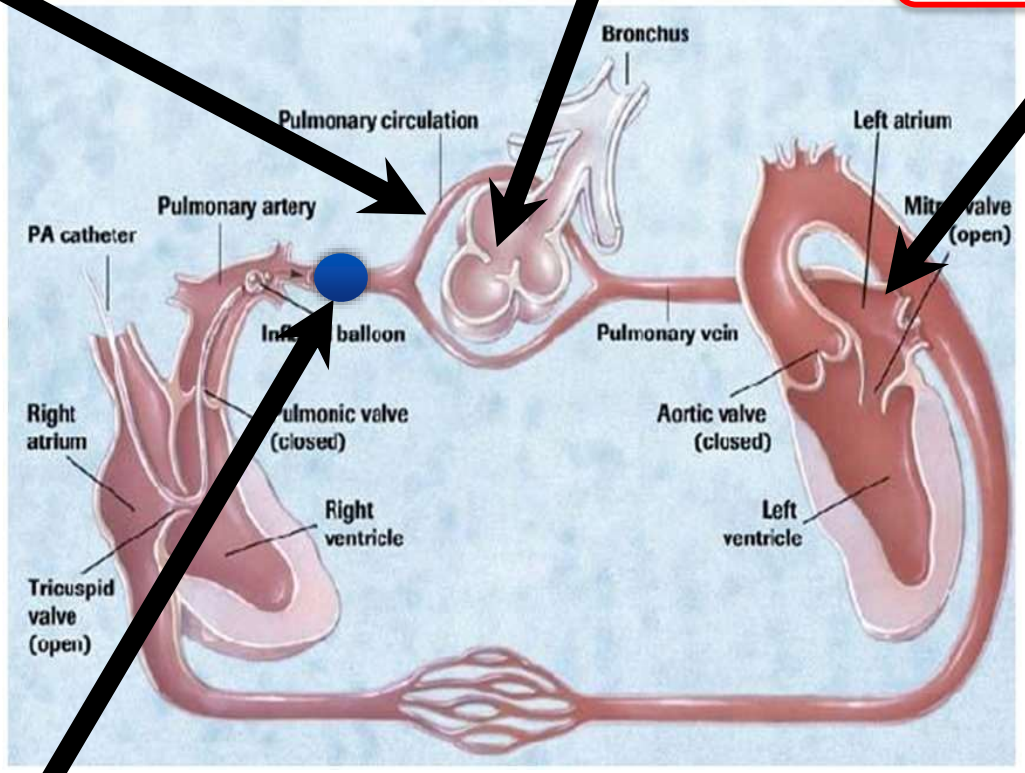
1. Pulmonary Arterial Hypertension

3. Chronic Hypoxemia

2. Left Heart Disease



4. Thromboembolic

5. Miscelaneous

-Sarcoid, fibrosing mediastinitis

Group 2 Pulmonary Hypertension

- PH is a **common complication of LHDs** (PH-LHD), **frequently** occurring as a 'symptom' of the underlying condition and often related to disease severity.
- When present, PH-LHD **results in more severe symptoms** and **worse exercise tolerance** and exerts a **negative impact on outcome**.
- The **true prevalence** of PH-LHD remains **unknown**, mostly because the definition of PH in epidemiological studies has been based on echocardiography, with a variety of cut-off values.

European Heart Journal 2016;37:67–119 -doi:10.1093/eurheartj/ehv317
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Group 2 Pulmonary Hypertension

- The **prevalence of PH** in patients with chronic HF **increases with the progression of functional class** impairment.
- Up to **60% of patients with severe left ventricular systolic dysfunction** and up to **70% of patients with HFpEF** may present with PH.
- In left-sided valvular diseases, the prevalence of PH increases with the severity of the defect and of the symptoms.
- PH can be found in virtually all patients with severe symptomatic mitral valve disease and in up to 65% of those with symptomatic aortic stenosis.

European Heart Journal 2016;37:67–119 -doi:10.1093/eurheartj/ehv317
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PH Epidemiology in NCCHK

2008	ATRIAL SEPTAL DEFECT	1
	VENTRICULAR SEPTAL DEFECT	0
	MITRAL STENOSIS AND TRICUSPID REGURGITATION	**4**
	CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION	0
	PATENT DUCTUS ARTERIOSUS	1
	PRIMARY PULMONARY HYPERTENSION	23
	TOTAL	28

Under-diagnosed???

	PATENT DUCTUS ARTERIOSUS	0
	PRIMARY PULMONARY HYPERTENSION	13
	TOTAL	20
2010	ATRIAL SEPTAL DEFECT	2
	VENTRICULAR SEPTAL DEFECT	0
	MITRAL STENOSIS AND TRICUSPID REGURGITATION	**3**
	CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION	0
	PATENT DUCTUS ARTERIOSUS	1
	PRIMARY PULMONARY HYPERTENSION	12
	TOTAL	15

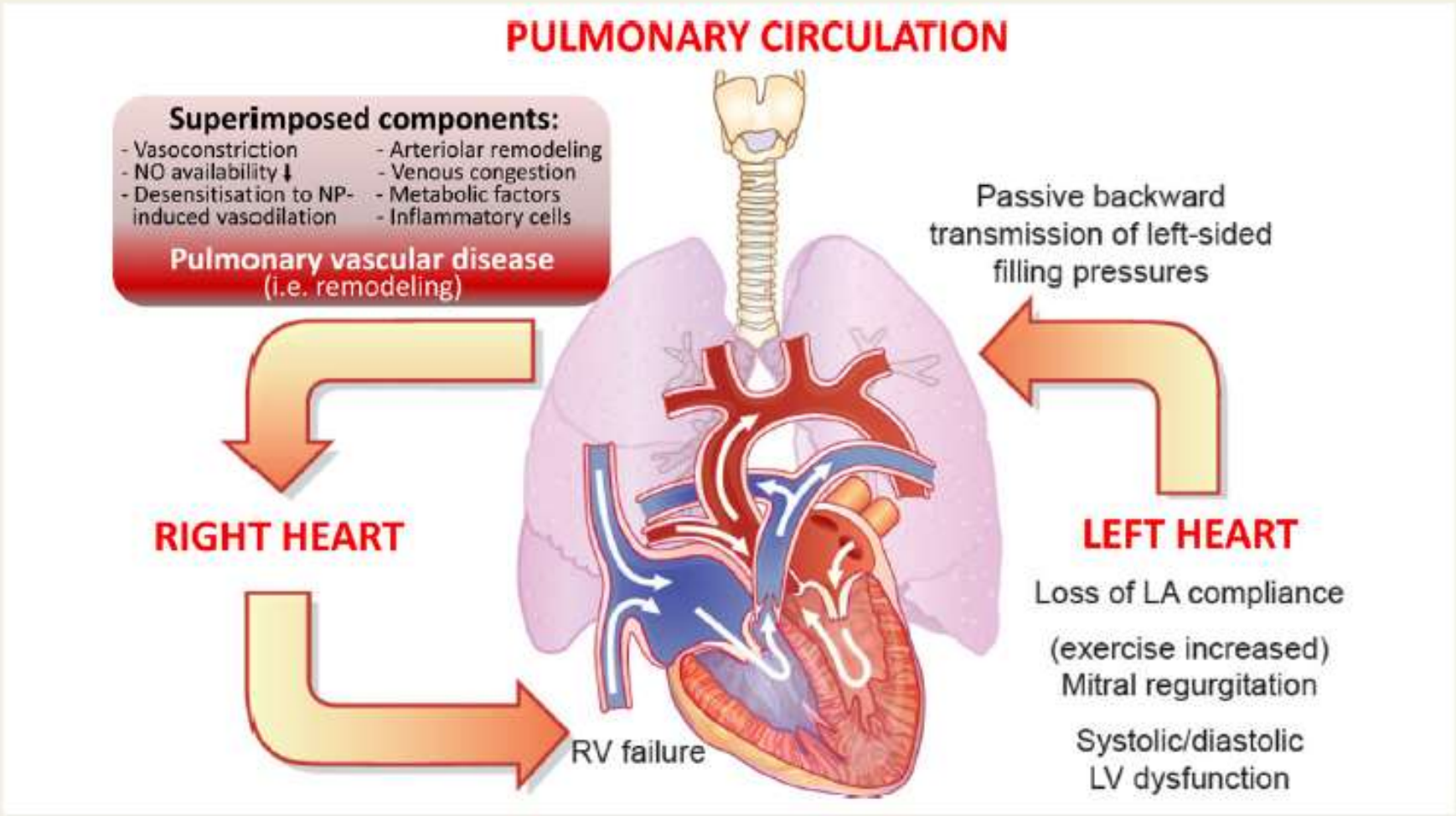
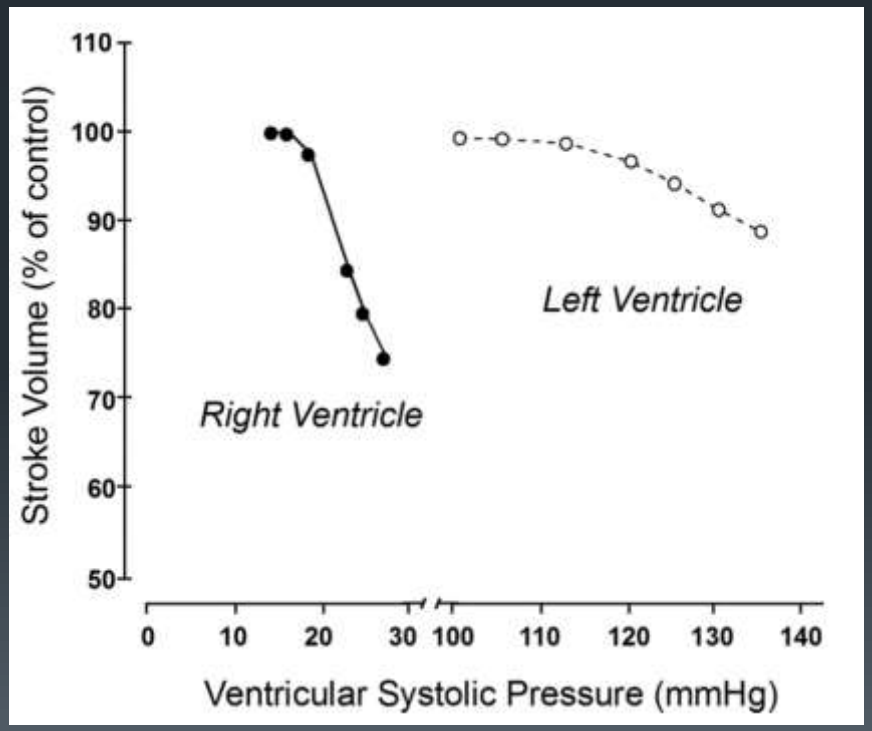


Figure 1 Cardiopulmonary interaction and pathobiology of pulmonary hypertension (PH) in left ventricular heart failure. Shown is (i) the backward transmission of elevated left ventricular filling pressures into the pulmonary circulation (*post-capillary haemodynamic profile*), (ii) potential superimposed components contributing to the extent of PH (leading to a *pre-capillary component*),[11] which may be associated with (iii) pulmonary vascular remodelling in some patients, thus leading to (iv) right ventricular strain and dysfunction over time. Right ventricular (RV) dilation and increase in wall stress/tension (internal RV afterload) result in elevated myocardial oxygen consumption, which with concomitant reduction in coronary perfusion gradient leads to RV ischaemia and progressive RV failure.

RV – PA coupling

- RV differs from LV
- Well suited accommodate an increase in volume load, sensitive to afterload
- Acute pressure overload causes great reduction in SV
- Even mild PH led uncoupling of RV–PA
- Chronically, RV may adapt with hypertrophy
- RV output reduction may lead to LV underfilling in advanced HF



Circulation 2012;126:975-990

Diagnostic Algorithm for Pulmonary Hypertension

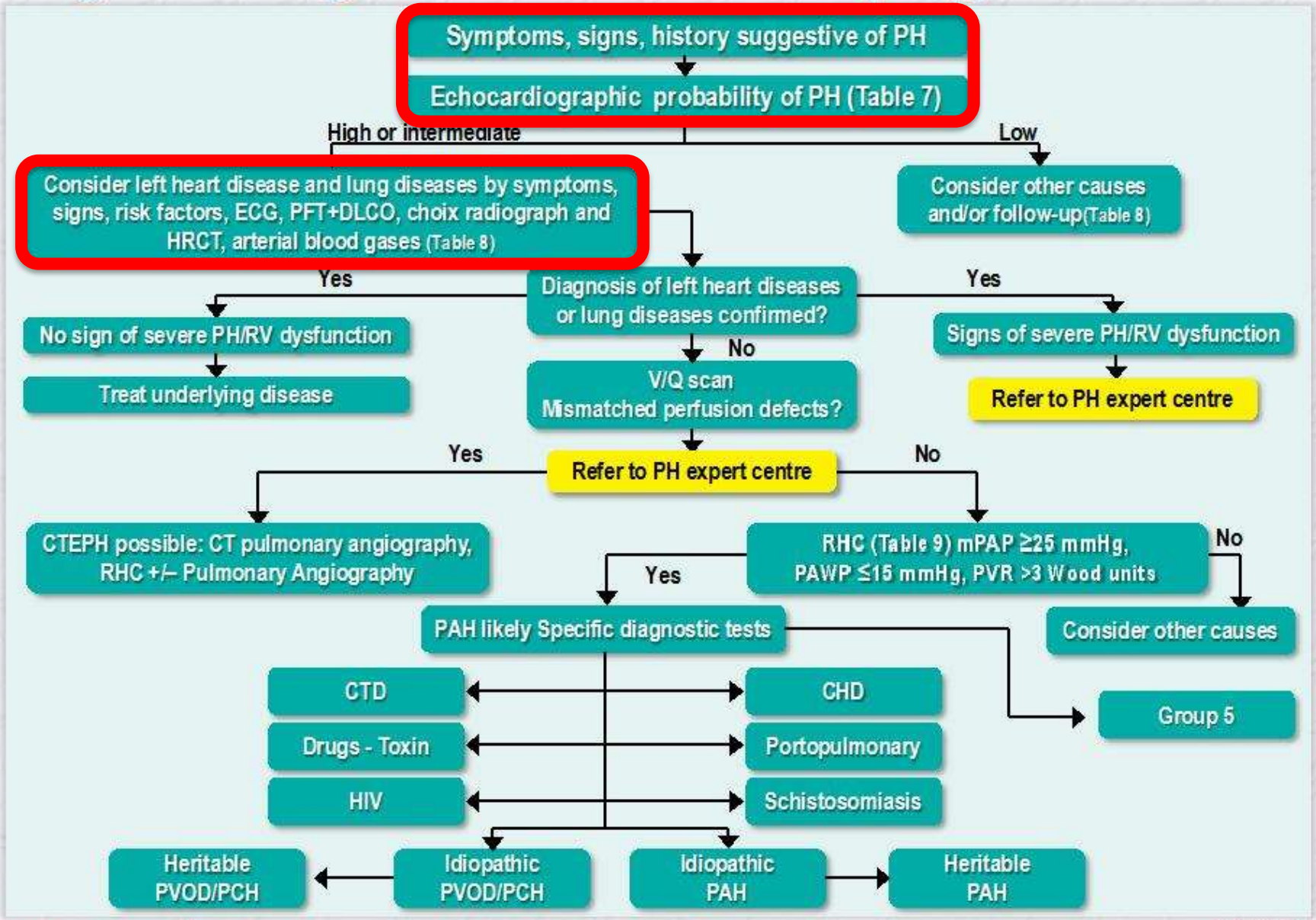


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Table 8A Echocardiographic probability of pulmonary hypertension in symptomatic patients with a suspicion of pulmonary hypertension

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	

Table 8B Echocardiographic signs suggesting pulmonary hypertension used to assess the probability of pulmonary hypertension in addition to tricuspid regurgitation velocity measurement in *Table 8A*

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 msec 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.	

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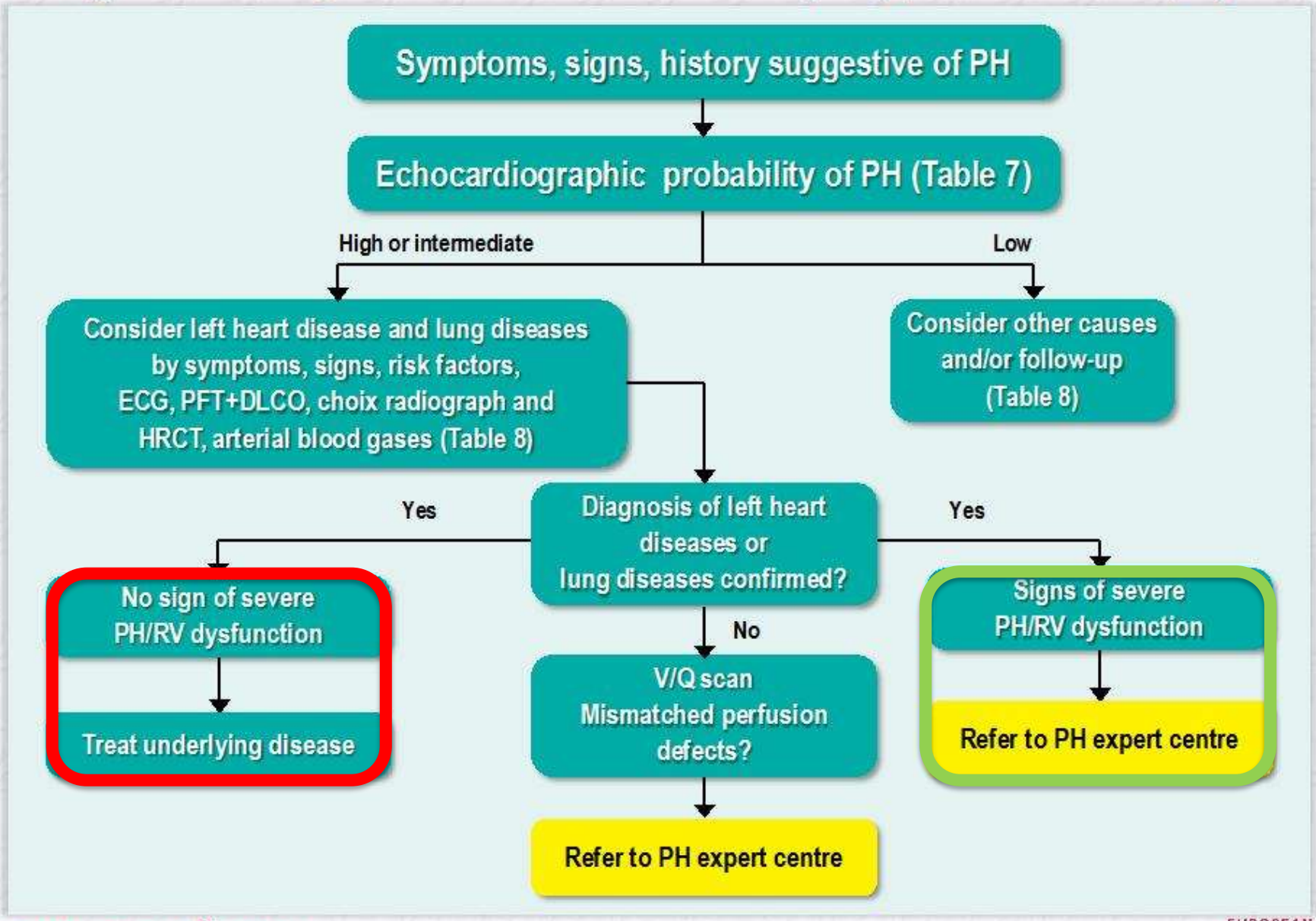
Diagnostic Algorithm for Pulmonary Hypertension (1)



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Diagnostic strategy

Recommendations	Class	Level
Echocardiography is recommended as a first-line non-invasive diagnostic investigation in case of suspicion of PH.	I	C
Ventilation/perfusion or perfusion lung scan is recommended in patients with unexplained PH to exclude CTEPH.	I	C
Contrast CT angiography of the PA is recommended in the work-up of patients with CTEPH.	I	C
Routine biochemistry, haematology, immunology, HIV testing and thyroid function tests are recommended in all patients with PAH to identify the specific associated condition.	I	C
Abdominal ultrasound is recommended for the screening of portal hypertension.	I	C
Lung function test with DLCO is recommended in the initial evaluation of patients with PH.	I	C
High-resolution CT should be considered in all patients with PH.	IIa	C
Pulmonary angiography should be considered in the work-up of patients with CTEPH.	IIa	C
Open or thoracoscopic lung biopsy is not recommended in patients with PAH.	III	C

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Examples of key factors suggestive of Group 2 pulmonary hypertension

Clinical presentation	Echocardiography	Other features
Age >65 years	Structural left heart abnormality · Disease of left heart valves · LA enlargement (>4.2 cm) · Bowing of the IAS to the right · LV dysfunction · Concentric LV hypertrophy and/or increased LV mass	ECG · LVH and/or LAH · AF/Afib · LBBB · Presence of Q waves
Symptoms of left heart failure	Doppler indices of increased filling pressures · Increased E/e' · >Type 2-3 mitral flow abnormality	Other imaging · Kerley B lines · Pleural effusion · Pulmonary oedema · LA enlargement
Features of metabolic syndrome	Absence of: · RV dysfunction · Mid systolic notching of the PA flow · Pericardial effusion	
History of heart disease (past or current)		
Persistent atrial fibrillation		

AF = atrial flutter; Afib = atrial fibrillation; ECG = electrocardiogram; IAS = inter-atrial septum; LA = left atrium; LAH = left anterior hemiblock; LBBB= left bundle branch block; LV = left ventricle; LVH = left ventricular hypertrophy; PA = pulmonary artery; RV = right ventricle.

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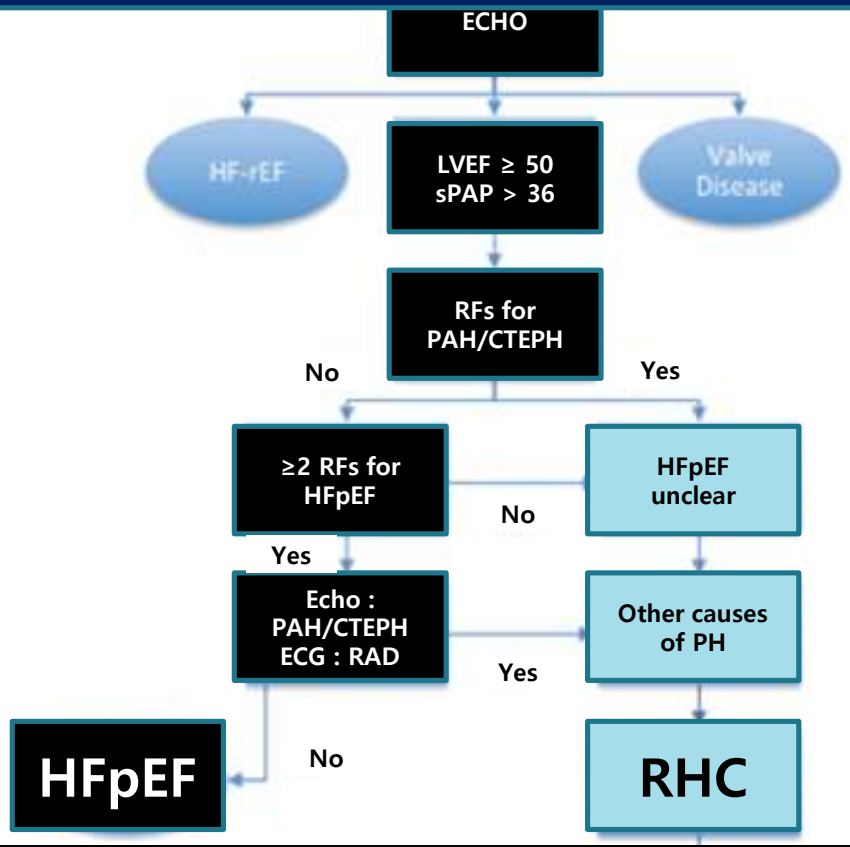
Table 2 **Results of non-invasive diagnostic tests may be suggestive of either pulmonary arterial hypertension or pulmonary hypertension associated with left heart disease**

	Suggestive of PAH (Nice group 1)	Suggestive of PH-LHD (Nice group 2)
a. Clinical features	Younger age, familial cases, bendopnea[a], risk factors for PAH: CTD, CHD, severe liver disease, portal hypertension, HIV	Older age, hypertension, diabetes, CAD, BMI >30, pulmonary congestion, history of pulmonary oedema, orthopnoea
b. ECG	RV hypertrophy, right axis, RV strain	LV hypertrophy (Sokolow–Lyon index: S in V1 + R in V6), left axis, atrial fibrillation
c. ECHO[b]	No signs of LHD, PASP elevated, RV > LV, RV hypertrophy/dysfunction (TAPSE), RVOT notching[c], small LA, dilated IVC	Enlarged LA, LV hypertrophy, signs of systolic (EF) and/ordiastolic (*E*/*A*, DT, *E*/*E*′) LV dysfunction, valvular disease
d. Chest X-ray	Enlarged right heart chambers, dilated PA, peripheral PA pruning	Pulmonary congestion, Kerley B lines, pleural effusions, enlargement of left heart chambers
e. PFT/DLCO	Normal/mild obstructive spirometry, normal or moderately decreased DLCO[d], low p_cCO_2 ($\leq$36 mmHg)[e]	Normal/obstructive spirometry, normal DLCO (may be decreased due to comorbid COPD), high p_cCO_2 (>36 mmHg)[e]
f. Biomarkers	BNP/NTproBNP elevated (not discriminate between Groups 1 and 2)	BNP/NTproBNP elevated (not discriminate between group 1 and 2)
g. CPET	Low $P_{ET}CO_2$ at AT, decreasing during exercise; high VE/VCO_2, increasing during exercise	$P_{ET}CO_2$ at AT normal or slightly lowered, not decreasing during exercise, VE/VCO_2 not increasing during exercise
h. HR-CT	To diagnose or rule out parenchymal lung disease (not discriminate between Groups 1 and 2)	To diagnose or rule out parenchymal lung disease (not discriminate between Groups 1 and 2)
i. V/Q scan	To diagnose or rule out CTEPH (not discriminate between Groups 1 and 2)	To diagnose or rule out CTEPH (not discriminate between Groups 1 and 2)

HFpEF or PAH ??

Hypertension	
Age >65yrs	
Obesity	
CAD	
DM	
AF	
ECHO features	
LA dilatation	
LVH	
E/e' >15	



Mixed connective tissue	5%
Previous PE/DVT	3.8%
Liver cirrhosis	5%
SLE	<1%
HIV	0.5%
Family history of PAH	
Recreational drug use	
* ECHO features	
Mod-severe RV impairment	
Paradoxical septal motion	
sPAP >70mmHg	

RHC ??

Table 9 Diagnostic management suggested according to echocardiographic probability of pulmonary hypertension in patients with symptoms compatible with pulmonary hypertension, with or without risk factors for pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension

Echocardiographic probability of PH	Without risk factors or associated condition for PAH or CTEPH[d]	Class[a]	Level[b]	With risk factors or associated conditions for PAH or CTEPH[c]	Class[a]	Level[b]	Ref[c]
Low	Alternative diagnosis should be considered	IIa	C	Echo follow-up should be considered	IIa	C	
Intermediate	Alternative diagnosis, echo follow-up, should be considered	IIa	C	Further assessment of PH including RHC should be considered[e]	IIa	B	45, 46
	Further investigation of PH may be considered[e]	IIb					
High	Further investigation of PH (including RHC[e]) is recommended	I	C	Further investigation of PH[e] including RHC is recommended	I	C	

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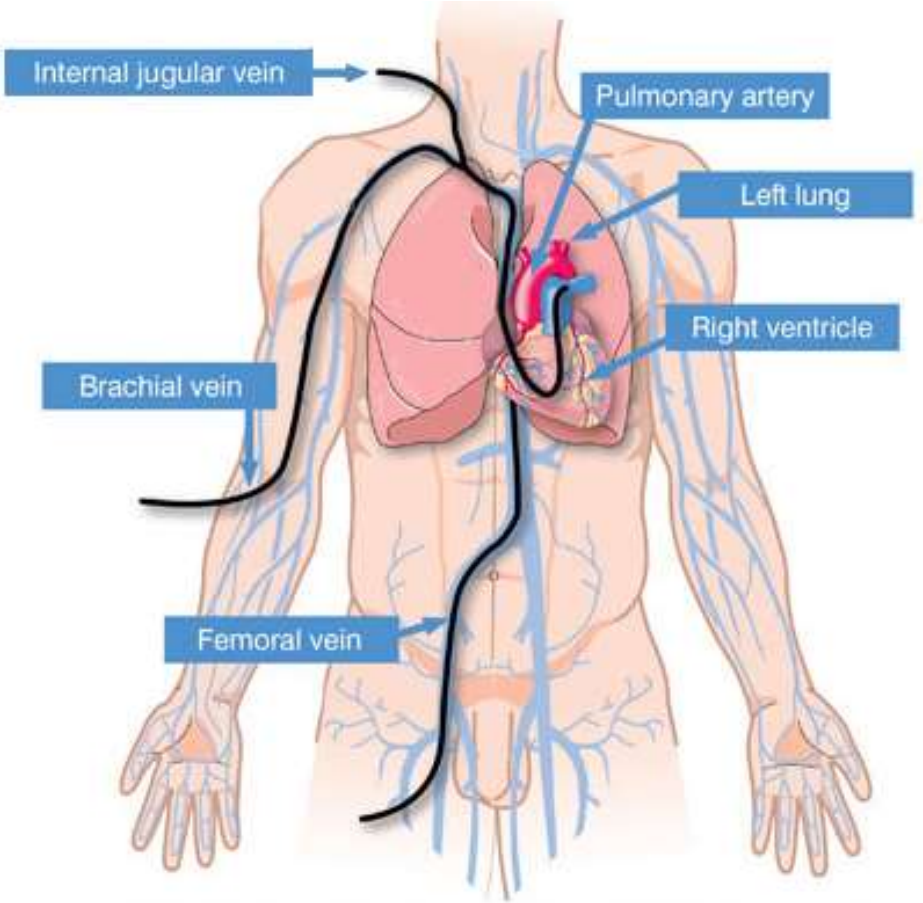
Right heart catheterisation

- the diagnostic gold standard[1]

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

PAH is defined by

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



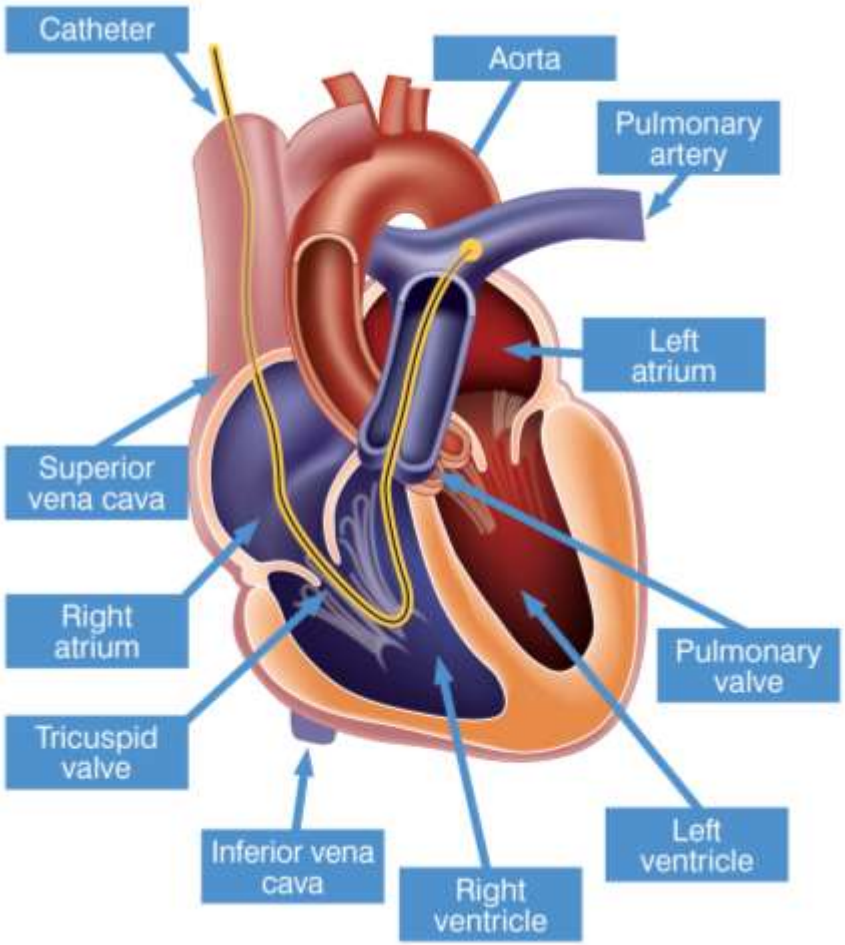
Standard approaches for catheter access

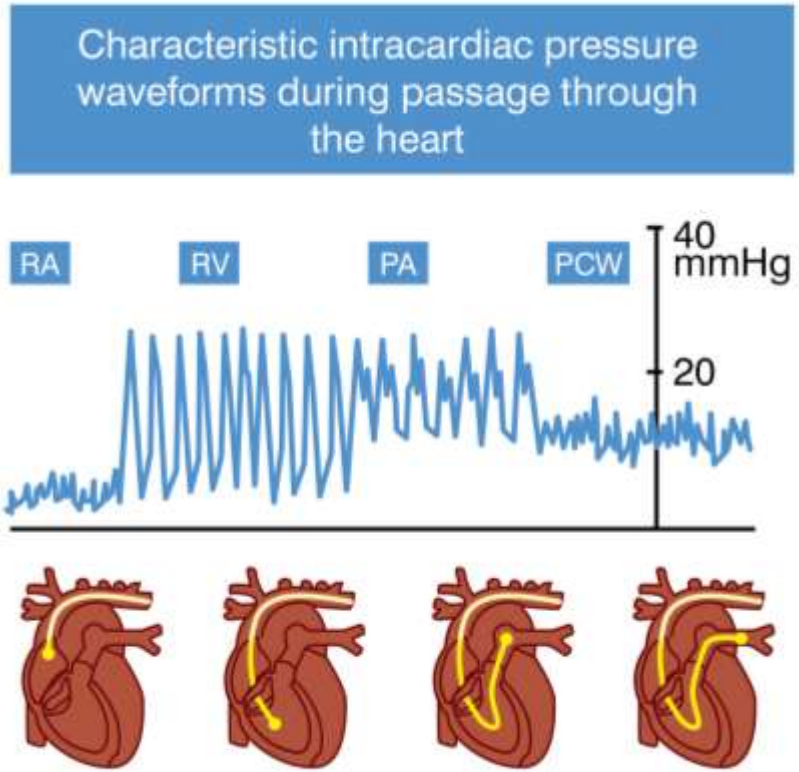
Galié et al. *Eur Heart J* 2009.

1. Galiè N et al. *Eur Heart J* 2009

Right heart catheterisation

- the diagnostic gold standard[1]





1. Galiè N et al. *Eur Heart J* 2009

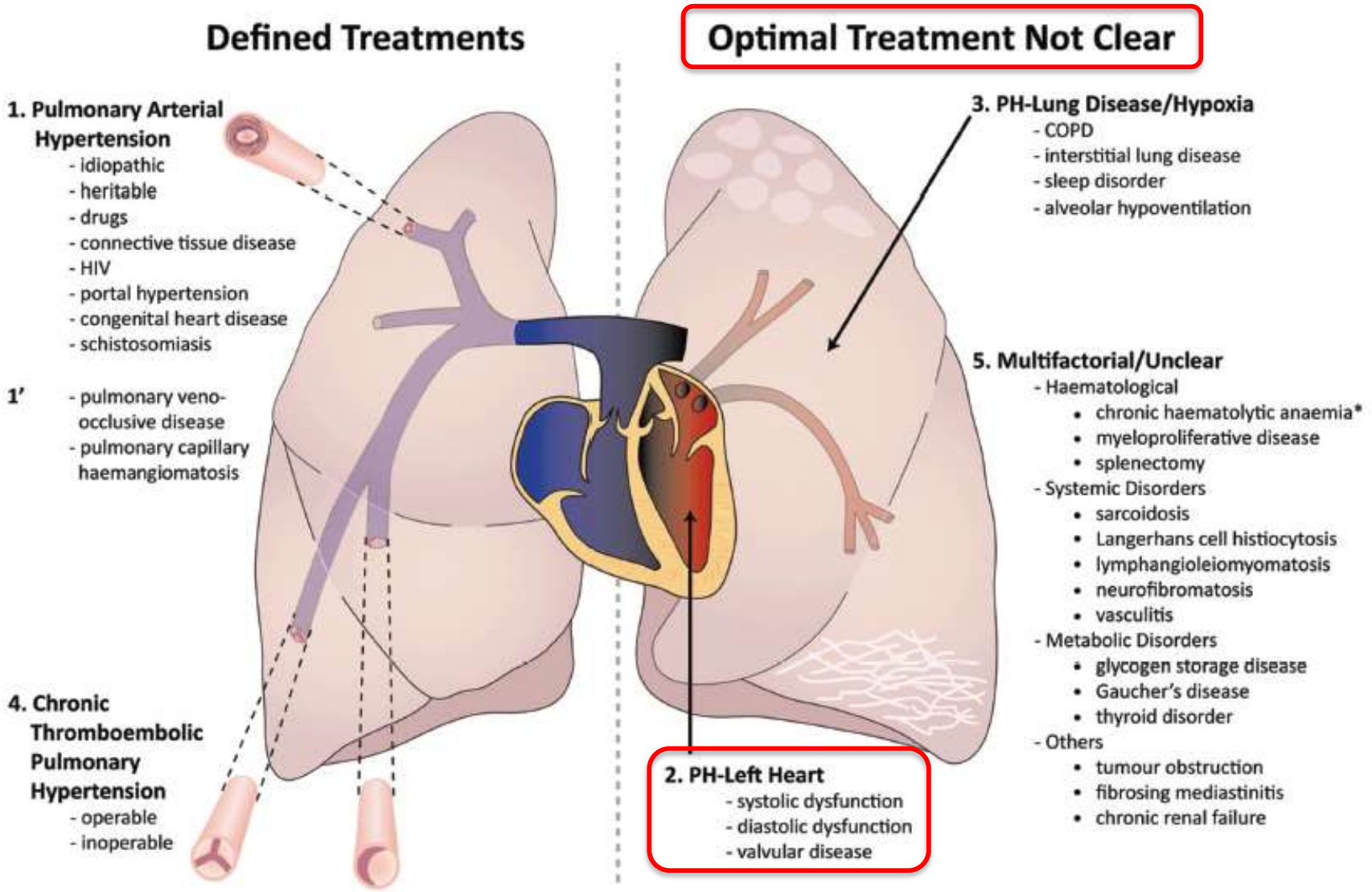


Figure 1. Classification of adult pulmonary hypertension. Adapted from Figure 1 of Kiely et al.[3] COPD: chronic obstructive pulmonary disease; PH: pulmonary hypertension.

PAH supportive therapy

Recommendations	Class	Level
Diuretic treatment is recommended in PAH patients with signs of RV failure and fluid retention.	I	C
Continuous long-term O_2 therapy is recommended in PAH patients when arterial blood O_2 pressure is consistently less than 8 kPa (60 mmHg).	I	C
Oral anticoagulant treatment may be considered in patients with IPAH, HPAH and PAH due to use of anorexigens.	IIb	C
Correction of anaemia and/or iron status may be considered in PAH patients.	IIb	C
The use of angiotensin-converting enzyme inhibitors, angiotensin-2 receptor antagonists, beta-blockers and ivabradine is not recommended in patients with PAH unless required by co-morbidities (i.e. high blood pressure, coronary artery disease or left heart failure).	III	C

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European Respiratory Journal 2015 46: 903-975;

Management of pulmonary hypertension in left heart disease

Recommendations	Class	Level
Optimization of the treatment of the underlying condition is recommended before considering assessment of PH-LHD (i.e. treating structural heart disease).	I	B
It is recommended to identify other causes of PH (i.e. COPD, SAS, PE, CTEPH) and to treat them when appropriate before considering assessment of PH-LHD.	I	C
It is recommended to perform invasive assessment of PH in patients on optimized volume status.	I	C
Patients with PH-LHD and a severe pre-capillary component as indicated by a high DPG and/or high PVR should be referred to an expert PH centre for a complete diagnostic work-up and an individual treatment decision.	IIa	C
The importance and role of vasoreactivity testing is not established in PH-LHD, except in patients who are candidates for heart transplantation and/or LV assist device implantation.	III	C
The use of PAH approved therapies is not recommended in PH-LHD.	III	C

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Pulmonary Hypertension secondary to CHF (Systolic and Diastolic)

↓

Chronic post-capillary PH

↓

Pulmonary Vascular Remodeling

↓

RV dysfunction

Passive PH
TPG < 12 mmHg

Reactive PH
TPG > 12 mmHg

Traditional Medical Therapy

- Diuretic
- ACEi/ARB
- Aldosterone Antagonists
- Beta Blockade

Advanced Treatment Options

- Sildenafil/others ??
- LVAD/Bivent. Support ??

Table 19 Recommendations for efficacy of drug monotherapy for pulmonary arterial hypertension (group 1) according to World Health Organization functional class. The sequence is by pharmacological group, by rating and by alphabetical order

Measure/treatment			Class[a]-Level[b]						Ref.[c]
			WHO-FC II		WHO-FC III		WHO-FC IV		
Calcium channel blockers			I	C[d]	I	C[d]	-	-	84,85
Endothelin receptor antagonists	Ambrisentan		I	A	I	A	IIb	C	194
	Bosentan		I	A	I	A	IIb	C	196–200
	Macitentan[e]		I	B	I	B	IIb	C	201
Phosphodiesterase type 5 inhibitors	Sildenafil		I	A	I	A	IIb	C	205–208
	Tadalafil		I	B	I	B	IIb	C	211
	Vardenafil[g]		IIb	B	IIb	B	IIb	C	212
Guanylate cyclase stimulators	Riociguat		I	B	I	B	IIb	C	214
Prostacyclin analogues	Epoprostenol	Intravenous[e]	-	-	I	A	I	A	220–222
	Iloprost	Inhaled	-	-	I	B	IIb	C	229–231
		Intravenous[g]	-	-	IIa	C	IIb	C	232
	Treprostinil	Subcutaneous	-	-	I	B	IIb	C	233
		Inhaled[g]	-	-	I	B	IIb	C	237
		Intravenous[f]	-	-	IIa	C	IIb	C	234
		Oral[g]	-	-	IIb	B	-	-	238–240
	Beraprost[g]		-	-	IIb	B	-	-	218
IP receptor agonists	Selexipag (oral)[g]		I	B	I	B	-	-	241,248

EMA = European Medicines Agency; PAH = pulmonary arterial hypertension; RCT = randomized controlled trial; WHO-FC = World Health Organization functional class.

[a]Class of recommendation.

[b]Level of evidence.

[c]Reference(s) supporting recommendations.

[d]Only in responders to acute vasoreactivity tests = class I, for idiopathic PAH, heritable PAH and PAH due to drugs; class IIa, for conditions associated with PAH.

[e]Time to clinical worsening as primary endpoint in RCTs or drugs with demonstrated reduction in all-cause mortality.

[f]In patients not tolerating the subcutaneous form.

[g]This drug is not approved by the EMA at the time of publication of these guidelines.

European Heart Journal (2016) **37**, 67–119
doi:10.1093/eurheartj/ehv317

SUPER-1

Sildenafil Use in Pulmonary Arterial HypERtension

Galiè N, *et al. New Engl J Med* 2005;353:2148–57.

SUPER-2

Long-Term Treatment with Sildenafil Citrate in Pulmonary Arterial Hypertension

Rubin LJ, et al. Long-term treatment with sildenafil citrate in pulmonary arterial hypertension: SUPER-2. *Chest*. Epub May 2011

SUPER-1: conclusions

- Sildenafil significantly improved (*vs* placebo)
  - 6MWD
  - mPAP, PVR, CI
  - WHO FC
- Other favourable clinical trends included:
  - Fewer hospitalisations for PAH
  - Reduced breathlessness during exercise
- Sildenafil is generally well tolerated
- Sildenafil is efficacious in treating patients with PAH

CI = cardiac index ; FC = functional class; mPAP = mean pulmonary arterial pressure; 6MWD = 6-minute walk distance; PAH = pulmonary arterial hypertension; PVR = pulmonary vascular resistance; WHO = World Health Organization

Galiè N, *et al. New Engl J Med* 2005;353:2148–57.

SUPER-2: conclusions

- After 3 years
  - 46% of patients maintained or improved 6MWD
  - 60% of patients maintained or improved their functional status
  - Kaplan-Meier estimated survival was 79%
- Most treatment-related adverse events were mild to moderate in severity, and included headache, dyspepsia, diarrhoea, blurred vision, nausea, and abdominal pain

6MWD = 6-minute walk distance

Rubin LJ, et al. Long-term treatment with sildenafil citrate in pulmonary arterial hypertension: SUPER-2. *Chest*. Epub May 2011

Goal of Therapy for PH-LHD

- To improve global management of the underlying condition prior to considering specific measures to treat PH.
  - **Repair** of valvular heart disease when indicated
  - **Aggressive therapy** for HFrEF.
- Risk factors for cardiovascular diseases and features of **metabolic syndrome should be controlled**.
- In contrast, there is **no strong evidence-based** recommendation for the treatment **for HF-pEF**.
- There is **no new evidence supporting the use of PAH therapies in PH-LHD**, due in part to the absence of studies specifically for PH.

European Heart Journal 2016;37:67–119 -doi:10.1093/eurheartj/ehv317
European Respiratory Journal 2015 46: 903-975;

The Ten Commandments

1. Right heart catheterization is recommended to confirm the diagnosis of pulmonary arterial hypertension (PAH - Group 1) and to support treatment decisions.
2. Vasoreactivity testing performed during right heart catheterization is recommended in patients with idiopathic PAH, heritable PAH and PAH induced by drugs or toxins use to detect patients who can be treated with high doses of a calcium channel blocker.
3. It is recommended to evaluate the severity of PAH patients with a panel of data derived from clinical assessment, exercise tests, biochemical markers, and echocardiographic and haemodynamic evaluation and to perform regular follow-up assessments every 3-6 months in stable patients.
4. It is recommended to avoid pregnancy in patients with PAH.
5. It is recommended for referral centres to provide care by a multi-professional team (cardiology and respiratory medicine physicians, clinical nurse specialist, radiologists, psychological and social work support, appropriate on-call expertise).

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European Heart Journal 2016;37;67–119 -doi:10.1093/eurheartj/ehv317
European Respiratory Journal 2015 46: 903-975;

The Ten Commandments

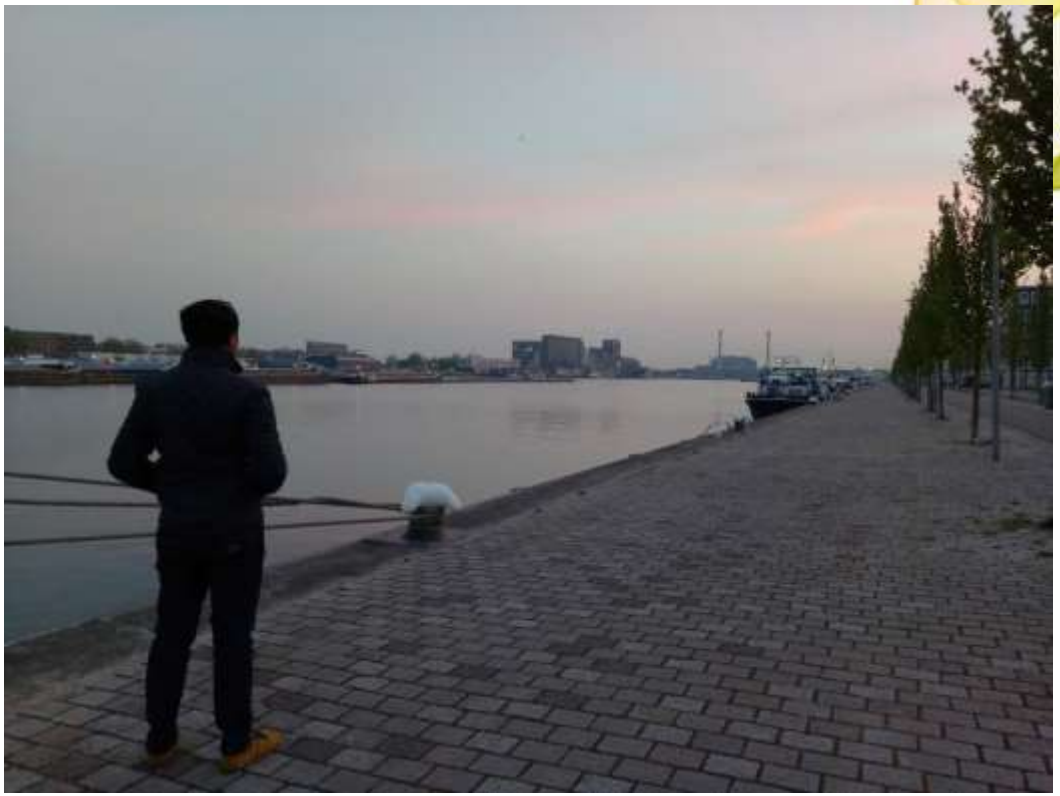
6. Initial drugs monotherapy or initial oral drugs combination therapy is recommended in treatment naïve, low or intermediate risk patients with PAH.
7. Sequential drugs combination therapy is recommended in PAH patients with inadequate treatment response to initial monotherapy or to initial oral drugs combination therapy.
8. Initial combination therapy including an intravenous prostacyclin analogue is recommended in high risk PAH patients.
9. The use of PAH approved therapies is not recommended in patients with pulmonary hypertension due to left heart disease or lung diseases.
10. Surgical pulmonary endarterectomy in deep hypothermia circulatory arrest is recommended for patients with CTEPH and it is recommended that the assessment of operability and decisions regarding other treatment strategies (drugs therapy or balloon pulmonary angioplasty) be made by a multidisciplinary team of experts.

European Heart Journal 2016:37;67–119 -doi:10.1093/eurheartj/ehv317
European Respiratory Journal 2015 46: 903-975;

CONCLUSION

- PH is common in HF, unfortunately still under-diagnosed
- This condition increases morbidity and mortality
- Management remains lacking evidence-based approach
- Treat and optimize treatment of underlying disease in PH-LHD

Thank You



End of Presentation

Functional class

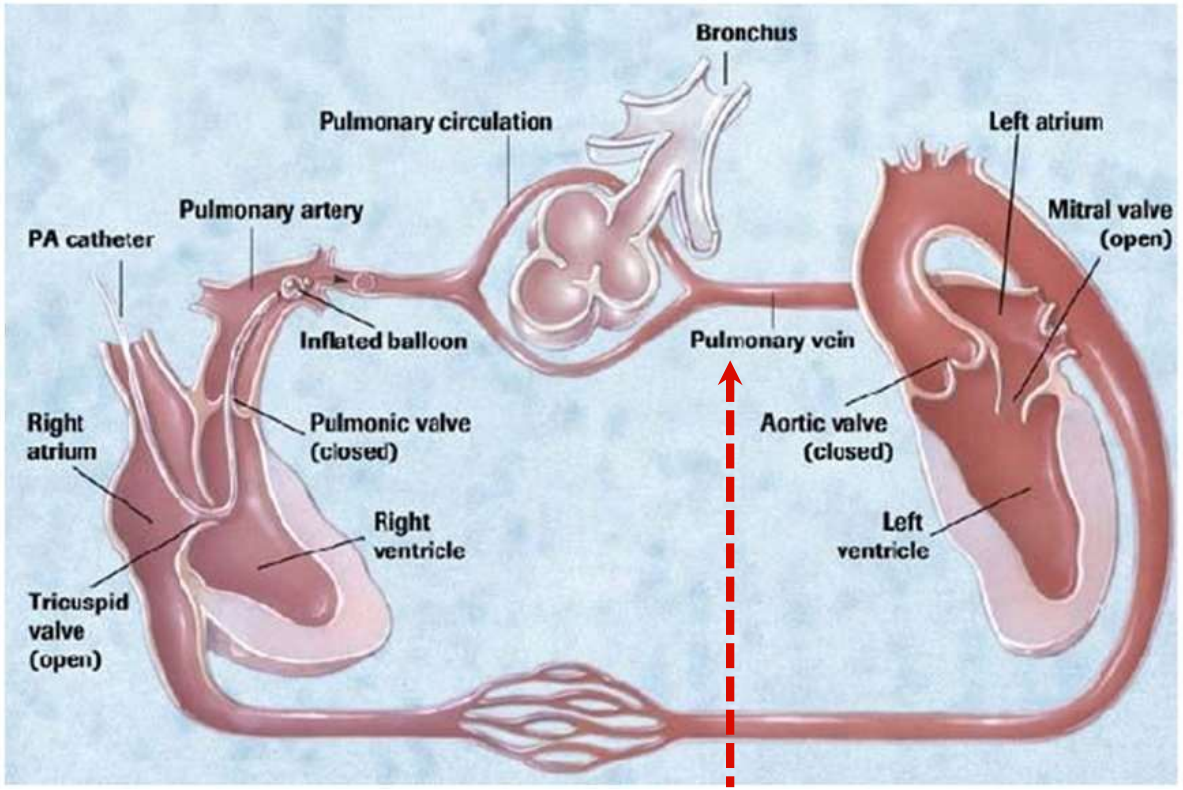
Funct. Class	Symptomatic Profile
I	Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause dyspnoea or fatigue, chest pain, or near syncope
II	Patients with pulmonary hypertension resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnoea or fatigue, chest pain, or near syncope
III	Patients with pulmonary hypertension resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnoea or fatigue, chest pain, or near syncope.
IV	Patients with pulmonary hypertension with inability to carry out any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnoea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity

Adapted from guidelines for the diagnosis and treatment of pulmonary hypertension[1]

Galiè N et al. *Eur Heart J* 2009

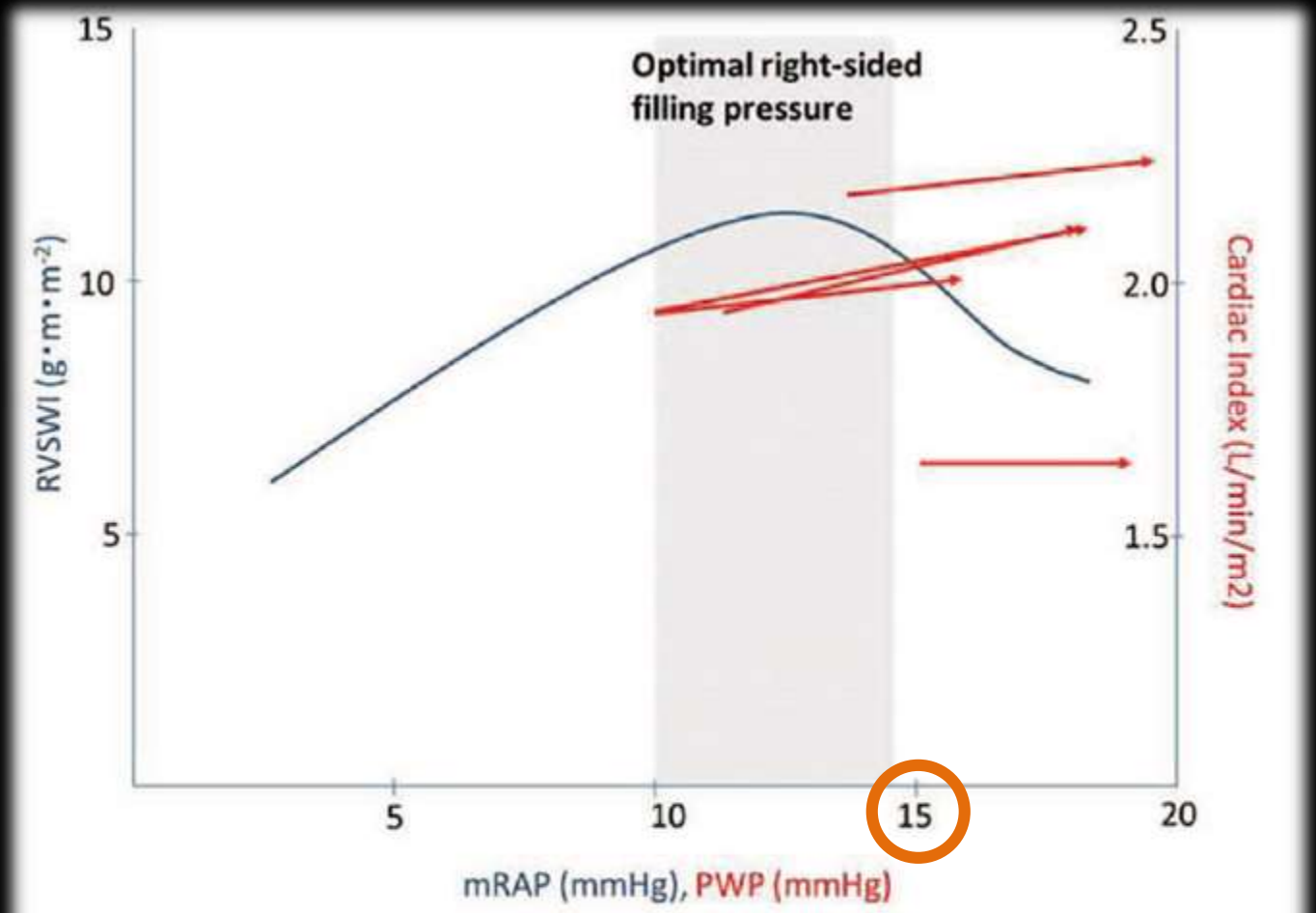
Relationship of HF and PH

Passive Congestion (Elevated PCWP)



Increased LVEDP (PCWP)

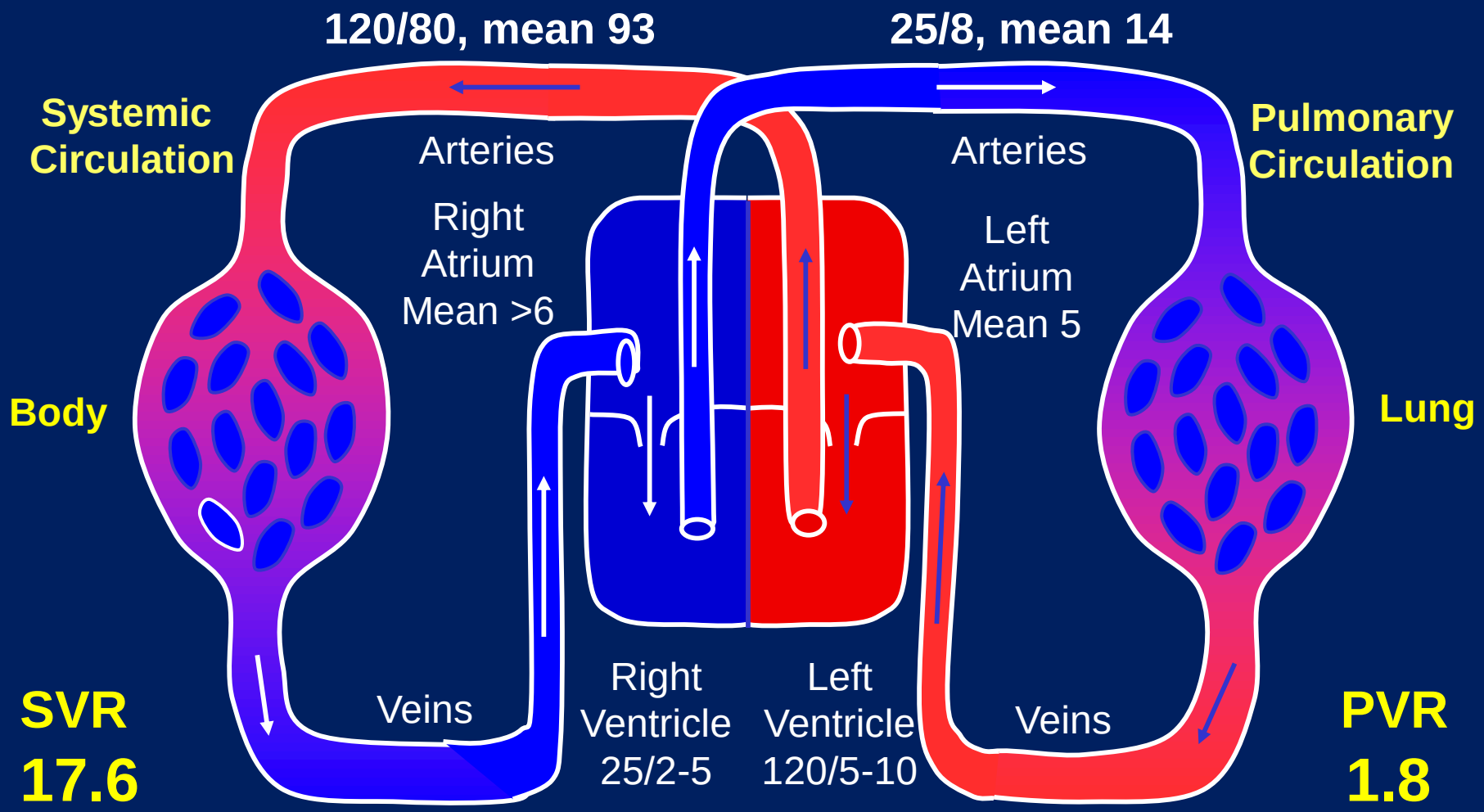
Pre - Capillary vs Post - Capillary



	N	Target	mRAP	PWP	CI
Dell'Italia wt al., 1985	13	PWP 15–18	11→15	10→18	1.9→2.1
Shah wt al., 1985	43	PWP 15–18	10→16	10→16	1.9→2.0
Dhainaut et al., 1990	20	RAP 20	10→18	12→18	1.9→2.1
Siniorakis et al., 1994	11	PWP 18–24	12→19	14→20	2.3→2.4
Ferrario et al., 1994	11	RAP 20	15→19	15→19	1.6→1.6

Inohara et al. European heart journal Acute cardiovascular care 2013;2:226-34.

Vascular Pressure in Systemic and Pulmonary Circulations (mmHg)



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