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PH

Addressing PH Subtypes: Raising Awareness of Understudied Populations

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Learning Objectives

- Review characteristics of PH patient groups that fall outside of the idiopathic category
- Discuss the screening, diagnosis and expedient referral of non-idiopathic patients to PH specialty centers from community generalists and specialty healthcare providers
- Focus on understudied PH groups that require special diagnostic attention by all healthcare providers
- Review treatment and management approaches to these understudied PH patients

Setting the Stage – What Are the Understudied PH Populations?

Where Have Studies of PAH Been Focused?

- The current classification scheme for pulmonary hypertension is comprised of 5 major groups
- Historically, Group 1 PAH has been the most often studied class of adult PH
- PAH therapy trials have mainly enrolled white females in their 40s and 50s and have consistently excluded non-WHO Group 1 forms of PH[1]
- Initial clinical trials performed in newly diagnosed PAH and CTEPH patients were single agent, placebo controlled, of short duration, focused on changes in measures of exercise capacity and comprised of relatively small populations of patients[2]
- Over the past decade, clinical trial designs for PAH have evolved into much larger, placebo controlled, on background therapy and upfront combination therapy trials

1. Hill NS, et al. *Proc Am Thorac Soc,* 2008; 5:603–609
2. Sitbon O, et al. *Eur Respir J,* 2019; 53: 1801908 [https://doi.org/10.1183/13993003.01908-2018].

WSPH 2018: Clinical Classification of PH

1. Pulmonary Arterial Hypertension

1.1 Idiopathic PAH
1.2 PAH with vasoreactivity
1.3 Heritable PAH
1.4 Drugs and toxins induced
1.5 Associated with:
1.5.1 Connective tissue disease
1.5.2 HIV infection
1.5.3 Portal hypertension
1.5.4 Congenital heart disease
1.6 PAH with overt signs of venous/capillaires (PVOD/PCH) involvement
1.7 Persistent PH of the Newborn syndrome

2. PH due to left heart disease

2.1 PH due to heart failure with preserved EF
2.2 PH due to heart failure with reduced EF
2.3 Valvular heart disease
2.4 Congenital post-capillary obstructive lesions

3. PH due to lung diseases and/or hypoxia

3.1 Obstructive lung disease
3.2 Restrictive lung disease (with respect to SSc)
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4. PH due to pulmonary artery obstruction

4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions

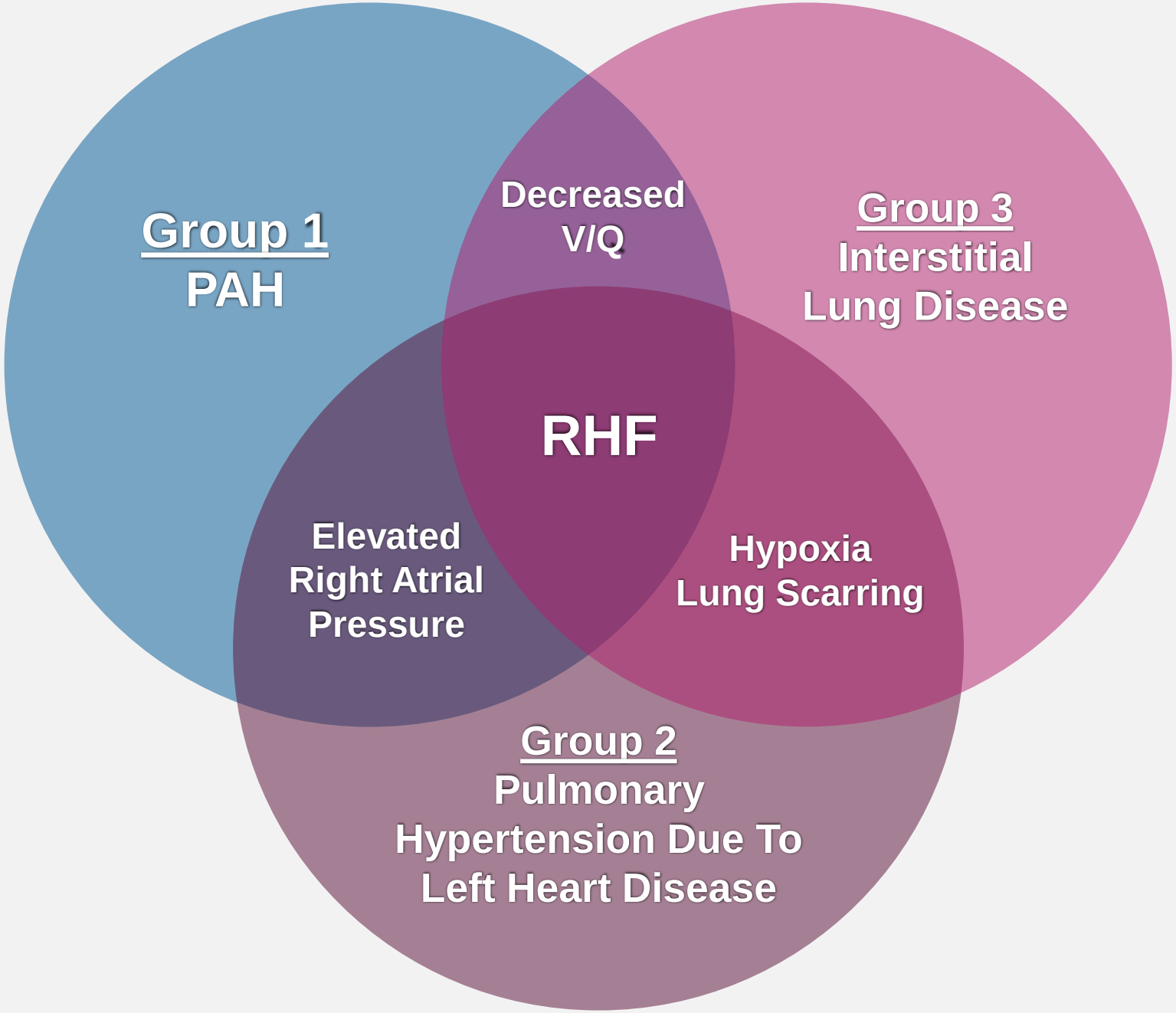
5. PH with unclear mechanisms

5.1 Hematologic disorders
5.2 Systemic disorders
5.3 Others
5.4 Complex congenital heart disease

Simonneau G, et al. *Eur Respir J.* 2019 Jan 24;53(1):1801913. doi: 10.1183/13993003.01913-2018

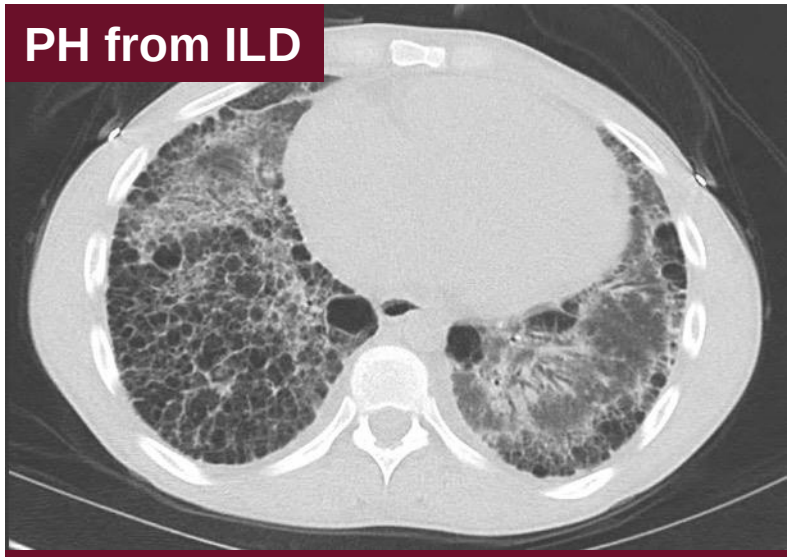
Connective Tissue Diseases (CTD): Identifying Patients with PH

Patients With SSc Can Have Different Reasons For Their PH



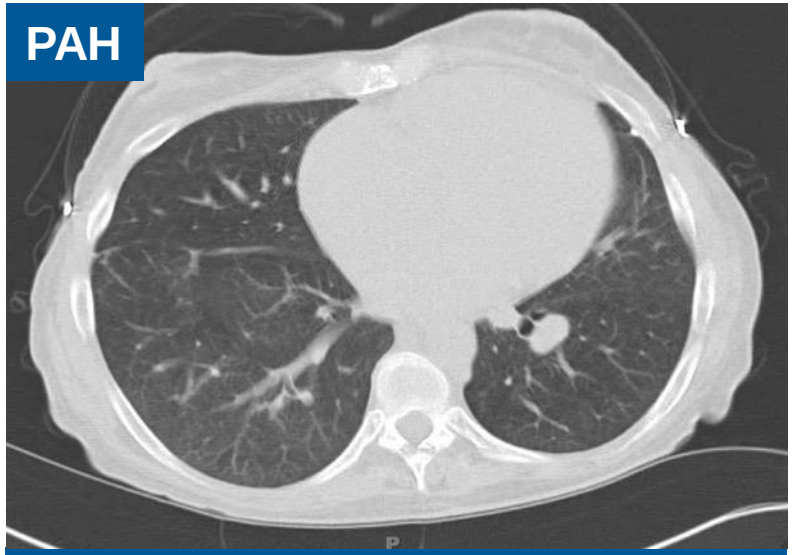
Different Spectrums of PH That Can Be Seen in SSc:
Classic Examples

PH from ILD



- Diffuse >> limited
- Very abnormal lung architecture
- Reduced vital capacity
- **Chronic hypoxia**
- Normal to moderate PA pressure elevation

PAH



- Limited >> diffuse
- Normal or minimally abnormal lung architecture
- Mild basilar fibrosis common
- **Very low DLco, normal vital capacity** (%FVC / %DLco >**1.6**)
- **Evidence of RV dysfunction**
- Elevated PA pressure

Courtesy of Dinesh Khanna, MD

CTD-Associated PAH – Perspectives for Rheumatologists and Pulmonologists: Working Together To Build Clinical Suspicion

How Commonly Is PAH Associated With Systemic Sclerosis?

- Connective tissue disorders (CTDs) are commonly associated with PAH
- Systemic sclerosis (SSc) is the most frequent CTD complicated by PAH (8%–12%), accounting for ~75% of CTD-PAH cases[1]
- PAH is a leading cause of death in SSc and associated with a worse prognosis than iPAH[2]
- PAH can be detected in 1%–5% of patients affected with systemic lupus erythematosus (SLE) and ~3%–4% of mixed connective tissue disease (MCTD)[3]
- Data on the prevalence of PAH in CTDs other than SSc are much less reliable owing to the lack of screening (recommended only for SSc) and RHCs

1. Zanatta E, et al. *Experimental Biology and Medicine* 2019; 244: 120–131.
2. Launay D, et al. *Ann Rheum Dis* 2013;72:1940–6
3. Bazan IS, et al. *Respir Med* 2018;134:42–6

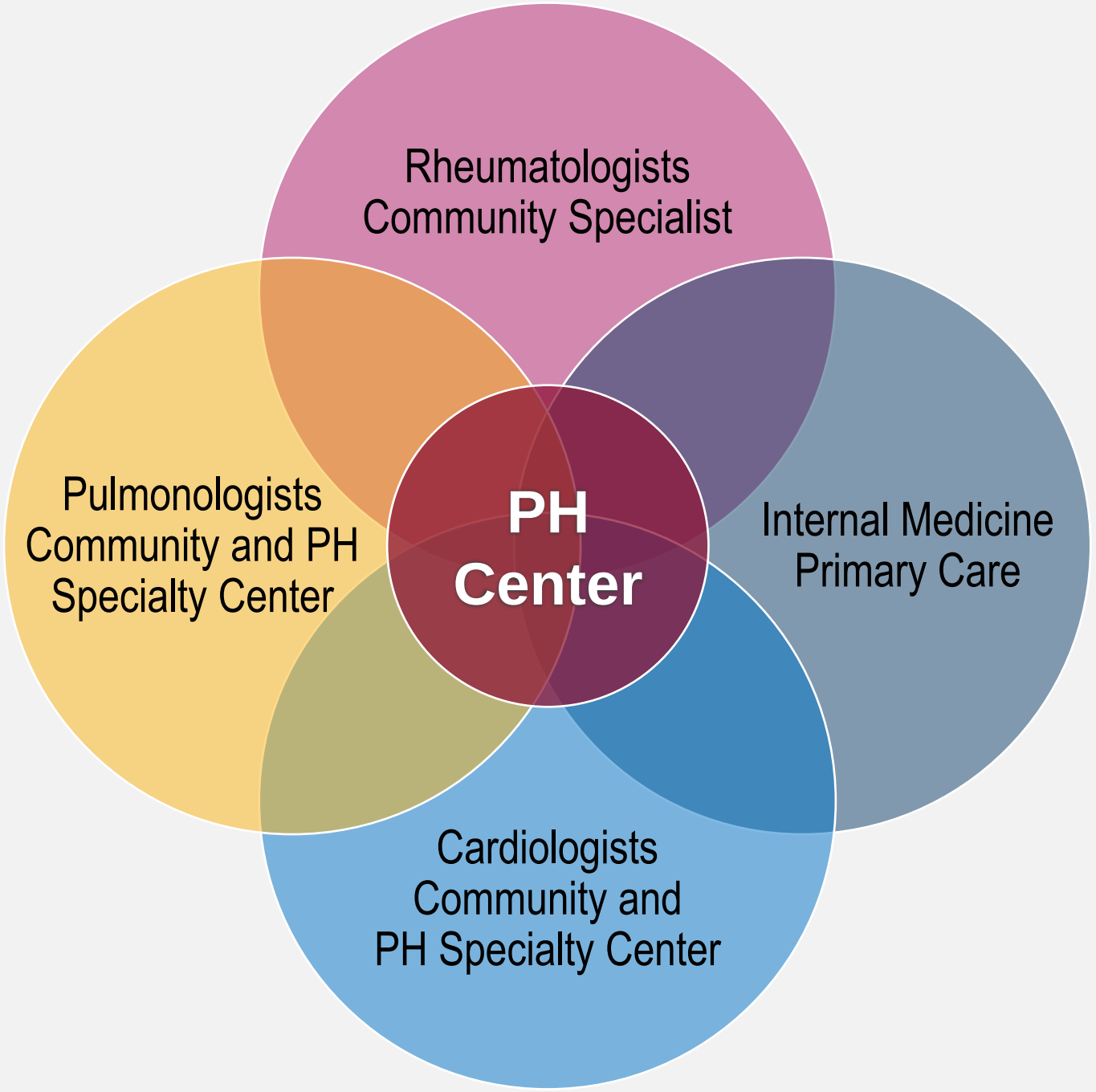
Building a Clinical Suspicion of PAH

- **General Symptoms** (nonspecific)
  - Dyspnea
  - Weakness
  - Chest pain
  - Light-headedness / syncope
  - Cough (less frequent)

- **Signs and symptoms in advanced disease**
  - Progressive right-sided heart failure (edema, ascites, abdominal distension)
  - Hemoptysis
  - Ortner's syndrome/hoarseness (unilateral vocal cord paralysis) very rare
  - 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
  - Right sided S3 gallop

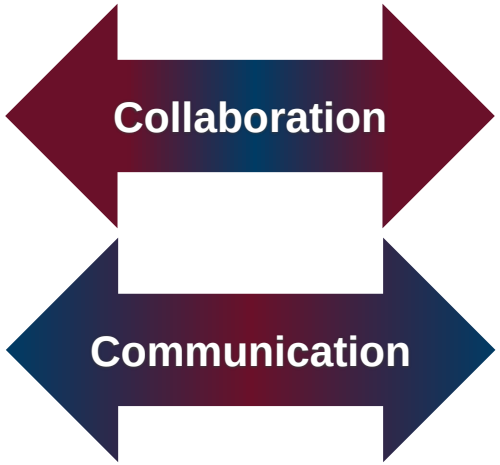
Successful Identification and Management of PAH Requires Collaboration



The Community Physician and the PH Center: Disease Identification and Treatment Must Be a Collaborative Approach

Community
Generalists and Specialists
"Initial Assessment"

- At-risk patient population
- Primary provider of care
- Identification of disease
- Screening of at-risk populations (e.g. SSc)
- Routine medical care after diagnosis

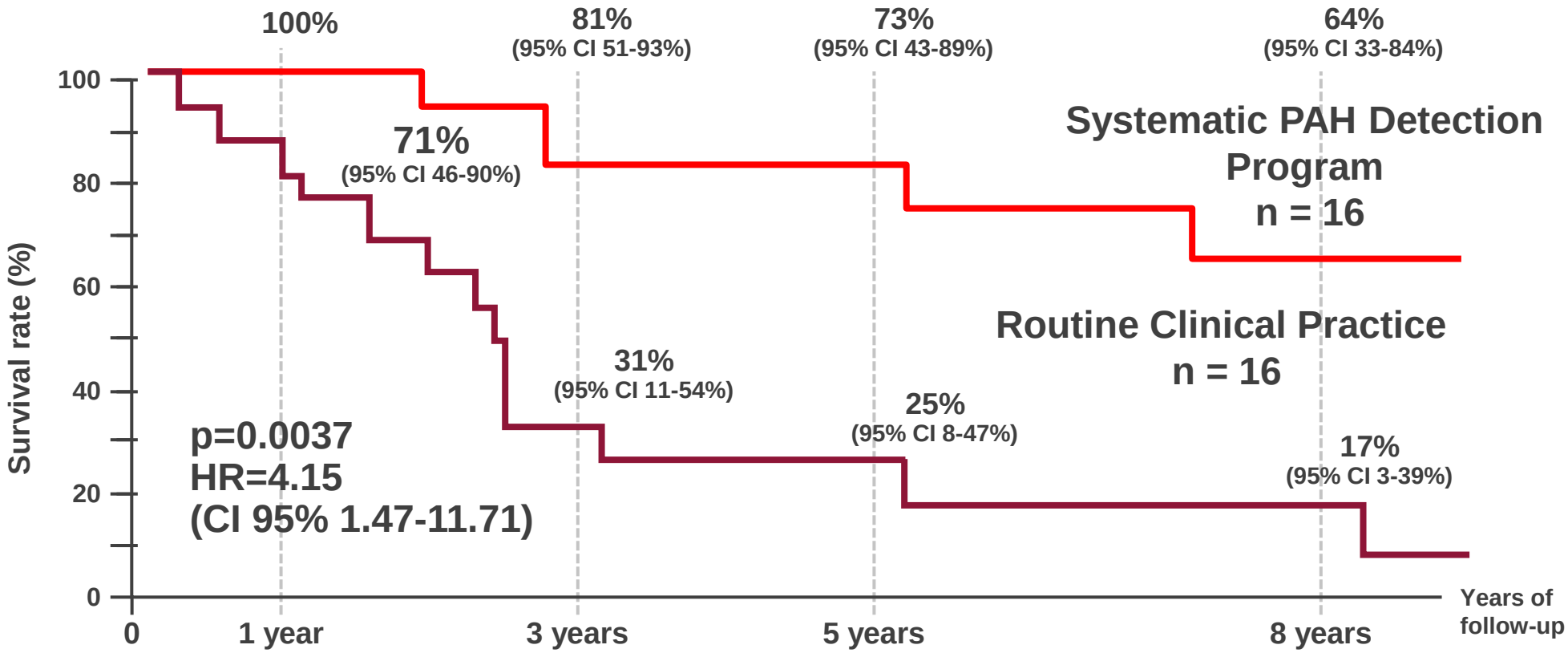


PH Specialty Center
"Confirmation of diagnostics where there is uncertainty"

- PAH specialty physicians
- Advanced diagnostics
- Experienced in advanced therapies (incl. prostacyclins and IP receptor agonists)
- PAH trials
- Lung transplantation
- Presence of support groups
- Nursing expertise and support teams
- Advanced patient education programs

Screening the CTD Patient For Development of PAH: Why Must We Do This?

Active Screening Identifies Patients Earlier and Earlier Detection = Better Survival



Values at each time point are the survival rate with 95% confidence interval ; (95% CI), HR = hazard ratio

Adapted from Humbert M, et al. *Arthritis Rheum.* 2011;63:3522-3530.

Screening of High-Risk Populations for PAH

- Annual screening recommended in asymptomatic patients with the SSc spectrum of diseases and should include:
  - 2-step approach: look for presence of telangiectasia, ACA, PFT and DLco measurements, electrocardiogram, and biomarkers (NT-proBNP and uric acid) in the initial stage
  - Echocardiography and consideration of RHC in patients with abnormal findings
- Screening should be part of a scientific protocol or registry, whenever possible
- Patients with SSc and other CTDs with clinical signs and symptoms of PH should be evaluated by RHC
- Scleroderma (systemic sclerosis) and scleroderma spectrum
  - Annual screening for SSc and SSc spectrum with uncorrected DL_{CO} <80% of predicted,
  - Screening tools: DETECT algorithm, 2015 ESC/ERS recommendations for TTE or FVC/DL_{CO} ratio >1.6 (assuming none-to-mild ILD) and >2-fold ULN of NT-proBNP
  - If any tests are positive, refer for RHC
  - When uncorrected DL_{CO} is ≥ 80% of predicted, TTE screening may be used

Hoeper MM, et al. *J Am Coll Cardiol.* 2013;62:D42-D50.

Bottom Line: If Your Patient Has SSc, Screen Them Annually for Development of PH

SCREEN: If The Patient Presents With…SSc or MCTD with Scleroderma Features	
How often?	Annually
How do I screen?	Echo, PFTs, and NT-Pro-BNP or DETECT protocol (if DL_{CO} < 80%)
If results are abnormal, then…	Send for RHC
Other annual tests	TTE (esp. if new symptoms), NT-proBNP, PFT with DL_{CO} (esp. if new symptoms develop), or DETECT algorithm

SCREEN: If The Patient Presents With…Other CTDs	
How often?	Not recommended due to low prevalence
If symptoms	F/U ERS/ESC recommendations for work up

Khanna D, et al. *Arthritis Rheum.* 2013;65:3194-201
Galie N, et al.. *European Respiratory Journal.* 2009; 34(6):1219–1263.

How Do We Determine If a SSc Patient Needs to Be Sent to a PH Specialty Center?

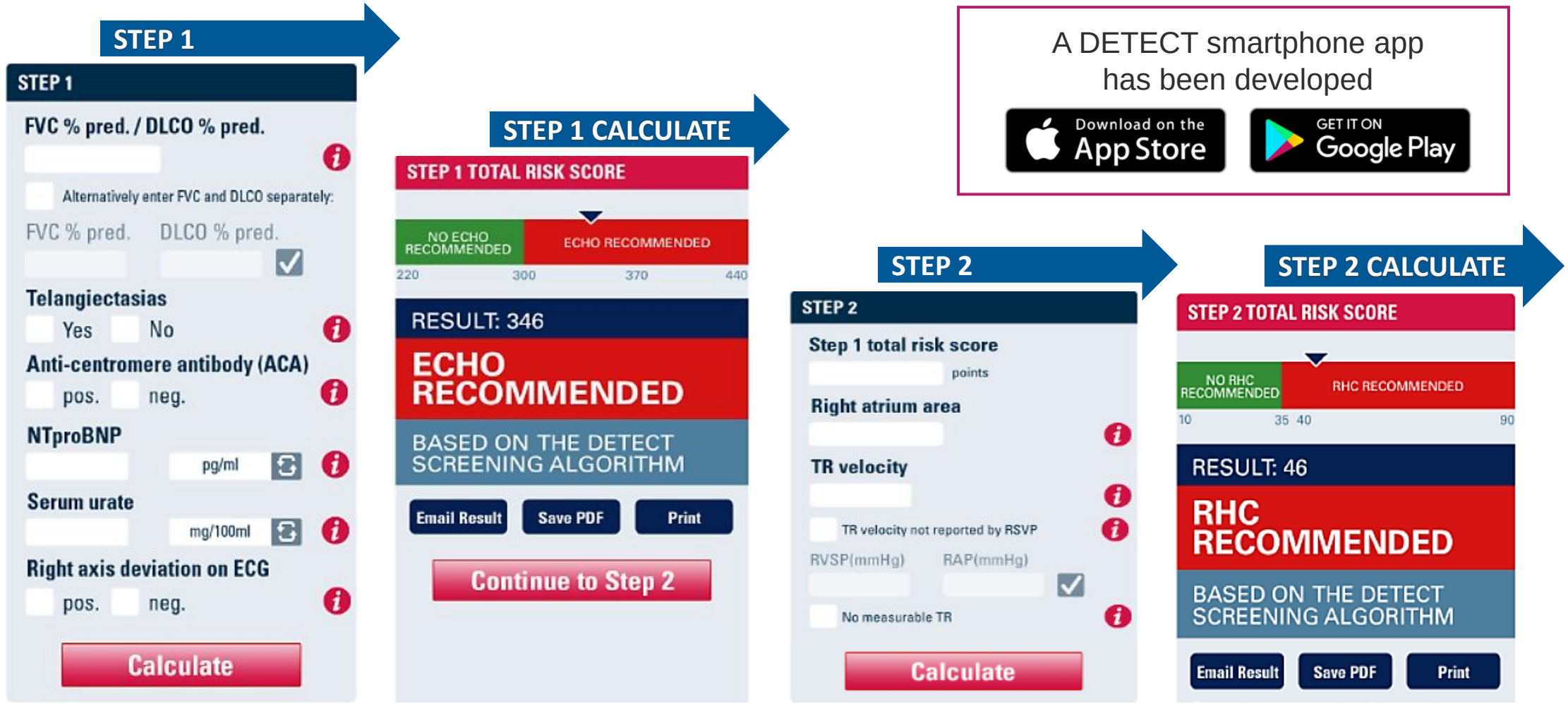
Rationale for the Two Steps of the DETECT Algorithm

Step 1 Non-echocardiographic data (6 variables)	Step 2 Echocardiographic data (2 variables)
Easily obtained by a rheumatologist to determine need for echocardiography	If rheumatologist assessment from the indicates a need for echocardiography, the cardiologist determines this next stage

By using 2 steps to determine referral for RHC, DETECT optimizes resource usage and reduces the burden on particular medical departments

Coghlan JG, et al. *Ann Rheum Dis.* 2013;73:1340-1349.

DETECT Protocol: A Two-Step Decision Tree for Screening For SSc-PAH



Coghlan JG, et al. *Ann Rheum Dis,* 2014; 73:1340-9.

DETECT v2.0 was released in January 2019

Collaborative Assessment of the PAH Patient: Data to Collect and Where Testing Should Occur

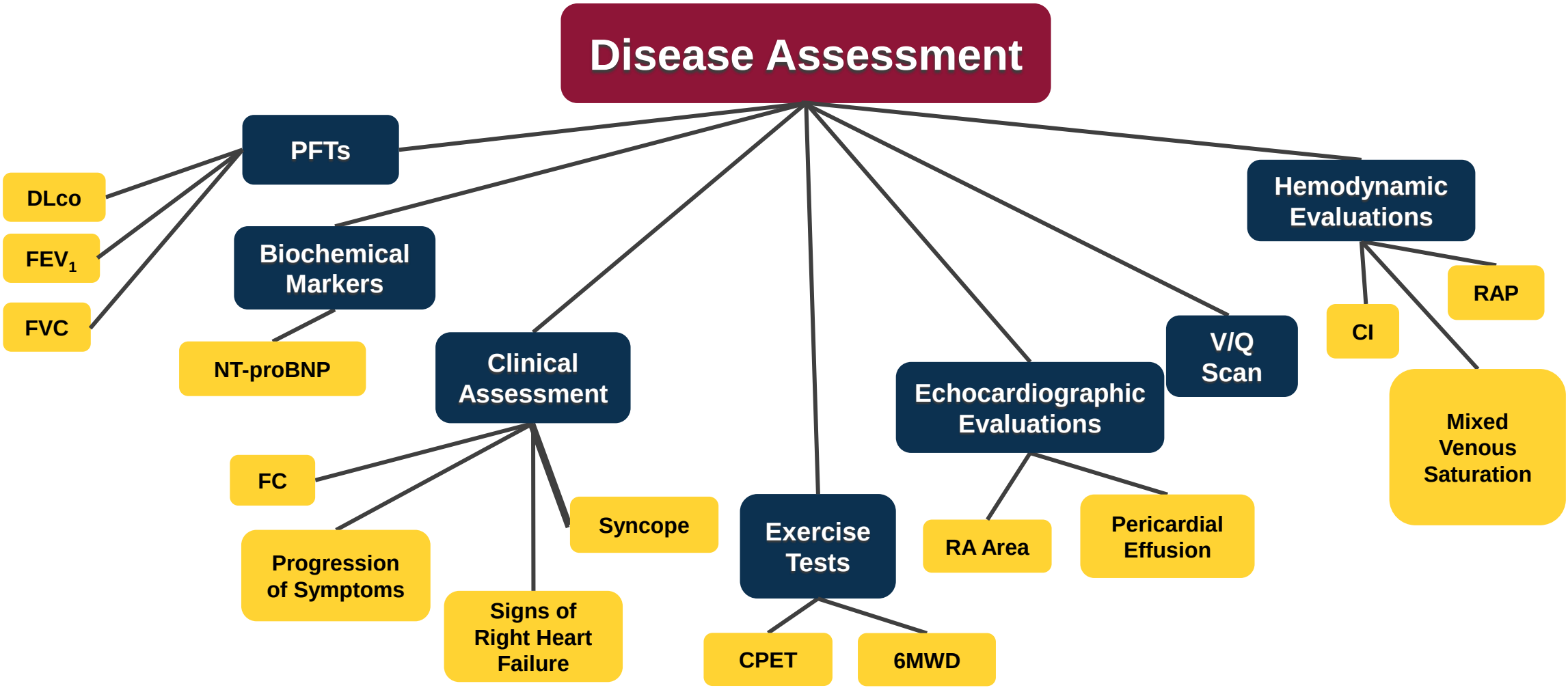


Diagram adapted from Galiè N, et al. *Eur Heart J.* 2016;37:67-119.
Thakkar V, et al. *Arthritis Res Ther.* 2013;15:R193.

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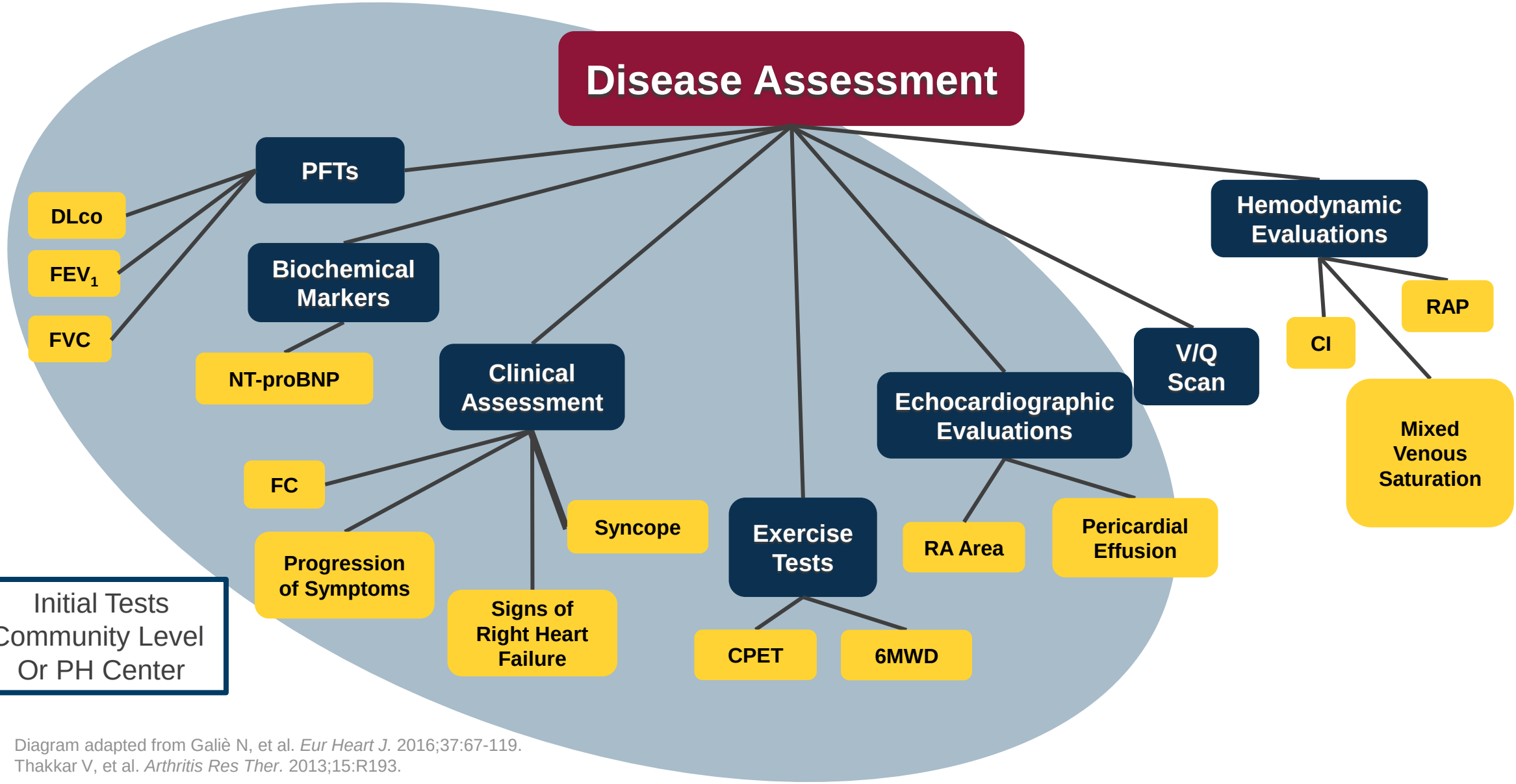

Diagram adapted from Galiè N, et al. *Eur Heart J.* 2016;37:67-119.
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Collaborative Assessment of the PAH Patient: Data to Collect and Where Testing Should Occur

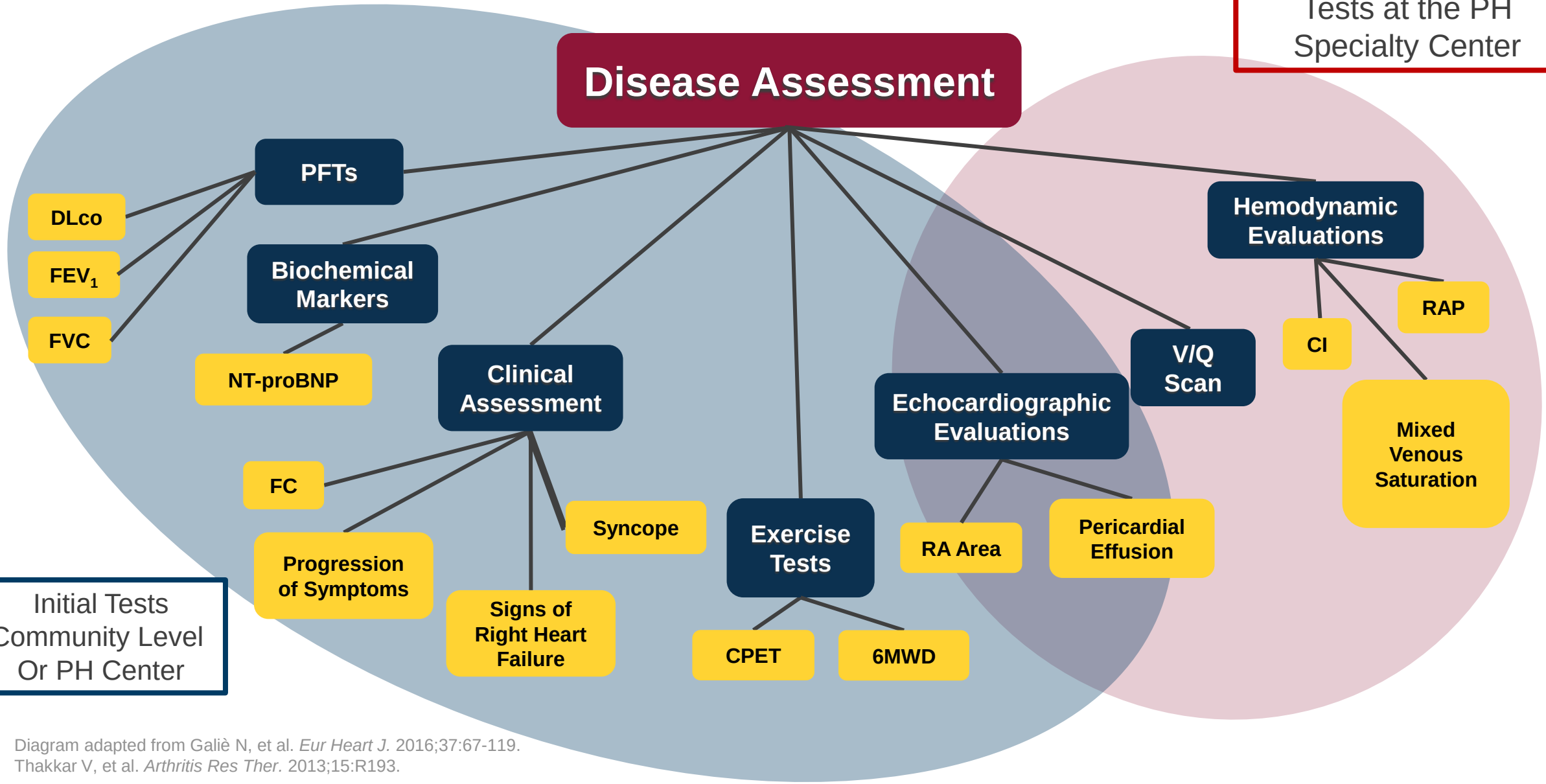
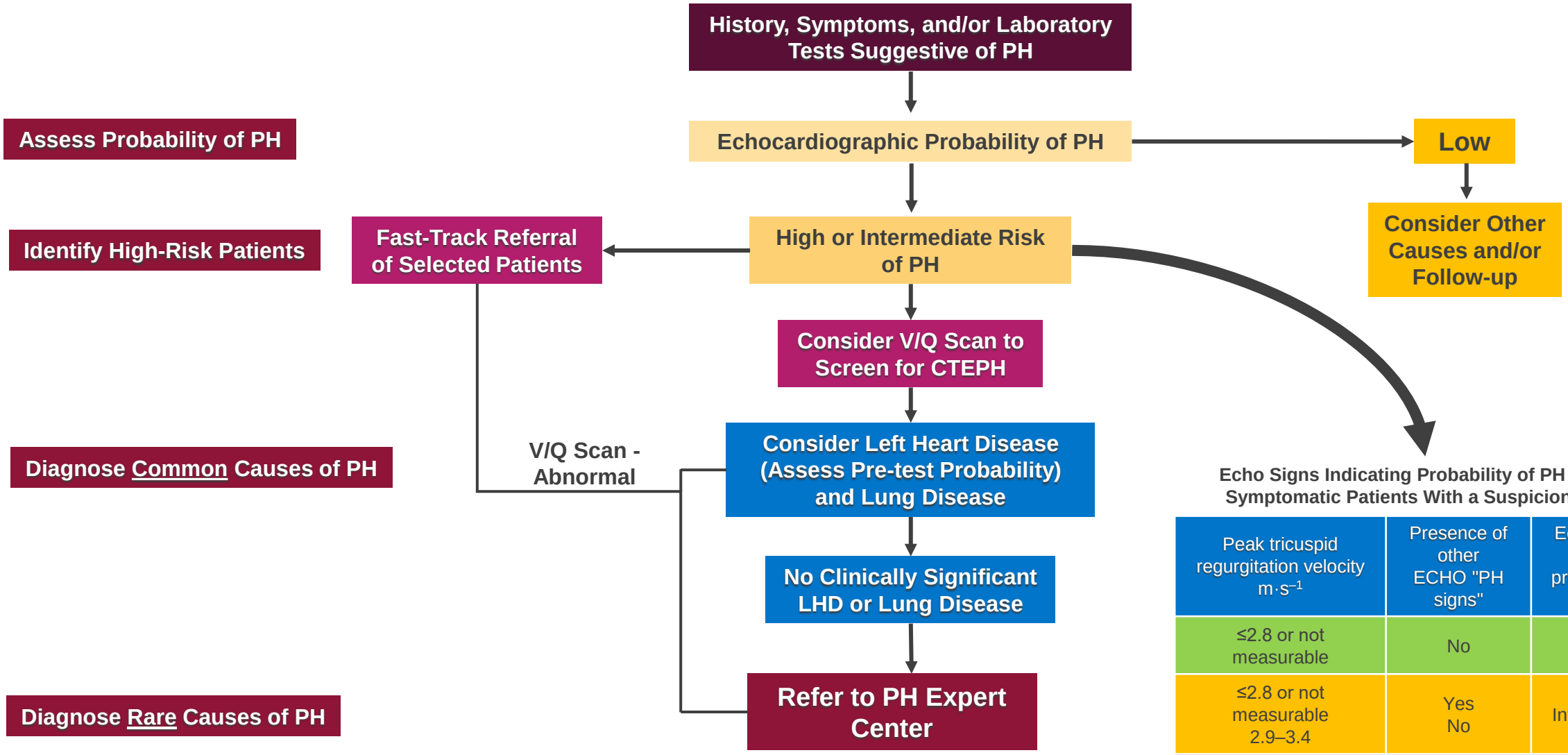


Diagram adapted from Galiè N, et al. *Eur Heart J.* 2016;37:67-119.
Thakkar V, et al. *Arthritis Res Ther.* 2013;15:R193.

The Revised Diagnostic Algorithm Must Be Seen in 2 Parts:

Step 1: Triage and Diagnosis of Common Conditions – Community Level

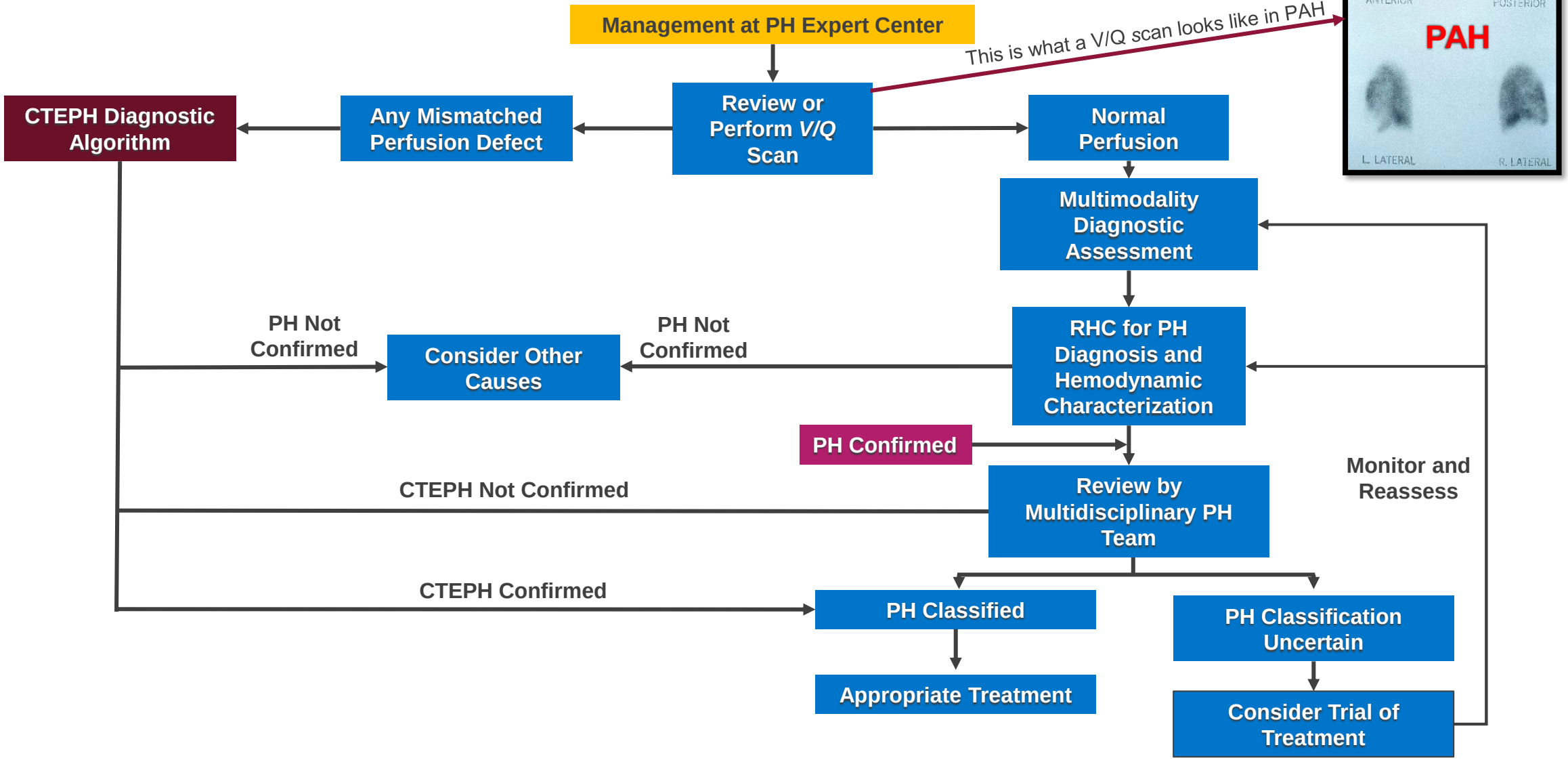


Echo Signs Indicating Probability of PH Risk in Symptomatic Patients With a Suspicion of PH

Peak tricuspid regurgitation velocity $m \cdot s^{-1}$	Presence of other ECHO "PH signs"	Echocardio-graphic 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

Frost AA, et al. *Eur Respir J.* 2019 Jan 24;53(1). pii: 1801904. doi: 10.1183/13993003.01904-2018. Print 2019 Jan

Revised Diagnostic Algorithm:
Step 2: Role of the PH Expert Center



Frost AA, et al. *Eur Respir J.* 2019 Jan 24;53(1). pii: 1801904. doi: 10.1183/13993003.01904-2018. Print 2019 Jan

The Echocardiogram Is of Central Importance to CTD-PAH (and All Types of PH) Diagnosis and Referral

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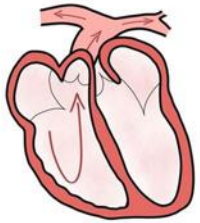
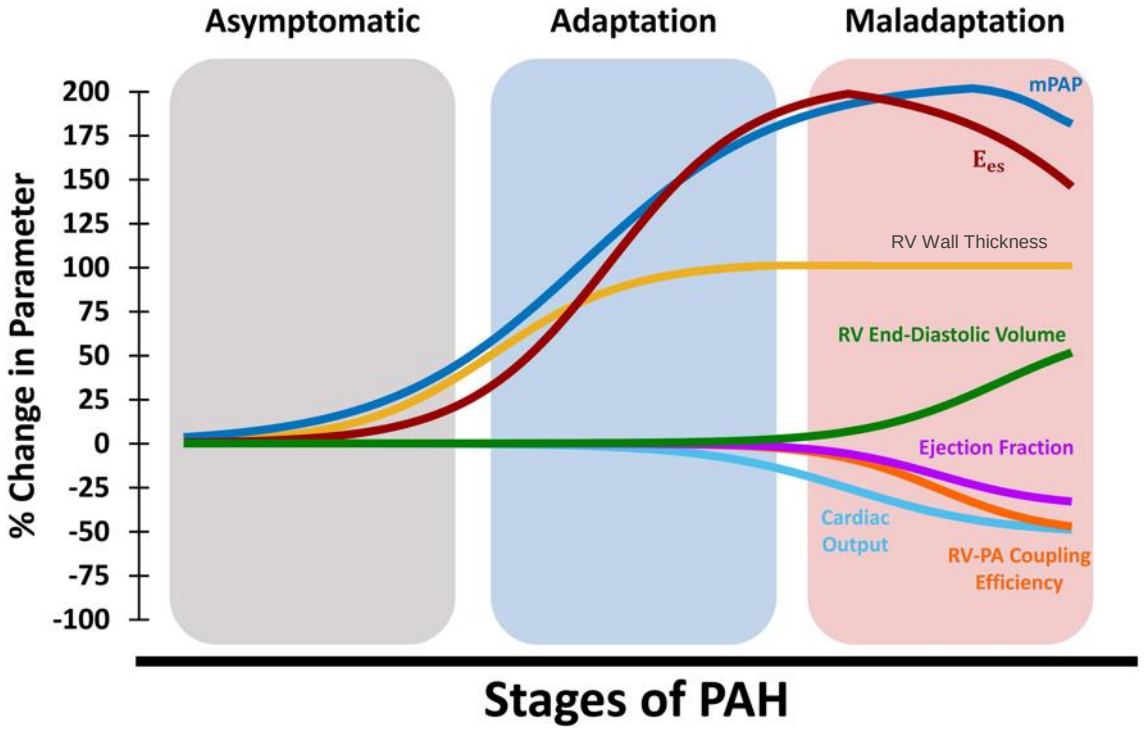
Importance of Structural Changes in the RV in PAH

- **Right ventricular (RV) function is the single most important prognostic determinant of survival in various forms of pulmonary hypertension (PH)**[1]
- PAH 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]

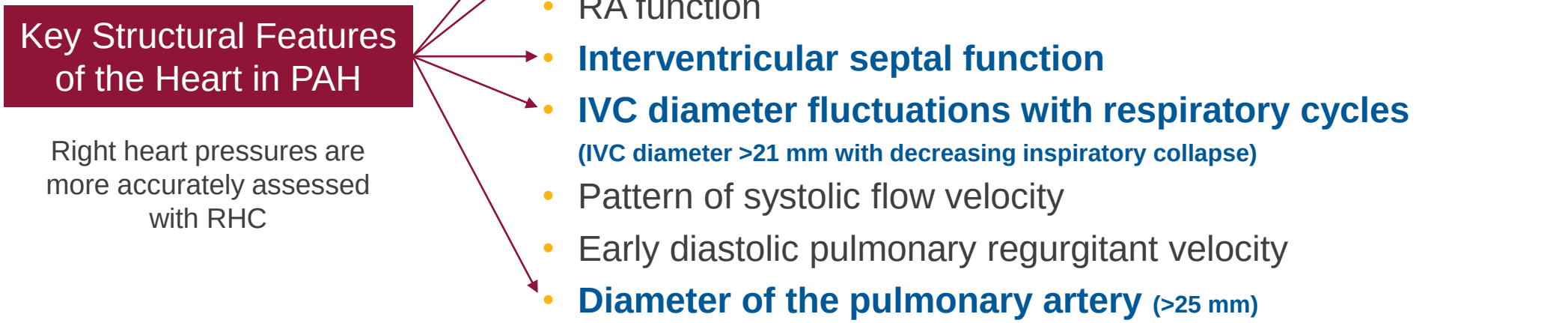




1. Lahm T, *et al*. *Am J Respir Crit Care Med, 2018;* 198:e15–e43
2. Hill MR, *et al. Ann. Biomed. Eng*, 2014; 42: 2451–2465.doi: 10.1007/s10439-014-1096-3
3. Wang, Z, *et al. J. Appl. Physiol,* 2018; 124:1244–1253. doi: 10.1152/japplphysiol.00725.2017
4. Vonk Noordegraaf A*, et al*. *J. Am. Coll. Cardiol.*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

Using Echo To Uncover Ph Related Changes in Heart Structure: You Absolutely Need Good Images of the Right Heart!

- 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
- Pressures obtained are useful but are <u>estimates</u> only



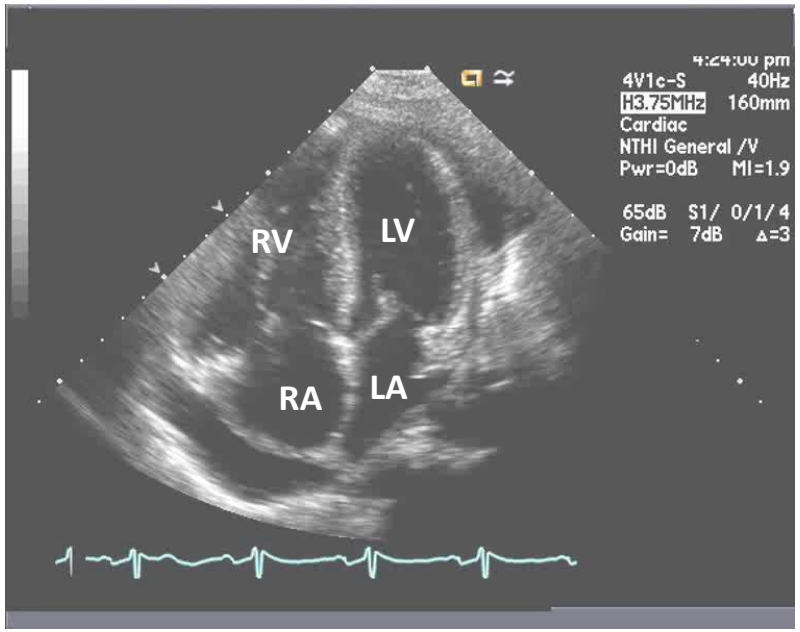
Frost A, et al. *Eur Respir J*. 2019;53(1):1801904.

ECHO: It's Not All About Pressures –Structural Images Essential

Precapillary PH

Group 1

RV Dilation and Dysfunction

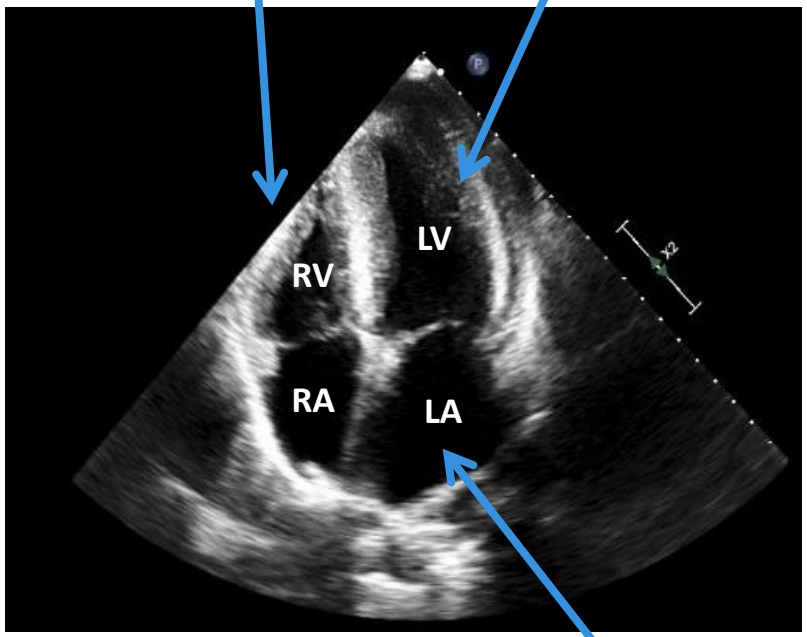


Pericardial Effusion

Small LA w/ Shifted Septum

Normal Right Sided Chambers

LVH



LA Enlargement

Postcapillary PH

Group 2

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

Roles of the Pulmonologist and Cardiologist at the PH Center: Confirming the Diagnosis

Hemodynamic Evaluation Of Suspected PH

- RHC is still the only validated method to confirm and grade PH and is best performed at the PH center
- 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]
- Screening and referral of CTD (esp. SSc) patients to the PH center may allow use of cardiopulmonary exercise testing that may uncover latent PAH
- 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 all these reasons, hemodynamic evaluation of suspected PH is best performed 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.

Recommendations for RHC for SSc and Scleroderma Spectrum Disorders

	Signs or Symptoms Required for RHC†	Quality of Evidence
Transthoracic Echocardiogram		
TR jet velocity 2.5–2.8 meters/second	**Yes**	**High**
2.8 meters/second	**No**	**High**
RA or RV enlargement (RA major dimension 53 mm and RV mid-cavity dimension 35 mm), irrespective of TR jet velocity	**No**	**High**
PFTs		
FVC:DLCO ratio >1.6 and/or DLCO <60% pred	**Yes**	**High**
FVC:DLCO ratio >1.6 and/or DLCO <60% pred and NT-proBNP 2X ULN	**No**	**High**
Composite Measure		
Meets DETECT algorithm in patients with DLCO <60% predicted and disease duration 3 years‡	**No**	**Moderate**

† Signs include loud pulmonic sound and peripheral edema. Symptoms include dyspnea on rest or exercise, fatigue, presyncope/syncope, chest pain, palpitations, dizziness, and lightheadedness.
‡ Where a transthoracic echocardiogram did not reveal overt systolic dysfunction, greater than grade I diastolic dysfunction, greater than mild mitral or aortic valve disease, or evidence of PH (as defined in the transthoracic echocardiogram section).

Rao V, Khanna D. *Int J Adv Rheumatol.* 2010;8:53-62.

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.

Congenital Heart Disease (CHD)-PAH:

What To Look for and When Should You Refer to the PH Center?

A Short Tour of Congenital Heart Disease Associated PAH (CHD-PAH)

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Specifics of PAH in Adult Congenital Heart Disease (ACHD)

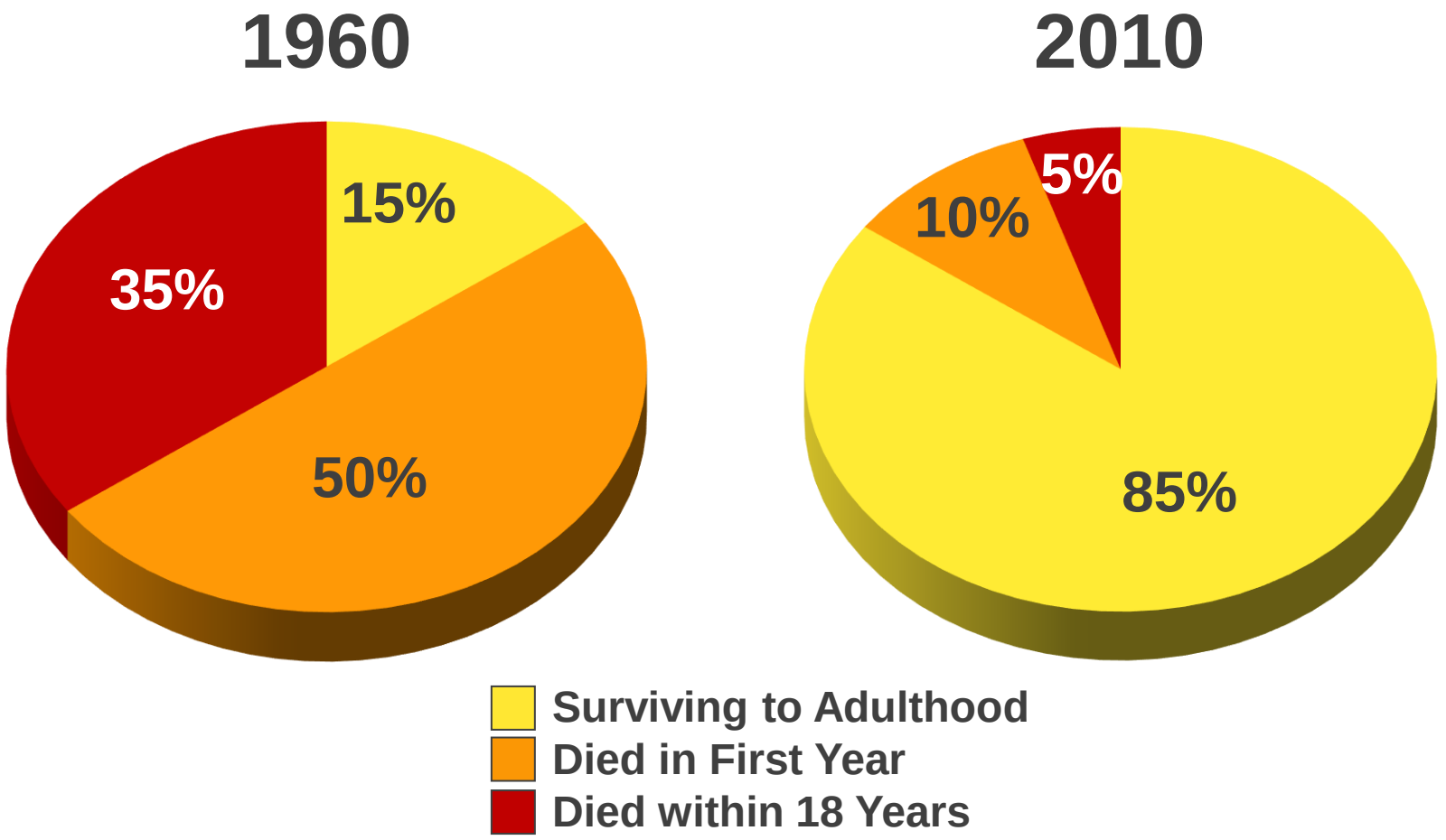
- CHD affects 0.8% of live births in the U.S. (excluding bicuspid AV and MVP)
- PH is a common complication of CHD (5-10%), particularly if significant and unrepaired[1]
- With newer and improved diagnostic techniques and evolving medical, catheter-based and surgical interventions, there are now >1,400,000 adults with congenital heart disease (adults>children)
- Unfortunately, most physicians get minimal exposure to CHD patients during training
- All ACHD patients should be seen by an ACHD specialist at least once – complex patients need follow-up every 6-12 months at an accredited ACHD center[1]

Specific Aspects of PH in ACHD[2]

- Higher flow and more downstream shunt lesions are more likely to cause PAH
- Like any PH, ACHD-PH can be pulmonary venous or pulmonary arterial
- Same hemodynamic criteria used for diagnosis as other Group 1 disease
- Differentiation of etiology can dramatically impact management
- Diagnostic catheterization is essential for proper diagnosis and should be performed by a board certified ACHD physician

1. Gilboa SM, et al. *Circulation.* 2016;134:101–109.
2. Goldstein SA, Krasuski RA. *Cardiol Clin,* 2022; 40:55–67 https://doi.org/10.1016/j.ccl.2021.08.006

Advances In CHD Management Have Led to Growing Adult Population with New Problems and Concerns



- >1,400,000 adults with CHD (adults>children)
- Most patients only palliated
  - Lesions can recur
  - Palliative methods can cause problems
- Simple lesions can result in **PH**, arrhythmias, and heart failure, even after successful repair
- Epidemiologic studies limited
  - Complexity varied
  - No centralized database

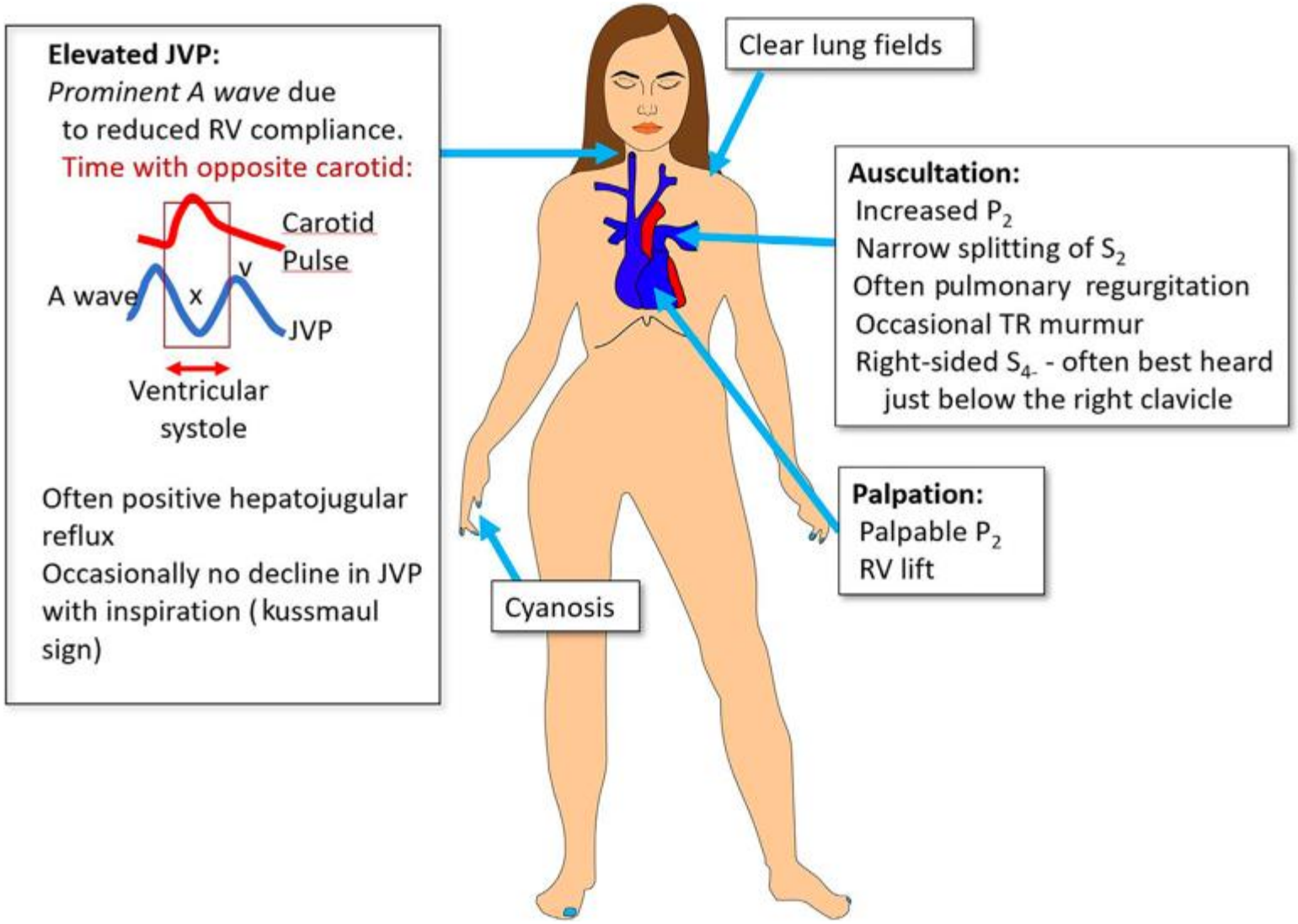
van der Velde ET, et al. *Eur J Epidemiol* 2005;20:549-57
Warnes CA, et al. *Circulation* 2008;118:e714-e833;
Gilboa SM, et al. *Circulation* 2016;134:101-9

Categorizing Congenital Heart Disease and PH

- In CHD, PAH can be classified into 4 distinct subgroups of patients:
  1. Eisenmenger syndrome
  2. Persistent systemic-to-pulmonary shunts
  3. Small, coincidental defects
  4. Patients who have undergone defect correction
- Patients with shunts, repaired and unrepaired, need to be screened at an ACHD center for the development of PAH
- 2018 WSPH Recommendations
  - Post-operative PAH screening in subgroup 4 without PAH should include clinical, echocardiographic and ECG screening during follow-up visits 3–6 months after correction and then throughout their planned long-term cardiovascular follow-up

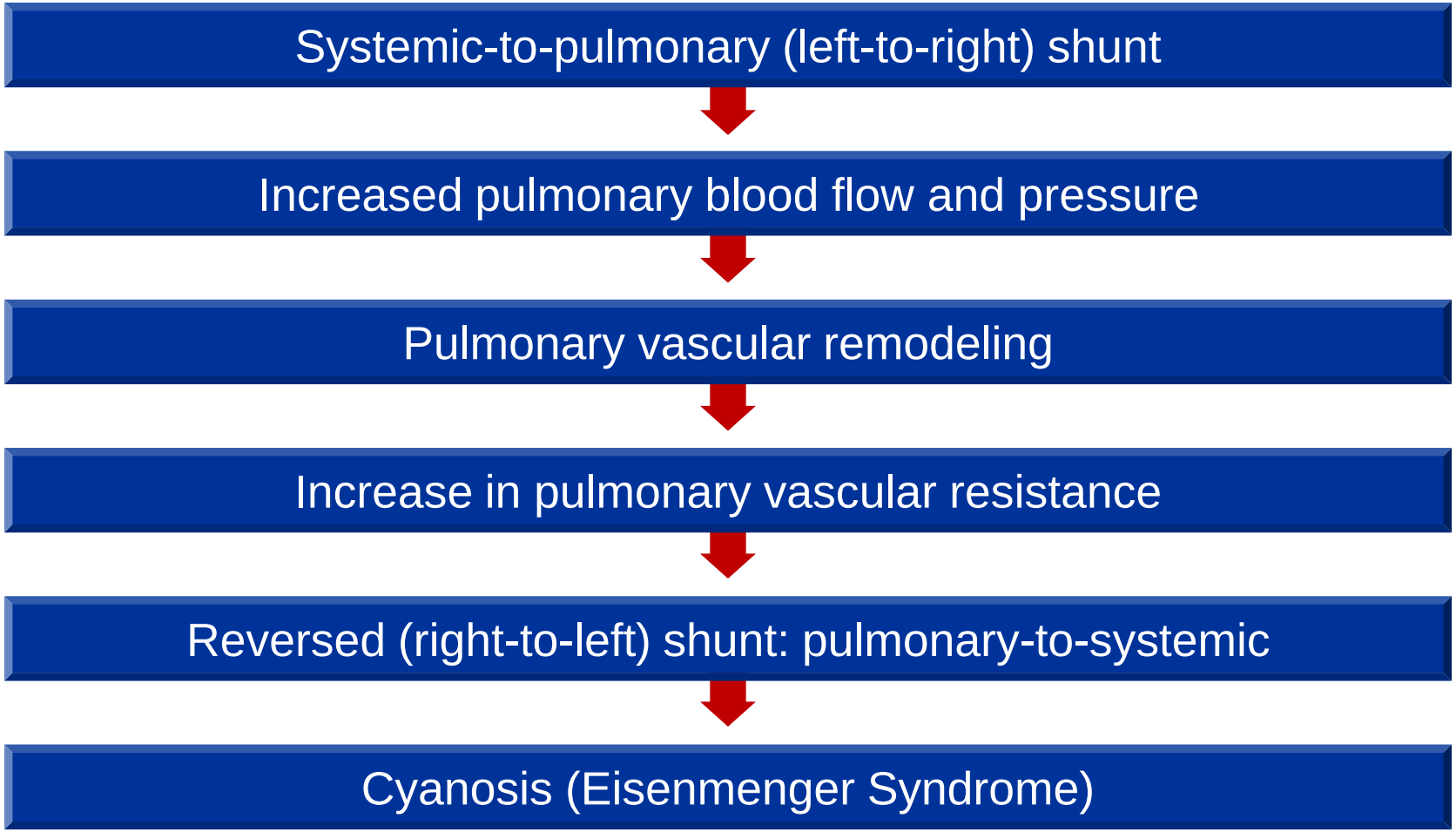
Simonneau G, et al. *JACC.* 2004;43(suppl 1):S5-S12.

Physical Manifestations and Common Examination Findings in a Patient With PAH-CHD



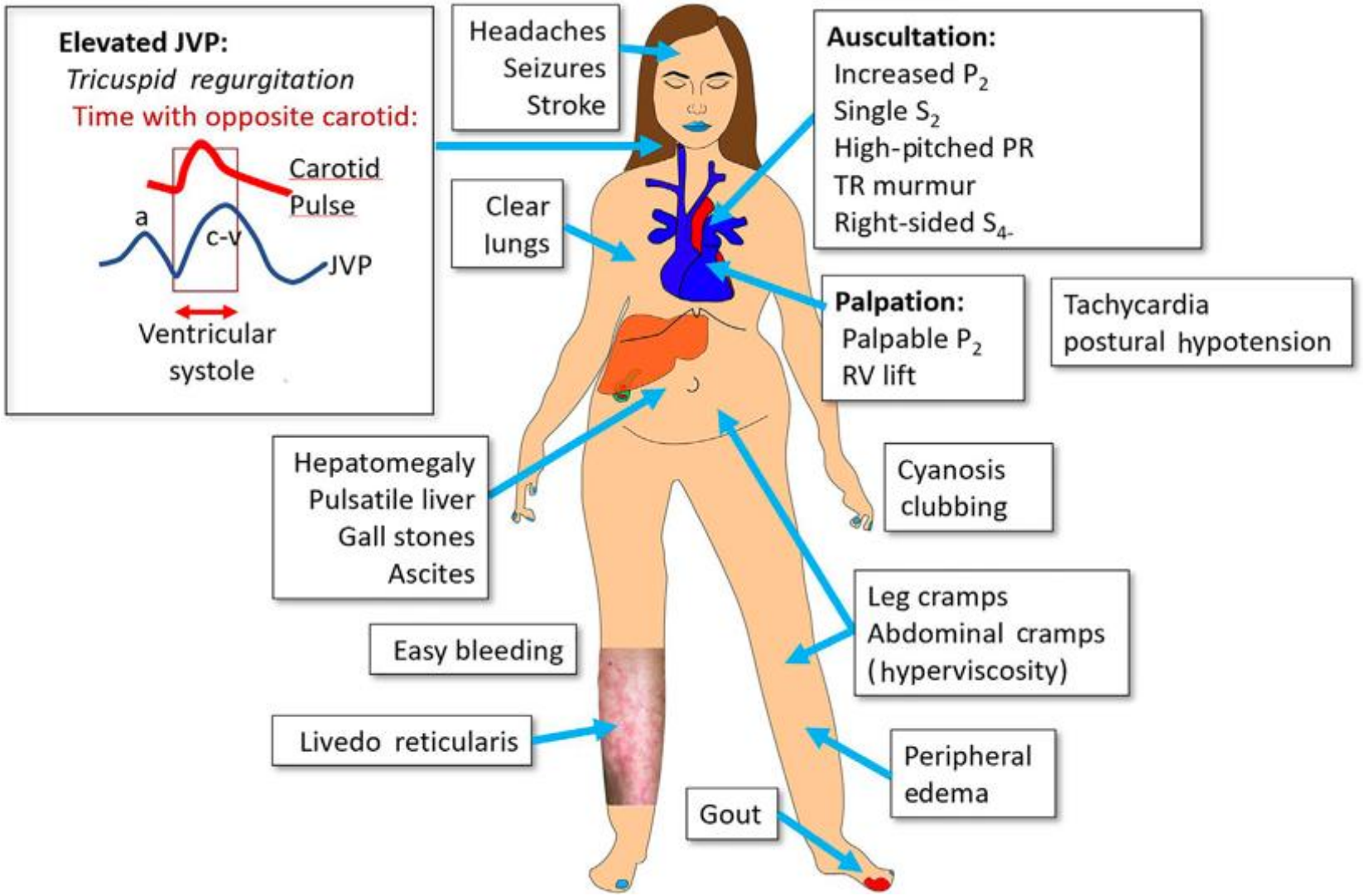
Goldstein SA, Krasuski RA. *Cardiol Clin,* 2022; 40:55–67 https://doi.org/10.1016/j.ccl.2021.08.006

Progression of PAH-CHD to Eisenmenger Syndrome



Galiè N, et al. *Drugs* 2008;68:1049-66
Vongpatanasin W, et al. *Ann Intern Med* 1998;128:745-55

Eisenmengers Syndrome: Physical Manifestations and Common Examination Findings



Goldstein SA, Krasuski RA. *Cardiol Clin,* 2022; 40:55–67 https://doi.org/10.1016/j.ccl.2021.08.006

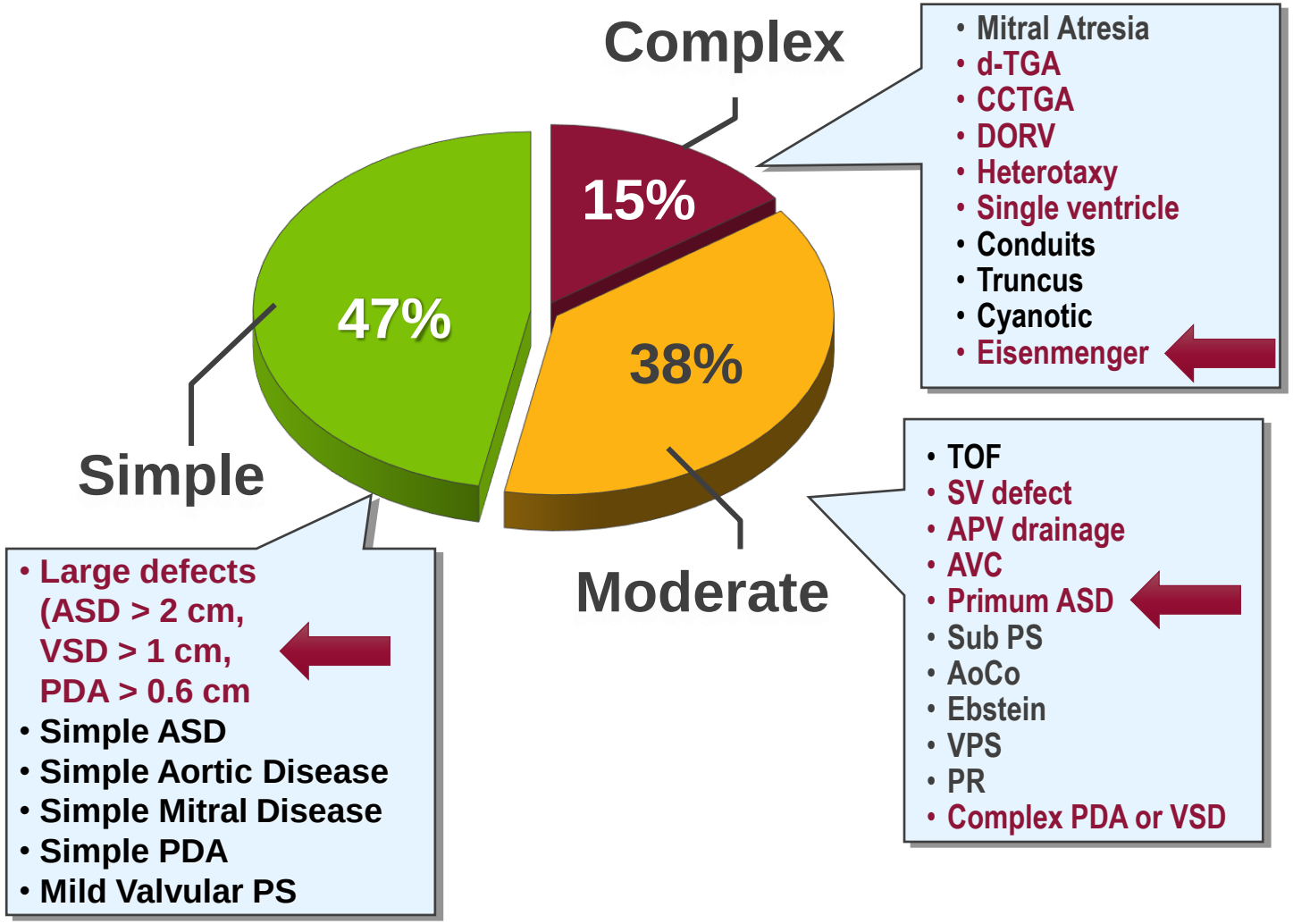
Unique Considerations In The CHD-PAH Patient

- Is there too much or too little pulmonary blood flow?
- If a defect is present, is it correctable?
- If a defect is correctable, what is the best manner in which to correct it?
- Have advanced medical therapies been adequately tested and do they work in CHD patients?

ACHD: Basic Lesion Types

IMPACT LIVE
IMProving Approaches to Care and Treatment
PH

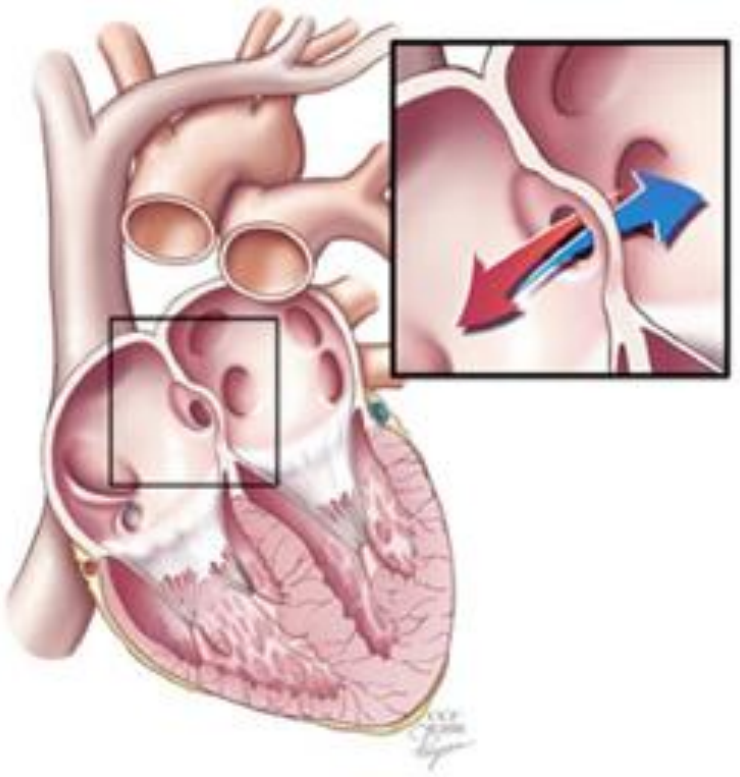
Many Different Lesions Result in PH, BUT Very Few Have Been Included in Prospective Studies



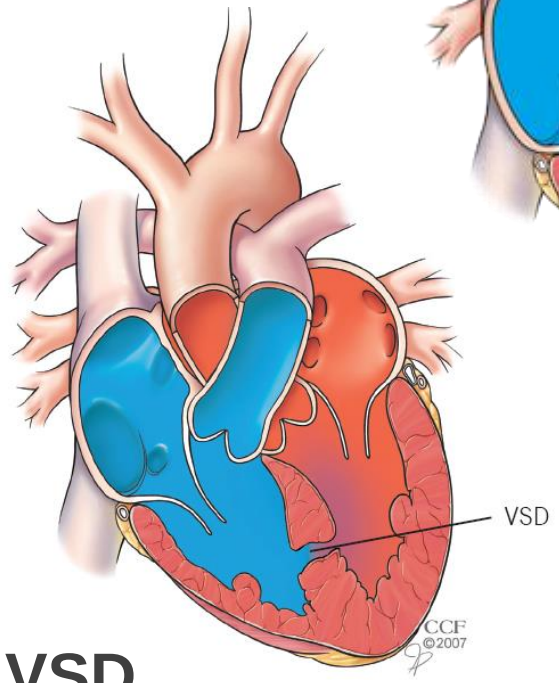
- Studies have mainly focused on Eisenmenger Syndrome patients and repaired shunts
- Many lesions exist for which the effects of advanced medical therapy for PAH are poorly understood

Marelli A et al. *Am Heart J* 2009;157:1-8
Warnes C et al. *J Am Coll Cardiol* 2001;37:1170-5

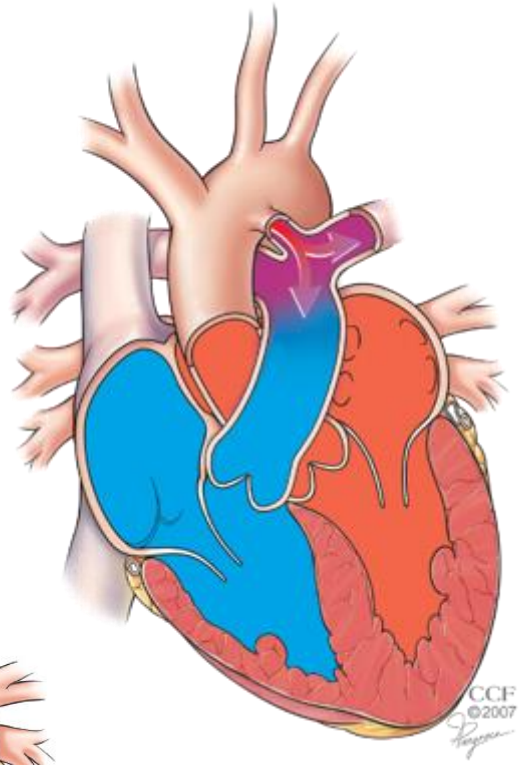
Shunt Lesions ARE Most Common Cause OF PAH



ASD



VSD



PDA

- Patients with repaired and unrepaired defects can develop PAH (~2-10%)
- Increasing dyspnea, declining exercise capacity, and progressive increase in PVR are clinical hallmarks
- 25%-50% of CHD-PAH patients unabated can progress to Eisenmenger syndrome

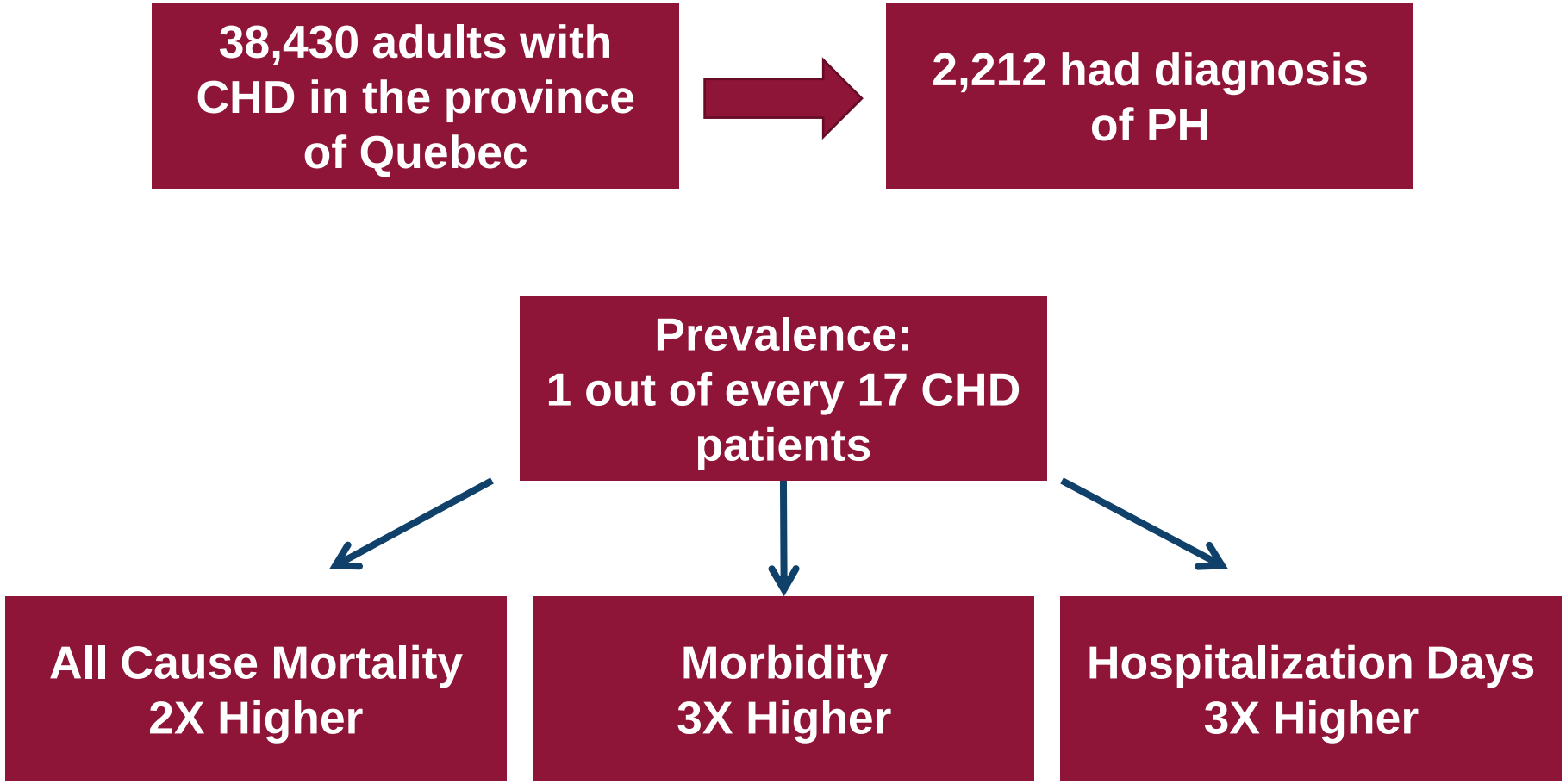
Engelfriet PM et al. *Heart* 2007;93:682-7
Gaine S *JAMA* 2000;284:3160-8
Galiè N et al. *Drugs*. 2008;68:1049-66

PAH-CHD Clinical Subgroups and Characteristics

SUBGROUP	1 Eisenmenger syndrome (ES)	2 PAH associated with persistent systemic-to-pulmonary shunts	3 PAH with small/coincidental shunts	4 PAH after defect correction
CHARACTERISTICS	• Large intra- and extra-cardiac defects systemic-to-pulmonary shunts • Cyanosis • Secondary erythrocytosis • Multisystem involvement	1. **Correctable** with surgery or intravascular percutaneous procedure 2. **Non-correctable** • Moderate to large defects • PVR mildly to moderately increased • Systemic-to-pulmonary shunting still prevalent • No cyanosis at rest	• PVR elevation with small cardiac defects (which do not account for elevated PVR) • Clinical picture similar to iPAH • Defect closure contraindicated	• Congenital heart disease repaired • PAH immediately after or recurs/develops months/years after correction, in absence of significant postoperative haemodynamic lesions

Simonneau G et al. *J Am Coll Cardiol* 2013;62:D34-41;
Xu ZY et al. *Zhonghua Xin Xue Guan Bing Za Zhi* 2020;48:315-22

Morbidity and Mortality Are Higher in PAH-CHD



Lowe BS, et al. *J Am Coll Cardiol.* 2011;58:538-46.

Imaging in ACHD-PAH – What the PH/CHD Specialty Center Offers

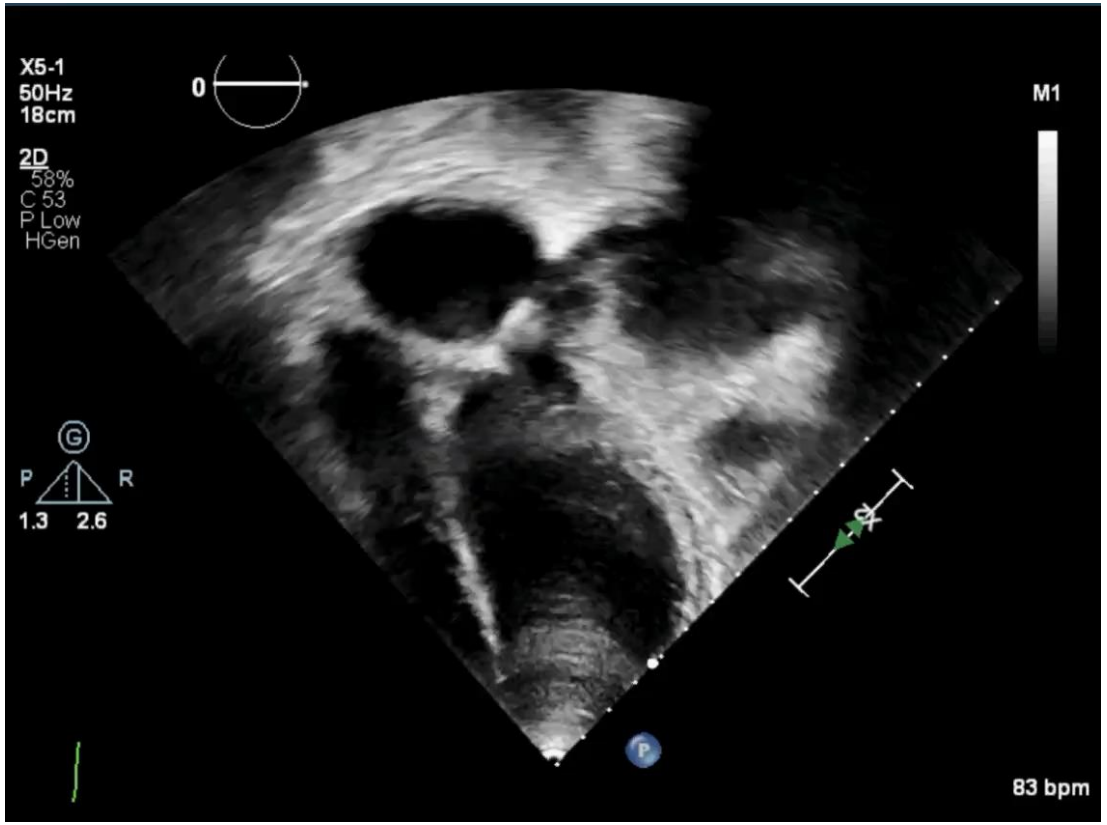
Imaging of Congenital Heart Disease

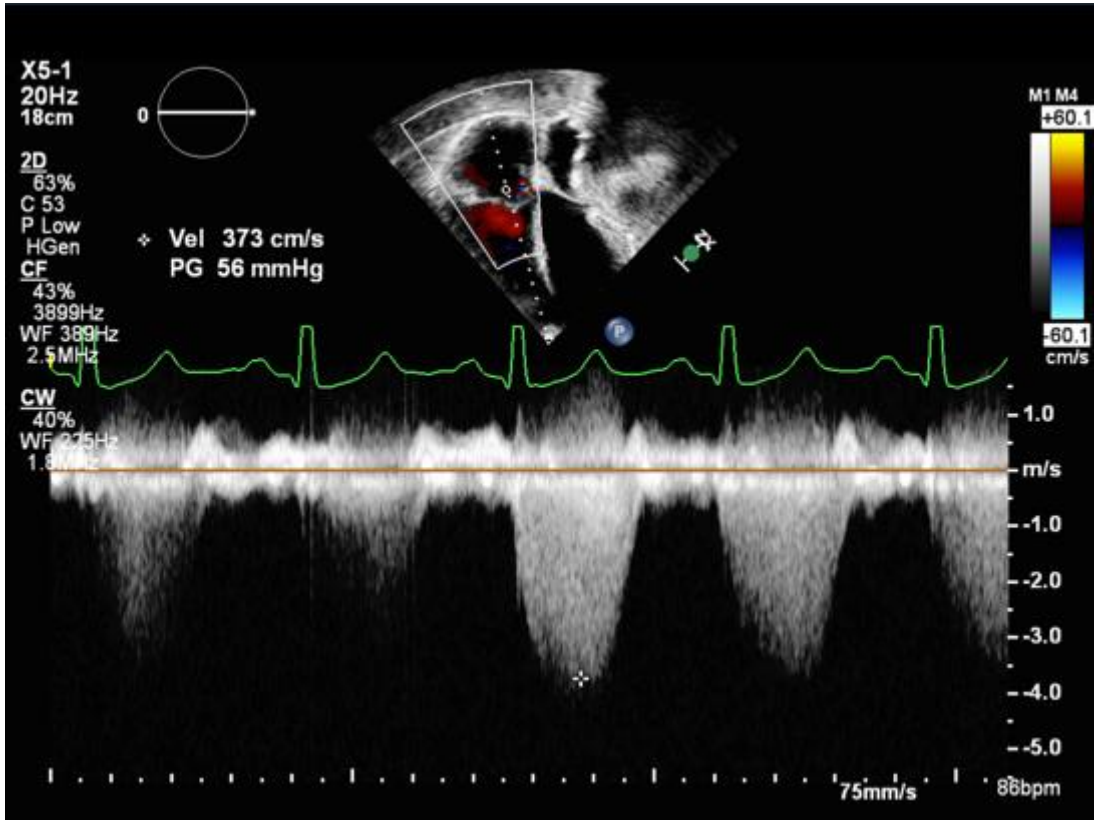
- Goals of Imaging ACHD patient with PAH
  - Determine original and current (post-op) anatomical relationships
  - Assess for residual lesions
    - Shunts (ASD, VSD, PDA, collaterals)
    - Valve stenosis or regurgitation
    - Vascular obstructions (pulmonary arteries and veins, right and left ventricular outflow tracts)
  - Measure differential pulmonary blood flow
  - Evaluation of ventricular size, thickness and function
  - Appraisal for myocardial injury

Imaging of Congenital Heart Disease: Pros and Cons

	✓ Pro	✕ Con
Echocardiography	Noninvasive, No radiation, Readily available, No sedation, Visualization of intracardiac anatomy, Excellent temporal resolution	Poor acoustic windows Poor visualization of extracardiac anatomy
Nuclear Perfusion	Noninvasive, Can quantify pulmonary blood flow	Limited information, Radiation
CT	Noninvasive, Excellent spatial resolution	Radiation, Limited intracardiac anatomy and hemodynamic data
CMR	Noninvasive, No radiation, Can assess intra and extracardiac anatomy, ventricular function and myocardial viability, hemodynamic data, lung perfusion	Not readily available Time consuming Metallic artifact and some devices still contraindicated
Angiography	Visualization of extracardiac anatomy, Hemodynamics, Facilitates interventions	Invasive, Need for sedation, Radiation, Poor visualization of intracardiac anatomy

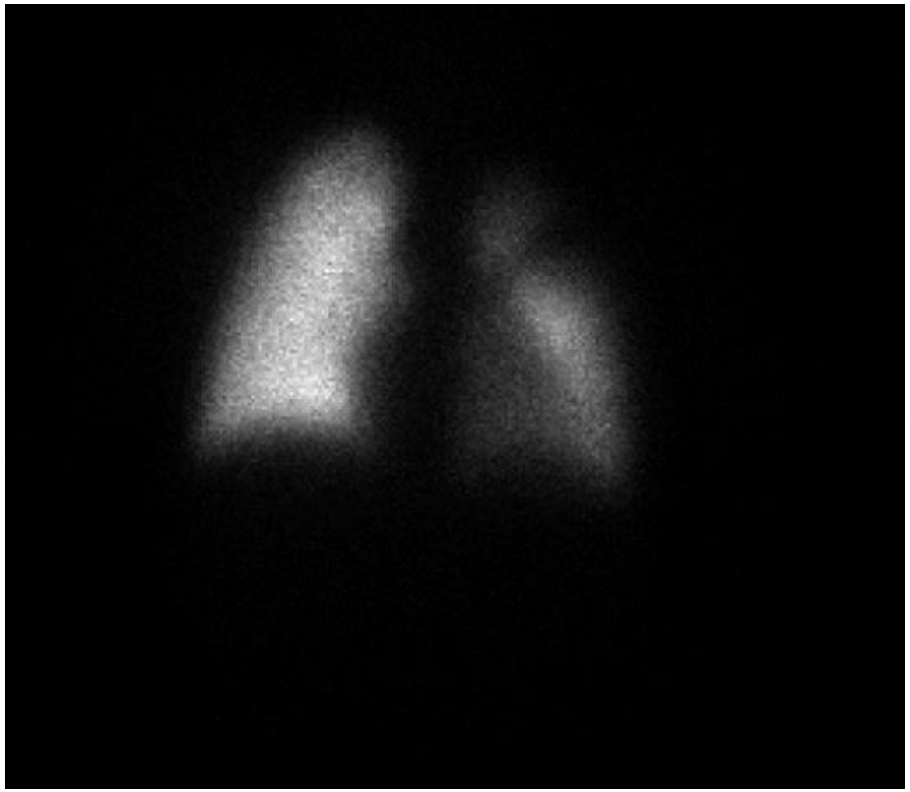
Non-Invasive Imaging: Echocardiography

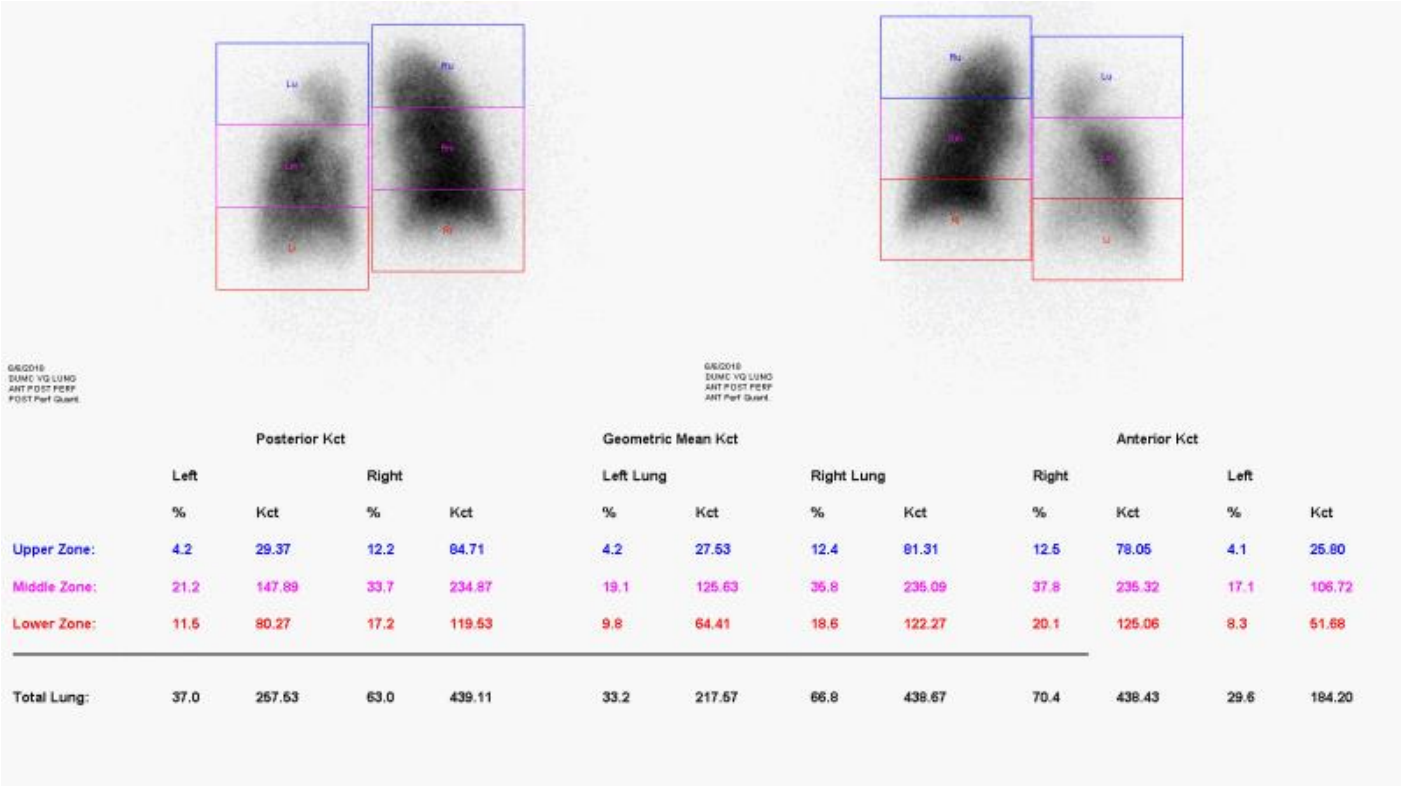




Images courtesy of Richard Krasuski, MD, Duke University Medical Center

Non-Invasive Imaging: Nuclear Perfusion Scan

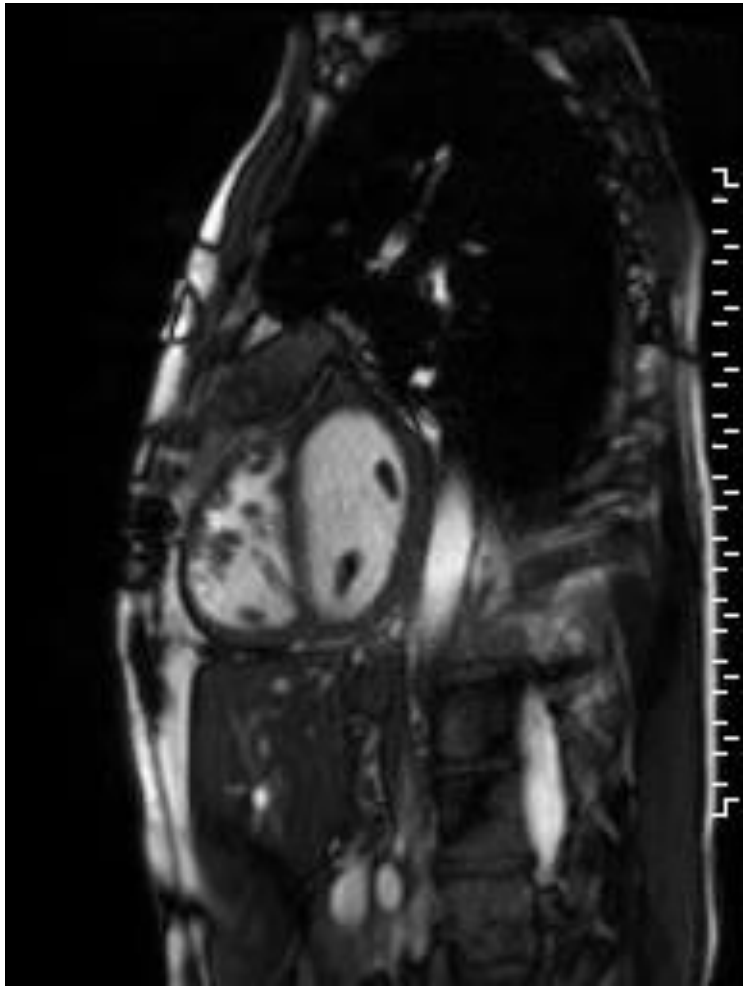


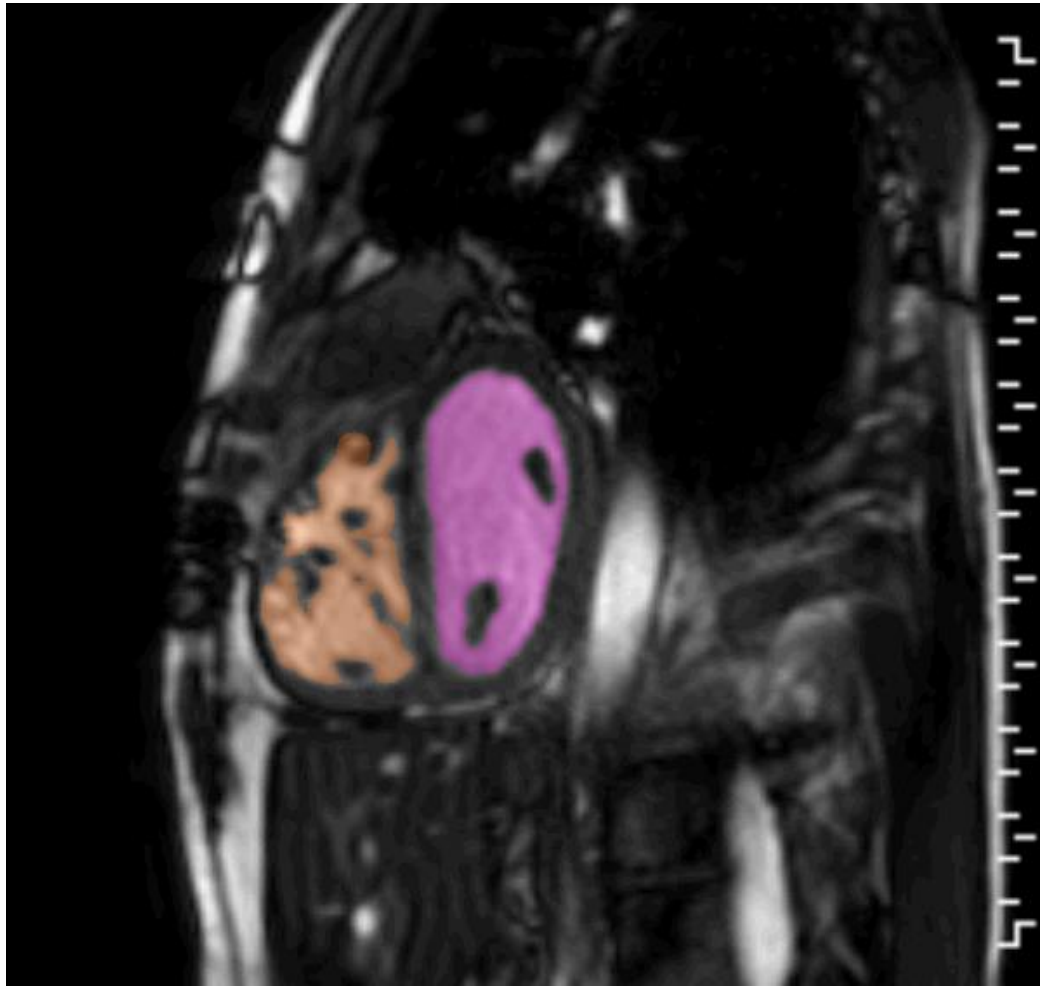


	Posterior Kct				Geometric Mean Kct				Anterior Kct			
	Left		Right		Left Lung		Right Lung		Right		Left	
	%	Kct	%	Kct	%	Kct	%	Kct	%	Kct	%	Kct
Upper Zone:	4.2	29.37	12.2	84.71	4.2	27.53	12.4	81.31	12.5	78.05	4.1	25.80
Middle Zone:	21.2	147.89	33.7	234.87	19.1	125.63	35.8	235.09	37.8	235.32	17.1	106.72
Lower Zone:	11.5	80.27	17.2	119.53	9.8	64.41	18.6	122.27	20.1	125.06	8.3	51.68
Total Lung:	37.0	257.53	63.0	439.11	33.2	217.57	66.8	438.67	70.4	438.43	29.6	184.20

Images courtesy of Dr. Jay Campbell, Duke University Medical Center

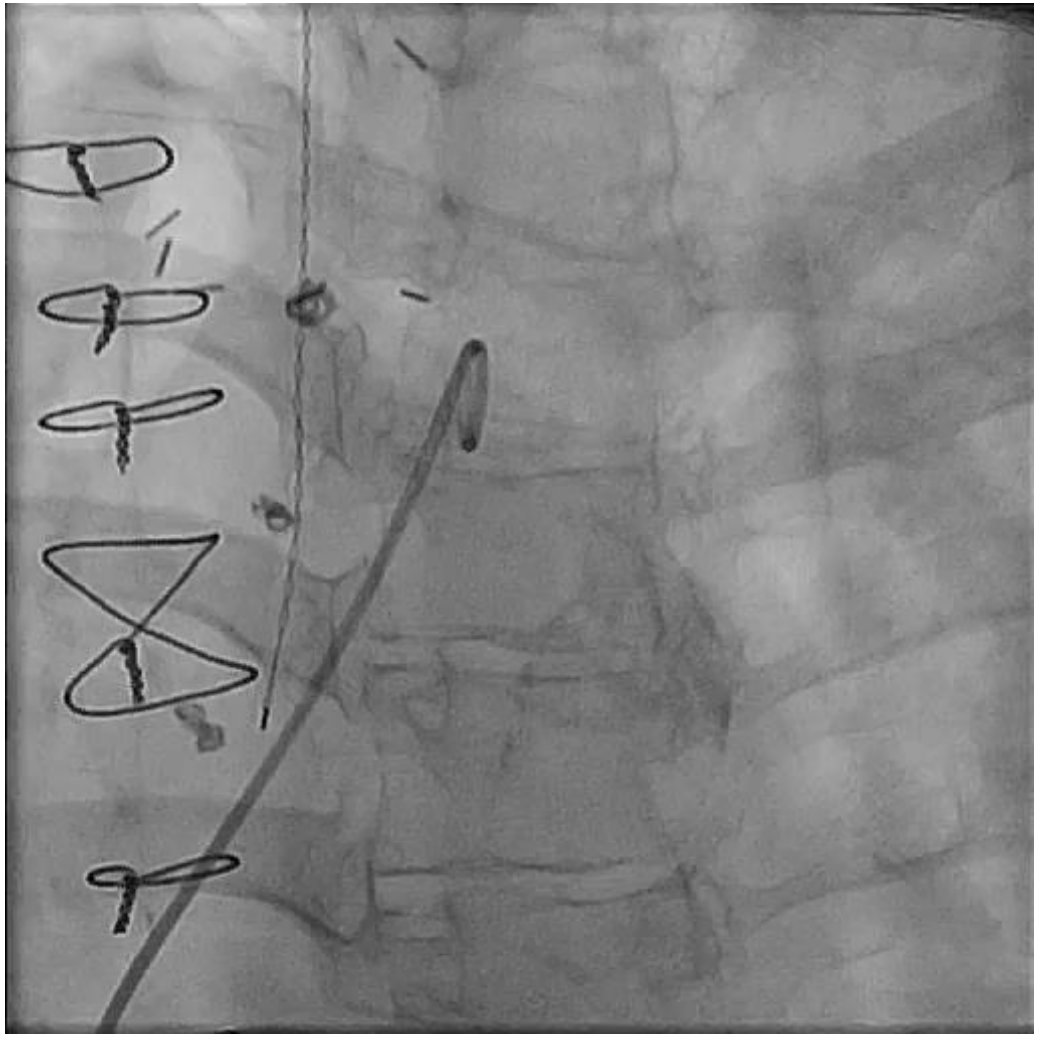
Non-Invasive Imaging: CMRI/CT

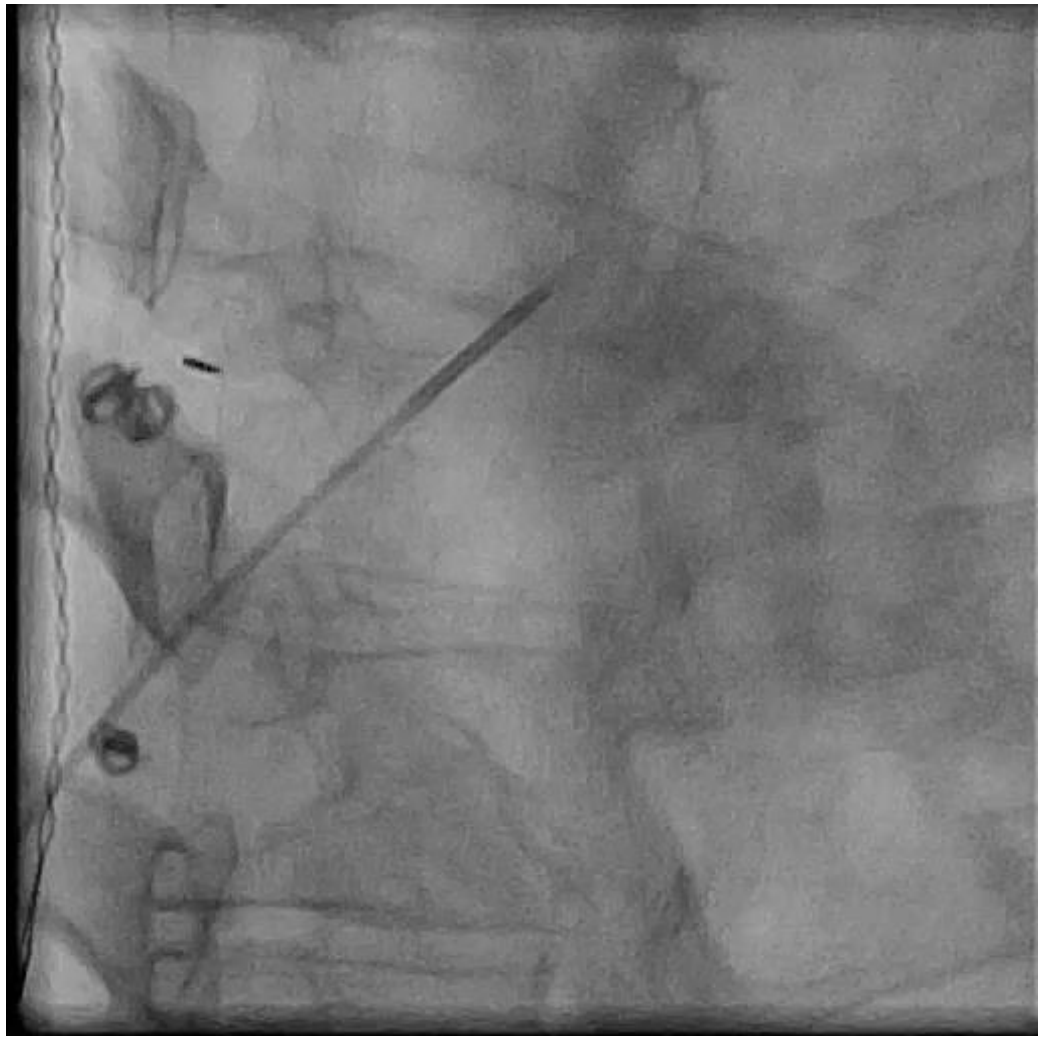




Images courtesy of Dr. Richard Krasuski, Duke University Medical Center

Selective Pulmonary Angiography





Images courtesy of Dr. Richard Krasuski, Duke University Medical Center

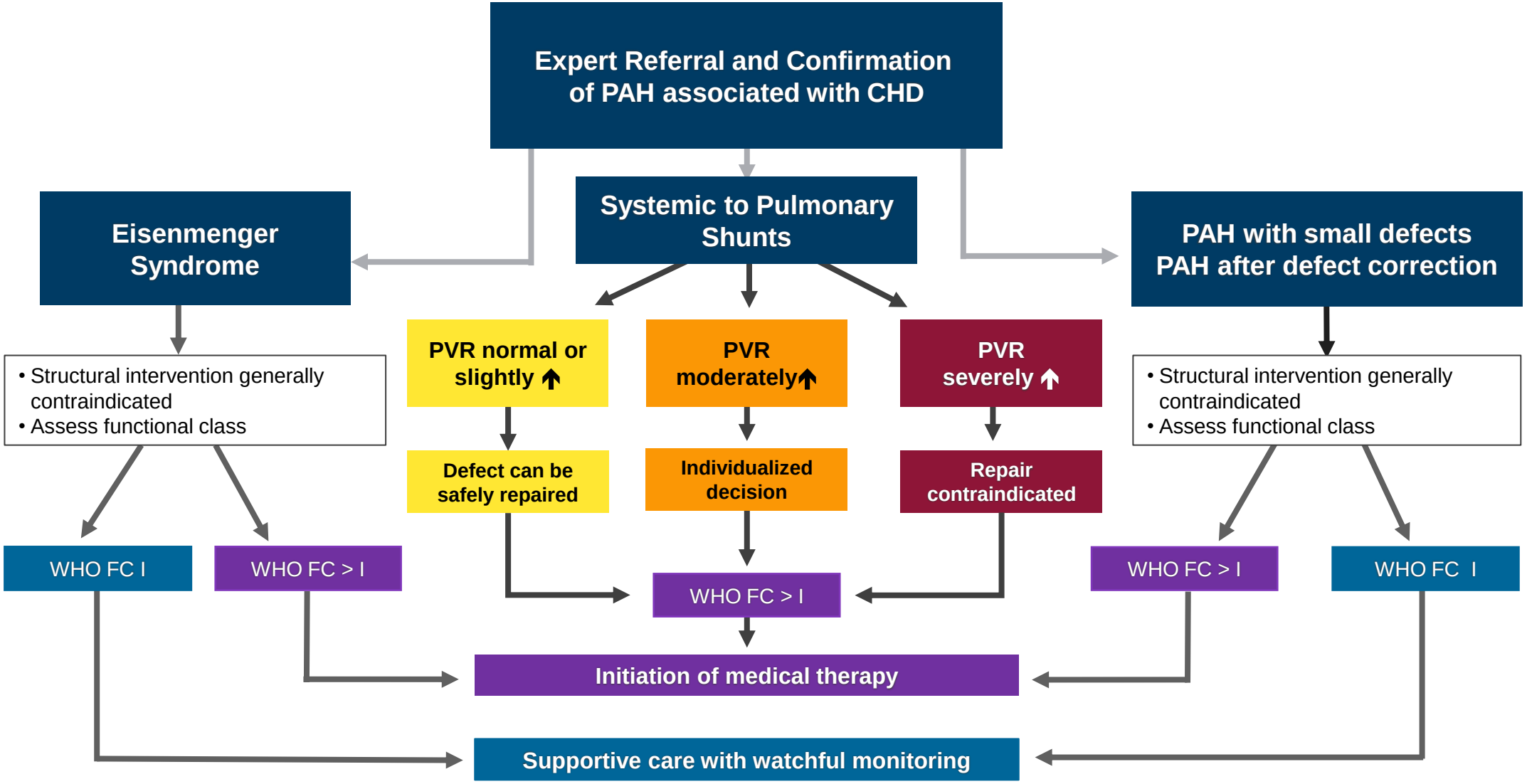
Management of CHD-PAH – General Considerations

Managing PAH In Adult Congenital Heart Disease: General Principles

- All patients with PAH should receive lifelong tertiary care
- Patients and their families should be made aware of major risk of pregnancy (mortality as high as 1/3, and considerable morbidity)
  - effective contraception should be provided
- Encourage regular exercise and maintenance of active lifestyle
- Periodic 6MWD or CPET is recommended to provide prognostic information and guide management
- Immunization against COVID-19, influenza and pneumococcal infections
- Provide psychosocial support

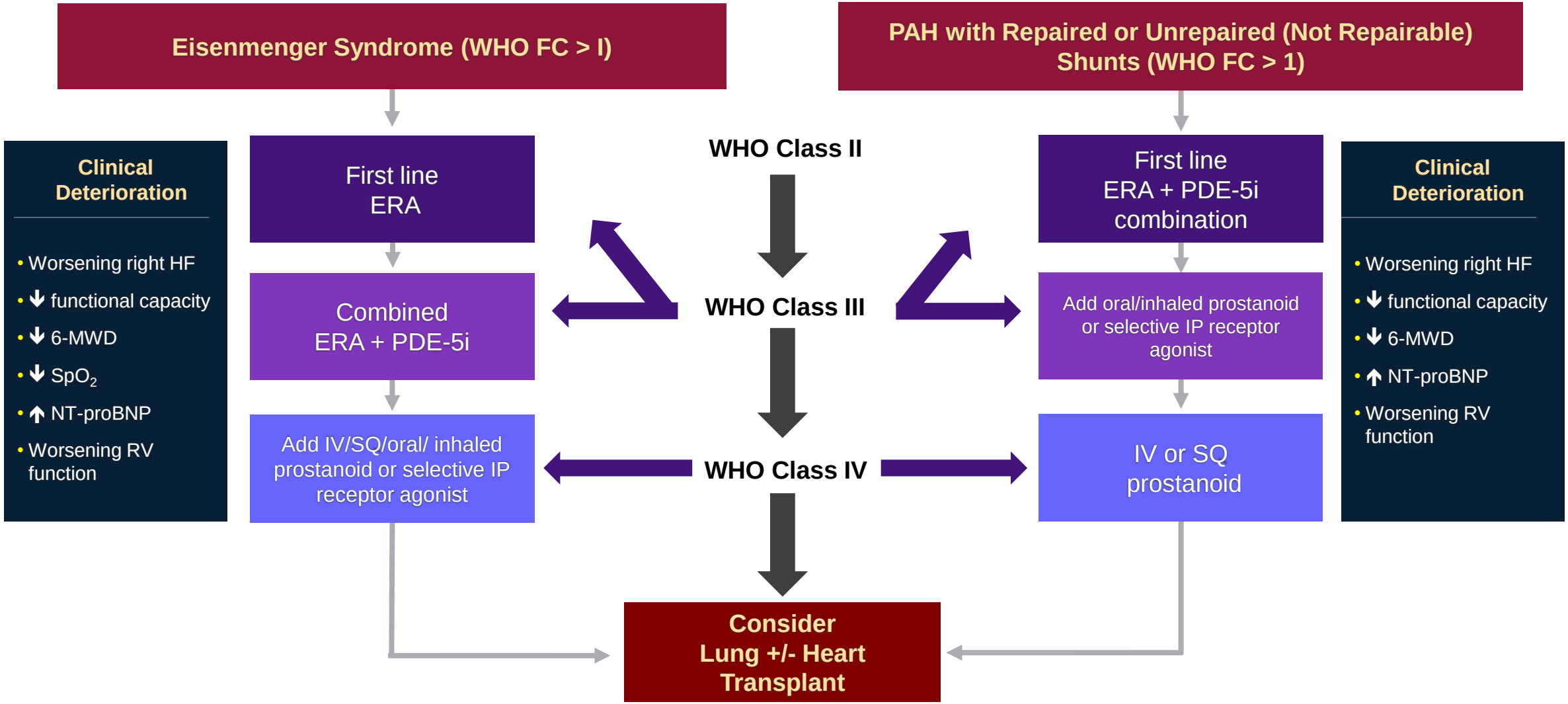
Adapted from Brida M, Gatzoulis MA. *Heart* 2018;0:1–7.

Management of PAH Associated with CHD and/or Eisenmenger Syndrome



Adapted from Fathallah F and Krasuski RA. *Prog Cardiovasc Dis* 2018;61:320-27.

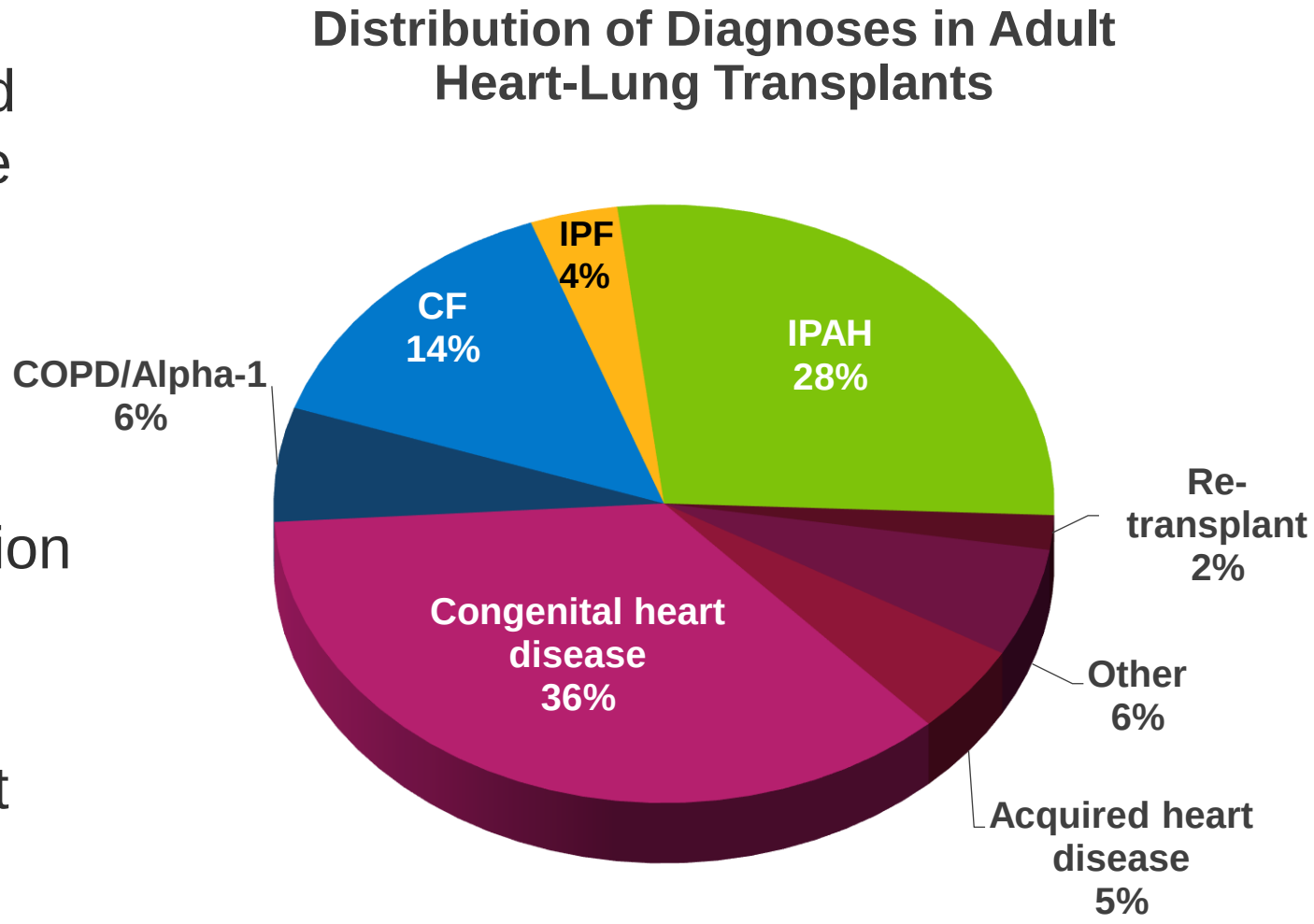
Management of PAH Associated with CHD and/or Eisenmenger Syndrome



Adapted from Fathallah F and Krasuski RA. *Prog Cardiovasc Dis* 2018;61:320-27.

Organ Transplant Requires Extensive Discussion and Collaboration

- Transplant options for advanced complex CHD with PH are more complicated:
  - Lung
  - Heart-lung
  - Lung and defect repair
- CHD accounts for large proportion of heart-lung transplants
- Support options are becoming available as bridge to transplant



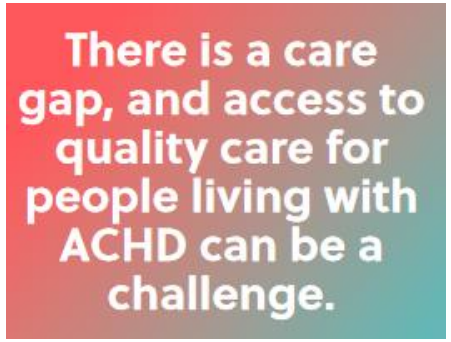
Serfas JD, Krasuski RA. *Adv in Pulm Hypertension* 2019;18(1): 31-2
Hertz MI, et al. *J Heart Lung Transplant* 2011;30 (10):1071-1132

The Importance of Referring the PAH-ACHD Patient to an Accredited Specialty Center

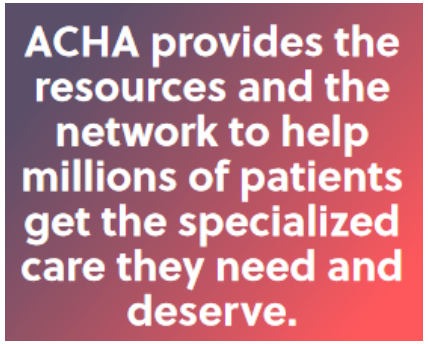
Why Accreditation of ACHD Programs is Important

- Ensures a minimum standard of care for a very complicated patient population – fluid process with continuous feedback
- Helps identify various specialists in institutions and ensures their participation in care provision
- Helps identify gaps in programs and opportunities to improve provision of care
- Helps empower patients to select, participate in and influence their own care

- 47 ACHA ACHD Accredited Centers in 28 different states in a combination of both Adult and Pediatric Hospitals (https://www.achaheart.org/)



Adult Congenital Heart Association



https://www.achaheart.org/your-heart/programs/accreditation/

ACHA Accreditation Criteria

- 20 different categories of criteria
- Patients with CHD have unique characteristics that need to be met, not only with regard to their heart issues
- Plethora of innovative ways that programs meet patient needs and serve the community
- ACHA ACHD Accreditation Steering Committee meets regularly to update criteria
- Providers at centers who may not be able to become accredited can use criteria to elevate the level of care at their individual institutions

A.	ACHD Cardiologist
B.	ACHD Medical Program Director
C.	Advanced Practice Nurse/Physician Assistant
D.	Registered Nurse
E.	Cardiothoracic Surgery and Cardiothoracic Intensive Care Unit
F.	Heart Failure, Heart Transplant, Heart/Lung Transplantation
G.	Interventional Cardiac Catheterization
H.	Interventional Electrophysiology
I.	Inpatient Services
J.	Outpatient Services
K.	Transitional Services
L.	Patient-Centered Care
M.	Echocardiography
N.	Cardiac Magnetic Resonance Imaging
O.	Cardiac Computed Tomography
P.	Pulmonary Arterial Hypertension
Q.	Exercise Testing and Cardiac Rehabilitation
R.	Reproductive Services
S.	Psychology and Social Work
T.	Cardiac Anesthesia

https://www.achaheart.org/your-heart/programs/accreditation/
https://www.achaheart.org/media/3471/accreditationprogramcriteria2022.pdf

Summing Up - Understudied PH Populations

Summary

- While Group 1 PAH has been the most studied form of the disease with the greatest number of approved medications, some subgroups within Group 1 and other PH Groups have received less attention
- It is important for all healthcare providers, at both the community and specialty center levels, to be able to recognize these sub-classifications of PH
- While the diagnosis of all types of PH follows a similar path, each form of the disease may require added attention to certain diagnostic modalities

Key Take-Aways

- For CTD patients with unexplained dyspnea, annual screening is mandated to detect the presence of PAH
- The DETECT protocol is a useful tool for screening CTD-PAH patients
- Knowing when a patient must be referred to a PH specialty center is critical to the timely diagnosis and initiation of treatment for all PH patients
- For CTD with Group 3 PH, there is a complex pathophysiology with at least 3 pathways potentially contributing to the increased vascular resistance through the lungs
- Treatment options within the Group 1 subcategory of CTD-PAH may benefit from approved Group 1 PH medications and strategies as outlined in current guidelines

Take Aways

- CHD-PAH may present at various ages based on severity of lesions and type/age at time of repair
- Specific diagnosis of the underlying cause of CHD-PAH and consideration of medical/surgical/transcatheter intervention should occur at an accredited CHD-PAH center of excellence
- Timely referral from the community level to the specialty center is extremely important
- Other than for corrected shunts and Eisenmenger syndrome, the benefit of Group 1 medications in CHD-PAH remains uncertain

Final Thoughts…

- PH comes in many forms, is influenced by presence of comorbid conditions and does not have effective treatment in all cases
- Each patient at risk of PH requires regular and complete risk evaluation
- Community providers are the front line of PH detection and must work in concert with PH specialty centers to begin the diagnostic process and later cooperate in patient management
- It is critical, in all cases where PH is suspected, that timely referral from the community level to the PH specialty center occurs, accompanied by high quality preliminary screening and diagnostic data collection
- Cooperative management between PH specialty centers and community providers is the best option way to optimize patient outcomes