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Sleuthing Unexplained Dyspnea: Diagnostic Tools

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Learning Objectives

1. Review the potential causes of unexplained dyspnea and the implications of delayed diagnosis of underlying causes as they pertain to pulmonary hypertension
2. Discuss collaborative diagnostic roles of the community physician and the PH specialty center in determining the potential presence of pulmonary hypertension and the need for expedient referral to the specialty center
3. Compare and contrast the diagnostic tools available to determine the presence, cause and severity of pulmonary hypertension and newer diagnostic modalities that are influencing the diagnostic process
4. Review the necessary diagnostic values and implications needed to create an “index of suspicion” that pulmonary hypertension is at the core of a patient’s unexplained dyspnea

Dyspnea: Many Possible Causes, Always To Be Taken Seriously

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Revisiting Unexplained Dyspnea – Possible Causes

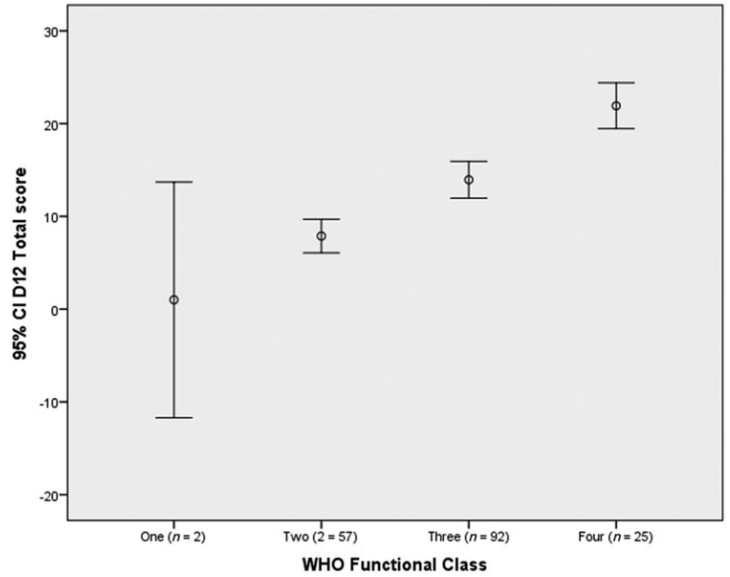
Acute dyspnea could be due to…well…almost any medical condition, it seems…

Possible Causes of Unexplained Dyspnea		
Asthma	CO Exposure	Pleurisy / Inflammation
Lung Infections	Collapsed Lung	COPD/ILD
Anxiety	Hypotension	Heart Failure
Choking/Blocked Airway	Hiatal Hernia	Pulmonary Embolism
Allergic Reactions	Croup	Pulmonary Edema
Anemia	Traumatic Lung Injury	Sarcoidosis
Serious Blood Loss	Lung Cancer	Pulmonary Hypertension

It is essential to ask the right questions and do the correct diagnostics to determine the cause of the patient's dyspnea.
You cannot assume it is due to the simplest, most common cause

How Bad Is It? – Assessing Your Patients' Dyspnea

- Breathlessness is a predominant symptom among patients with cardiopulmonary disease and has been shown to have a strong correlation with anxiety, depression, health-related quality of life (HRQL), activity limitation and mortality
- The Dyspnoea-12 (D-12) is a short instrument that assesses breathlessness severity and taps its physical and emotional components[1]
- The D-12 has acceptable reliability and validity for use in patients with PAH and correlates with WHO Functional Class[2]

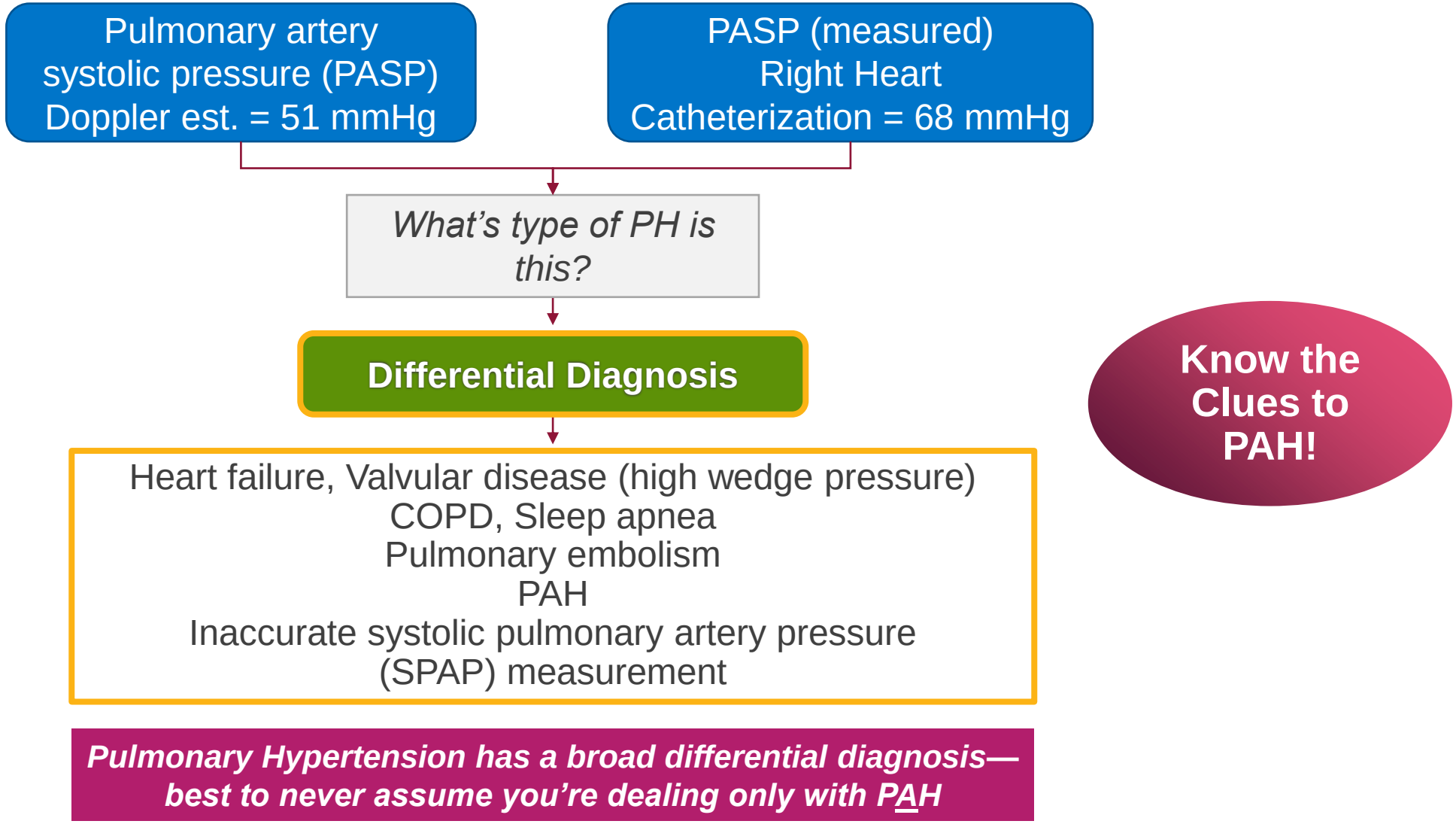


DYSPNEA 12 Questionnaire

Item	None	Mild	Moderate	Severe
1. My breath does not go in all the way				
2. My breathing requires more work				
3. I feel short of breath				
4. I have difficulty catching my breath				
5. I cannot get enough air				
6. My breathing is uncomfortable				
7. My breathing is exhausting				
8. My breathing makes me feel depressed				
9. My breathing makes me feel miserable				
10. My breathing is distressing				
11. My breathing makes me agitated				
12. My breathing is irritating				

1. Yorke J, et al. *Thorax,* 2010; 65: 21–26
2. Yorke J, Armstrong I. *Eur J Cardiovascular Nursing,* 2014; 13:506–514

Always Suspect It Could Be PAH, But Never ASSUME It's PAH



Know the Clues to PAH!

When the Patient Has Underlying Disease[1,2], You Expect Them to Be at Risk for PAH and You Must Test for It

- Systemic sclerosis (SSc)
- Lupus erythematosus
- Pulmonary fibrosis
- Connective tissue diseases (MCTD, rheumatoid arthritis, etc.)
- Congenital heart disease
- Liver disease
- HIV
- Obstructive sleep apnea (OSA)
- Sickle cell disease
- Pulmonary embolism (risk for CTEPH)
- Schistosomiasis

1. Shahane A. *Rheumatol Int.* 2013;33(7):1655-1667.
2. Pulmonary Hypertension Association. Associated conditions. https://phassociation.org/patients/aboutph/diseases-and-conditions-associated-with-ph/

If Unexplained Dyspnea Is Not Fully Explored, What Are the Implications…Especially if It Is PH?

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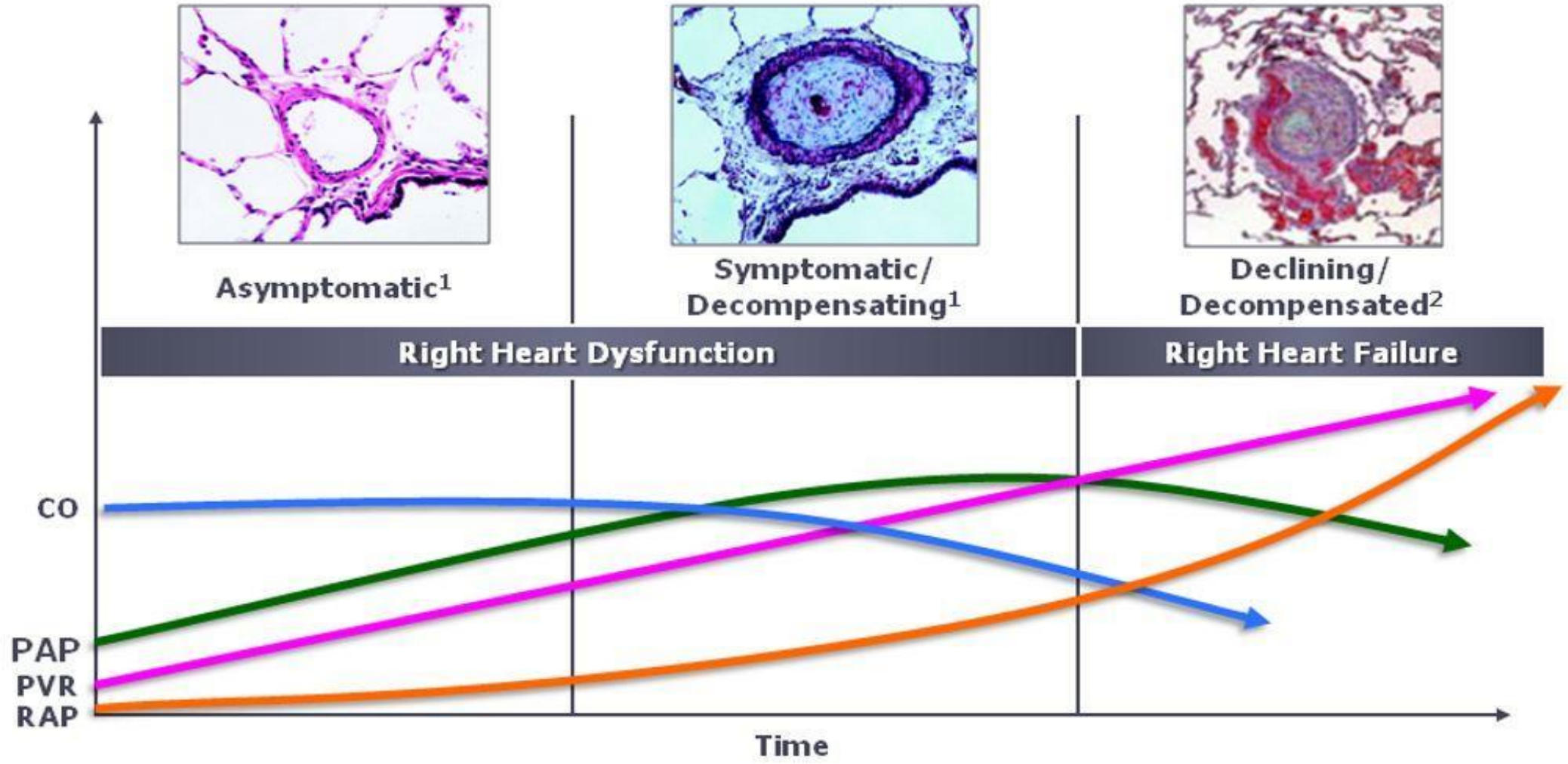
Common Pitfalls in PAH Patient Care

- It is easy to dismiss dyspnea as something else[1]
  - This often results in physicians waiting too long after patients are symptomatic to refer patients to a PH specialty center
- Lack of screening of at-risk PH populations[2]
  - E.g. Scleroderma, MCTD, familial PAH (genetic screens)
- Relying on sPAP measurements from the ECHO imaging instead of obtaining evidence for **structural** signs of RV dysfunction
- ***Not confirming diagnosis with a right heart catheterization***
- Lack of risk reassessment leading to delay in correct therapy and escalation

1. Brown LM, et al. *Chest.* 2011;140:19-26.
2. Steen V, et al. *Arthritis Rheum*. 2003;48:516-522.

PAH Is Progressive – Structural Changes Start Before Functional Changes*



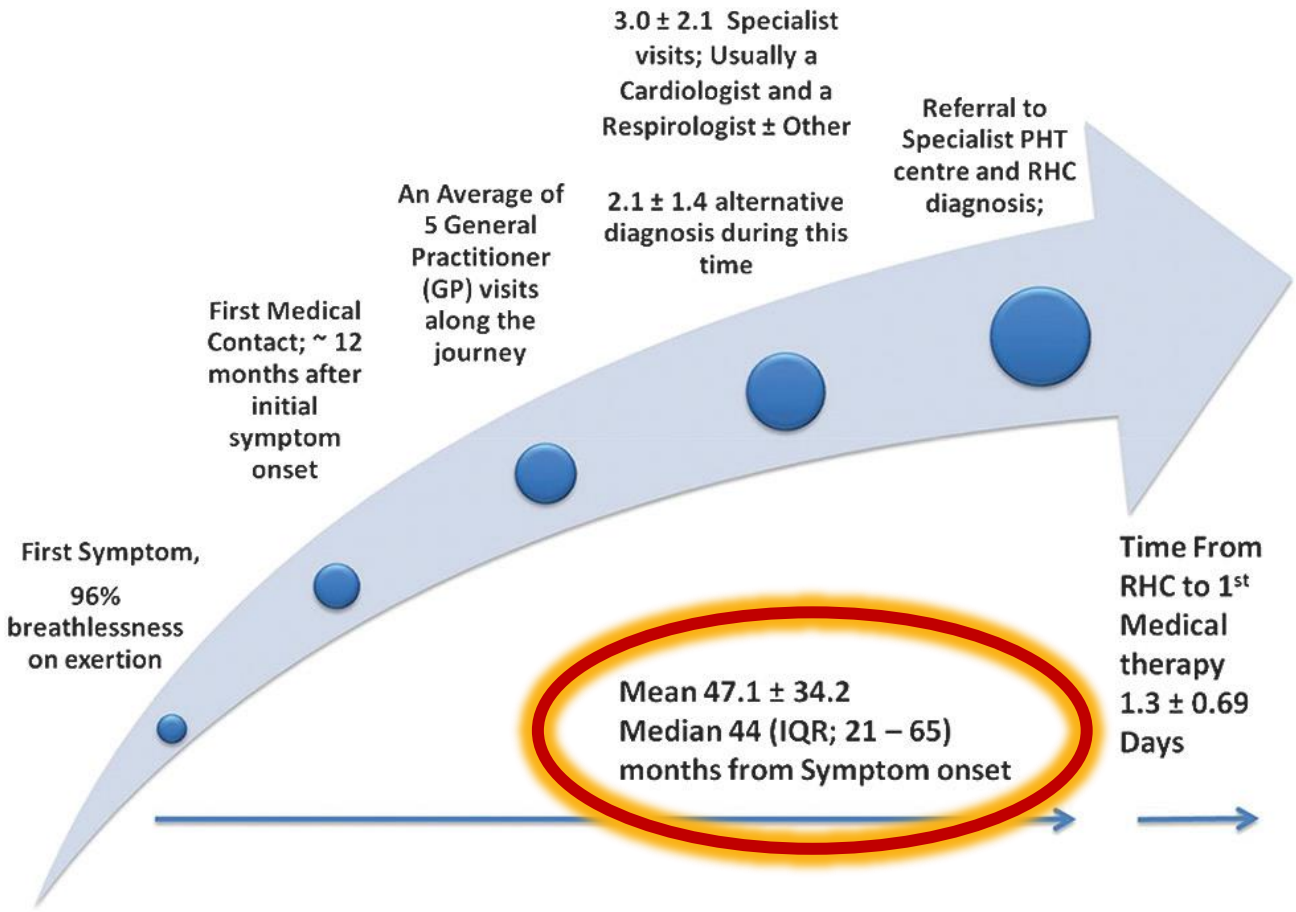
*These observations are based on reports from *in vitro*, animal, and human trials.

Adapted from:

1. Trembath RC, et al. *Pediatr Res.* 2003;53:883-888.
2. Minai OA, et al. *Cleve Clin J Med.* 2007;74:737-747.

What Factors Influence Time to Definitive PAH Diagnosis?

- Time between patient-reported onset of symptoms and a definitive iPAH diagnosis is consistently delayed
- The DELAY study (Australia) retrospectively examined factors contributing to diagnostic delays and the time to definitive iPAH diagnosis
- In 32 patients (69% female) reporting exertional dyspnea, mean time from symptom onset to diagnosis was 47 ± 34 mo.
- Patients reported 5.3 ± 3.8 general practitioner (GP) visits and 3.0 ± 2.1 specialist reviews before being seen at a PH center
- Factors significantly associated with delayed diagnosis were:
  - advanced age
  - number of GP visits
  - heart rate
  - systolic blood pressure



From the time of first medical contact to the time of RHC diagnosis, women moved through this phase in significantly shorter time vs. men (24 ± 30.31 months vs. 45 ± 39.95 months, respectively, *P*=.043).

Strange G, et al. *Pulm Circ.* 2013;3:89-94.

How Can We Make It Easier to Develop That "Index of Suspicion" for PAH?

Roles of the community physician and the PH center in reaching the correct diagnosis and promoting referral

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Building a Clinical Suspicion of PAH

- **General Symptoms (nonspecific)**
  - Dyspnea
  - Weakness
  - Chest pain
  - Light-headedness/syncope
  - Cough (less frequent)
- **In more progressed disease, one may also observe…**
  - Progressive right-sided heart failure (edema, ascites, abdominal distension)
  - Hemoptysis
  - Ortner’s syndrome/hoarseness (rare) (unilateral vocal cord paralysis)
  - Arrhythmias
- **Physical Findings**
  - Augmented second heart sound (P2 component)
  - Right ventricular lift
  - Jugular venous distension
  - Hepatojugular reflux
  - Ascites
  - Hepatomegaly and/or splenomegaly
  - Edema
  - Tricuspid regurgitant or pulmonary regurgitant murmurs
  - S3 gallop

In the Current Era, What Clinical Data Are Needed for Assessment of the PAH Patient?

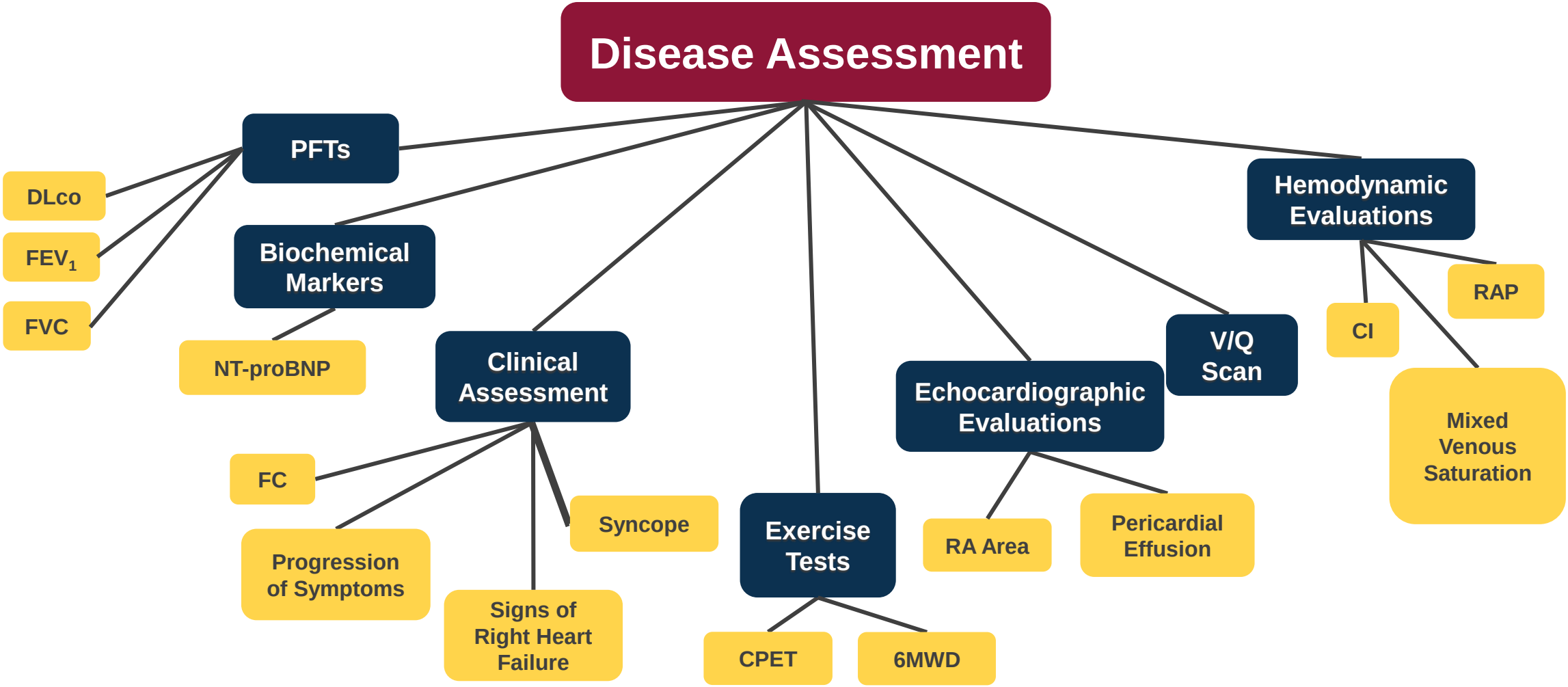

Diagram adapted from Galiè N, et al. *Eur Heart J.* 2016;37:67-119.
Thakkar V, et al. *Arthritis Res Ther.* 2013;15:R193.

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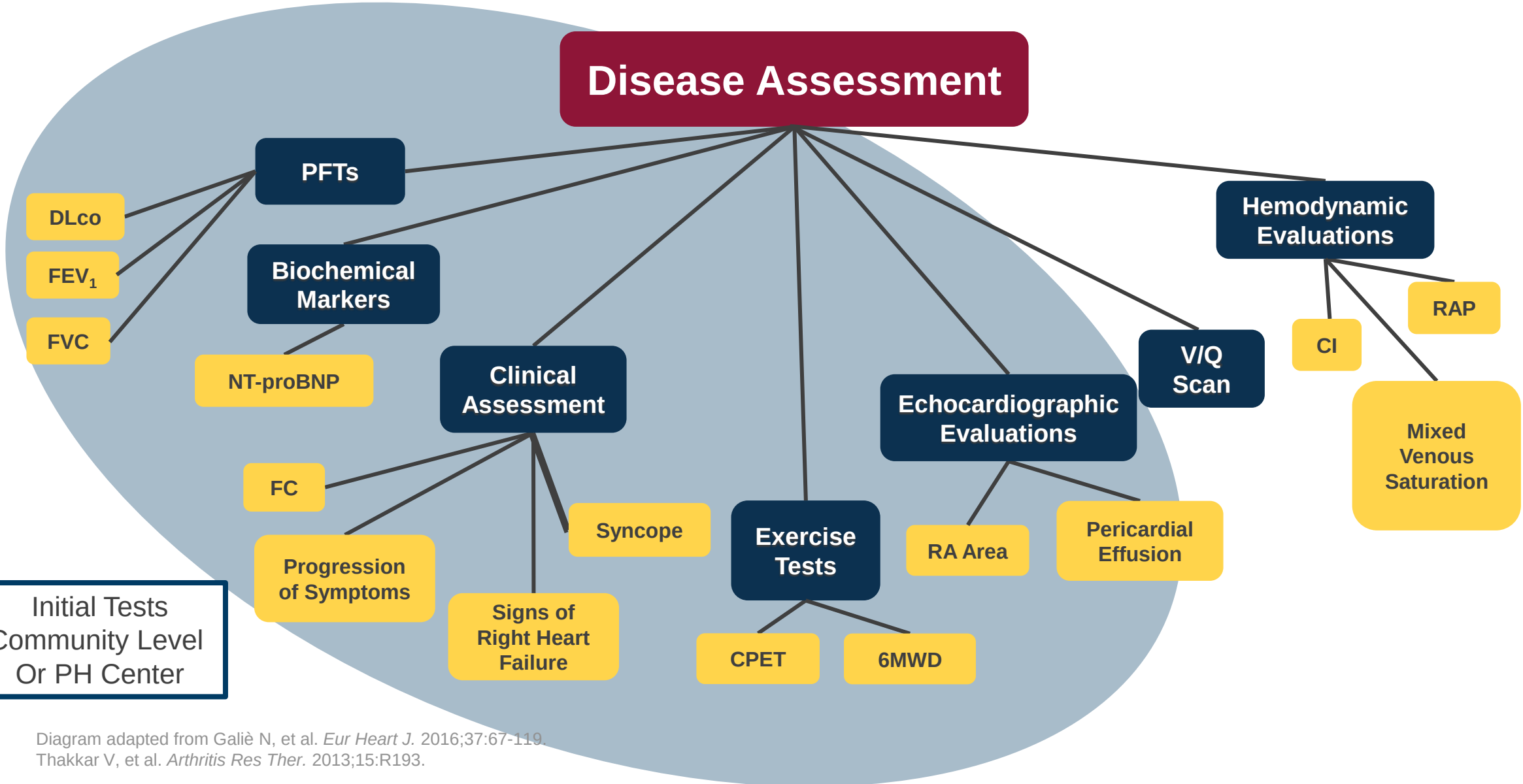

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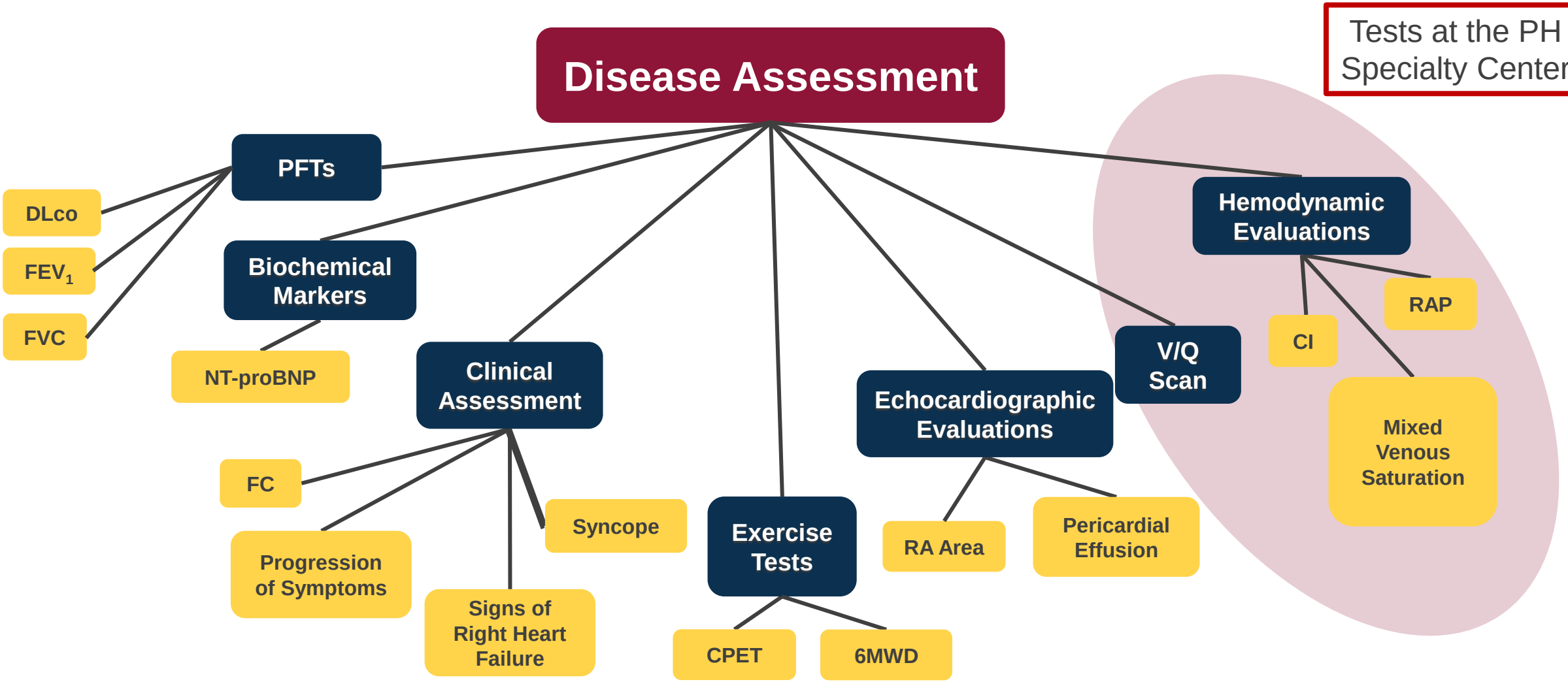

Diagram adapted from Galiè N, et al. *Eur Heart J.* 2016;37:67-119.
Thakkar V, et al. *Arthritis Res Ther.* 2013;15:R193.

What Information Should You Get From PFTs?

- Always obtain “full” PFTs in PAH workup (spirometry, lung volumes, DLCO [diffusing capacity of carbon monoxide])

- Normal PFTs: FEV_1 80-120%, FVC 80-120%, DLCO 60-120%

FEV_1 = Forced expiratory volume in 1st second; FVC = Forced vital capacity;

“Classic” pattern in PAH: normal or mildly restricted spirometry + decreased DLCO.

E.g.: FEV_1 89%, FVC 92%, DLCO 42%

- Presence of markedly abnormal PFT (obstruction/restriction) should prompt further pulmonary investigation (ILD, COPD)

Importance of Biochemical Markers: Assessment With Point-of-Care Testing To Improve Diagnosis and Prognosis

- Active B-type natriuretic peptide (BNP) and the functionally inert N-terminal prohormone of BNP (NT-proBNP) are well-established clinical biomarkers used in PAH and other cardiovascular disorders[1]
- Elevated levels of BNP and NT-proBNP are incorporated into several PAH risk stratification tools and screening algorithms to aid diagnosis of systemic sclerosis[2]
- Point of care testing has been shown to confer benefits including improved patient outcomes through reduced time-to-diagnosis and cost effectiveness[2]

Comparison of Select Variables Used in the European Society of Cardiology (ESC)/European Respiratory Society (ERS) and REVEAL 2.0 Prognostic Tools

	ERS/ESC Guidelines			REVEAL 2.0 Risk Score Calculator		
NHYA Functional Class	I,II	III	IV	I	III	IV
6MWD	>440 m	165 – 440 m	<165 m	⩾440 m	320 – <440 m	<165 m
BNP/NT-proBNP plasma levels	BNP <50 ng·L^{-1} NT-proBNP <300 ng·L^{-1}	BNP 50–300 ng·L^{-1} NT-proBNP 300–1400 ng·L^{-1}	BNP >500 ng·L^{-1} NT-proBNP >1400 ng·L^{-1}	BNP<50 ng·L^{-1} NT-proBNP <300 ng·L^{-1}	BNP 200–800 ng·L^{-1}	BNP ⩾800 ng·L−1 NT-proBNP ⩾1100 ng·L^{-1}

1. Galie N, et al. *Eur Heart J,* 2016; 37: 67–119
2. Lewis RA, et al. *Eur Respir Rev,* 2020; 29: 200009 [https://doi.org/10.1183/16000617.0009-2020]

Echocardiography: Not Definitive for PH, but Essential To Determine Need for Referral to PH Center

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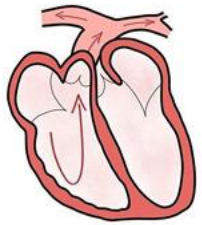
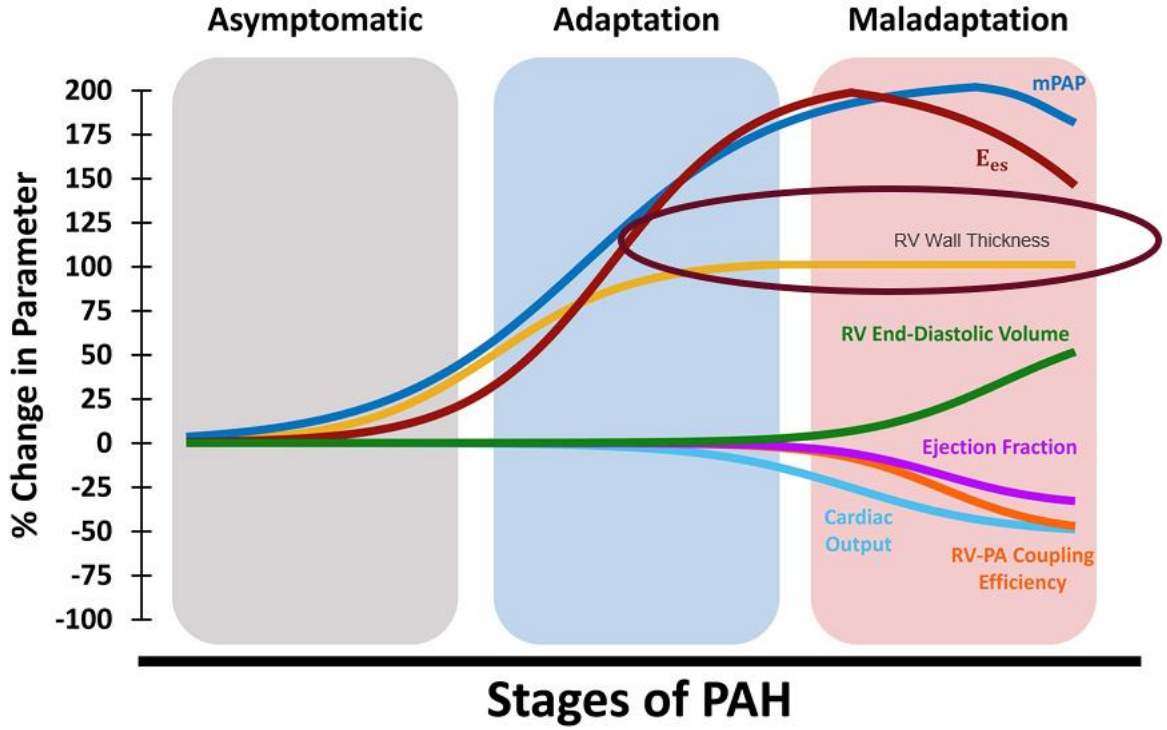
Importance of Structural Changes in the RV in PAH

- Right ventricular (RV) function is the single most important prognostic determinant of survival in various forms of pulmonary hypertension (PH)[1]
- Pulmonary arterial hypertension has been shown to result in RV remodeling at different scales (organ-level hemodynamics to tissue stiffening, fiber reorientation, and altered myocyte contractility and mitochondrial energetics)[2]
- The RV initially responds to increased pressures in PAH by undergoing concentric hypertrophy, which helps reducing RV wall stress and results in increased organ-level contractility
- Increased wall thickness results in maintained cardiac output and ejection fraction during the early stages of RV remodeling with further progression of PAH, RV hypertrophy reaches a plateau[3] while PA pressures continue to rise[4]





1. Lahm T, et al. *Am J Respir Crit Care Med,* 2018; 198:e15–e43
2. Hill MR, et al. *Ann. Biomed. Eng,* 2014; 42: 2451–2465.doi: 10.1007/s10439-014-1096-3
3. Wang, Z, et al. *J. Appl. Physiol,* 2018; 124:1244–1253. doi: 10.1152/japplphysiol.00725.2017
4. Vonk Noordegraaf A, et al. *J. Am. Coll. Cardiol.* 2017; 69, 236–243. doi: 10.1016/j.jacc.2016.10.047

Using ECHO to Uncover PH

- The most common opportunity to spot a new PAH patient is either in the ECHO review or in the ECHO report
- Emphasis of echocardiogram should not be on pressures, but on **structural changes** associated with the heart

Key Structural Features of the Heart in PAH

Pressures you can get with the right heart cath!

- Tricuspid regurgitant velocity
- **Right ventricular size** **(right ventricle/left ventricle basal diameter ratio >1.0)**
- **RA size** **(RA area [end-systole] >18 cm^2)**
- RA function
- **Interventricular septal function**
- IVC diameter fluctuations with respiratory cycles (IVC diameter >21 mm with decreasing inspiratory collapse)
- Pattern of systolic flow velocity
- Early diastolic pulmonary regurgitant velocity
- Diameter of the pulmonary artery (>25 mm)

Frost A, et al. *Eur Respir J.* 2019;53(1):1801904.

Echo: Probability of PH in Symptomatic Patients With a Suspicion of PH – Key Considerations

Peak tricuspid regurgitation velocity $m \cdot s^{-1}$	Presence of other echocardiographic "PH signs"	Echocardiographic probability of PH
≤2.8 or not measurable	No	Low
≤2.8 or not measurable 2.9–3.4	Yes No	Intermediate
2.9–3.4 >3.4	Yes Not Required	High

Galiè N, Humbert M, Vachiery J-L, *et al.* 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Respir J.* 2015; 46: 903–975.

Echo Signs Suggesting PH Can Be Used To Assess the Probability of PH in Addition to TRjet Velocity Measurement

A: The ventricles	B: Pulmonary artery	C: Inferior vena cava and right atrium
Right ventricle/left ventricle basal diameter ratio >1.0	Right ventricular outflow Doppler acceleration time <105 ms and/or mid-systolic notching	Inferior vena 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 $m \cdot s^{-1}$ Pulmonary artery diameter >25 mm	Right atrial area (end-systole) >18 cm^2
Echocardiographic signs from at least two different categories (A/B/C) from the list should be present to alter the level of echocardiographic probability of PH.		

Galiè N, *et al. Eur Respir J.* 2015; 46: 903–975

Using Echocardiography To Get a Handle on Heart Structure and Function in PH

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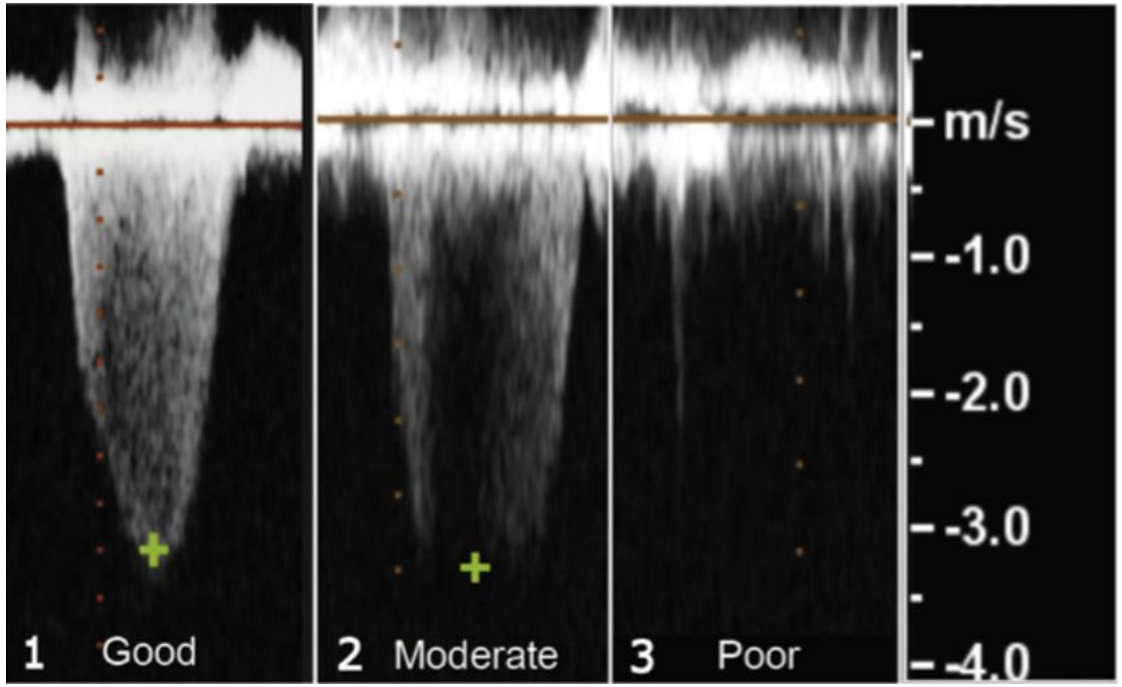
Echocardiogram: TR_{jet} Gives Only an Estimate Of PAP

- PAP is estimated from TR jet using simplified Bernoulli equation:
  - **Peak grad = 4 x V2 + RA**
- The quality of the TR jet and the expertise of echocardiography reader matters!

Quality of TR jet



Review the echocardiography images

Amsallem M, *et al*. *J Am Soc Echocardiogr*. 2016; 29:93-102.

ECHO: It's Not All About Pressures – Structural Images Can Tell Us A Lot!

Precapillary PH

RV Dilation and Dysfunction

PLACE VIDEO HERE
THEN OVERLAY THE
GRAPHIC NAMED
"Mod3_slide25_overlay.png"

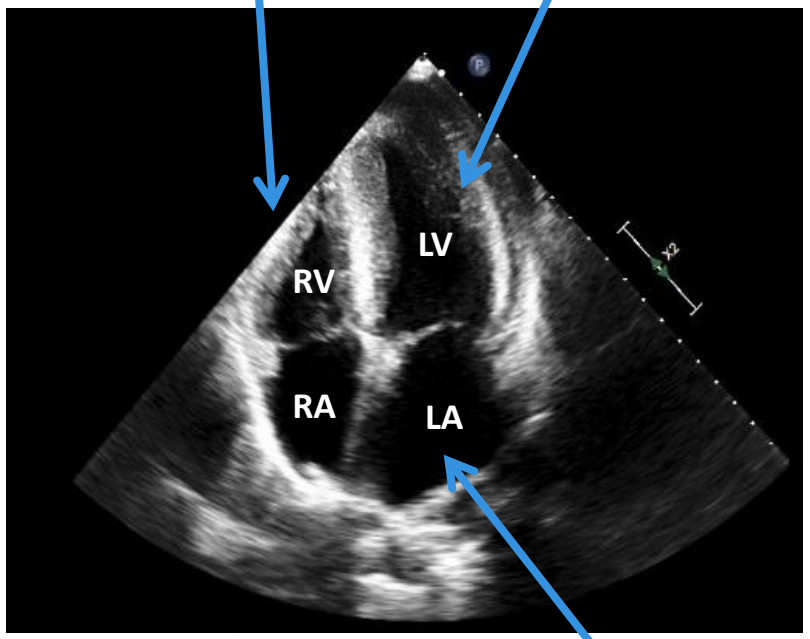
(HAS THE BLUE ARROWS)

Pericardial Effusion

Small LA w Shifted Septum

Normal Right Sided Chambers

LVH



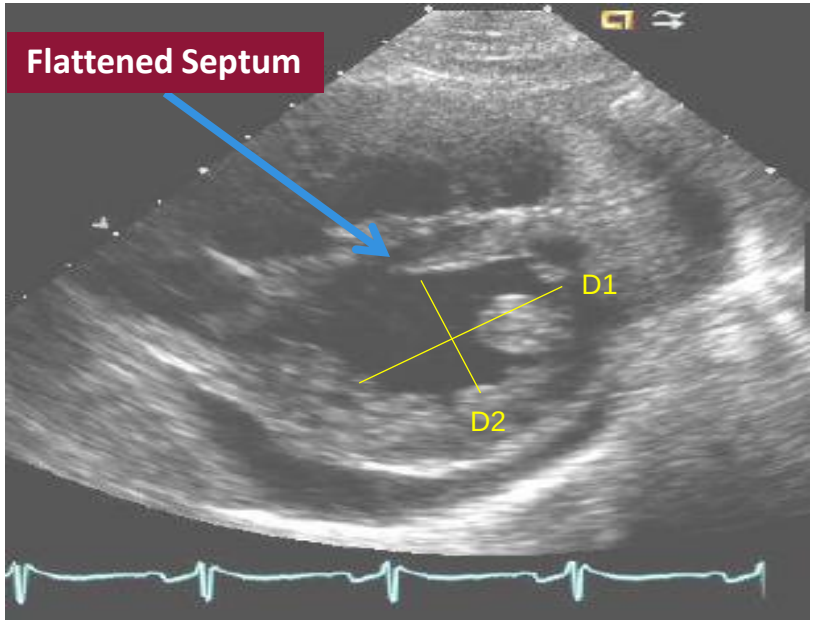
LA Enlargement

Postcapillary PH

LA=left atrium/atrial
LV=left ventricle/ventricular
RA=right atrium/atrial
RV=right ventricle/ventricular

Other Echocardiographic Parameters That May Be Useful

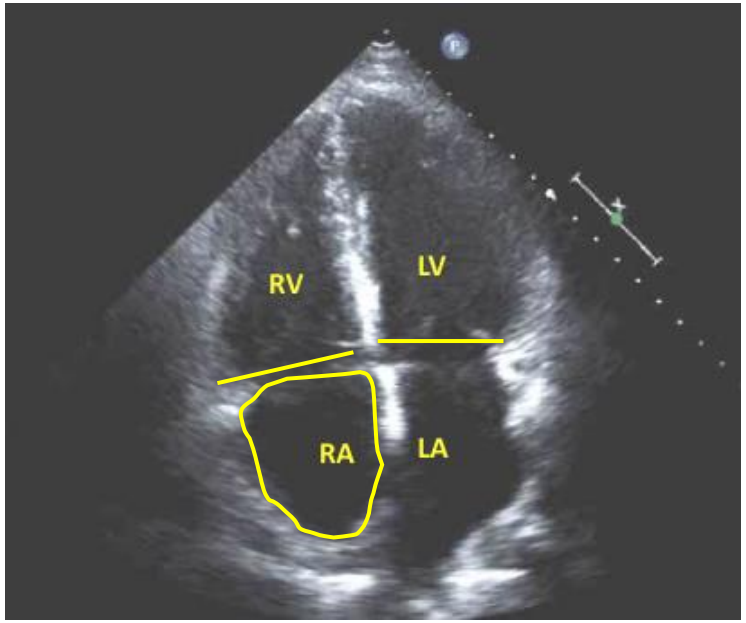
Parasternal Short Axis View



Eccentricity Index (D1/D2) > 1.1

- RV is enlarged

Apical 4 Chamber View



RV/LV Ratio > 1

RA Area > 18 cm^2

- Dilation of Right Sided Chambers

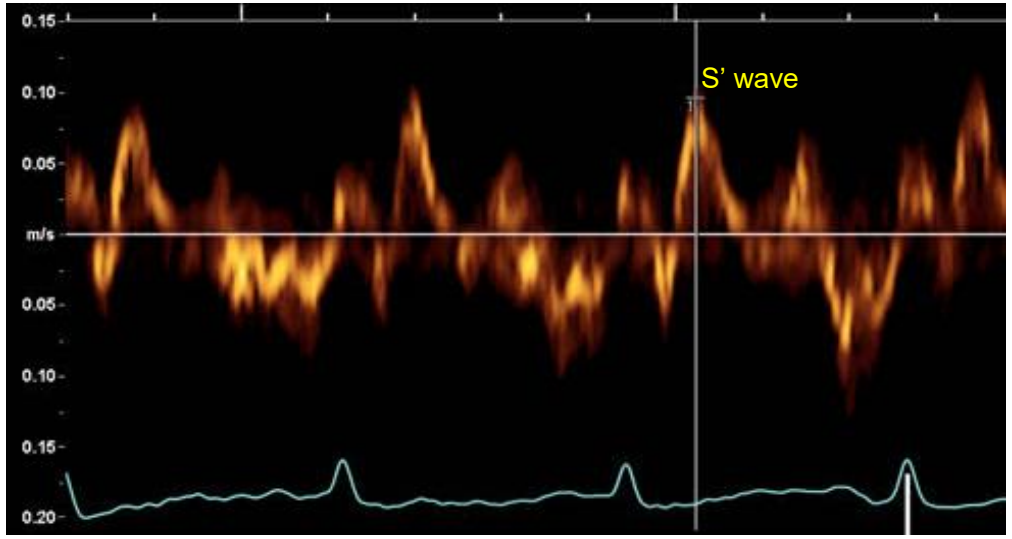
Galié N, et al. *Eur. Heart J* (2016) 37, 67–119

Other Echocardiographic Parameters That May Be Useful

Tissue Doppler (S')

- Indicative of RV function
- Simple and reproducible
- Represents regional wall motion

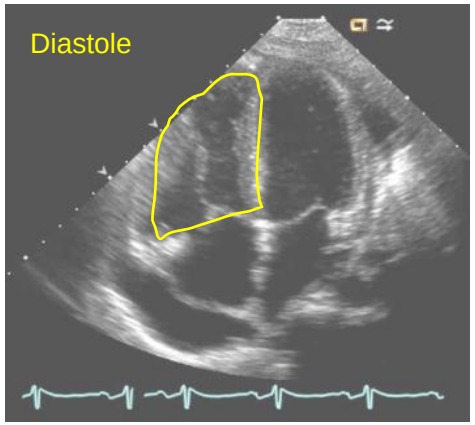
Tissue Doppler TV Annulus

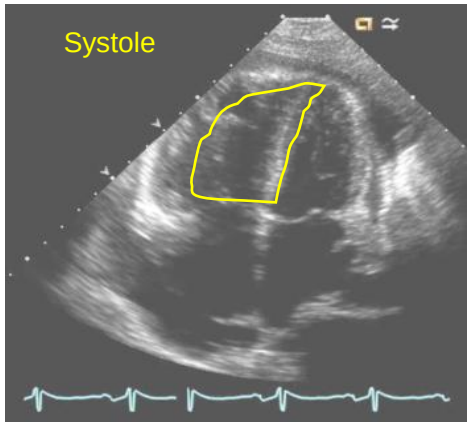


Fractional Area Change (FAC)

- Indicative of RV function
- High inter-observer variability
- May be a good test for follow up

RV Area Measured in Diastole and Systole





Graspa J, et al. *Circ Cardiovasc Imaging.* 2015;8:e002107.

Imaging Modalities: Newer Tools for PAH Diagnosis at the PH Center

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What Are the New PAH Diagnostic Modalities… and What They Can Illuminate?

- V/Q single photon emission CT (SPECT): pulmonary perfusion and embolism[1]
- Dual-energy CT (DECT): pulmonary perfusion[2]
- Three-dimensional dynamic contrast-enhanced magnetic resonance: lung perfusion[3]
- Functional magnetic resonance imaging: ventilation[4]
- Cardiac MRI: Subclinical right ventricular dysfunction
  - Parametric mapping[5]
  - Right ventricular strain[6]
  - Pulmonary artery four-dimensional flow imaging[7]
- Intravascular ultrasound and optical coherence tomography in PAH[8]
- Wearable technologies
- Artificial Intelligence analysis of diagnostic data

1. Grüning T, et al. *Clin Imaging* 2014; 38: 831–835
2. Giordano J, et al. *Eur Radiol* 2017; 27: 1631–1639.
3. Johns CS, et al. *J Magn Reson Imaging* 2017; 46: 1693–1697
4. Nakagawa T, et al. *J Magn Reson Imaging* 2001; 14: 419–424
5. Wang N, et al. *Can J Cardiol* 2014; 30: 455–463
6. De Siqueira ME, et al. *J Cardiovasc Magn Reson* 2016; 18: 39
7. Reiter G, et al. *Circ Cardiovasc Imaging* 2008; 1: 23–30
8. Dai Z, et al. *JACC Cardiovasc Imaging* 2014; 7: 843–845.

Relative Strengths and Weaknesses of Imaging Modalities in the Context of PH

Variable	Chest Radiography	V/Q Scan	SPECT/CT V/Q	Single-energy CT Angiography*	Dual-energy CT Angiography	MRI	Pulmonary Angiography
PH detection	+	-	-	+	+	+	-
Evaluation of anatomic compartments							
Lung	+	-	+	+++	+++	-	-
Cardiac chambers	+	-	-	++	++	+++	-
Pulmonary vessels	+	+	+	+++	++++	++	++
Mediastinum	-	-	-	+++	+++	+++	-
Assessment of PH etiology	++	++	+++	++++	++	++	++
General strengths	Readily available	Screening for CTEPH; SPECT(tomographic V/Q) currently replacing planar V/Q	Combined evaluation of lung parenchyma with lung perfusion	Excellent evaluation of etiologies of PH	Assessment of anatomy and lung perfusion (iodine maps) in a single test	No radiation; excellent evaluation of cardiac function and pulmonary flow in one examination	Planning of endovascular treatment (PEA, BPA)
Weaknesses	Limited role in the assessment of etiology	Need further imaging to assess the cause of PH; interpretive limitations in patients with comorbid conditions	Lung assessment limited; needs more validation; radiation dose added with use of CT	Limited hemodynamic assessment; limited evaluation of distal pulmonary arteries (beyond subsegmental level)	Needs validation for all dual-energy CT technologies	Limited in evaluation of lung parenchyma; not widely available; more technical expertise needed	Absence of perivascular structure evaluation; invasive test
Average effective radiation exposure (mSv)	0.05	2.2	2.6 – 3.5	2 - 5	3 - 5	none	10 - 30

BPA = balloon pulmonary angioplasty, PEA = pulmonary endarterectomy, PH = pulmonary hypertension, V/Q scan = ventilation-perfusion scintigraphy. 2 = no utility, 1 = limited utility, 11 = moderately useful, 111 = useful, 1111 = very useful.
*Non-electrocardiogram-gated CT.

Remy-Jardin M. *et al*. *Radiology*, 2021; 298:531–549

V/Q Scans and Computed Tomographic Approaches to PH Diagnosis: Finding CTEPH

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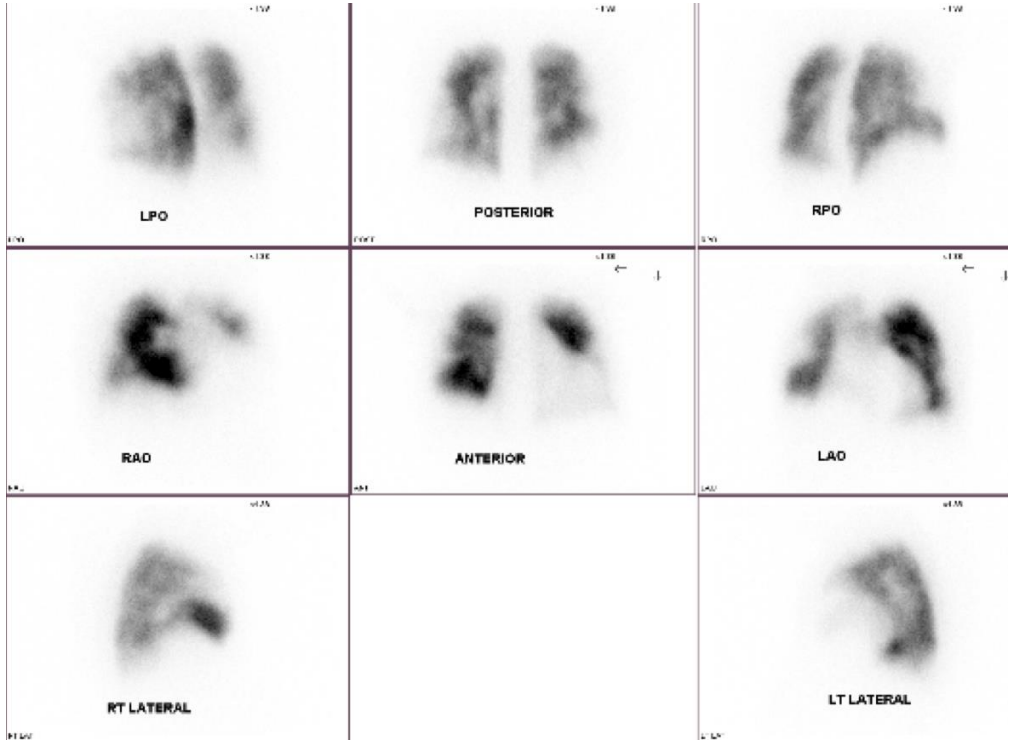
Always Rule Out CTEPH: VQ Scan is the Screening Test of Choice

CTEPH

Organized thrombus that becomes part of the intima.

Lung Perfusion



V/Q Scan Looks At Perfused vs Non Perfused Areas.
Sensitivity > 95%
Specificity > 95%

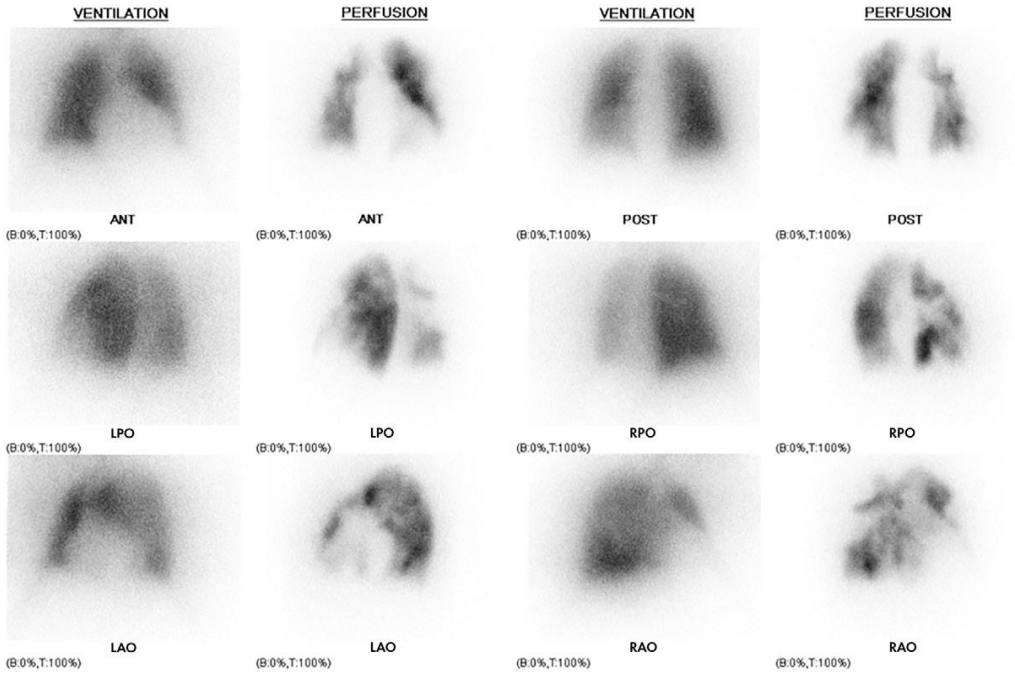
V/Q Scintigraphy and SPECT

- SPECT scan is an imaging test that shows how blood flows to tissues and organs
- It may be used to help diagnose seizures, stroke, stress fractures, infections, and tumors in the spine

Top Images:
Planar ventilation (81m krypton) and perfusion (99m Tc macroaggregate albumin) imaging shows multiple segmental and subsegmental defects in normally ventilated lungs, highly suggestive of CTEPH

Lower Images
SPECT perfusion images provide detailed analysis of perfusion defects in coronal plane

ANT = anterior, LAO = left anterior oblique, LPO = left posterior oblique, POST = posterior, RAO = right anterior oblique, RPO = right posterior oblique.



Remy-Jardin M. et al. *Radiology,* 2021; 298:531–549

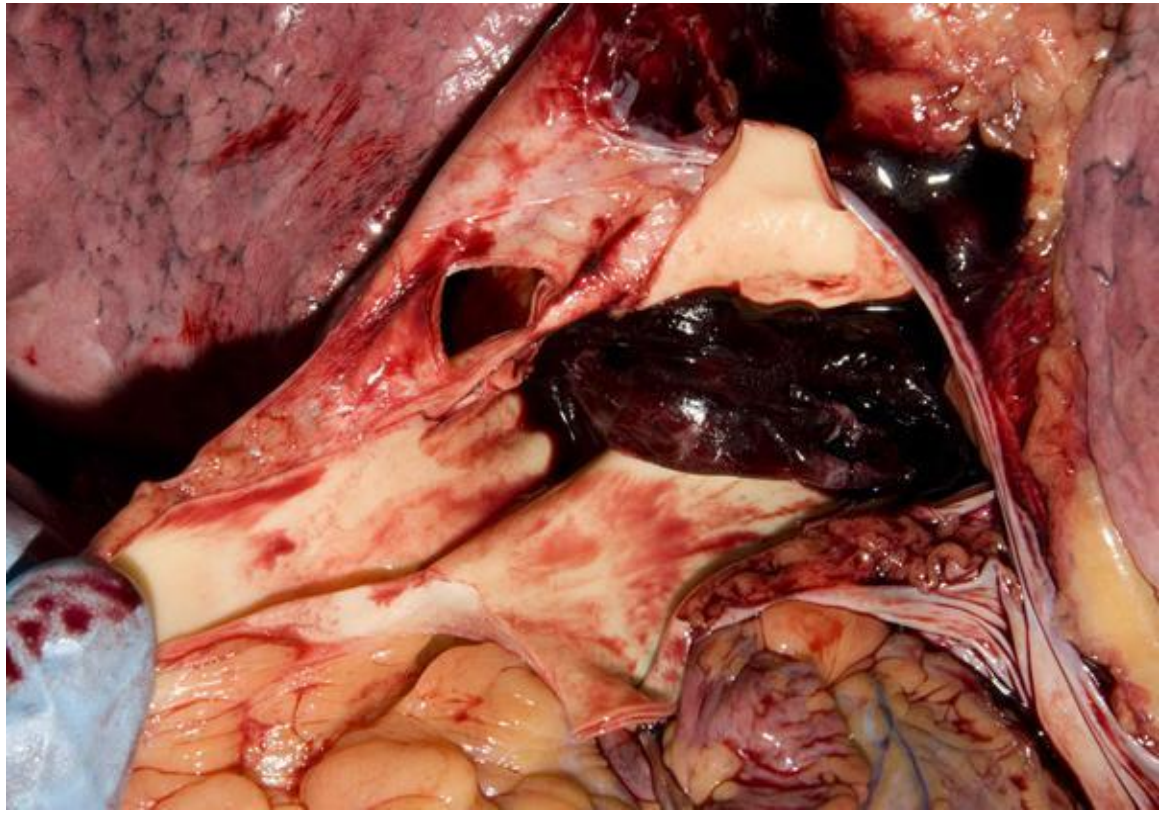
Computed Tomography With Angiography (CTA)

- Advanced CTA of the lung has sensitivity and specificity regarding CTEPH related changes of 92–100% and 95–97%, respectively at the main/lobar and segmental pulmonary artery levels[1]
- Conventional CTA does not provide functional information concerning pulmonary perfusion
  - Single source CTA has a sensitivity of 64–70% for depiction of subsegmental chronic thromboembolism compared to selective pulmonary angiography[2]
- CTA can naturally show direct vascular signs of CTEPH such as complete obstruction, partial obstruction, bands or web
- Main pulmonary enlargement or mosaic lung pattern are signs of pulmonary hypertension[3]

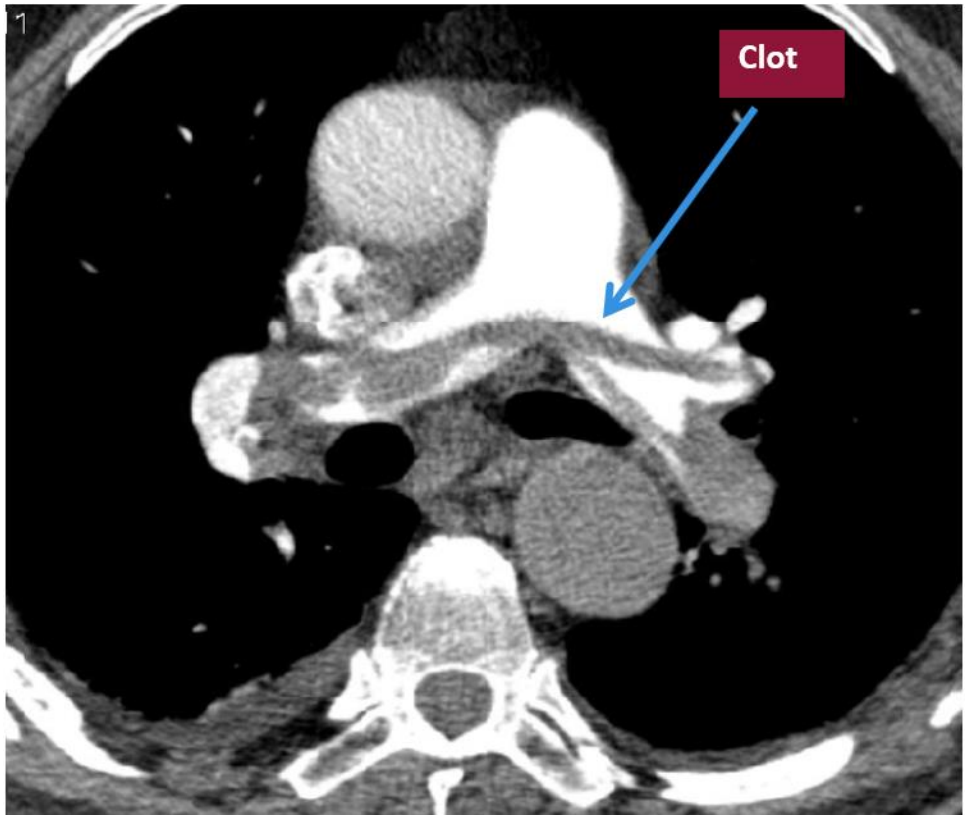
1. Ley S, et al. Eur. *Radiol.,* 2012; 22:607-616
2. Pitton MB, et al, *RöFo,* 2002; 174:474–479
3. Castaner et al, *Radiographics,* 2009; 29:31–50

A CT Scan Is the Test of Choice To Diagnose Acute Pulmonary Embolism

Acute Pulmonary Embolism

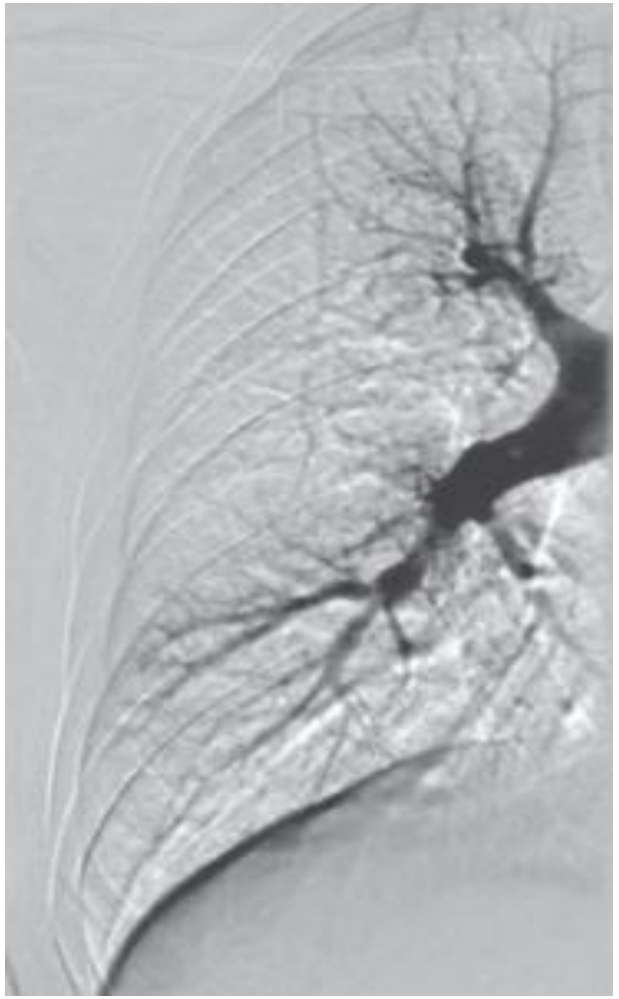


Fresh clot in the lumen of the pulmonary artery



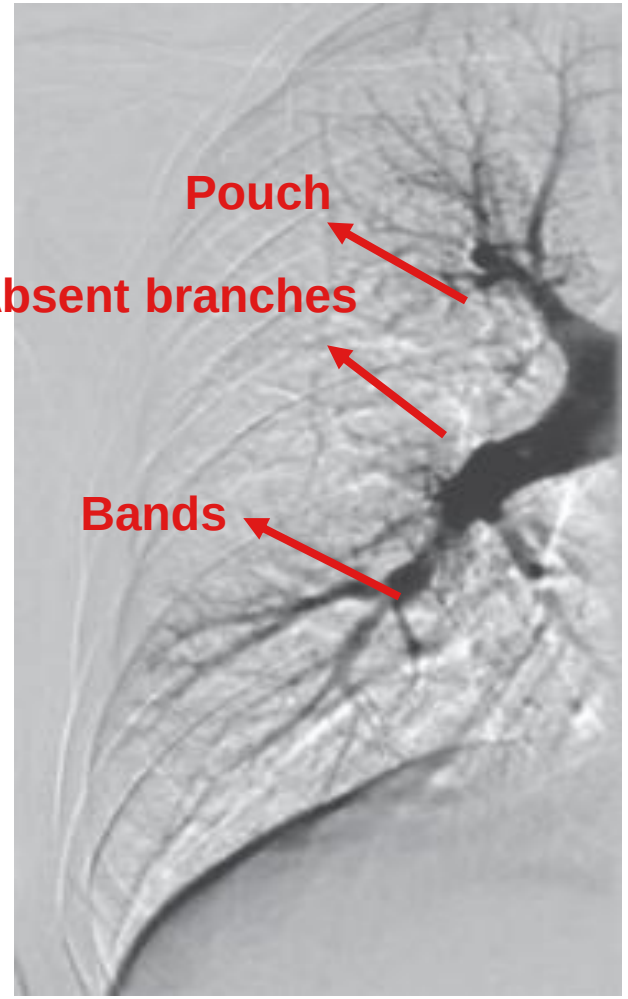
CT scan can miss organized thrombus

Angiography: Confirms CTEPH / Allows Surgical Planning



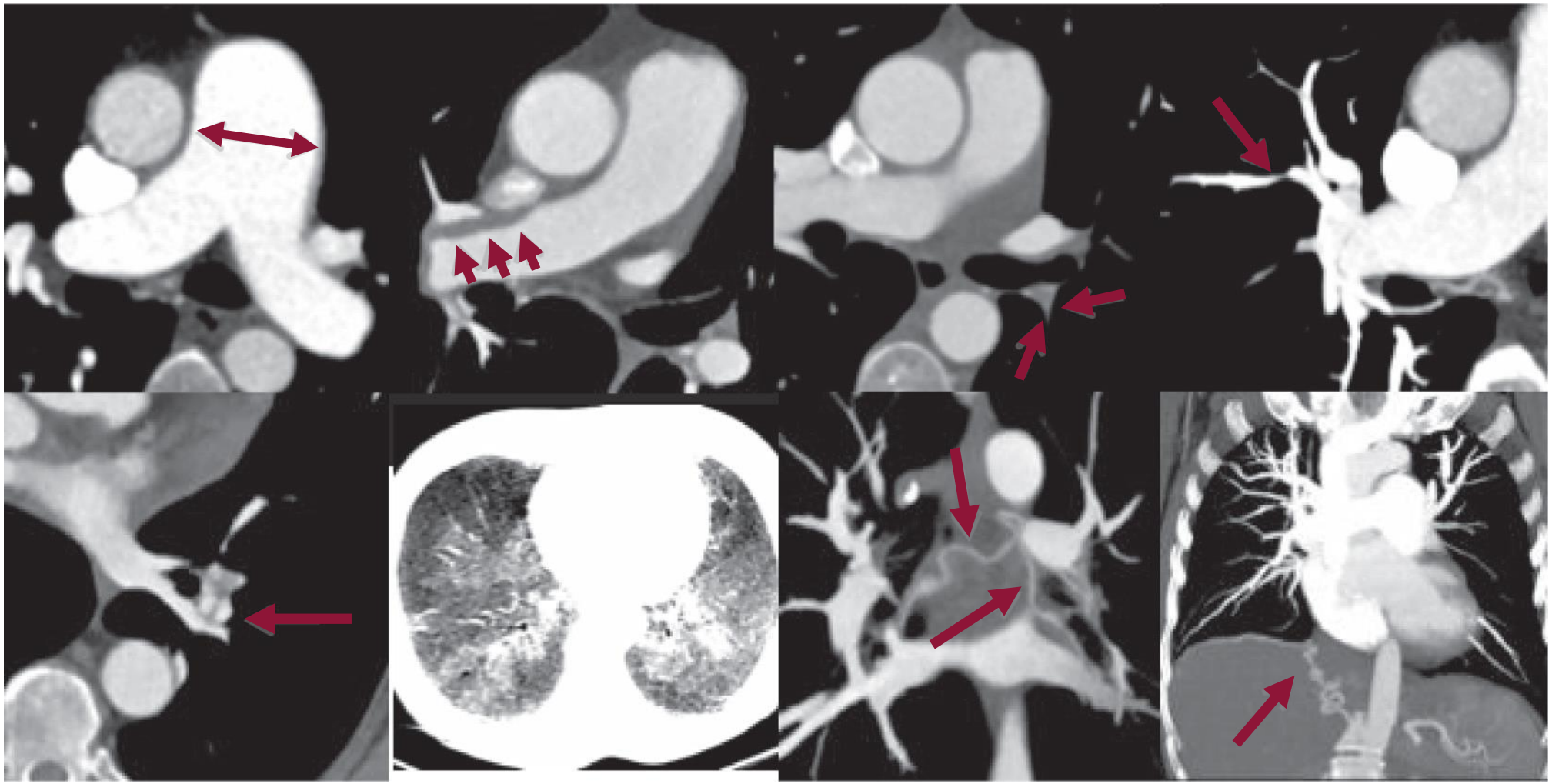
Jenkins D. *Eur Resp Rev*. 2015; 24:263-271.

Angiography: Confirms CTEPH / Allows Surgical Planning



Jenkins D. *Eur Resp Rev*. 2015; 24:263-271.

CTA: Examples

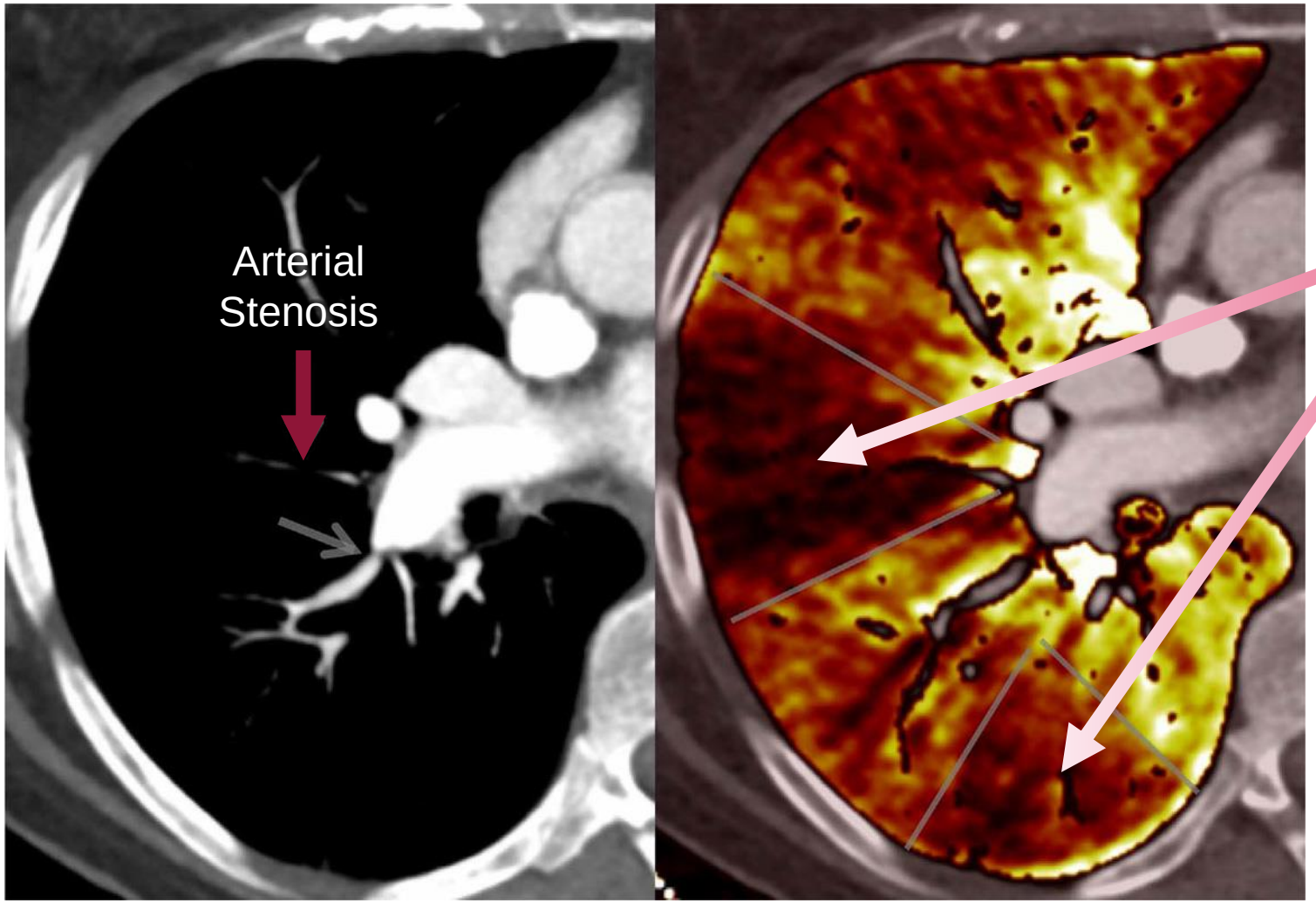


Modern Imaging:
Dual-Energy Computed Tomography Angiography (DECT)

- Enables a combined functional and morphological analysis of the lung
- Attenuation properties of iodine occur at two different photon energies (80 and 140 kV), this **dual energy** technique can generate pulmonary blood volume maps correlated to pulmonary perfusion[1]
- In comparison with a conventional CT, no additional intravenous iodine contrast medium injection
- Functional image processing is simply added.
- DECT is not associated with increased radiation levels[2]
- Study examining correlation between DECT and single photon emission computed tomography (SPECT) in 51 patients found that the DECT with iodine maps has a sensitivity of 96% and a specificity of 76% for CTEPH[3]

1. Johnson TR, et al, *Eur. Radiol.,* 2007; 17:1510–1517.
2. Thieme SF, et al. *Semin. Ultrasound CT MR,* 2010; 31:301–308
3. Nakazawa T, et al., *J. Comput. Assist. Tomogr*. 2011; 35: 590–595.

DECT: High Resolution Blood Maps Of The Lung



Consequences Of Segmental Perfusion Defects

DECT gives “superior anatomic and functional comprehension” by simultaneously recording vascular anatomy, parenchymal morphology and functional perfusion without extra radiation exposure

Kharat A, et al. *Thromb Res,* 2018; 163-260-265

Cardiac Magnetic Resonance Imaging (CMRI)

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PH

Cardiac And Lung Perfusion MRI

- MRI can provides anatomical and functional assessment of both pulmonary circulation and heart, with the major advantage of not using ionized radiation
- Diagnostic for congenital abnormalities
- With video techniques, gives robust qualitative and quantitative assessment of right ventricle (RV) with EDV, ESV, EF and CI[1]
- Curvature of the LV septal wall is a classic sign to depict elevated RV systolic pressure[2]
- Phase-contrast MRI can quantify blood flow and peak velocity not only in the main pulmonary artery but also in all of vessels of the chest
- Sequences assess differential blood flow to the right and left lung[3] and seem to reflect PAP measurements obtained by invasive RHC[4]

1. Abolmaali N, et al. *J. Magn. Reson. Imaging,* 2007; 26:646–653
2. Dellegrottaglie S, et al. *Radiology*, 2007; 243:63–69
3. Nikolaou K et al. *Investig. Radiol.,* 2004; 39:537–545.
4. Reiter G, et al, *Radiology,* 2015, 275 71–79

Is There a Role For Cardiac Magnetic Resonance Imaging (CMRI) In PH?

Three dimensional imaging technique that provides detailed morphology of cardiac chambers and accurate quantification of volumes, mass and flow.

Pros

- Non-invasive and highly reproducible
- Aids in diagnosis and prognosis
- Accurate RV function assessment
- Able to evaluate potential congenital or associated conditions

Cons

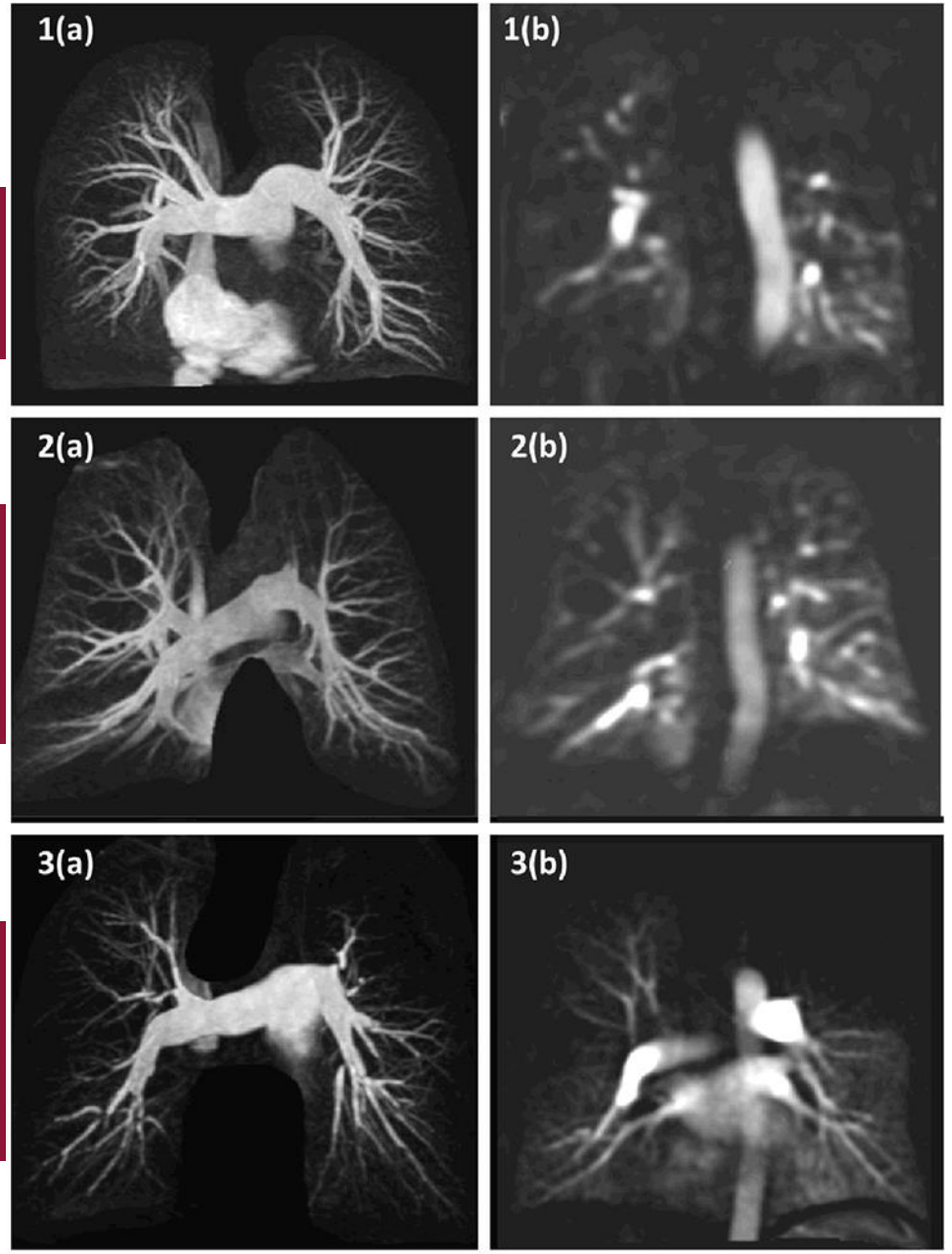
- Difficult for patients receiving pump therapy
- Claustrophobia

Magnetic Resonance Angiograms (a) and Perfusion Images (b)

IPAH: Shows vessel tortuosity and patchy perfusion

PH-COPD: Typical vessel splaying seen in patients with COPD/emphysema and associated reduced perfusion in the upper zones

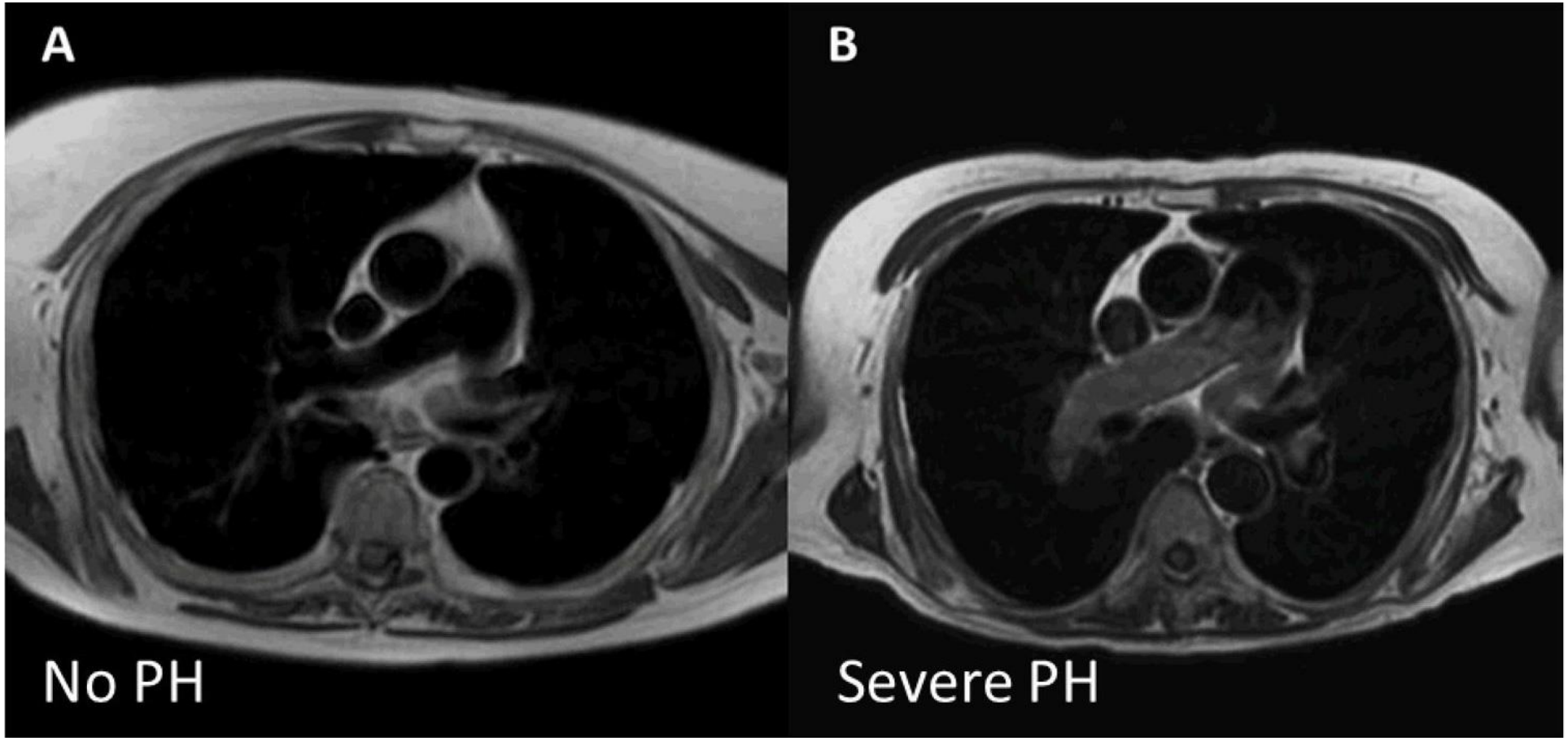
CTEPH: Vessel stenoses and occlusions typical of a patient with CTEPH and the associated segmental perfusion defects



Swift AJ, Wild JM, Nagle SK, et al. Quantitative MR imaging of pulmonary hypertension: A practical approach to the current state of the art. *J Thorac Imaging.* 2014;29(2): 68–79

MRI Investigation of Suspected PH: What We Can Learn

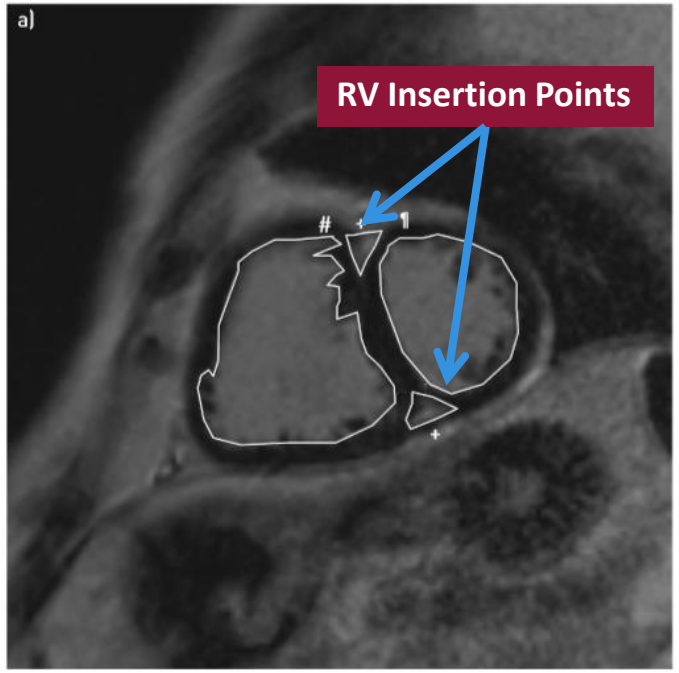
Axial Black Blood Images



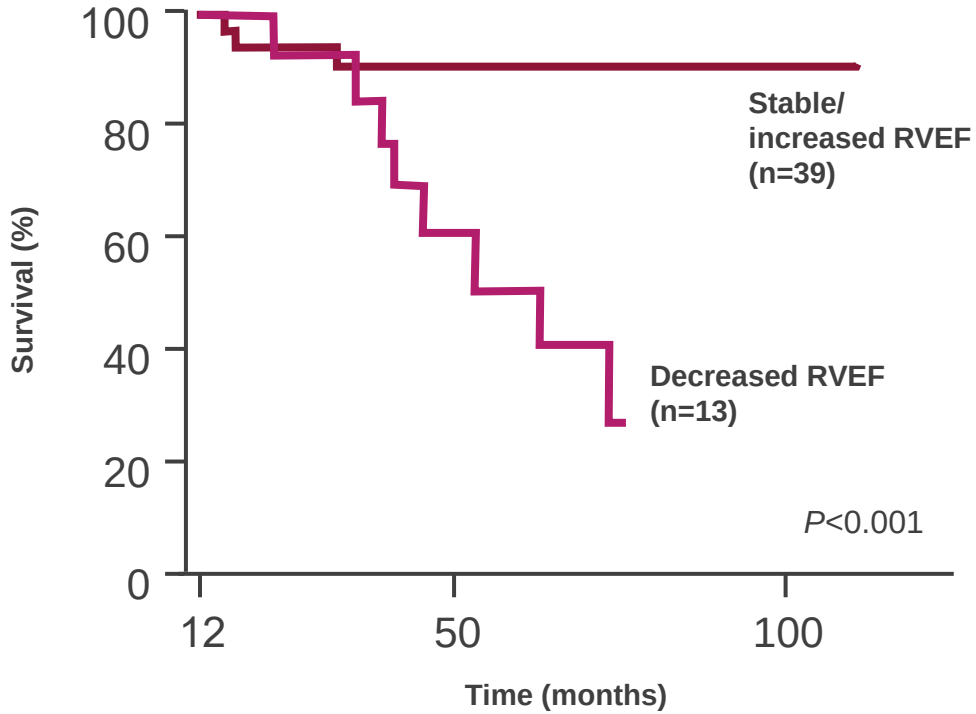
Swift AJ, et al. *J Thorac Imaging,* 2014; 29: 68–79

Certain cMRI Features Can Help Predict Outcomes in PAH

Short Axis with Late Gadolinium Enhancement



RV Ejection Fraction and Survival in Medically Treated PAH Patients



Grunig E, Peacock A. *Eur Respir Rev.* 2015; 24:653-664.
Van de Veerdonk, et al. *J Am Coll Cardiology.* 2011; 58:2511-2519.
Peacock, AJ, et al.. *Circ Cardiovasc Imaging.* 2014;7:107-114.

Know When to Refer Your Patients to the PH Center

Hemodynamic Evaluation Of Suspected PH

- Right heart catheterization is still the only validated method to confirm and grade PH, best performed at the PH center
- Recent studies have shown that even patients with mPAP < 20 mm Hg or mPAP between 21 and 24 mmHg at rest may develop PH during exercise, (exercise pulmonary hypertension)[1]
- Use of exercise hemodynamic measurements in symptomatic patients with pulmonary perfusion defects and normal resting mPAP can reveal presence of abnormal cardiodynamic response to effort[2], esp. in patients with chronic clots
- For these reasons, and more, hemodynamic evaluations of the suspected PH patients may best be done at the PH center

1. Lau EMT, et al. *Eur. Respir. J.,* 2016; 47:436–14
2. Kovacs G, et al. *Eur. Respir. J.,* 2012;39:319–328.

Essentials of PAH Diagnosis 3: Right Heart Catheterization

Diagnosis of PAH Requires Right Heart Catheterization!

- Confirms diagnosis
- Calculate resistance
- Guide therapy for PAH
- Excludes other etiologies of PH
  - Intracardiac or extracardiac shunts
  - Left-heart-disease
- Measures degree of RV dysfunction
  - RAP
  - CO

- O_2 Saturations (SVC, IVC, RV, PA, SA)
- RAP
- PAP, Systolic, diastolic, mean
- PAWP, or LVEDP
- CO/CI
- PVR
- Vasodilator challenge for idiopathic, heritable, and drugs and toxins.

Hemodynamic Values Used in the European Society of Cardiology (ESC)/European Respiratory Society (ERS)

	ERS/ESC Guidelines		
NHYA/WHO FC	I,II	III	IV
Hemodynamics/ right heart catheterization	RAP <8 mmHg CI ⩾2.5 L/min/m^2 SvO_2 >65%	RAP 8–14 mmHg CI 2.0–2.4 L/min/m^2 SvO_2 60–65%	RAP >14 mmHg CI <2.0 L/min/m^2 SvO_2 <60%

Galiè N, et al. *Eur Heart J.* 2016;37:67-119.

Summing Up: Know When Unexplained Dyspnea Is Something Really Serious

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Where’s the Air? – The Importance of Explaining the Unexplained Dyspnea

- Patients may develop dyspnea from many potential causes
- The importance of uncovering the cause of the dyspnea cannot be understated
- Route to diagnosis is multifactorial; involving community physicians and PH center specialists
- Key event: developing index of suspicion for PH and immediate referral from the community HCP to the PH center
- Certain diagnostic tools form essential components to constructing the suspicion that PH is the root cause of the dyspnea
- These tools include PFTs, measurement of biochemical markers (BNP), imaging of the heart and lungs and right heart catheterization to obtain hemodynamic measurements

Summing up…

- Echocardiogram: probably most important tool for the community physician and the PH center specialists
- The echo imaging must gather good structural pictures, particularly of the right heart, as pressures obtained are estimates only
- Other imaging techniques, such as V/Q scintigraphy with angiography can determine if PH is a result of pulmonary embolism
- Newer imaging techniques such as SPECT, DECT and cMRI provide vivid images of cardiac and pulmonary structures that can enhance diagnosis in CTEPH and help pinpoint area where surgical intervention may be an option
- Confirmation of PH must be accomplished via right heart catheterization, best done at the PH specialty center
- The interpretation of data and eventual management of the patient becomes a shared process between the PH center and the referring physician