YONSEI UNIVERSITY

호흡기내과 의사를 위한 Respiratory Review of 2025
: Pulmonary vascular disease

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Severance

Contents

- **Pulmonary hypertension(PH)**
  - **Definition of pulmonary hypertension**
  - **Imaging techniques for pulmonary hypertension**
  - **Pulmonary hypertension in chronic lung disease**
- **Chronic thromboembolic pulmonary disease**

Definition of pulmonary hypertension

Revision of definition of PH

- mPAP ≥ 25mmHg -> mPAP ≥ 20mmHg
- PVR > 3 WU -> 2 WU

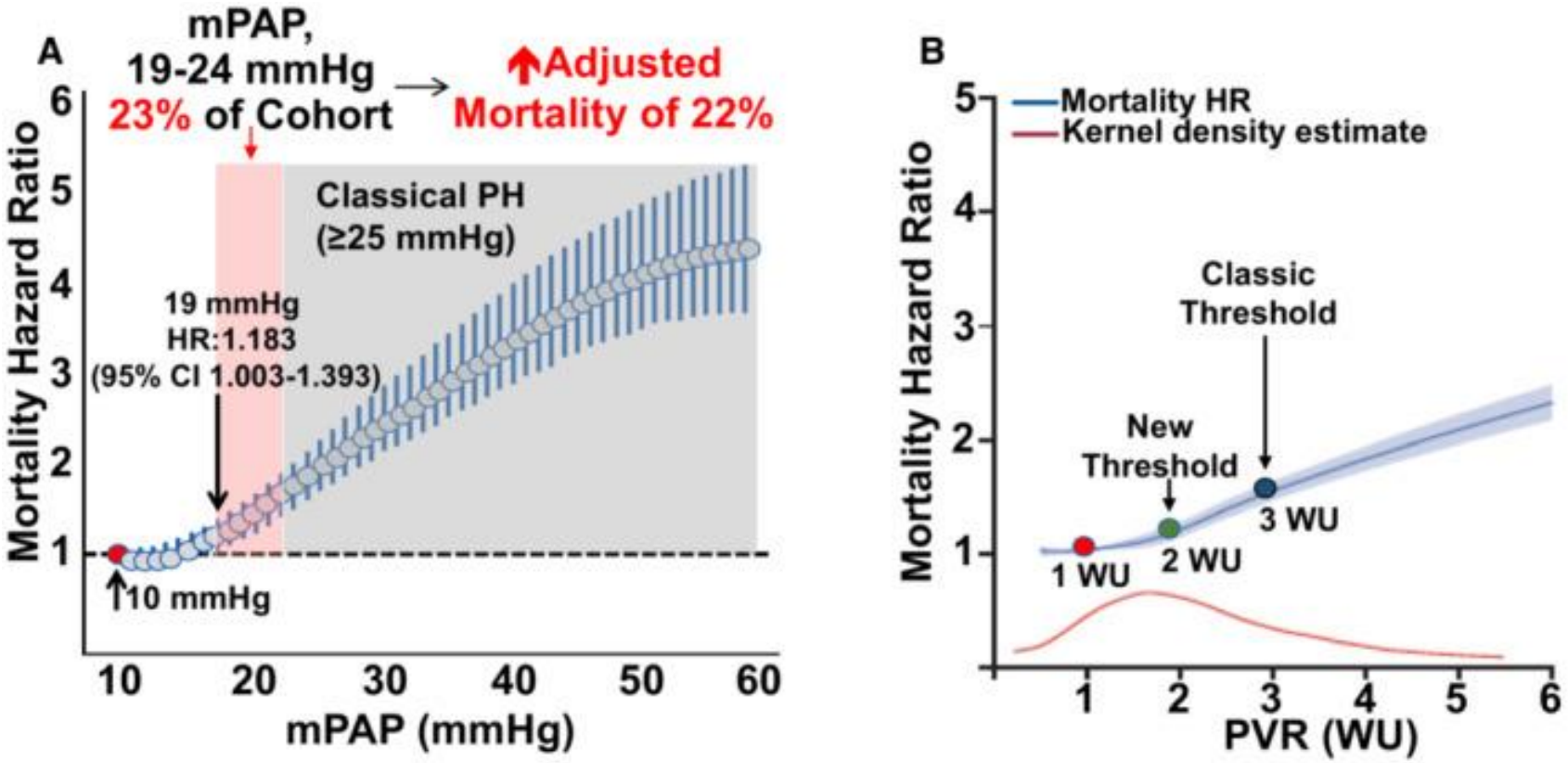
TABLE 1 Haemodynamic criteria of pulmonary hypertension (PH)

	Haemodynamic characteristics
PH	mPAP >20 mmHg
Pre-capillary PH	mPAP >20 mmHg PAWP ⩽15 mmHg PVR >2 WU
Isolated post-capillary PH (ipcPH)	mPAP >20 mmHg PAWP >15 mmHg PVR ⩽2 WU
Combined post- and pre-capillary PH (cpcPH)	mPAP >20 mmHg PAWP >15 mmHg PVR >2 WU
Exercise PH	mPAP/CO slope >3 mmHg/L/min between rest and exercise

mPAP: mean pulmonary arterial pressure; PAWP: pulmonary arterial wedge pressure; PVR: pulmonary vascular resistance; WU: Wood Units; CO: cardiac output.

Eur Respir J. 2022;2022:2200879
Eur Respir J. 2024 Oct 31;64(4):2401324.

Evidence of new definition



J Am Heart Assoc. 2023 Apr 18;12(8):e029024.

Changed definition of PH

- Earlier diagnosis

- In clinical management
  - Risk factor modification
  - Earlier referral to specialty center
  - Earlier treatment

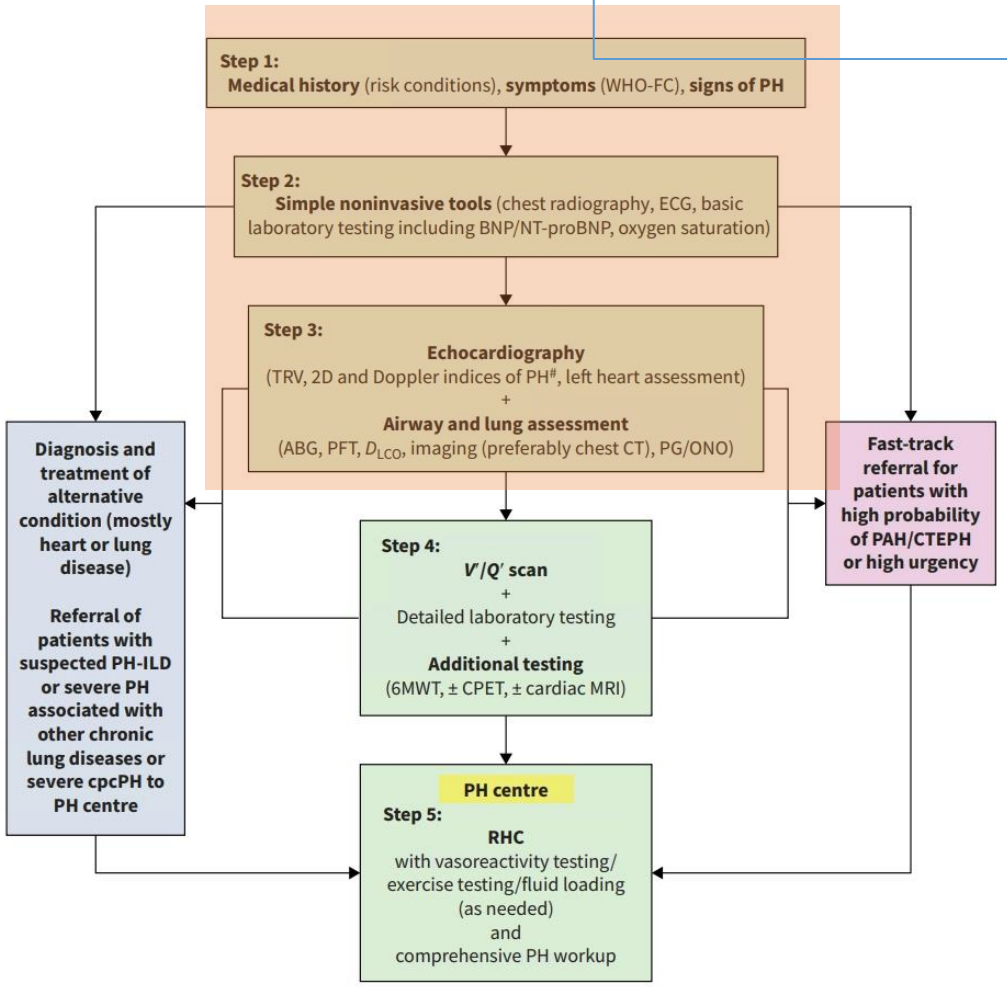
Imaging techniques for PH

Right heart catheterization, golden standard for diagnosis…

- Essential for diagnosis but invasive
- Cardiac output, cardia index, pulmonary arterial wedge pressure, pulmonary vascular resistance, mPAP, RAP, RVP, SVR….
- Hard to standardize
- PH specialty center

Suspect and Refer

Dyspnoea on exertion
Fatigue and rapid exhaustion
Bendopnoea (Dyspnoea when bending forward)
Weight gain due to fluid retention
Syncope during physical exertion



Eur Respir J. 2024 Oct 31;64(4):2401324.

Imaging techniques for pulmonary hypertension

Table 3 Overview of imaging modalities in pulmonary hypertension

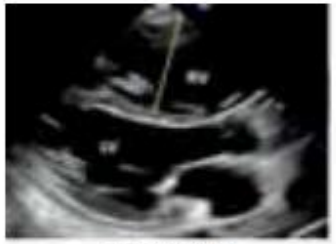
	Chest Radiography	Echocardiography	Chest NCT	Chest CTPA	Chest DECTA	CMRI	V/Q	Pulmonary angiography
PH detection	+	+ + +	+	+ +	+ +	+/–	–	–
Lung	+	–	+ + +	+ + +	+ + +	–	–	–
Heart	+/–	+ + +	+	+ +	+ +	+ + +	–	–
Pulmonary vessels	+/–	+	+	+ +	+ + +	+ +	+ + +	+ + +
Mediastinum	–	–	+	+ + +	+ + +	+ + +	–	–
PH etiology	+	+ +	+	+ +	+ +	+ +	+ +	+
Strengths	Availability; 1st line imaging	1st line imaging; define the probability of PH (low, intermediate, or high), thus prompting further investigation	Lung parenchyma evaluation	Comprehensive evaluation of all the chest compartments; PH etiology	Lung "perfusion" map	No radiation exposure; evaluation of right ventricle size and function	Pivotal in ruling out or detecting CTEPH	Endovascular treatment planning
Limitations	Unhelpful in mild PH and etiology assessment	Limited role in the assessment of etiology	Limited role in the assessment of heart and pulmonary vessels	Limited hemodynamics assessment; limited evaluation of distal pulmonary arteries	Needs more robust validation	Limited role in the evaluation of lung and vessels	Limited in case of patients with comorbidities; no comprehensive evaluation	Invasiveness

PH pulmonary hypertension, *NCT* non-contrast computed tomography, *CTPA CT* pulmonary angiography, *DECTA* dual-energy CT angiography, *CMRI* cardiac magnetic resonance imaging, *V/Q* ventilation/perfusion scan, *CTEPH* chronic thromboembolic pulmonary hypertension

Journal of Medical Imaging and Interventional Radiology (2024) 11:9

Imaging techniques for PH, Echocardiography

Parasternal Long axis

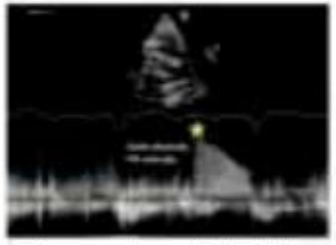


Enlarged RV

Parasternal Short axis (at level of valves)

Enlarged RA, RVOT and PA

Decreased RVOT/PV acceleration time <105 ms with mid-systolic notch



Increased peak diastolic pulmonic regurgitant velocity >2.2 $m \cdot s^{-1}$

Enlarged PA >25 mm

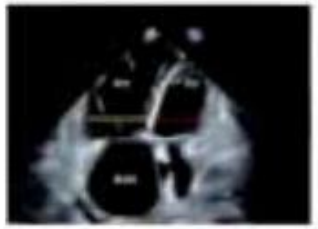
Parasternal Short axis (at mid-ventricle)

D-shaped LV; decreased LVEI (D2/D1) >1; Pericardial effusion

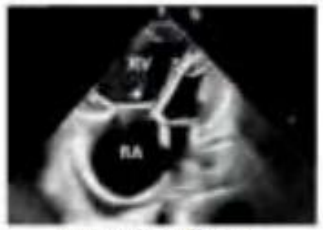
Eur Respir J. 2024 Oct 31;64(4):2401324.

Imaging techniques for PH, Echocardiography

4-chamber view



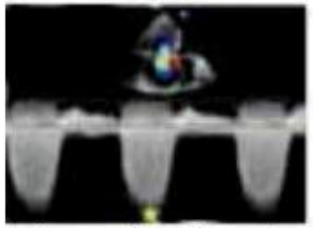
Dilated RV with basal RV/LV ratio >1.0; enlarged right atrial area >18 cm^2 (end-systole)



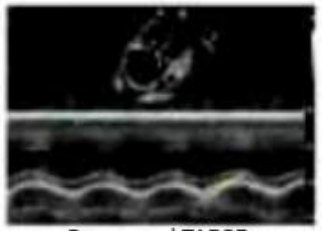
Pericardial effusion

Reduced RV fractional area change in systole *versus* diastole ((RVEDa-RVESa))/RVEDV) <35%

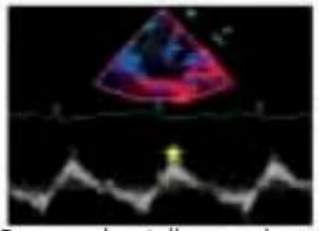
4-chamber view (Doppler and M-mode)



Increased systolic peak tricuspid regurgitant velocity >2.8 $m \cdot s^{-1}$ by Doppler



Decreased TAPSE <1.8 cm by M-mode



Decreased systolic excursion velocity (S') of tricuspid valve annulus <9.5 $cm \cdot s^{-1}$ by tissue Doppler imaging

IVC

Distended IVC >2.1 cm with diminished inspiratory collapsibility (<50% with a sniff or <20% with quiet inspiration)

Eur Respir J. 2024 Oct 31;64(4):2401324.

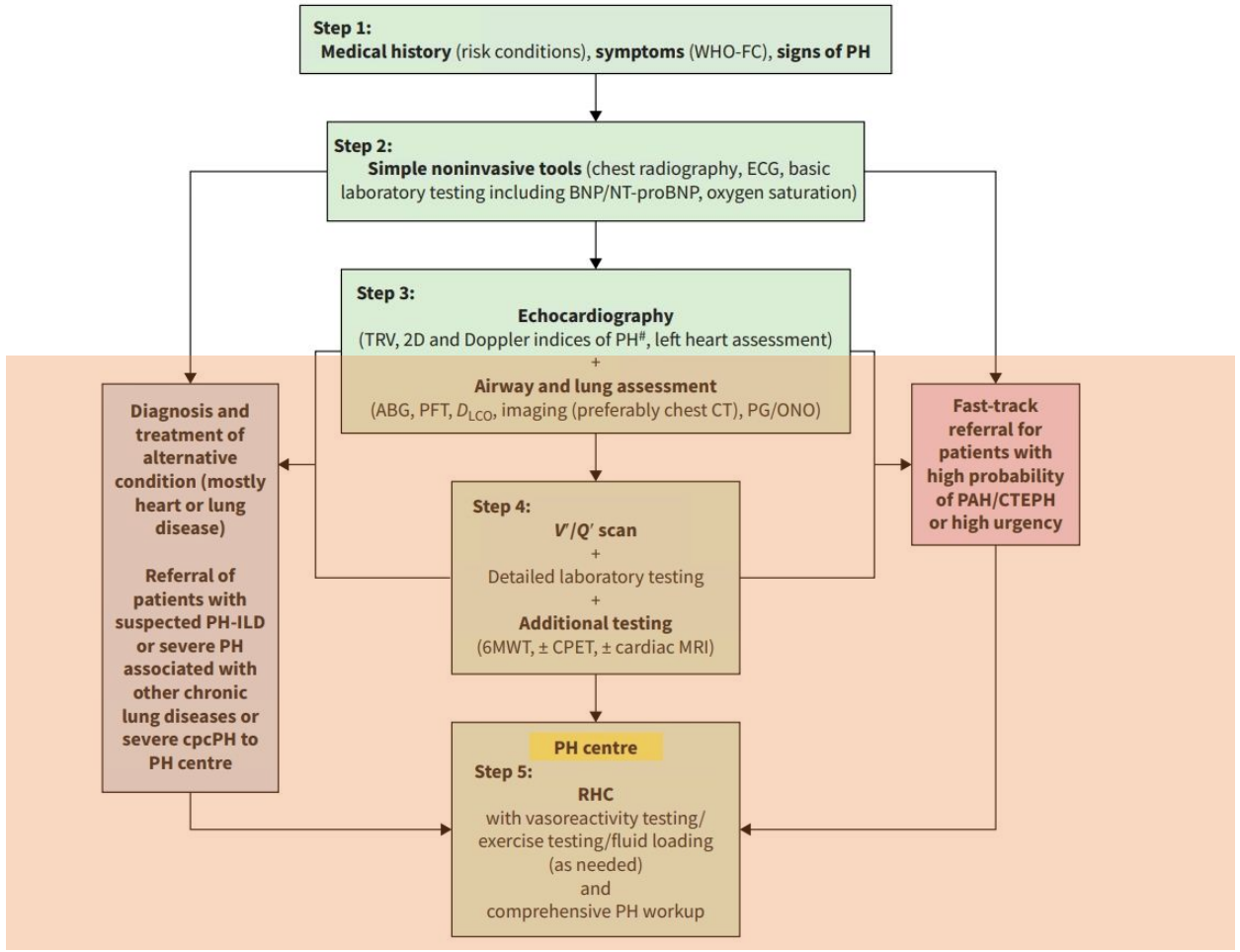
Chest CT findings suggestive of PH

- **Enlargement of Pulmonary Arteries**
  - Main Pulmonary Artery (MPA) Diameter > 29mm
  - MPA to Ascending Aorta Ratio > 1

- **Parenchymal and Vascular Patterns**
  - Mosaic attenuation in CTEPH
  - Centrilobular nodules in pulmonary capillary hemangiomatosis
  - Interlobular septal thickening and GGO in pulmonary venoocclusive disease

AJR 2012; 198:1320–1331
Front Cardiovasc Med. 2022 Oct 5;9:966257.

Suspect and Refer



Eur Respir J. 2024 Oct 31;64(4):2401324.

PH in chronic lung disease

Pulmonary hypertension in chronic lung disease

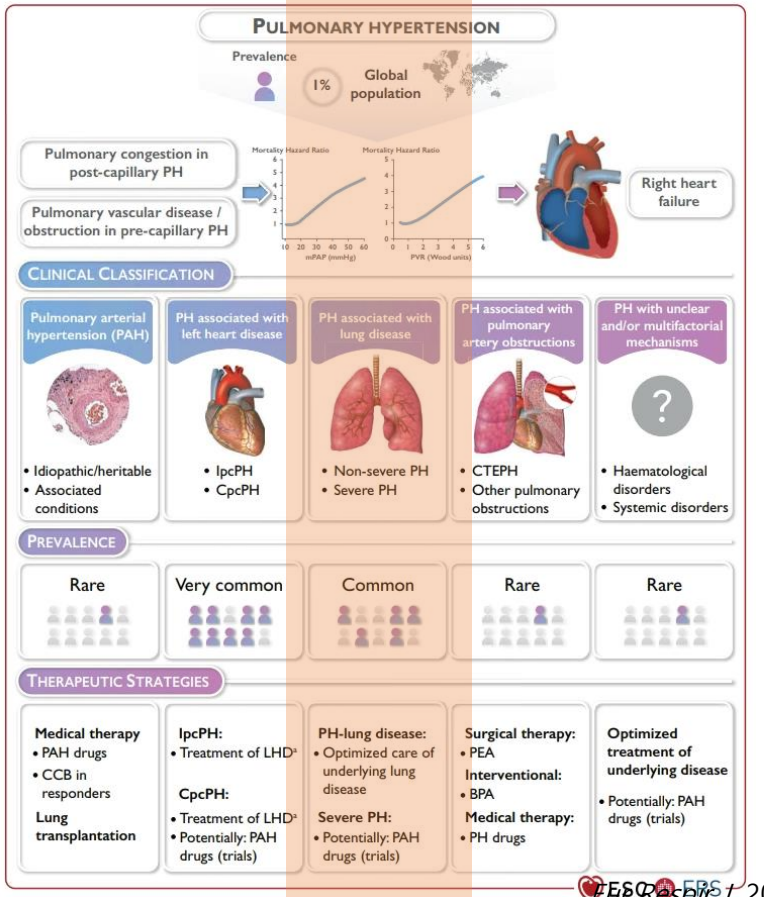
- **Pathophysiology**
  - Hypoxia-induced vasoconstriction
  - Vascular remodeling
  - Pulmonary vascular destruction

- **Prevalence**
  - COPD
    - ~30–90% develop PH (mPAP 20–35 mmHg); 1–5% of severe COPD cases show mPAP >35 mmHg
  - ILD

European Respiratory Journal 2019 54(suppl 63)

    - PH prevalence increases with advanced fibrosis

Current Opinion in Pulmonary Medicine 27(5):p 396-404



Eur Respir J. 2019 Jan 24;53(1):1801913.
Eur Respir J. 2024 Oct 31;64(4):2401324.

Updated clinical classification of G3 PH

Group 3: PH associated with lung diseases and/or hypoxia
3.1 COPD and/or emphysema
3.2 Interstitial lung disease
3.3 Combined pulmonary fibrosis and emphysema
3.4 Other parenchymal lung diseases[+]
3.5 Nonparenchymal restrictive diseases:
3.5.1 hypoventilation syndromes
3.5.2 pneumonectomy
3.6 Hypoxia without lung disease (*e.g.* high altitude)
3.7 Developmental lung diseases

Eur Respir J. 2024 Oct 31;64(4):2401324.

Management for PH in chronic lung disease

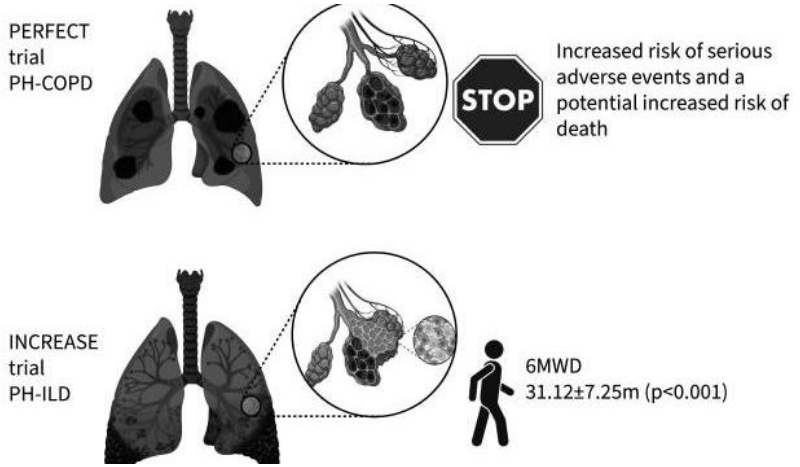
- **Optimizing the underlying lung disease**
  - Long-term oxygen therapy
  - Management of RV dysfunction
    - Diuretics, digoxin
  - Pulmonary rehabilitation
  - Continuous positive airway pressure/noninvasive ventilation

Breathe. 2023 Jan 10;18(4):220205

PH specific treatment in PH in CLD

- **Phosphodiesterase Type 5 Inhibitors (PDE5i)**
  - Sildenafil
  - Studies clinical benefit in COPD, ILD

- **Prostacyclin analogues**
  - Inhaled treprostinil
  - ILD with PH



Breathe. 2023 Jan 10;18(4):220205
Current Opinion in Pulmonary Medicine 27(5):p 396-404
Breathe (Sheff). 2025 Mar 18;21(1):240242

PH specific treatment in PH in CLD

폐고혈압 치료 타이바소, '진료필수약제 급여등재' 재도전

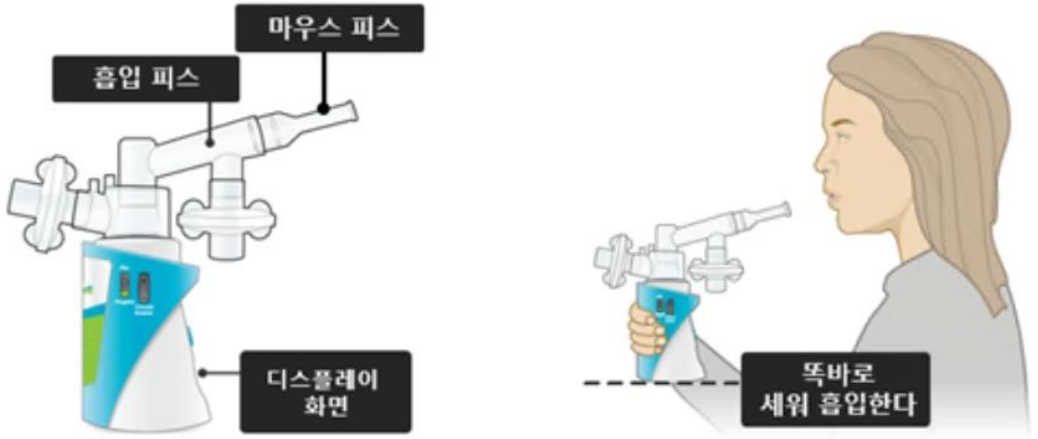
이현주 기자 | 입력 2025.03.12 06:06 | 수정 2025.03.14 05:38 | 댓글 0

가 가

타이바소흡입액0.6mg/mL(트레프로스티닐)

기본정보

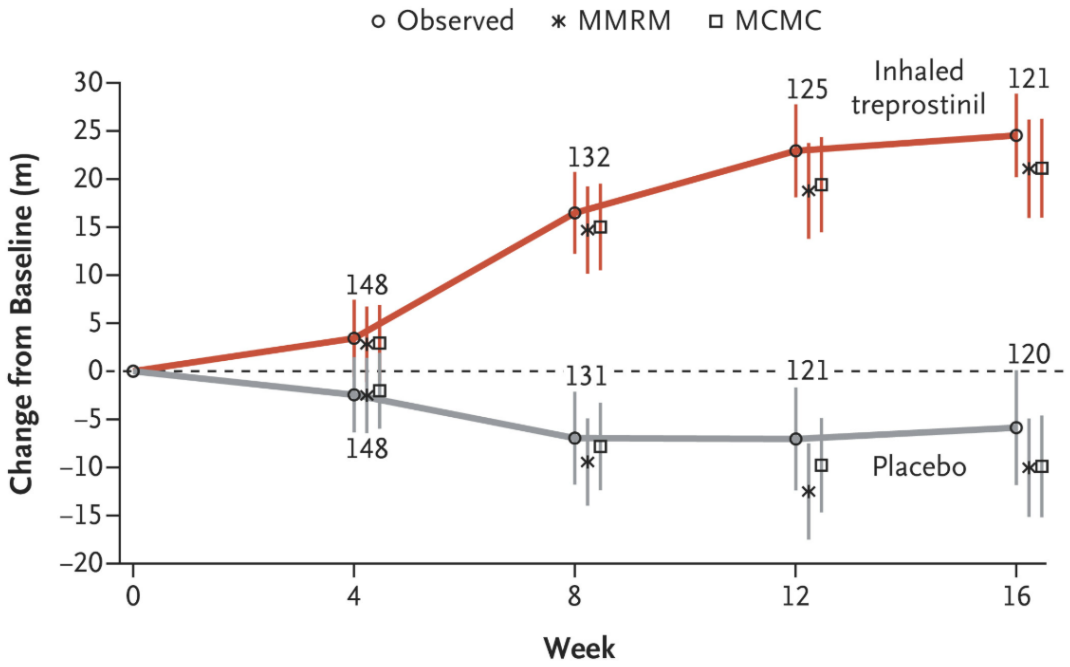
제품명	타이바소흡입액0.6mg/mL(트레프로스티닐)
성상	투명한 무색 또는 옅은 노란색의 액이 무색 플라스틱 용기에 든 액제
업체명	(주)안트로젠
위탁제조업체	
전문/일반	전문의약품(희귀)
허가일	2024-07-05
품목기준코드	202401656
표준코드	8806720001103, 8806720001110, 8806720001127
허가심사유형	자료제출의약품



하루 4회(최소 4시간 간격) 흡입

Inhaled Treprostinil in PH-ILD

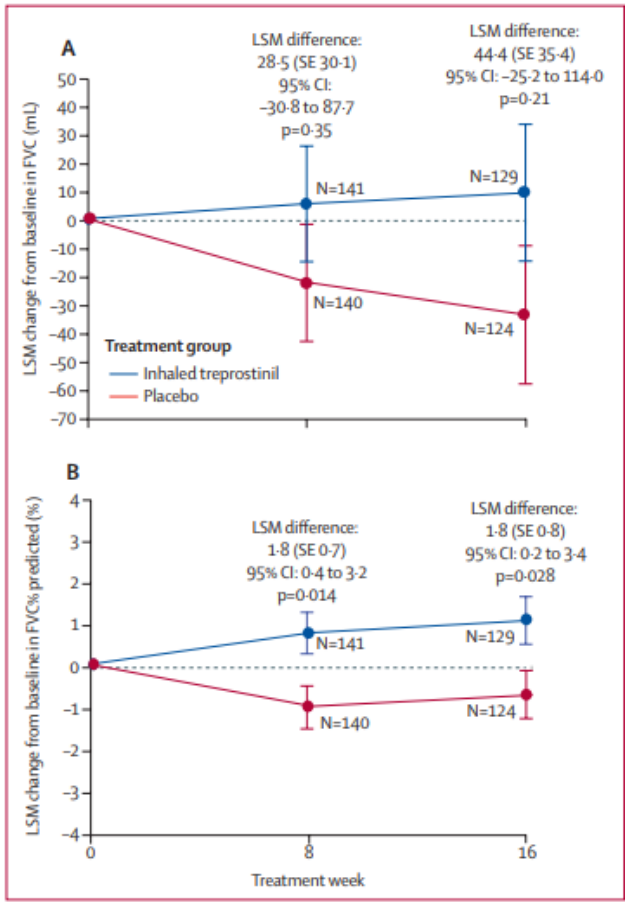
- **INCREASE study**
  - NT-proBNP ↓
  - Clinical outcome
    - Hospitalization ↓
    - Death ↓
    - Lung transplantation ↓
  - Adverse Event
    - Frequent
      - Cough, headache, dyspnea , dizziness
    - Significant
      - Throat irritation, Oropharyngeal pain
    - Discontinuation rate
      - 9.8% in the trepostinil



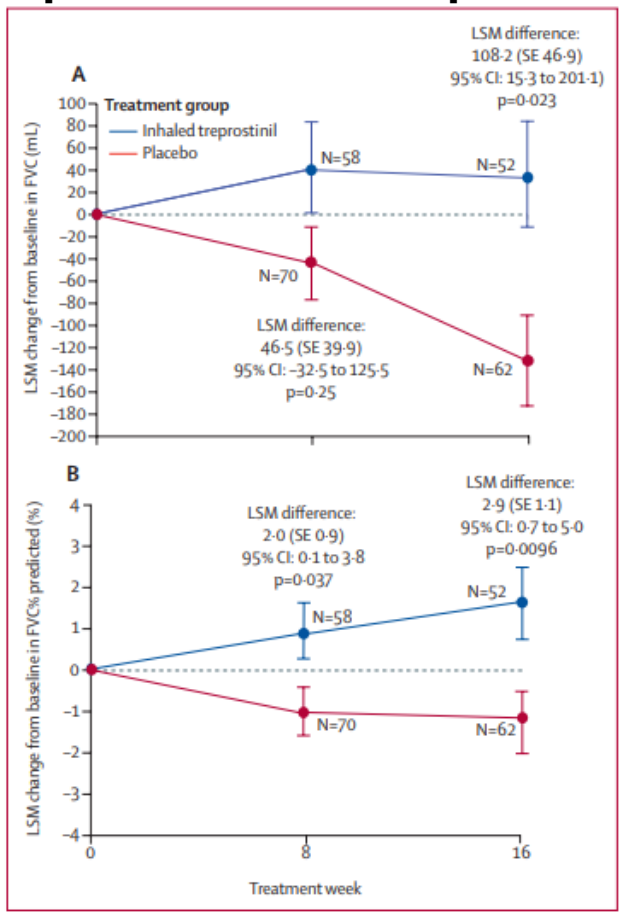
N Engl J Med 2021;384:325-334

Inhaled Treprostinil in PH-ILD: FVC

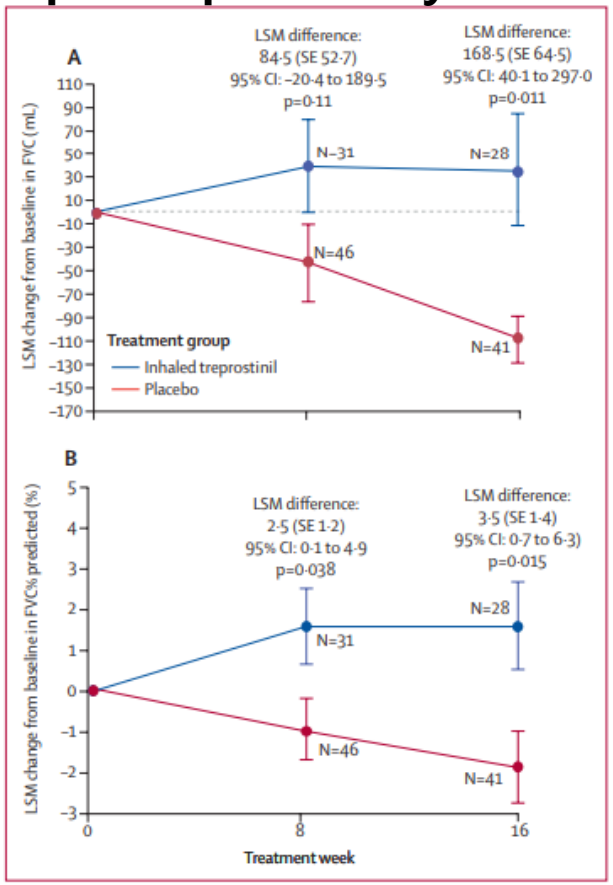
Overall population



Idiopathic interstitial pneumonia

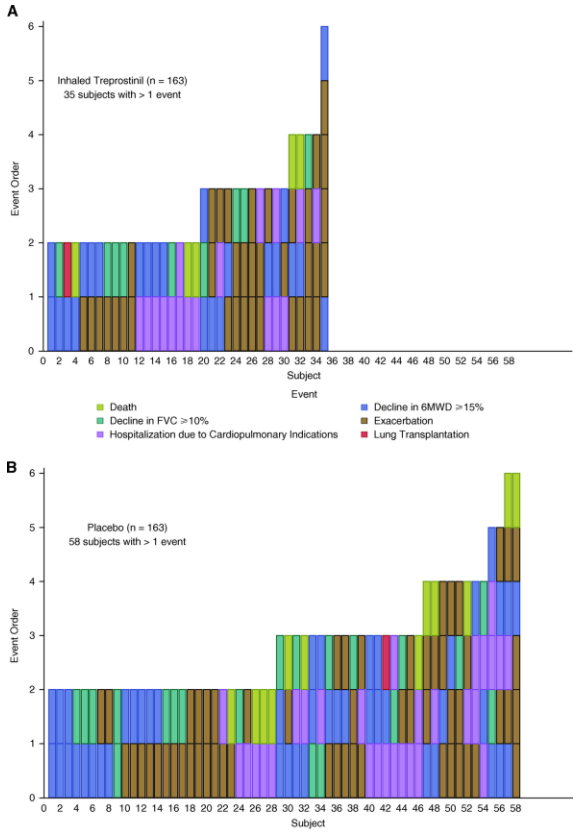


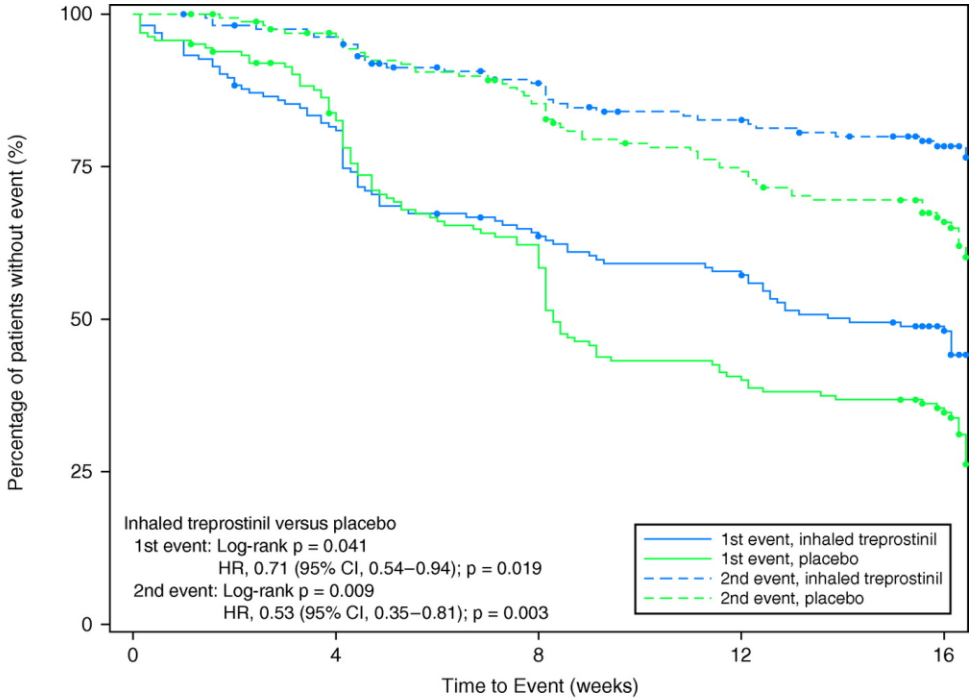
Idiopathic pulmonary fibrosis



Lancet Respir Med. 2021 Nov;9(11):1266-1274.

Inhaled Treprostinil in PH-ILD: Progression





No. at Risk:

1st event, inhaled treprostinil	163	132	102	91	61
1st event, placebo	163	132	98	64	49
2nd event, inhaled treprostinil	163	155	135	122	92
2nd event, placebo	163	152	132	113	84

- Death
- Decline in FVC ⩾10%
- Hospitalization due to Cardiopulmonary Indications
- Decline in 6MWD ⩾15%
- Exacerbation
- Lung Transplantation

Am J Respir Crit Care Med. 2022 Jan 15;205(2):198-207

Inhaled Treprostinil

Tyvaso prices

Inhalation Solution

0.6 mg/mL
Tyvaso inhalation solution

from **$3,311.20**
for 11.6 milliliters

Brand	Quantity	Per unit	Price
Tyvaso	11.6 (4 x 2.9 milliliters)	$285.45	$3,311.20
Tyvaso Refill Kit	81.2 (28 x 2.9 milliliters)	$284.77	$23,123.00
Tyvaso Starter Kit	81.2 (28 x 2.9 milliliters)	$317.66	$25,793.93
Tyvaso Starter Kit (Institutional)	11.6 (4 x 2.9 milliliters)	$515.70	$5,982.12

Important: When there is a range of pricing, consumers should normally expect to pay the lower price. However, due to stock shortages and other unknown variables we cannot provide any guarantee.

Chronic thromboembolic pulmonary disease

Chronic thromboembolic pulmonary disease

- Chronic thromboembolic pulmonary disease (CTEPD)
  - Chronic thromboembolic pulmonary hypertension (CTEPH)
  - CTEPD without pulmonary hypertension

- Incidence
  - 5–6 cases/million/year

- Treatment
  - Pulmonary endarterectomy (PEA) and balloon pulmonary angioplasty (BPA)

Eur Respir J . 2024 Oct 31;64(4):2401294.

Treatment of CTEPH

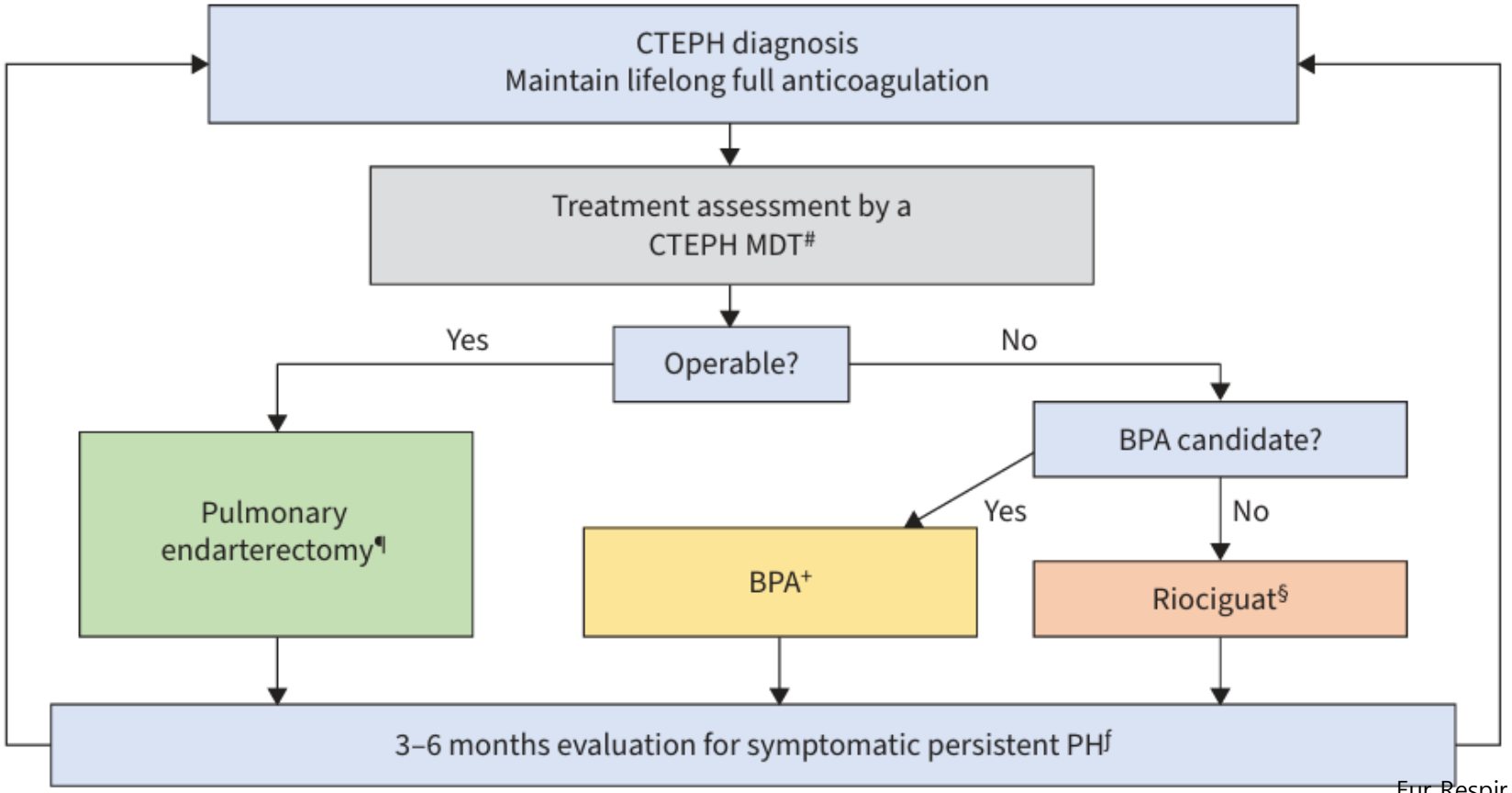
TABLE 3 Chronic thromboembolic pulmonary hypertension (CTEPH) multidisciplinary team (MDT) and centre expertise

	Requirements
MDT	PEA surgeon + BPA specialist + PH expert + pulmonary vascular radiologist
PEA centre	⩾20 surgeries per year with post-operative mortality rate <5%, ECMO support
Expert PEA centre	50 surgeries per year with mortality <3%, capable of treating segmental/ subsegmental disease, ECMO support
BPA centre	⩾50 procedures per year with procedure related mortality <3%
Expert BPA centre	>100 procedures per year with mortality <1%, ECMO support
Comprehensive CTEPH centre	Combined PEA + BPA + PH + ECMO expertise available with treatments based on centre MDT

PEA: pulmonary endartectomy; BPA: balloon pulmonary angioplasty; PH: pulmonary hypertension; ECMO: extracorporeal membrane oxygenation.

Eur Respir J . 2024 Oct 31;64(4):2401294.

Treatment of CTEPH



Eur Respir J . 2024 Oct 31;64(4):2401294.

Chronic thromboembolic pulmonary disease

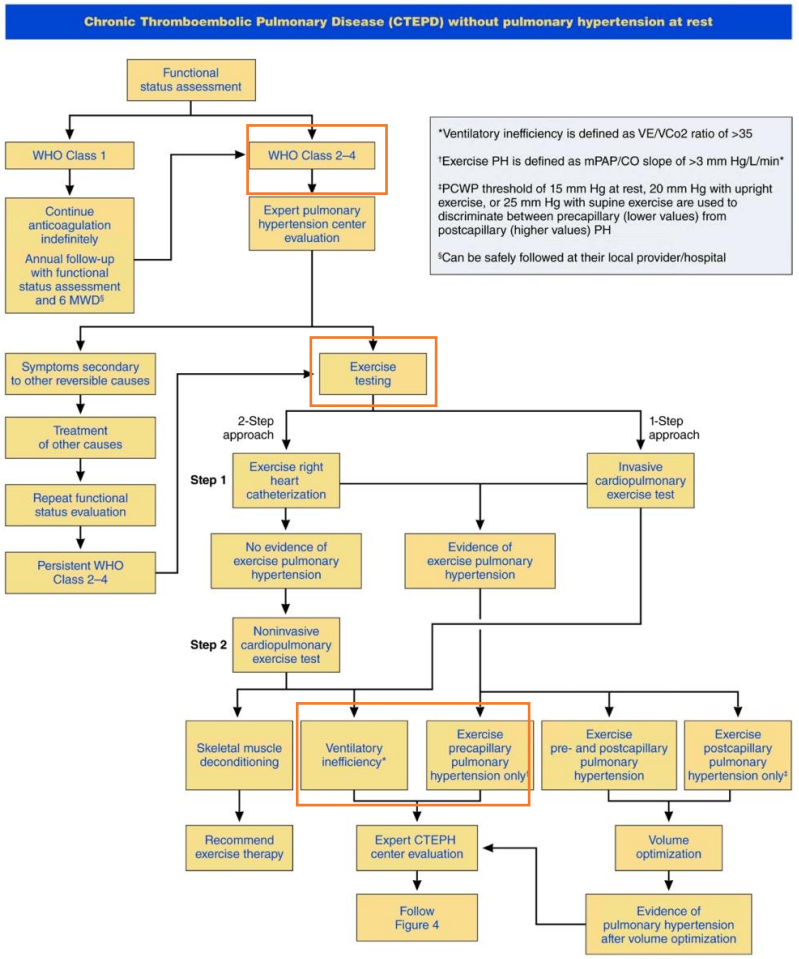
Circulation
Volume 149, Issue 15, 9 April 2024; Pages e1090-e1107
https://doi.org/10.1161/CIR.0000000000001197

American Heart Association

AHA SCIENTIFIC STATEMENTS

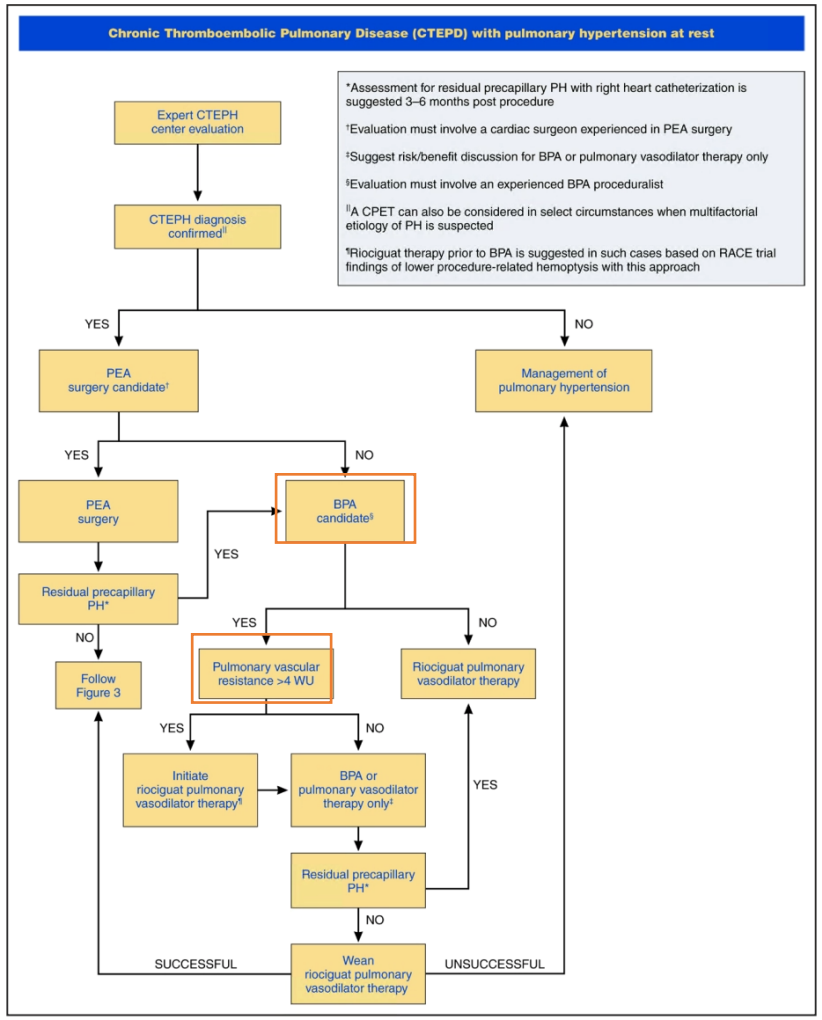
Status and Future Directions for Balloon Pulmonary Angioplasty in Chronic Thromboembolic Pulmonary Disease With and Without Pulmonary Hypertension: A Scientific Statement From the American Heart Association

BPA for CTEPD without PH



Circulation. 2024 Apr 9;149(15):e1090-e1107.

BPA for CTEPD with PH at rest



Circulation. 2024 Apr 9;149(15):e1090-e1107.

Suspect and Refer

Table 1. Suggested Competencies of an Expert CTEPH Center and an Expert PH Center

CTEPH care delivery competencies	Expert CTEPH center	Expert PH center	Referring centers/ physicians
Initial screening for CTEPD with ventilation-perfusion imaging	✓	✓	✓
Echocardiographic surveillance for PH	✓	✓	✓
Left- and right-sided heart catheterization, including exercise right-sided heart catheterization	✓	✓	✓
Initial management and stabilization for acute and chronic cor pulmonale, not including ECMO or pulmonary embolectomy (catheter or surgery)	✓	✓	✓
Systemic thrombolysis for high risk acute PE	✓	✓	✓
Counseling occupational and healthy living choices, including physical activity, rehabilitation, and anticoagulation management	✓	✓	✓
Venous health management	✓	✓	✓
Experienced PH physicians with expertise in all facets of PH medical management	✓	✓	
Advanced echocardiographic imaging expertise for right ventricular assessment	✓	✓	
Cross-sectional imaging expertise in diagnosis of pulmonary thromboembolic disease	✓	✓	
Catheter- and surgery-based acute pulmonary embolectomy or thrombolysis	✓	✓	
Expertise in performance and interpretation of both noninvasive and invasive CPET	✓	✓	
Comprehensive inpatient PE service and post-PE follow-up clinic	✓		
Nuclear medicine expertise in CTEPD diagnosis	✓		
Experienced diagnostic radiologist with expertise in CTEPH imaging interpretation	✓		
Invasive pulmonary angiogram performance and expertise in CTEPD diagnosis interpretation	✓		
Experienced PEA surgeon*	✓		
Experienced BPA interventionalist*	✓		
Onsite ECMO support availability	✓		
Lung transplantation	✓		

Summary

- **Revised definition**
  - Early referral/diagnosis/management
- **Imaging techniques for PH**
  - Screening and diagnosis
- **PH in chronic lung disease**
  - Update in subgroups
  - PH specific drug: inhaled treprostinil
- **Chronic thromboembolic pulmonary disease**
  - With/without PH
  - Referral to expert center

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