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The Role of Echocardiography in Early Detection and Evaluation of Treatment Response: Predicting Prognosis in Patients With PAH

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A DIVISION OF ULTIMATE MEDICAL ACADEMY

Supporter Acknowledgment

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Learning Objectives

- Describe the role of echocardiography in the early diagnosis of PAH and prediction of prognosis in patients with high-level risk factors.
- Summarize recent data regarding the impact of combination therapy on risk reduction and prognosis in patients with PAH.
- Discuss the value of patient-focused management and interdisciplinary approaches to support the care of patients with PAH.

PAH, pulmonary arterial hypertension.

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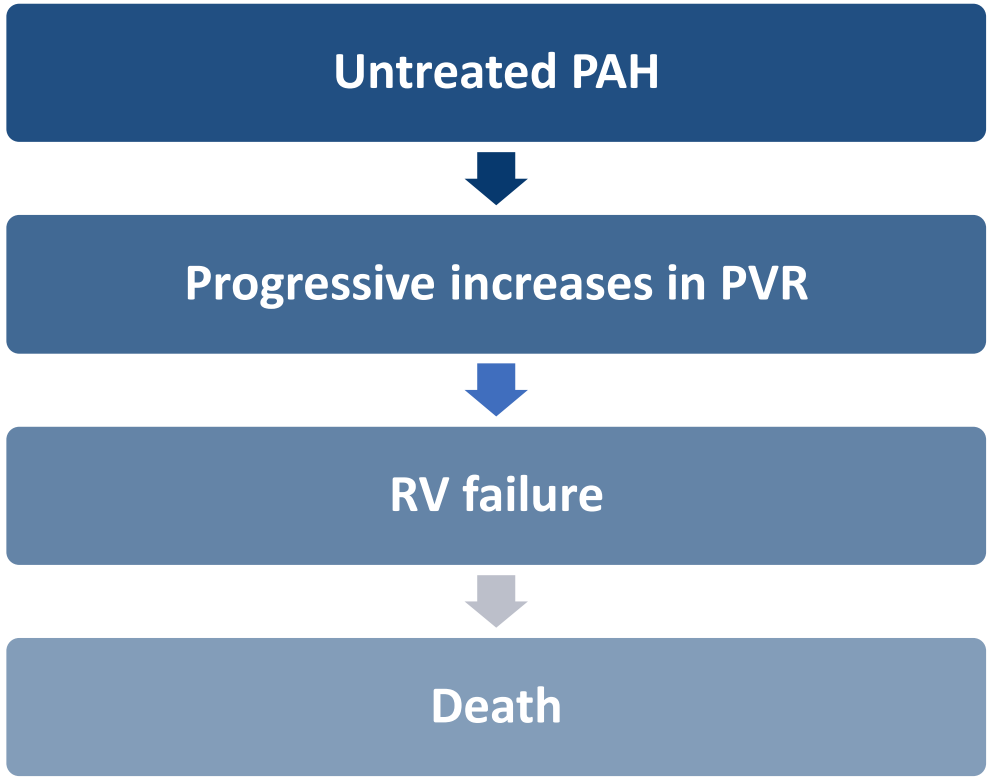
Overview of PAH

Pulmonary Arterial Hypertension

- Rare progressive disease
- ~500–1000 new cases each year in US
- More common in women
- All ages
- Most severe pulmonary hypertensive disease
- ~40% 5-Y mortality rate if untreated



PVR, pulmonary vascular resistance; RV, right ventricle.

Farber HW, et al. *Chest*. 2015;148(4):1043-1054; Humbert M, et al. *N Engl J Med*. 2004;351(14):1425-1436; National Organization for Rare Disorders. Pulmonary Arterial Hypertension. https://rarediseases.org/rare-diseases/pulmonary-arterial-hypertension/; Vazquez ZGS, et al. *Lung*. 2020;198(4):581-596.

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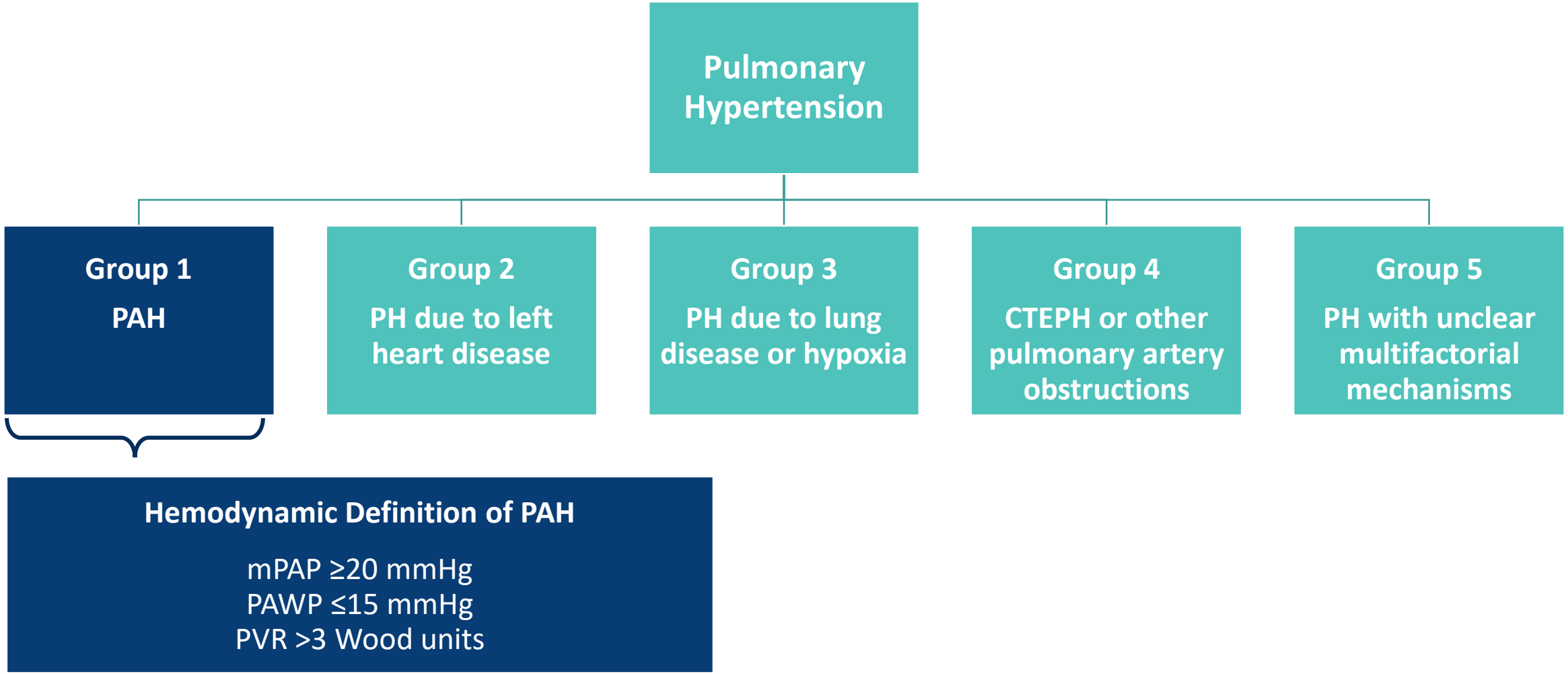
WHO Classification of Pulmonary Hypertension



CTEPH, chronic thromboembolic pulmonary hypertension; mPAP, mean pulmonary artery pressure; PAWP, pulmonary artery wedge pressure.

Hoeper MM, et al. *Lancet Respir Med*. 2016;4:306-22.

PAH Subtypes

- Idiopathic
- Heritable
- Drug & toxin-induced
- Condition-associated:
  - CTD
  - HIV infection
  - Portal hypertension
  - CHD
  - Schistosomiasis

- PVOD & pulmonary capillary hemangiomatosis
- Persistent PH of the newborn

CTD, connective tissue disease; HIV, human immunodeficiency virus; CHD, coronary heart disease; PVOD, pulmonary veno-occlusive disease.

Hoeper MM, et al. *Lancet Respir Med*. 2016;4:306-22.

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Diagnosis of PAH

Clinical Manifestations of PH

Initial symptoms
(nonspecific, induced by exertion)

Common:

- Dyspnea
- Fatigue
- Weakness
- Angina
- Syncope

Less common:

- Dry cough
- Exercise-induced nausea and vomiting

Advanced symptoms
(progressing RV failure, occur at rest)

- Abdominal distension
- Ankle edema

Symptoms specific to underlying/associated diseases or comorbidities

- Hemoptysis
- Hoarseness
- Wheeze
- Angina
- Telangiectasia, digital ulceration, & sclerodactyly (SSc)
- Inspiratory crackles (ILD)
- Spider naevi, testicular atrophy, & palmar erythema (liver disease)
- Digital clubbing (PVOD, cyanotic CHD, ILD, or liver disease)

SSc, systemic scleroderma; ILD, intersitial lung disease.
Galie N, et al. *Eur Heart J.* 2016;37(1):67-119.

Physical Signs of PH

May be present initially

- Parasternal lift
- Loud P2
- RV third heart sound
- Pansystolic murmur of tricuspid regurgitation
- Diastolic murmur of pulmonary regurgitation

More common in advanced disease

- Elevated JVP
- Hepatomegaly
- Ascites
- Peripheral edema
- Cool extremities

Not usually present

- Wheezes
- Crackles

JVP, jugular venous pressure.

Galie N, et al. *Eur Heart J*. 2016;37(1):67-119.

Differential Diagnosis

- CHF/cardiomyopathy
- CAD
- Left heart diseases
- Valvular disease
- PE
- Lung diseases (eg, COPD)

CHF, congestive heart failure; CAD, coronary artery disease; PE, pulmonary embolism; COPD, chronic obstructive pulmonary disease.

Galie N, et al. *Eur Heart J.* 2016;37(1):67–119; Stringham R, et al. *Am Fam Physician*. 2010;82(4):370-377; National Organization for Rare Disorders. Pulmonary Arterial Hypertension. https://rarediseases.org/rare-diseases/pulmonary-arterial-hypertension/

Diagnostic Evaluation for PAH

- Early referral and recognition
- Echocardiography
- V/Q scan
- PFTs
- Chest CT (usually HRCT)
- Biomarkers (BNP or NT-proBNP)
- 6MWT
- RHC/hemodynamic diagnosis

BNP, brain natriuretic peptide; CT, computed tomography; HRCT, high resolution CT; 6MWT, 6-minute walk test; NT-proBNP, N-terminal pro-BNP; PFTs, pulmonary function tests; RHC, right heart catheterization; V/Q scan, ventilation-perfusion scintigram.

Frost A, et al. *Eur Respir J*. 2019;53(1):1801904; Galie N, et al. *Eur Heart J*. 2016;37(1):67–119; Klinger JR, et al. *Chest*. 2019;155(3):565-586.

Guidelines for Echocardiographic Evaluation of Patients With Suspected PH

Echocardiographic probability of PH in symptomatic patients with a suspicion of PH

Peak TRV (m/s)	Presence of Other Echo 'PH Signs'*	Echocardiographic Probability of PH
≤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	

*See table at right; **Echocardiographic signs from ≥2 different categories (A/B/C) from the list should be present to alter the level of echocardiographic probability of PH.

LV, left ventricular; PA, pulmonary artery; TRV, tricuspid regurgitation velocity.

Galie N, et al. *Eur Heart J*. 2016;37(1):67-119.

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Echocardiographic signs suggesting PH used to assess the probability of PH in addition to TRV measurement

A: The Ventricles**	B: Pulmonary Artery**	C: Inferior Vena Cava and Right Atrium**
Right ventricle/left ventricle basal diameter ratio >1.0	RV 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 (LV 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	

Echocardiography is recommended to assess the "level of probability of PH," and results should be interpreted to support the decision to initiate cardiac catheterization.

*See table at right; **Echocardiographic signs from ≥2 different categories (A/B/C) from the list should be present to alter the level of echocardiographic probability of PH.

LV, left ventricular; PA, pulmonary artery; TRV, tricuspid regurgitation velocity.

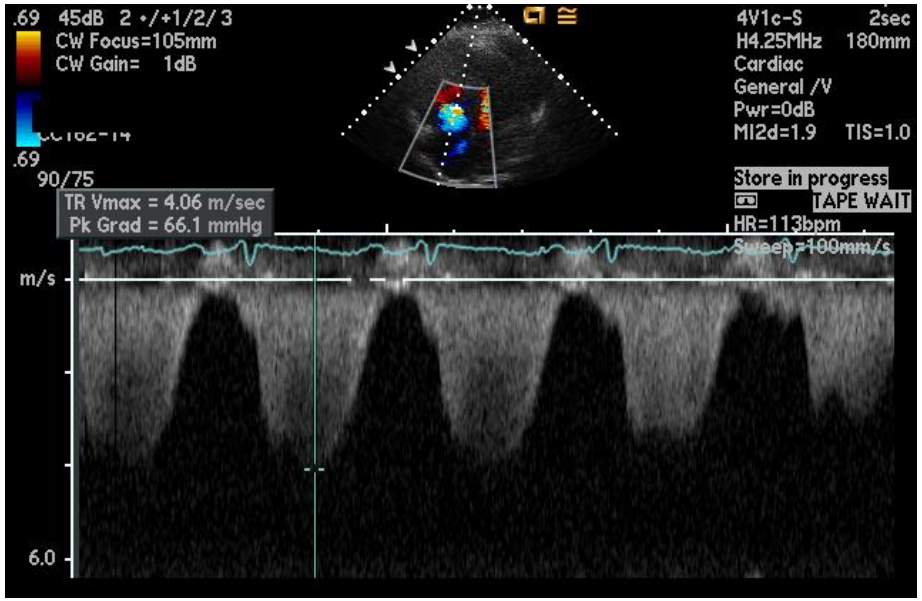
Galie N, et al. *Eur Heart J*. 2016;37(1):67-119.

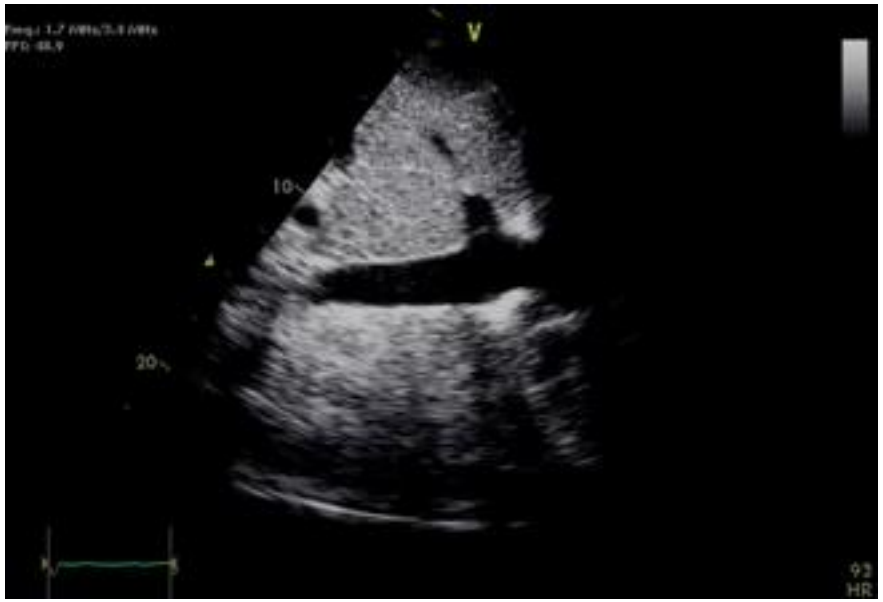
Which Patients Should Be Screened?

- ✓ CTD (eg, scleroderma, RA, GPA, SLE)
- ✓ HIV
- ✓ Sickle cell disease
- ✓ Liver disease
- ✓ Congenital heart disease (if symptomatic)

RA, rheumatoid arthritis; GPA, granulomatosis with polyangiitis; SLE, systemic lupus erythematosus.

Echocardiographic Measurement for Estimating PAP

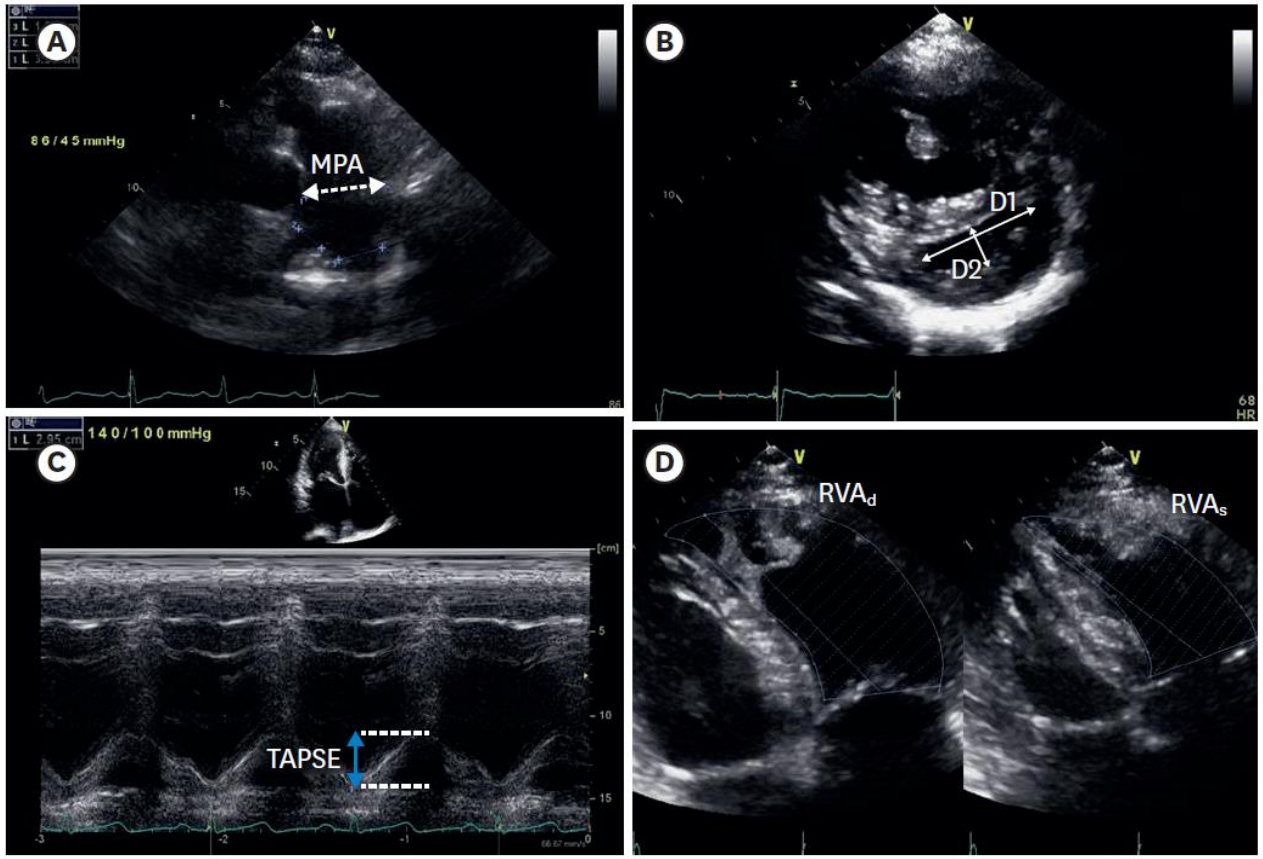




- RVSP = 4 (velocity of TR)^2 + RA pressure
  = 4(4)^2 + 20
  = ~84 mmHg
- PASP = RVSP in the absence of pulmonic outflow obstruction

RVSP, right ventricular systolic pressure; TR, tricuspid regurgitation; RA, right atrial; PASP, pulmonary artery systolic pressure.
Images courtesy of John Ryan, MD, University of Utah.

Echocardiographic Methods for Estimating RV Function



A) Assessment of MPA diameter; B) left ventricular eccentricity index; C) TAPSE; and D) RV fractional area change by measuring RVAd and RVAs for assessment of RV function.

D1, axis parallel to interventricular septum; D2, axis perpendicular to interventricular septum; MPA, main pulmonary artery; RVAd, RV area at diastole; RVAs, RV area at systole; TAPSE, tricuspid annular plane excursion.

Jang AY, et al. *J Cardiovasc Imaging*. 2020;28:1-9.

Checklist for Echocardiographic Assessments When PH Is Suspected

- ❑ Estimate pulmonary artery systolic pressure
- ❑ Evaluate severity of TR
- ❑ Evaluate right heart size and function
- ❑ Exclude left heart valvular disease and systolic dysfunction
- ❑ Exclude congenital heart disease
- ❑ Differentiate PAH from PH due to LHD
- ❑ Estimate RA pressure
- ❑ Evaluate for pericardial effusion

LHD, left heart disease.

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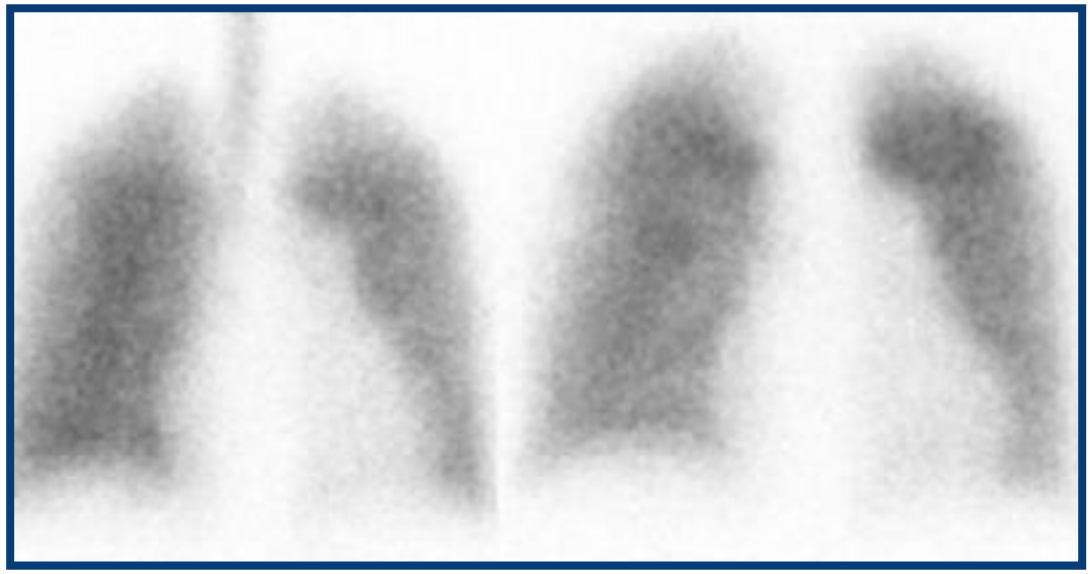
V/Q Scan

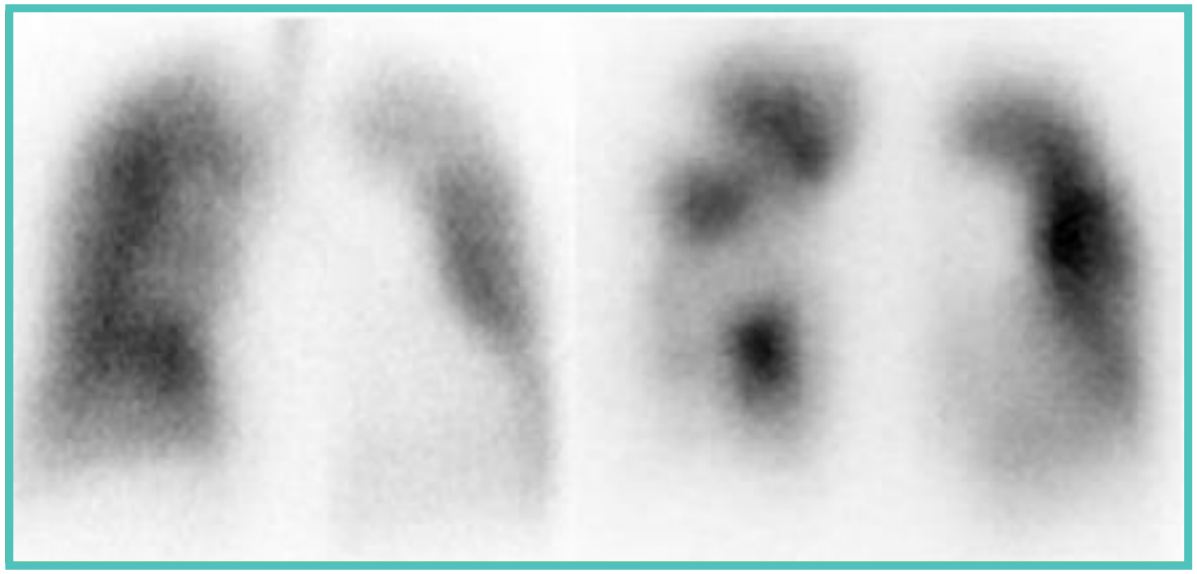
Ventilation **Perfusion**



Normal or Mottled Pattern

PAH

Ventilation **Perfusion**

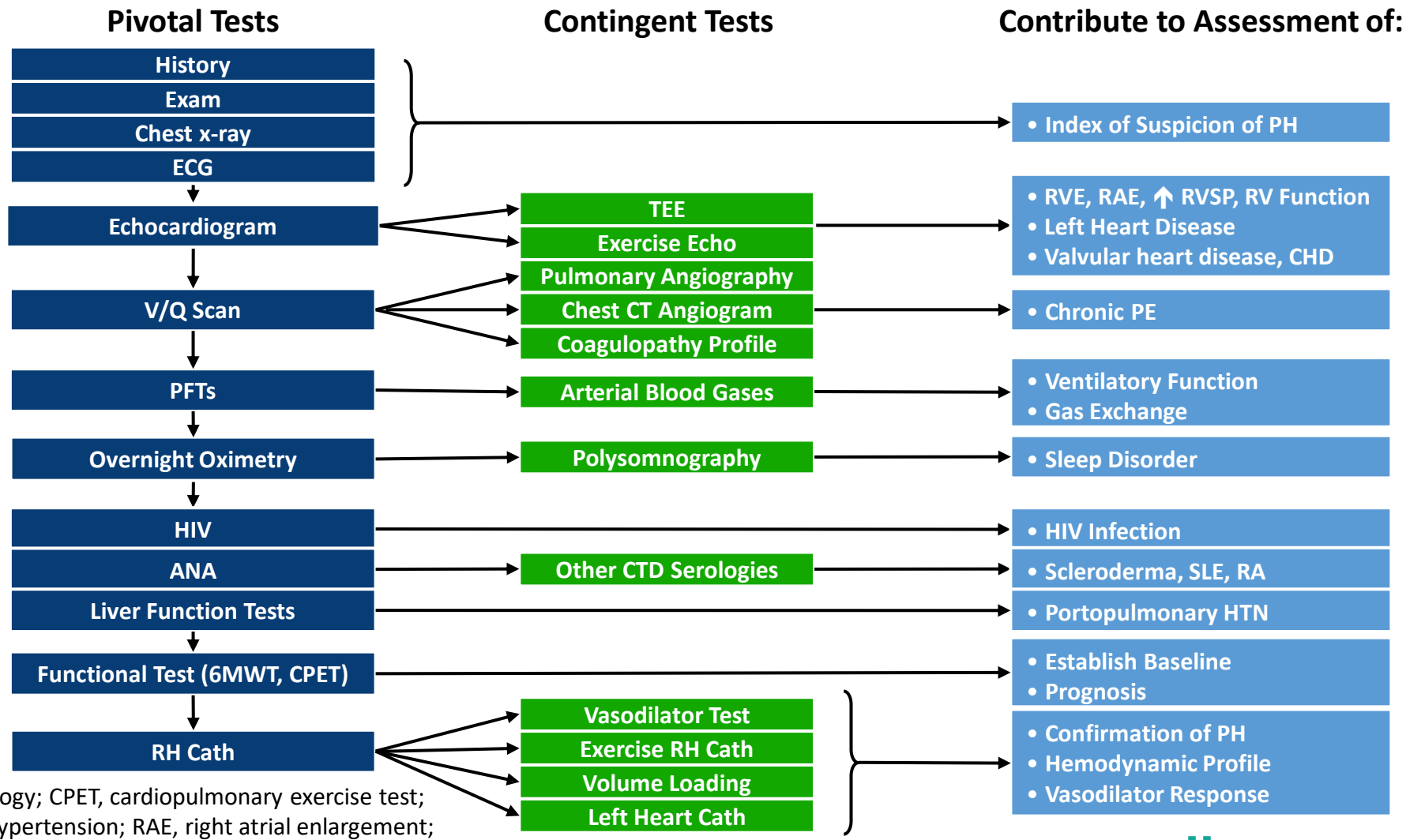


At least one segmental perfusion defect inconsistent with ventilation scan findings

CTEPH

Tanabe N, et al. *Respir Investig*. 2013;51(3):134-146.

ACCF/AHA Diagnostic Algorithm



ANA, antinuclear antibody serology; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; HTN, hypertension; RAE, right atrial enlargement; RVE, right ventricular enlargement; TEE, transesophageal echocardiography.

McLaughlin VV, et al. *J Am Coll Cardiol*. 2009;53:1573-1619.

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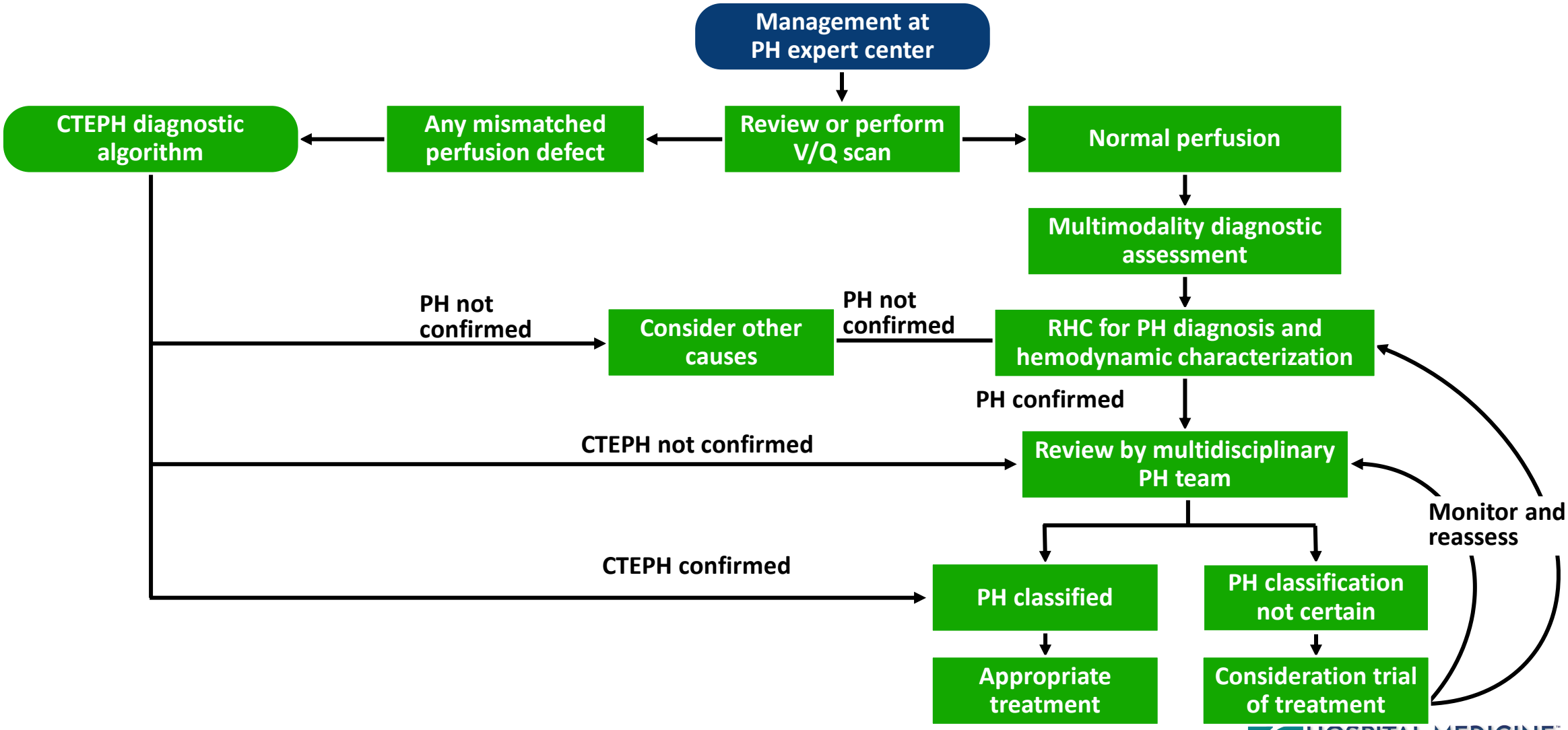
PH Diagnostic Algorithm: 2018 6th World Symposium



Adapted from Galie N, et al. *Eur Respir J.* 2019; 53 1801889.

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Evaluating Prognosis in PAH

WHO Functional Classification of PH*

Class I

- No limitation of physical activity
- Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope

Class II

- Slight limitation of physical activity
- Comfortable at rest
- Ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope

Class III

- Marked limitation of physical activity
- Comfortable at rest
- Less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope

Class IV

- Unable to carry out any physical activity without symptoms
- Manifest signs of RHF
- Dyspnea and/or fatigue may even be present at rest
- Discomfort increased by any physical activity
- Syncope

*Functional classification of pulmonary hypertension modified after the New York Heart Association functional classification according to the WHO 1998.

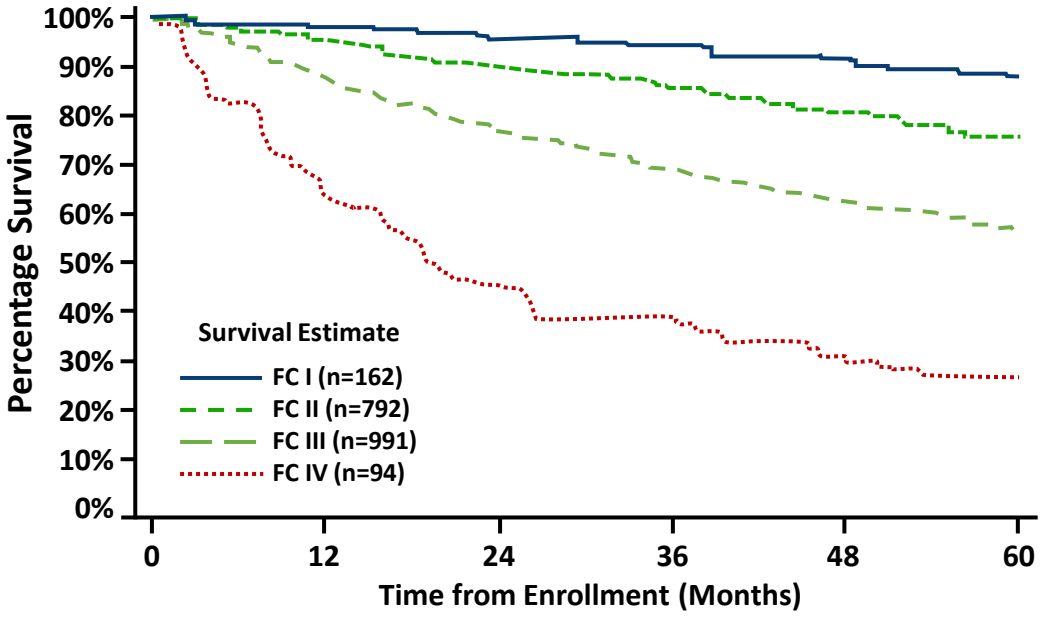
RHF, right heart failure.

Galiè N, et al. *Eur Heart J*. 2009;30(20):2493-537.

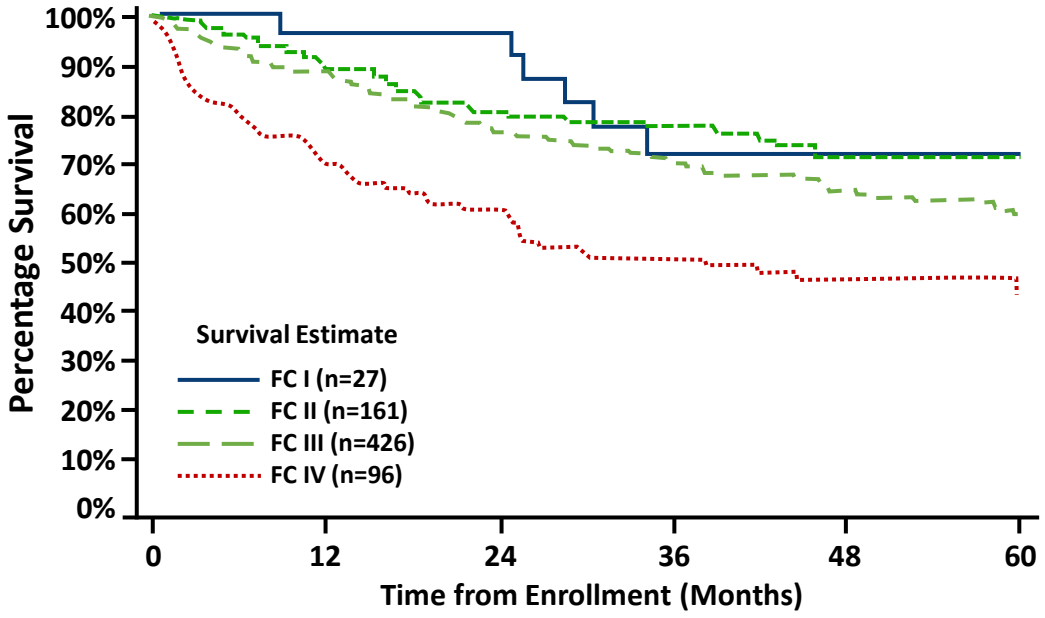
5-year Survival Among Patients With PAH by WHO FC

REVEAL Registry

Previously Diagnosed at Enrollment



Newly Diagnosed at Enrollment



NYHA FC is one of the most important predictors of survival among patients with PAH.

NYHA, New York Heart Association.

Farber HW, et al. *Chest*. 2015;148:1043-1054.

Assessment of Prognosis in PAH

Determinants of Prognosis*	Estimated 1-Year Mortality		
	Low Risk (<5%)	Intermediate Risk (5%–10%)	High Risk (>10%)
Clinical signs of right heart failure	Absent	Absent	Present
Progression of symptoms	No	Slow	Rapid
Syncope	No	Occasional syncope	Repeated syncope
WHO FC	I, II	III	IV
6MWD	>440 m	165–440 m	<165 m
Cardiopulmonary exercise testing	Peak VO_2 >15 ml/min/kg (>65% predicted) VE/VCO_2 slope <36	Peak VO_2 11–15 ml/min/kg (35–65% predicted) VE/VCO_2 slope 36–44.9	Peak VO_2 <11 ml/min/kg (<35% predicted) VE/VCO_2 slope ≥45
NT-proBNP plasma levels	BNP <50 ng/l NT-proBNP <300 ng/l	BNP 50–300 ng/l NT-proBNP 300–1400 ng/l	BNP >300 ng/l NT-proBNP >1400 ng/l
Imaging (echocardiography, CMRI)	Right atrium area <18 cm^2 No pericardial effusion	Right atrium area 18–26 cm^2 No or minimal, pericardial effusion	Right atrium area >26 cm^2 Pericardial effusion
Hemodynamics	RAP <8 mmHg Cardiac index ≥2.5 l/min/m^2 SvO_2 >65%	RAP 8–14 mmHg Cardiac index 2.0–2.4 l/min/m^2 SvO_2 60–65%	RAP >14 mmHg Cardiac index <2.0 l/min/m^2 SvO_2 <60%

*Mostly based on expert opinion and validated for idiopathic PAH. CMRI, cardiac MRI; RAP, right atrial pressure; SvO2, mixed venous oxygen saturation; VE/VCO2, minute ventilation - carbon dioxide output; VO2, oxygen uptake. Galie N, et al. *Eur Heart J.* 2016;37(1):67–119.

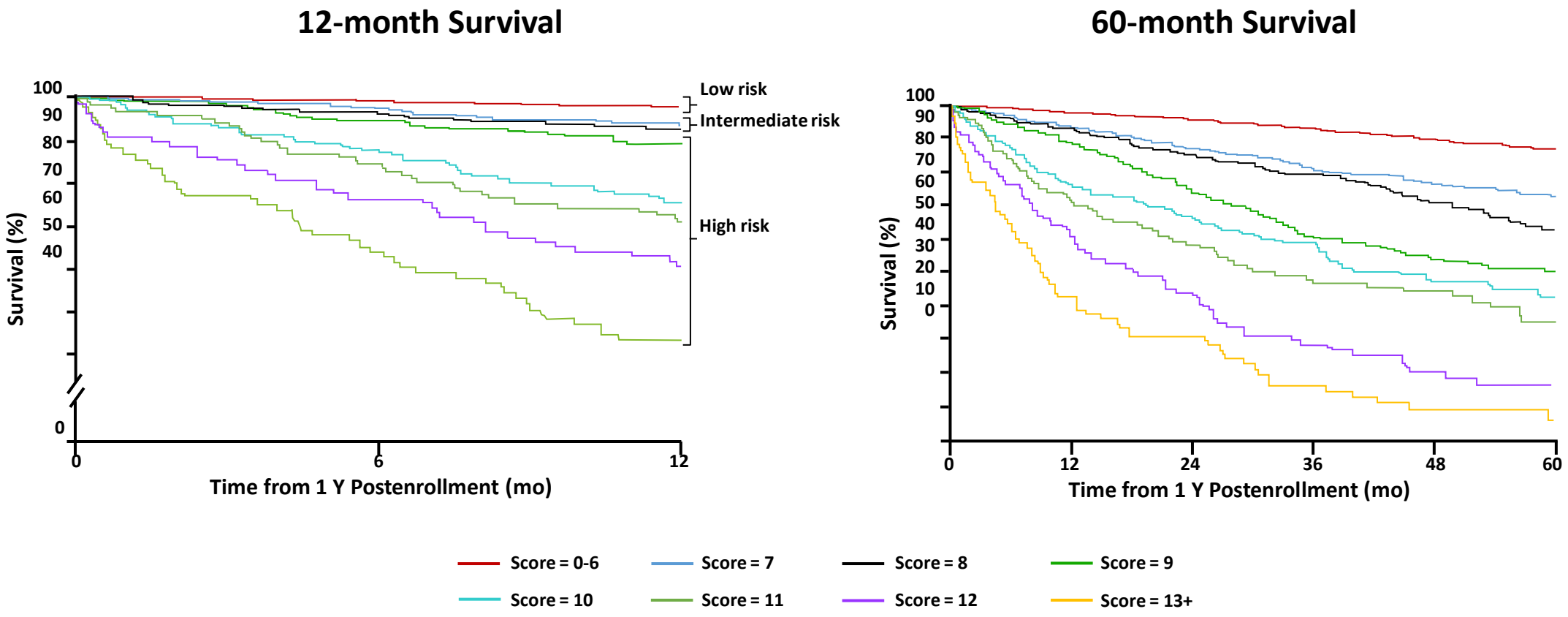
REVEAL 2.0 Risk Score Calculator

				Score
WHO Group 1 Subgroup	APAH-CTD +1	APAH-PoPH +3	FPAH +2	
Demographics	Males age >60 yr +2			
Comorbidities	eGFR <60 mL/min/1.73 m^2 or renal inefficiency (if eGFR is unavailable) +1			
NYHA/WHO FC	I -1	III +1	IV +2	
Vital Signs	SBP <110 mm Hg +1		HR >96 BPM +1	
All-Cause Hospitalizations ≤6m	All-cause hospitalizations within 6 mo +1			
6MWT	≥440 m -2	320 to <440 m -1	<165 m +1	
BNP	<50 pg/mL or or NT-proBNP <300 pg/ml -2	200 to <800 pg/mL +1	≥800 pg/mL or NT-proBNP ≥1100 pg/mL +2	
Echocardiogram	Pericardial effusion +1			
PFT	% predicted DI_{co} ≤40 +1			
RHC	mRAP >20 mm Hg within 1 year +1		PVR <5 Wood units -1	
			Sum of above	
				+6
			Risk Score	

Risk score	Risk
0–6	Low
7–8	Intermediate
≥9	High

Available at: https://www.pahinitiative.com/wp-content/uploads/2020/12/reveal-esc-ers-risk-poster.pdf

REVEAL 2.0 Risk Score Calculator: Predicting Survival in PAH



REVEAL 2.0 provided robust separation of risk among risk categories and predicted 12-month and 60-month survival in patients with PAH.

Note: REVEAL 2.0 also predicted 12- and 60-month clinical worsening (data not shown).
Benza RL, et al. *Chest*. 2019;156:323-337.

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Treatment of PAH

PAH Treatment Goals

Improve survival

Improve QoL

Improve exercise capacity
(6MWD, WHO FC)

Improve hemodynamics

Fewer/less severe symptoms

Prevent clinical worsening
(Treatment escalation hospitalization, LT, death)

LT, liver transplant.

General Management of Confirmed PAH

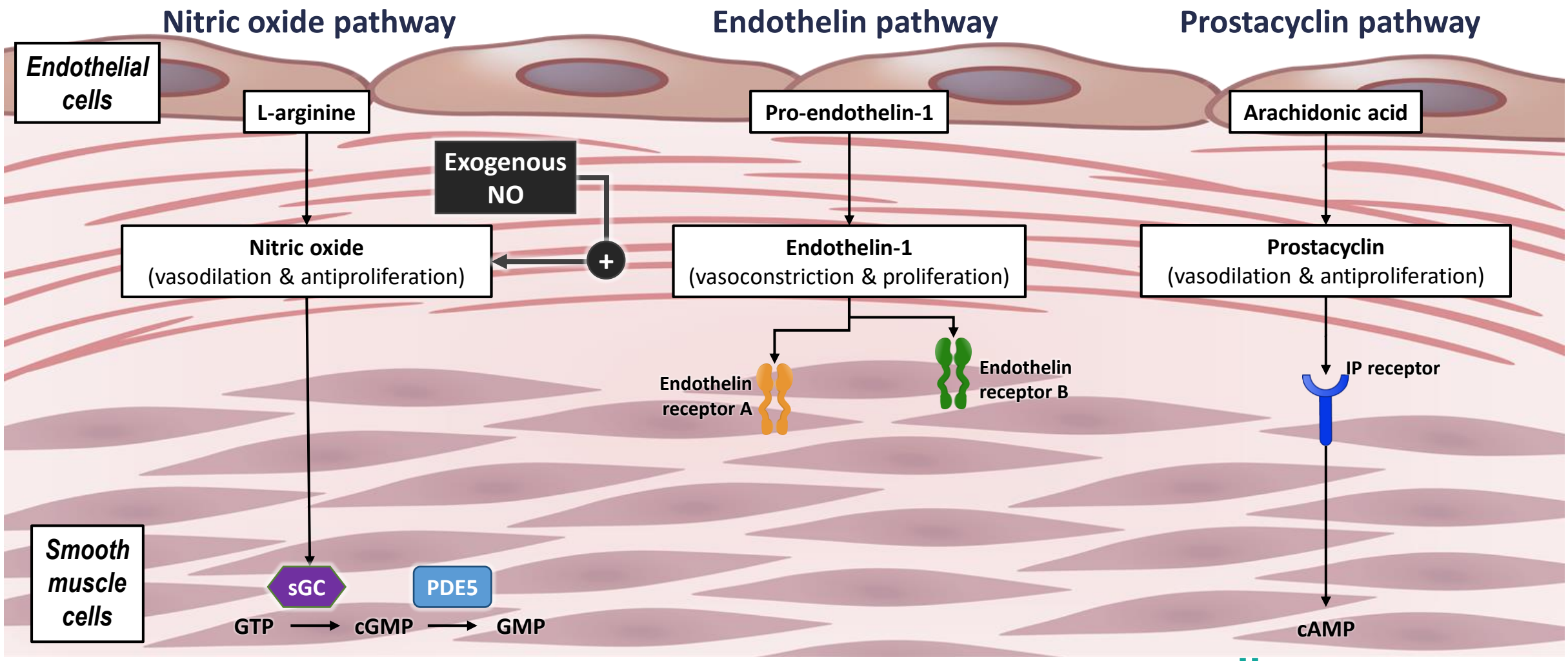
- Evaluate severity in a systematic and consistent manner
- Coordinate care between local physicians and PH centers
- Aggressively treat contributing causes
- Participate in supervised exercise activity
- Maintain current immunizations (influenza, pneumococcal pneumonia, and COVID)
- Consider when to incorporate palliative care services

Avoid the following:

- Pregnancy (if pregnancy does occur, PH center care is suggested)
- Use supplemental O_2 as needed to maintain saturations > 91% at high altitude
- Nonessential surgery (if necessary, PH center care is suggested)
- Avoid intubation (if necessary, PH center care is suggested)

Klinger JR, et al. *Chest*. 2019;155:565-586.

Therapeutic Targets of Approved PAH Treatments



GTP, guanosine triphosphate; cGMP, cyclic guanosine monophosphate; NO, nitric oxide; sGC, soluble guanylate cyclase.
Humbert M. *Eur Res Rev*. 2010;19:59-63; Yerly P, et al. *Swiss Med Wkly*. 2016;146:w14305-w14305.

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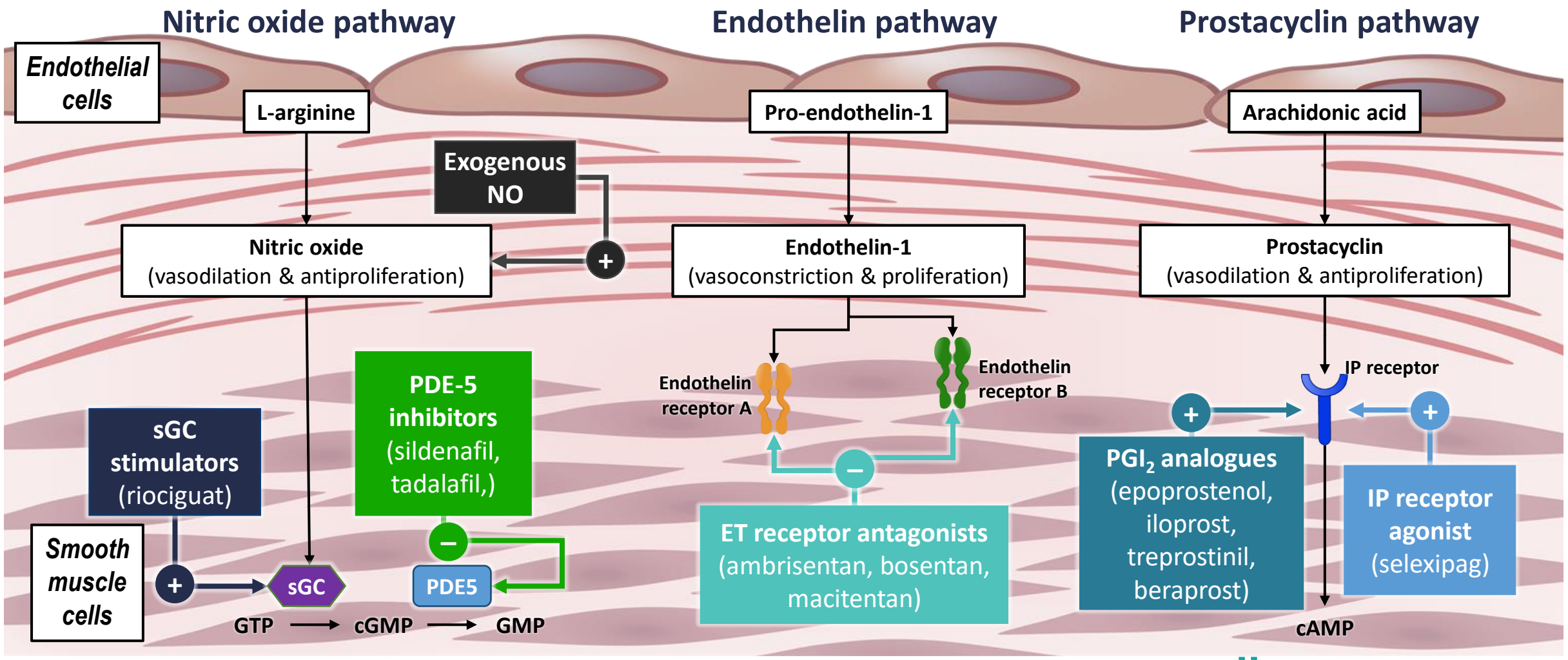

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Humbert M. *Eur Res Rev.* 2010;19:59-63; Yerly P, et al. *Swiss Med Wkly*. 2016;146:w14305-w14305.

Treatment of Symptomatic PAH: Select Clinical Trials

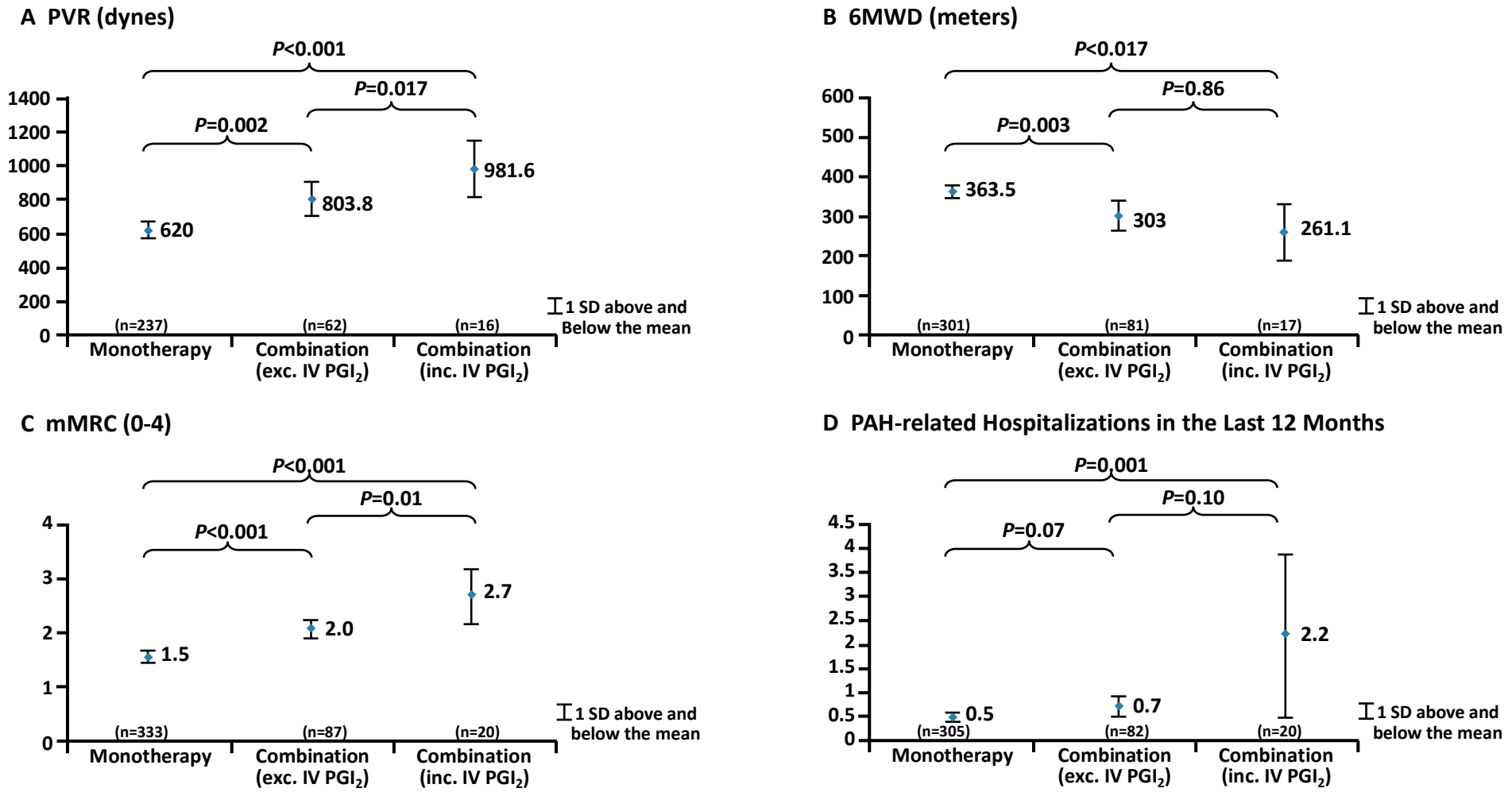
Clinical trial	Treatments	Efficacy findings	Safety and tolerability
SERAPHIN	• Macitentan 3 mg (n=250) or 10 mg (n=242) • PBO (n=250)	• Risk for worsening ↓ with 3-mg & 10-mg MAC vs PBO	• AEs more common with MAC: headache, nasopharyngitis, anemia
GRIPHON	• Selexipag (N=574) • PBO (N=582)	• Proportion of patients *without* an event* ↑ with selexipag vs PBO	• AEs more common with selexipag: headache, diarrhea, nausea, jaw pain
FREEDOM-EV	• Treprostinil (po; n=345) • PBO (n=345)	• Clinical worsening ↓ with TRE vs PBO	• AEs most common with TRE: headache, diarrhea, flushing, nausea, vomiting
PATENT 1 & 2	• Riociguat up to 2.5 mg tid (n=254) or 1.5 mg tid (n=63) • PBO (n=126)	• Improved 6MWD, PVR, NT-proBNP, WHO FC, time to clinical worsening, & dyspnea • 6MWD & WHO FC improvements persisted at 2Y	• Most common SAE with PBO & 2.5 mg–maximum group: syncope (4% & 1%, respectively)

*Death from any cause or PAH-related complication ≤7d after last dose.

AE, adverse event; MAC, macitentan; po, by mouth; SAE, serious adverse event; TRE, treprostinil.

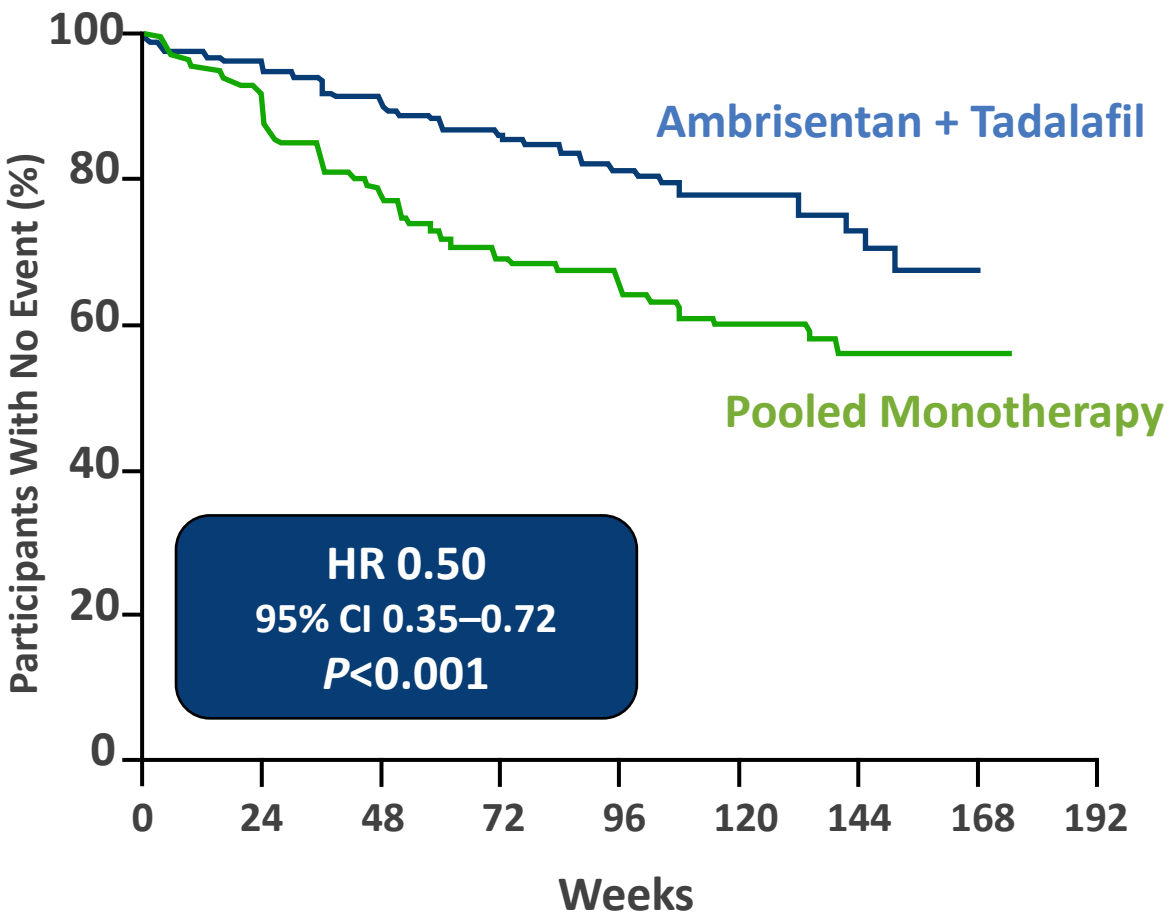
Pulido T, et al. *N Engl J Med*. 2013;369(9):809-818; Sitbon O, et al. *N Engl J Med*. 2015;373:2522-33; White RJ, et al. *Am J Respir Crit Care Med*. 2020;201(6):707-717.

Incremental Burden of Disease in Patients With PAH Receiving Monotherapy or Combination Therapy



Small M, et al. *Advances in Therapy*. 2014;31:168-179.

AMBITION: Combined Ambrisentan and Tadalafil in Patients With PAH



Study objective:

- Evaluate effect of initial combination therapy with ambrisentan & tadalafil on long-term PAH outcomes

Treatment:

- AMB + TAD (COMB; n=253) vs AMB or TAD alone (MONO; n=247)

Primary endpoint:

- Time to clinical failure

Findings:

- Clinical failure risk ↓ with COMB vs MONO (risk reduction: HR=0.50; 95%CI, 0.35 to 0.72; *P*<0.001)
- COMB vs MONO showed greater ↓ from baseline in NT-proBNP, clinical response rate, & 6MWT improvement
- AEs more common with COMB vs MONO: peripheral edema, headache, nasal congestion, anemia

AMB, ambrisentan; COMB, combination therapy; MONO, monotherapy; TAD, tadalafil.

Galiè N, et al. *N Engl J Med*. 2015;373(9):834-844.

TRITON: Triple vs Dual Combination Therapy

- **Study objective:**
  - Comparison of initial triple vs double therapy (macitentan + tadalafil + selexipag/placebo)
- **Efficacy findings:**

Outcome	Triple initial therapy (N=123)	Double initial therapy (N=124)	Ratio/Difference/HR	95% CI	*P* value
Change in PVR at Week 26	54% ↓	52% ↓	Ratio: 0.96	(0.86–1.07)	0.424
Change in 6MWD at Week 26	55.0 m ↑	56.4 m ↑	LSM Difference: −1.4m	(−19.4 to 16.5)	0.876
Change in NT-proBNP at Week 26	74% ↓	75% ↓	Ratio: 1.03	(0.77–1.37)	0.853
Time to disease progression*	Not reported	Not reported	HR: 0.59	(0.32-1.09)	0.087

- **Safety findings:**
  - AEs more frequent with triple vs double therapy: headache, diarrhea, nausea, extremity pain, jaw pain, & vomiting
  - Rate of selexipag/placebo discontinuation due to AEs was similar between groups

*Centrally adjudicated, until end of observation period +7d.

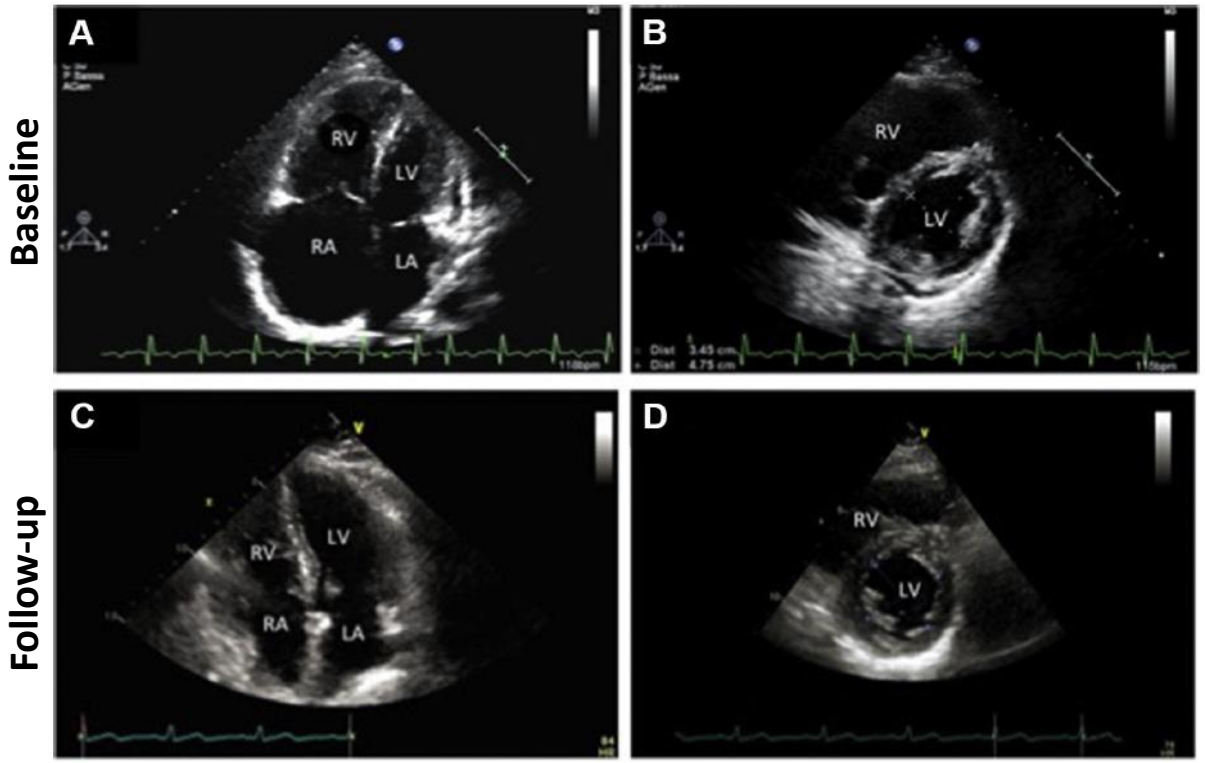
Chin K, et al. *Am J Respir Crit Care Med*. 2020;201:A2928.

Triple Upfront Combination Therapy With Ambrisentan, Tadalafil, and Treprostinil in Severe Nonreversible PAH

Hemodynamics at baseline and 24-m follow-up*

Variable	Baseline	Follow-up	Change (%)	P-Value
RAP, mmHg	13 ± 3	5 ± 2	–8 (–62)	<0.001
mPAP, mmHg	60 ± 9	42 ± 5	–18 (–30)	<0.001
PAWP, mmHg	8 ± 2	9 ± 3	1 (12)	0.545
Cardiac input, L/min/m^2	1.8 ± 0.3	3.5 ± 0.8	1.7 (94)	<0.001
PVR, WU	16.4 ± 4.4	5.5 ± 1.3	–10.9 (–69)	<0.001
SvO_2, %	56 ± 6	70 ± 7	14 (25)	<0.001

	Baseline	Follow-up
PVR (WU)	17.9	6.1
RVEDA (cm^2)	26	17
RVESA (cm^2)	19	10
LV-EI	1.5	1.1
REVEAL 2.0	11	7



Triple upfront combination therapy was associated with clinical and hemodynamic improvement and right-sided heart reverse remodeling.

*Values are expressed as mean ± SD or as otherwise indicated.
LV-EI; left ventricular ejection index; RVEDA, right ventricular end-diastolic area; RVESA, right ventricular end-systolic area; SvO_2, mixed venous oxygen saturation; WU, Wood unit.
D'Alto M, et al. *Chest*. 2020;157:376-383.

ESC/ERS Guidelines: Initial Combination Therapy for PAH

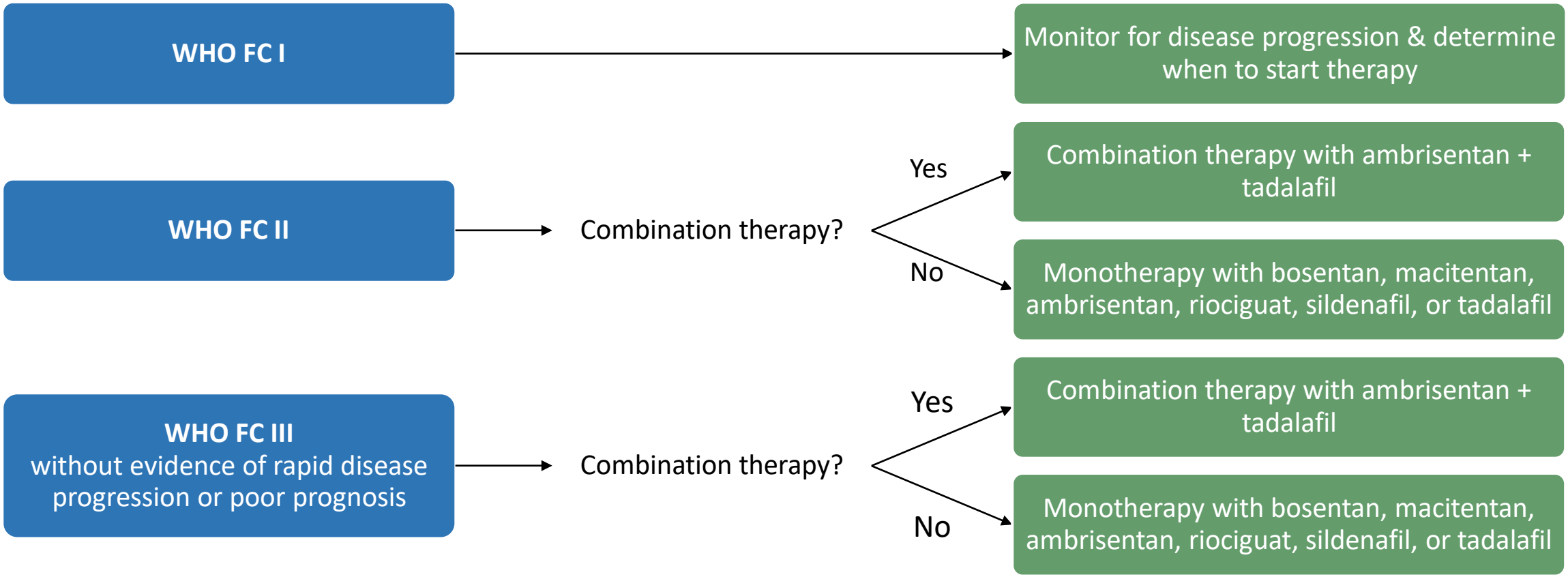
Class	Therapy	Indication		
		WHO-FC II	WHO-FC III	WHO-FC IV
ERA + PDE-5i	Ambrisentan + tadalafil	☑	☑	☑
	Other ERA + PDE-5i	☑	☑	☑
ERA + PDE-5i + prostacyclin analogue	Bosentan + sildenafil + IV epoprostenol		☑	☑
ERA/PDE-5i + prostacyclin analogue	Bosentan + IV epoprostenol		☑	☑
	Other ERA or PDE-5i + SC treprostinil		☑	☑
	Other ERA or PDE-5i + IV prostacyclin analogue		☑	☑

Sequence is by rating. Therapies/indications highlighted in orange have IB recommendations.

IV, intravenous; SC, subcutaneous.

Galie N, et al. *Eur Heart J.* 2016;37(1):67–119.

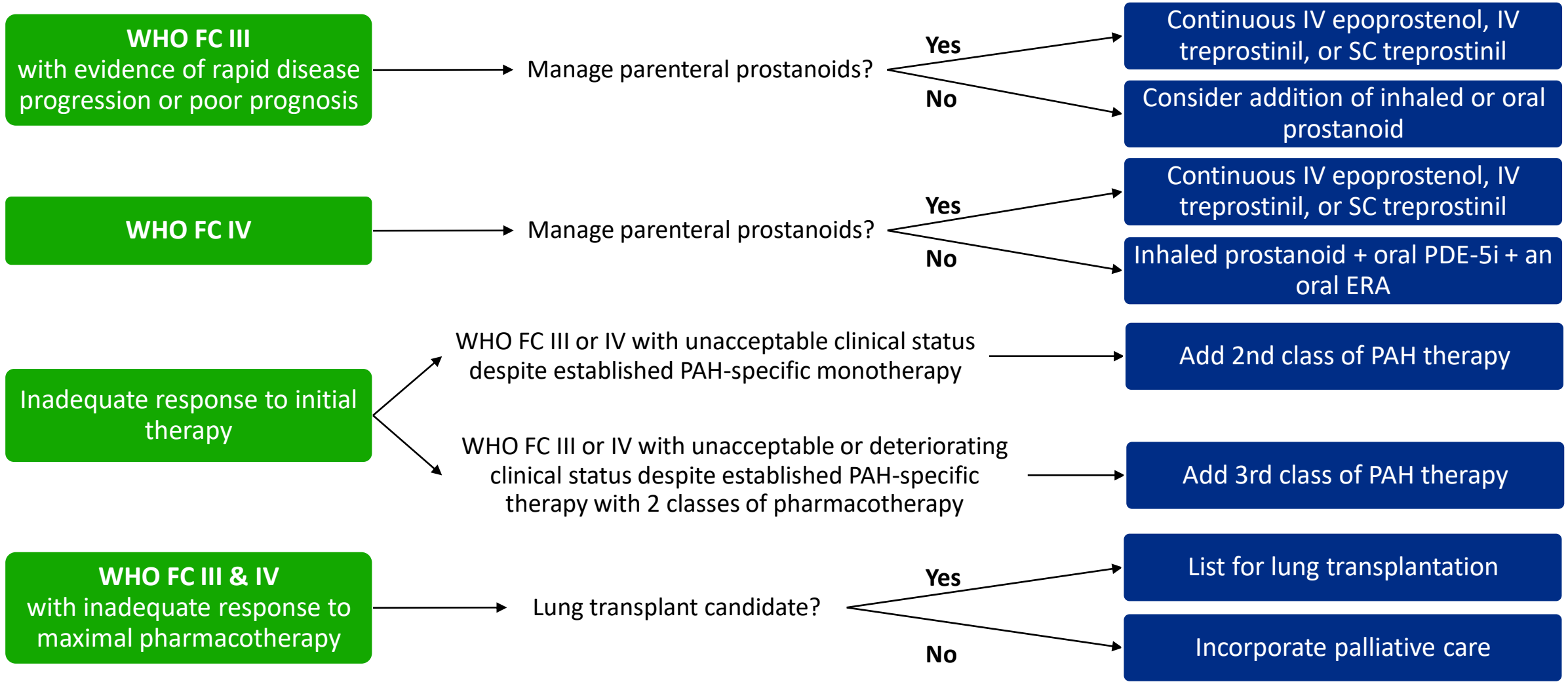
2019 CHEST Guidelines for Management of PAH in Treatment-Naïve Patients



*Calcium channel blockers are not recommended in patients with CTD-PAH, as long-term efficacy has been confirmed in only 0.6% of patients. (Zanatta E, et al. *Exp Biol Med (Maywood).* 2019;244(2):120-131.)

Klinger JR, et al. *Chest*. 2019;155:565-586.

2019 CHEST Guidelines for Management of PAH



Klinger JR, et al. *Chest*. 2019;155:565-586.

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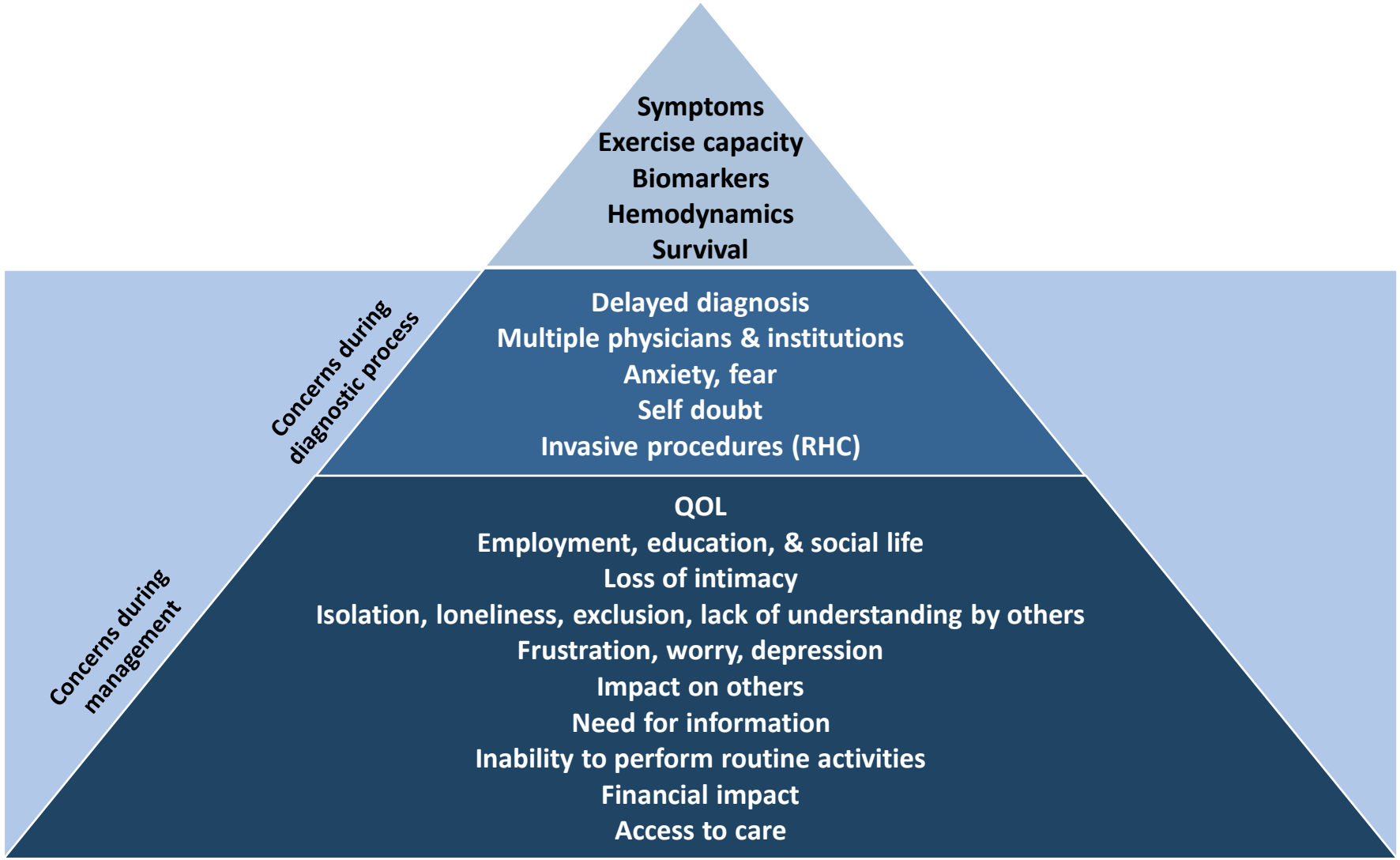
Multidisciplinary Approaches and Patient-Centered Care

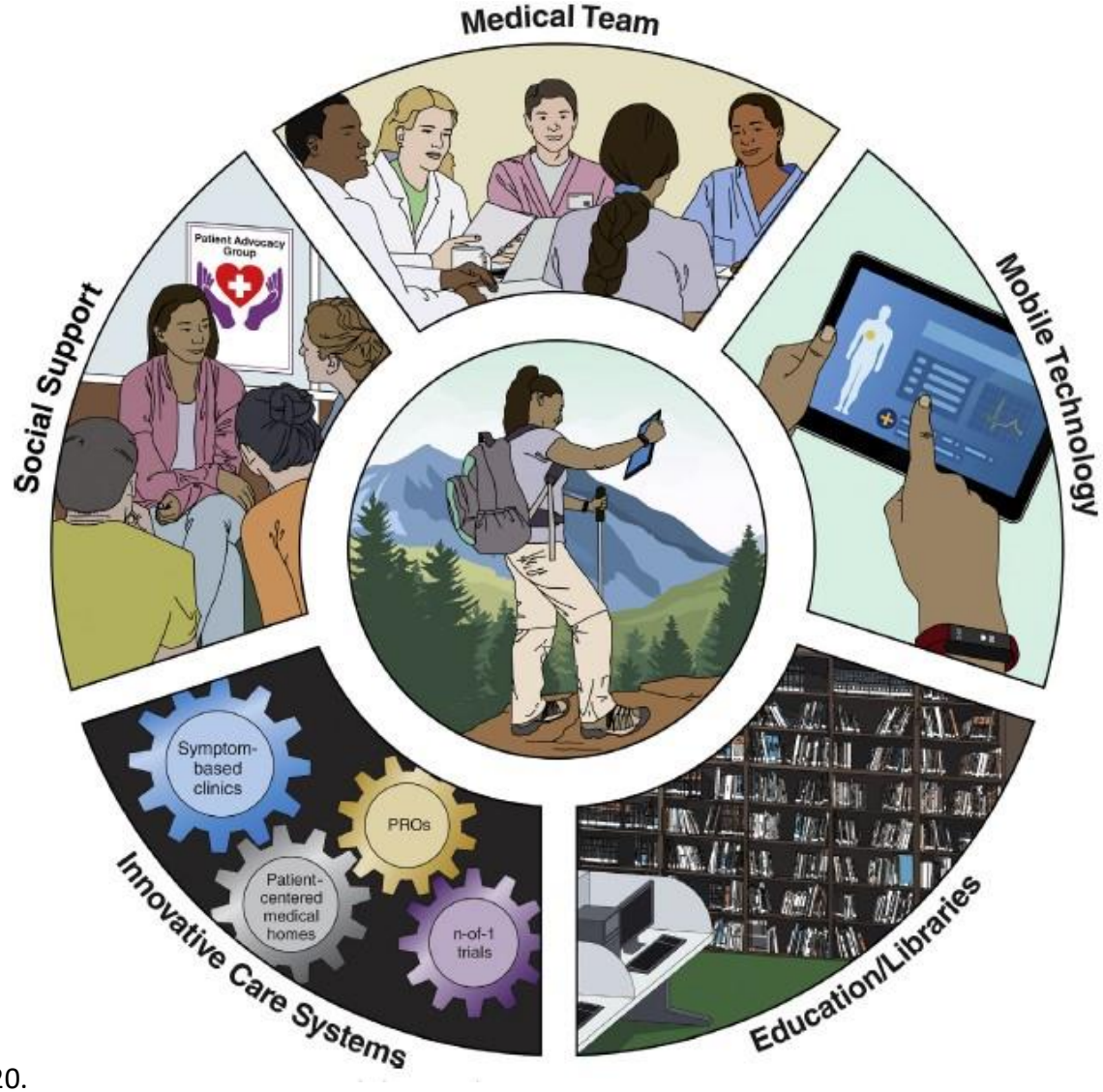
Concerns Regarding PAH Management: The Patient Perspective



Surveys of patients and caregivers suggest that traditional parameters of PH severity may be the "tip of the iceberg" when the broader range of patient concerns is considered.

McGoon MD, et al. *Eur Respir J*. 2019;53(1):1801919.

Collaborative PAH Care



Wohlfahrt P, et al. *Heart Fail Clin*. 2020;16:409-420.

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Case Study Assessments

Case 1: Patient Description

A 47-yr-old woman with history of Graves' disease (status post radioactive iodine: ablation) and MS presents with 6 mos of progressive dyspnea and inability to climb a flight of stairs. She has no chest pain, syncope, or palpitations.

Case 1: Physical Exam

Physical Exam Findings	
Wt: 171 lbs **BMI:** 29 mg/kg^2	**Heart:** Trivial systolic murmur at left lower sternal border, pronounced P2
HR: 97 bpm	**Chest:** + RV heave
RR: 16 bpm	**Neck:** JVP normal, negative HJR
BP: 115/87 mm Hg	**Lungs:** clear
SpO_2: 98% on room air	**Extremities:** no edema, clubbing, or cyanosis

BMI, body mass index; BP, blood pressure, HJR, hepatojugular reflux; HR, heart rate; RR, respiratory rate; Sp02, oxygen saturation.

Case Discussion Question

Which of the following would you include as part of the initial evaluation for this patient?

A. EKG
B. Echo
C. PFTs
D. V/Q scan
E. HIV
F. Autoimmune testing
G. 6MWD
H. BNP
I. Cardiac MRI
J. RHC

Echo, echocardiogram; EKG, electrocardiogram; MRI, magnetic resonance imaging.

Case 1: Initial Evaluation

Initial Evaluation Findings	
EKG: normal sinus rhythm, RVH, RA enlargement, right axis deviation	**Autoimmune testing:** ANA, RF, CCP negative
Echo: RA mildly dilated, RV severely enlarged & reduced function, small LV, EF 60%, estimated PASP 60 mmHg, small effusion	**6MWD:** 266 m, HR 97 to 137, 81% room air at end
PFTs: FEV1/FVC 0.74, TLC 95%, DLCO 72%	**BNP:** 723 ng/L
V/Q scan: low probability	**Cardiac MRI:** no congenital disease, RVEF 17%
HIV: nonreactive	

CCP, cyclic citrullinated peptide; DLCO, diffusing capacity of the lungs for carbon monoxide; EF, ejection fraction; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; TLC, total lung capacity.

Case Discussion Question

Based on her initial workup, the patient undergoes RHC and is diagnosed with IPAH. How would you characterize her prognosis?

A. High risk

B. Moderate risk

C. Low risk

IPAH, idiopathic pulmonary arterial hypertension.

Case Discussion Question

What type of treatment would you prescribe for this patient?

A. Continuous IV epoprostenol, IV treprostinil, or SC treprostinil

B. Combined ambrisentan + tadalafil

C. Monotherapy with bosentan, macitentan, ambrisentan, riociguat, sildenafil, or tadalafil

Case 2: Patient Description

66-yr-old woman with a history of HTN, T2DM, and obesity presents for 3Y of exertional dyspnea and fatigue. Her evaluation is unremarkable other than ECHO showing EF 58%, PASP 65 mmHg. She denies CP, LH, syncope, and LE edema. She has occasional palpitations and snores.

Current medications include verapamil 240 mg bid, atenolol 25 mg qd, metformin 1000 mg qd. She denies use of any substances and has no family history of group 1 PAH diseases.

T2DM, Type 2 diabetes mellitus.

Case 2: Physical Exam

Physical Exam Findings	
Ht: 5’ 4” **Wt:** 220 lbs	**Lungs:** Clear bilaterally
BP: 150/90 mm Hg	**Heart:** Palpable RV tap, RRR, loud S2, RS4, II/VI holosystolic murmur at LLSB
Gen: breathing comfortably at rest	**Abdomen:** Obese, S/NT/ND
Neck: JVP ~12 cm, normal carotid pulse	**Extremities:** Trace bilateral edema

LLSB, lower left sternal border; NT/ND, nontender/nondistended; RRR, regular rate and rhythm; RS4, right heart sound 4.

Case 2: Initial Evaluation

Test Findings	
ECG: sinus, normal axis, no chamber enlargement	**Labs:** ANA- and HIV-negative, Hgb 10.5, Cr 1.2, NT-pro BNP 220
Echo: EF 58%, borderline LVH, grade 1 diastolic dysfunction, normal RV size/function, moderate LA enlargement, normal RA size, normal valves with mild TR, mild moderate MR and mild AI, PASP 65 mmHg, RA pressure 15 mmHg	**V/Q:** normal perfusion scan
PFTs: slight restriction, DLCO normal	

AI, atrial insufficiency; LA, left atrial; LVH, left ventricular hypertrophy; MR, mitral regurgitation.

Case Discussion Question

What is your next step for this patient?

A. Initiate sildenafil

B. Perform right heart catheterization

C. Repeat echocardiogram in 6 months

D. Optimize volume status, optimize BP control, and screen for sleep apnea

Program Summary

- PAH is a chronic vascular disease characterized by abnormal thickening of the arterial wall leading to increased PVR, RV failure, and eventually heart failure, if left untreated.
- Early recognition, accurate diagnosis, and treatment that is appropriately tailored based on patient risk are central to avoiding morbidity and mortality.
- Thorough clinical assessment is central to the diagnosis, echocardiography plays a key role in detecting preclinical stages of disease, as well as evaluating prognosis and treatment options.
- Multiple treatments targeting the NO, endothelial, and prostacyclin pathways are approved and have shown good efficacy, particularly when used in combination.
- Additionally, collaborative management between specialty care centers, patients, and caregivers is needed to ensure optimal disease management over the long-term.

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Thank you!

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