The Pulmonary Circulation in Pediatric and Congenital Heart Disease

The Clinical Spectrum of PAH: Who has it? Is it the same disease in all?

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February 25, 2023

CARDIOLOGY 2023
26th Annual Update on Pediatric and Congenital Cardiovascular Disease

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Disclosures

Grant funding from NIH/NHLBI, Pediatric Heart Network, Actelion Pharmaceuticals, and United Therapeutics

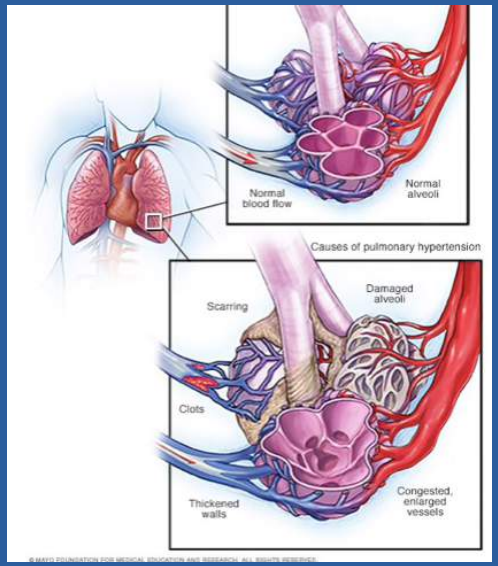
No way, it is not all the same!

PAH? PH? PHVD?

PAH: mean PA > 20 mm Hg, PCWP ≤ 15 mm Hg, and PVRi > 3 iWU

PH: mean PA > 20 mm Hg

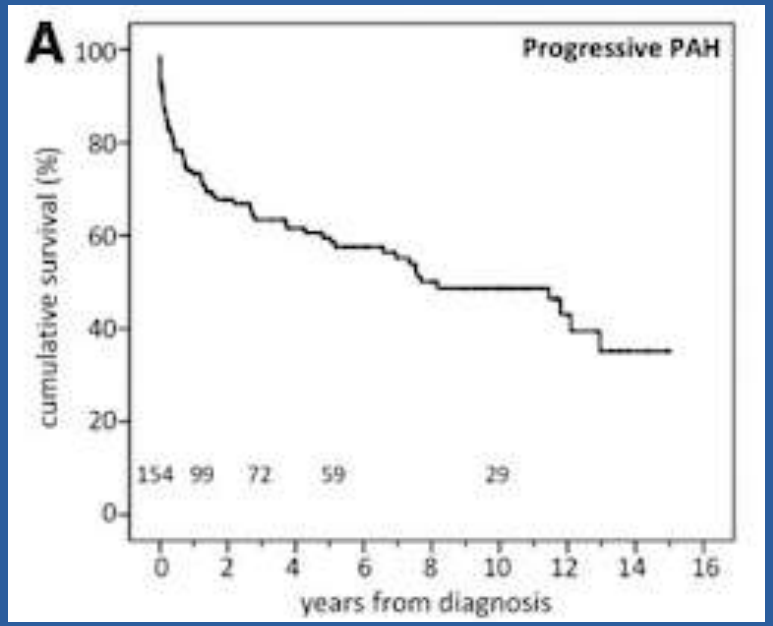
PHVD: TPG > ~~0~~ ~~g~~ or PVRi > 3



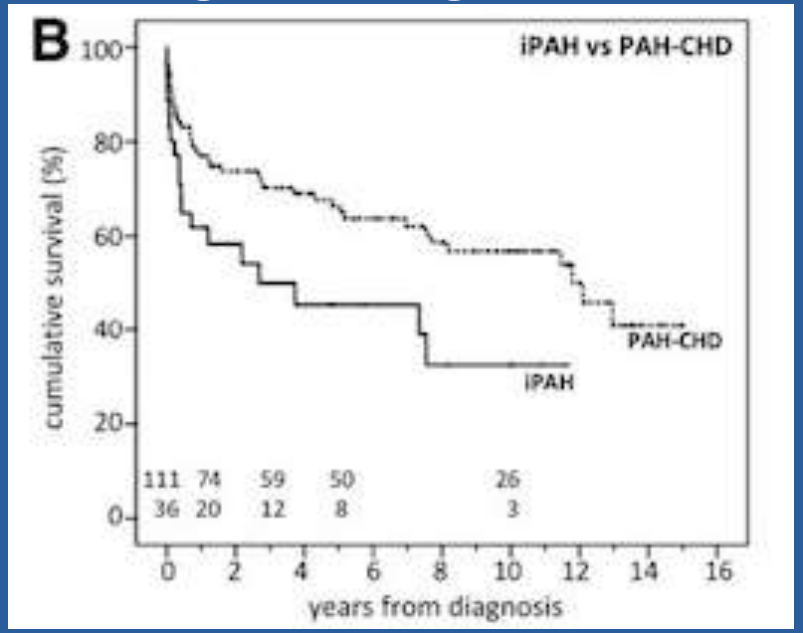
World Symposium of Pulmonary Hypertension 2018 Classification

1. Pulmonary arterial hypertension (PAH)
   1.4.4 PAH associated with CHD
2. PH with left heart disease
   2.4 Congenital/acquired condition → post-capillary PH
3. PH associated with lung disease and/or hypoxia
   3.5 Developmental or other lung disorders
4. PH due to pulmonary artery obstructions
   4.2 Other pulmonary artery obstructions
5. PH with unclear and/or multifactorial mechanisms
   5.4 Complex CHD (including SV-CHD)

Survival for PAH varies by subtype



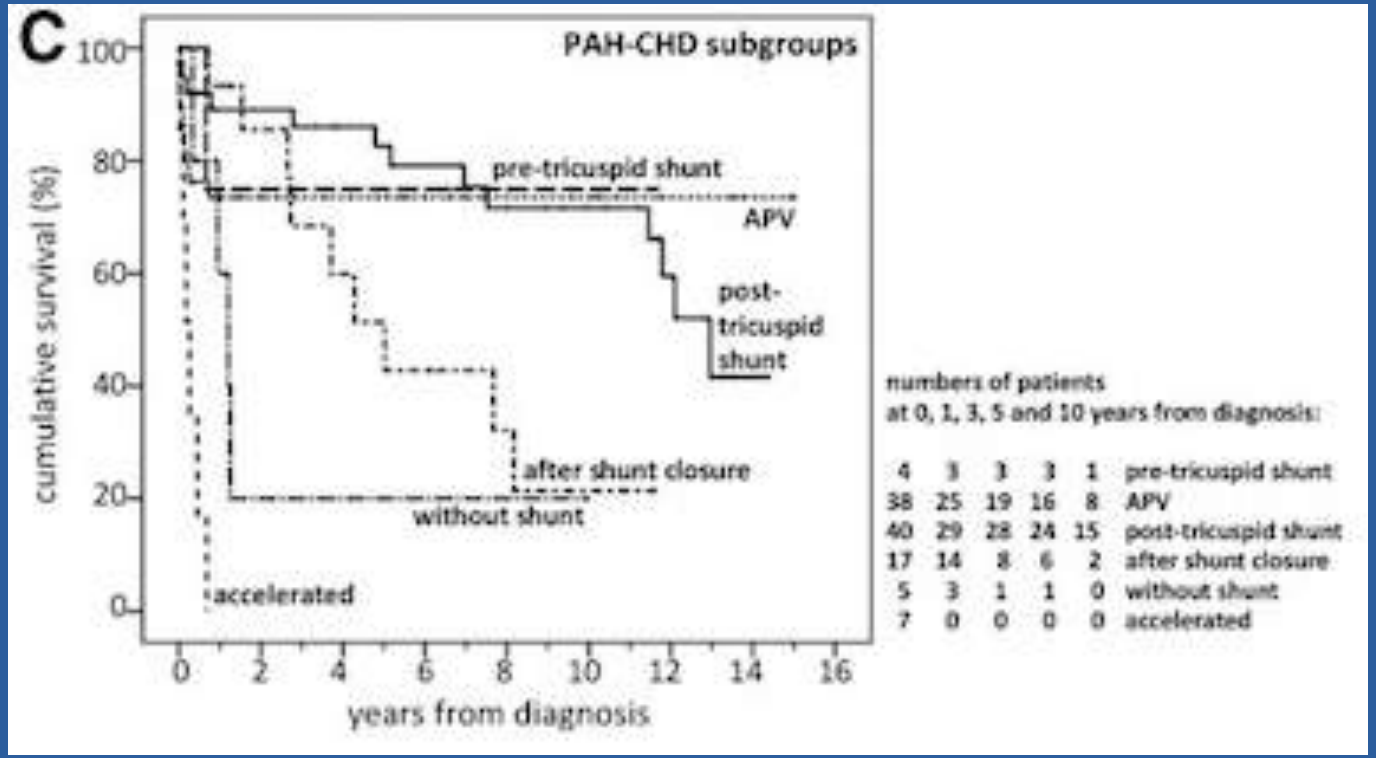
1, 3, 5 yr: 73%, 63%, 60%



CHD - 1, 3, 5 yr: 77%, 70%, 66%
IPAH - 1, 3, 5 yr: 62%, 50%, 46%

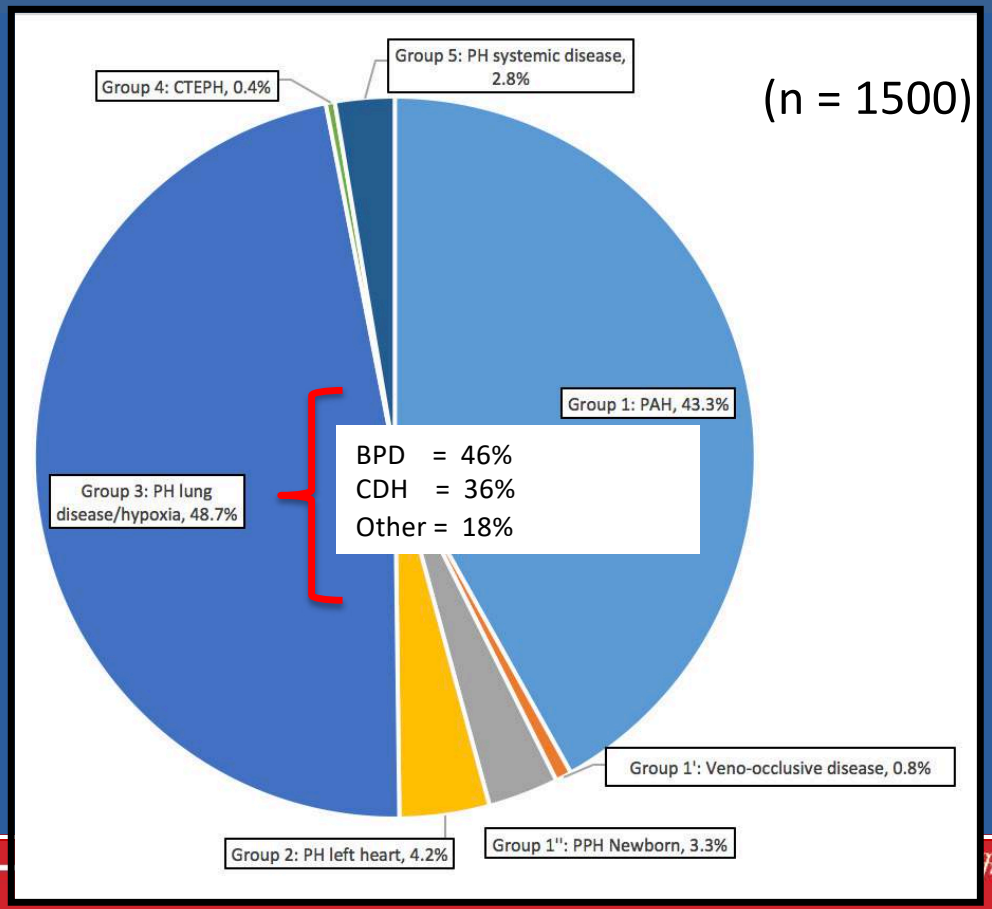
Van Loon RLE, et al. *Circulation,* 2011

Survival for CHD-PAH varies by subtype



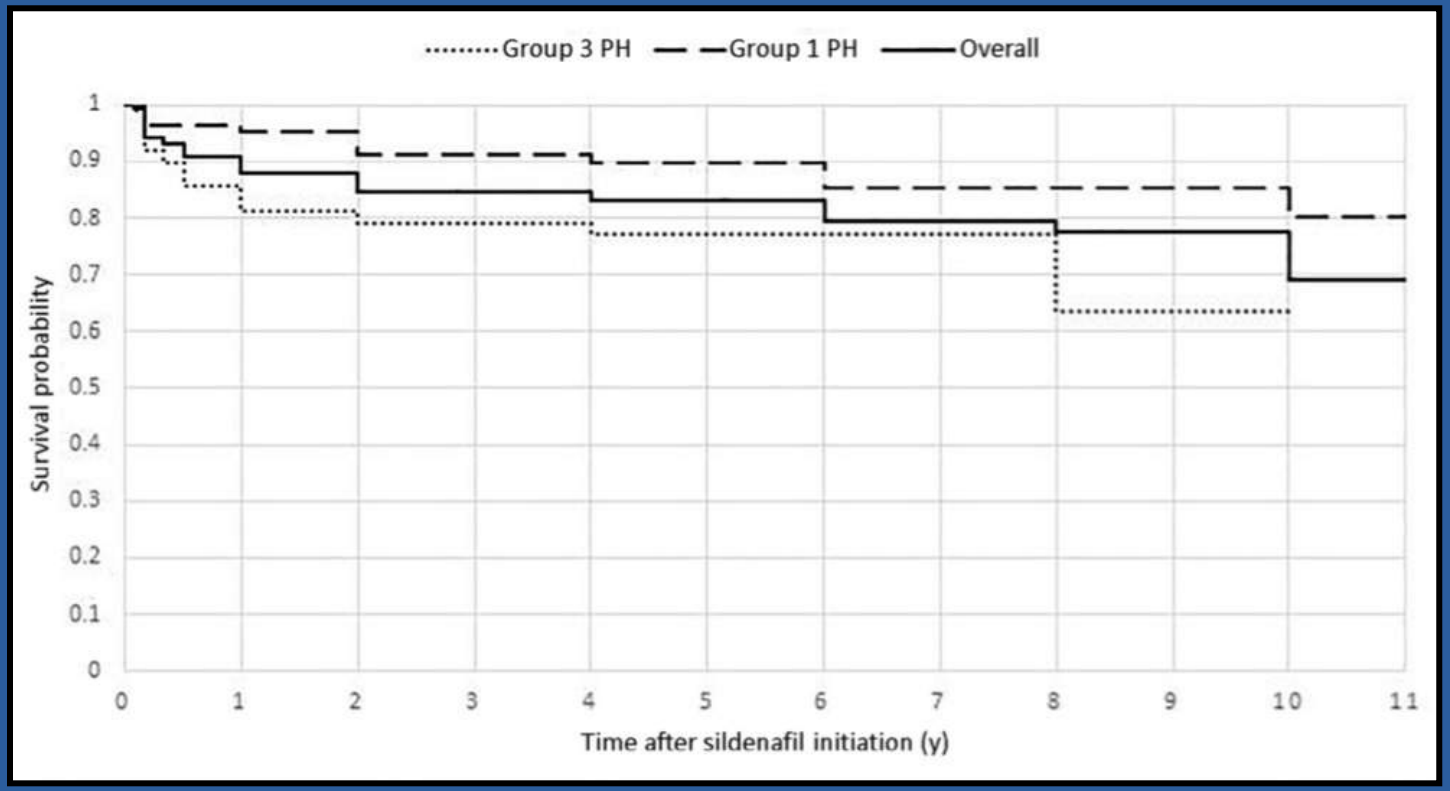
Van Loon RLE, et al. *Circulation,* 2011

Pediatric Pulmonary Hypertension Network (PPHNet) Registry: Nice Classification



S. Abman and PPHNet investigators. *Eur Respir J,* 2021

Survival on Sildenafil at Columbia

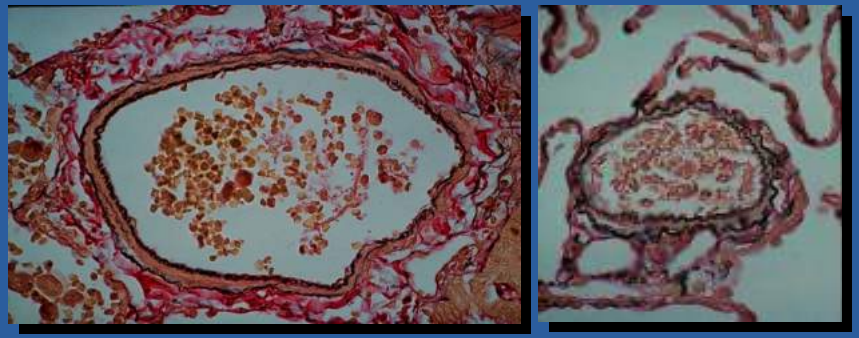


Cohen JL, et al. *J Pediatr,* 2019

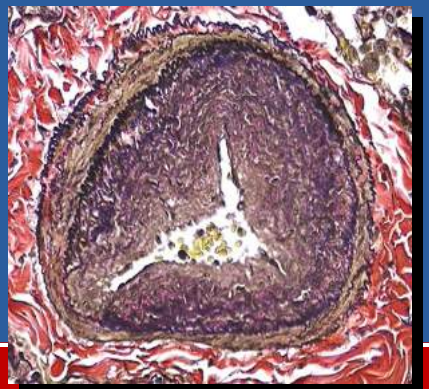
Ok…maybe it is all the same!

The Common Denominator of all PH

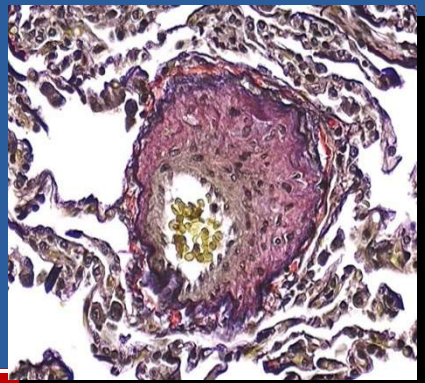
Normal



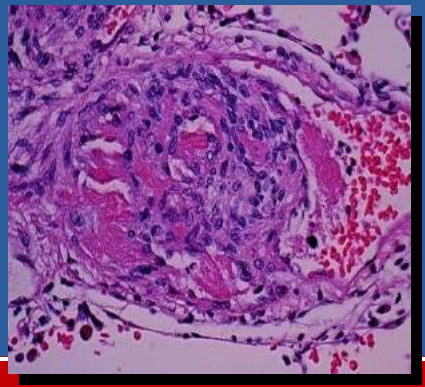
Intimal thickening due to endothelial proliferation



Medial thickening and muscularization



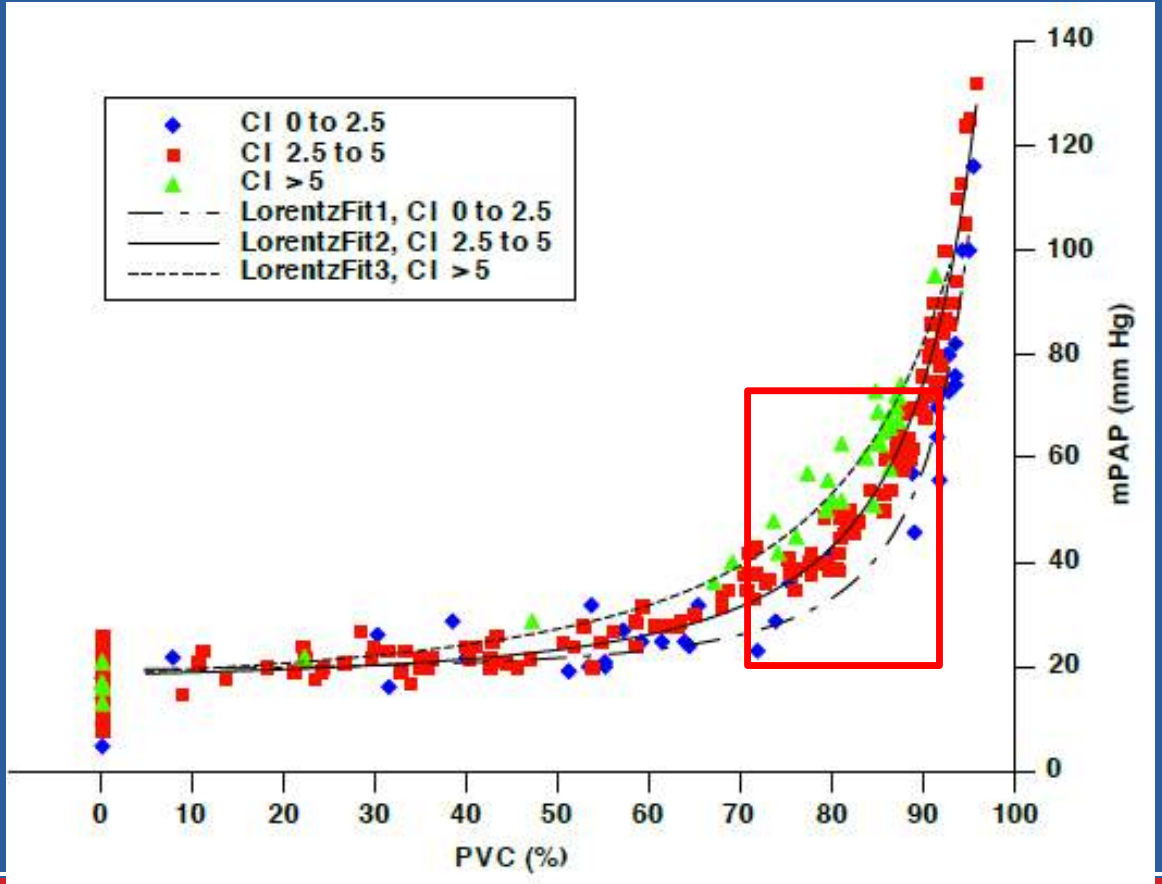
Plexiform lesions



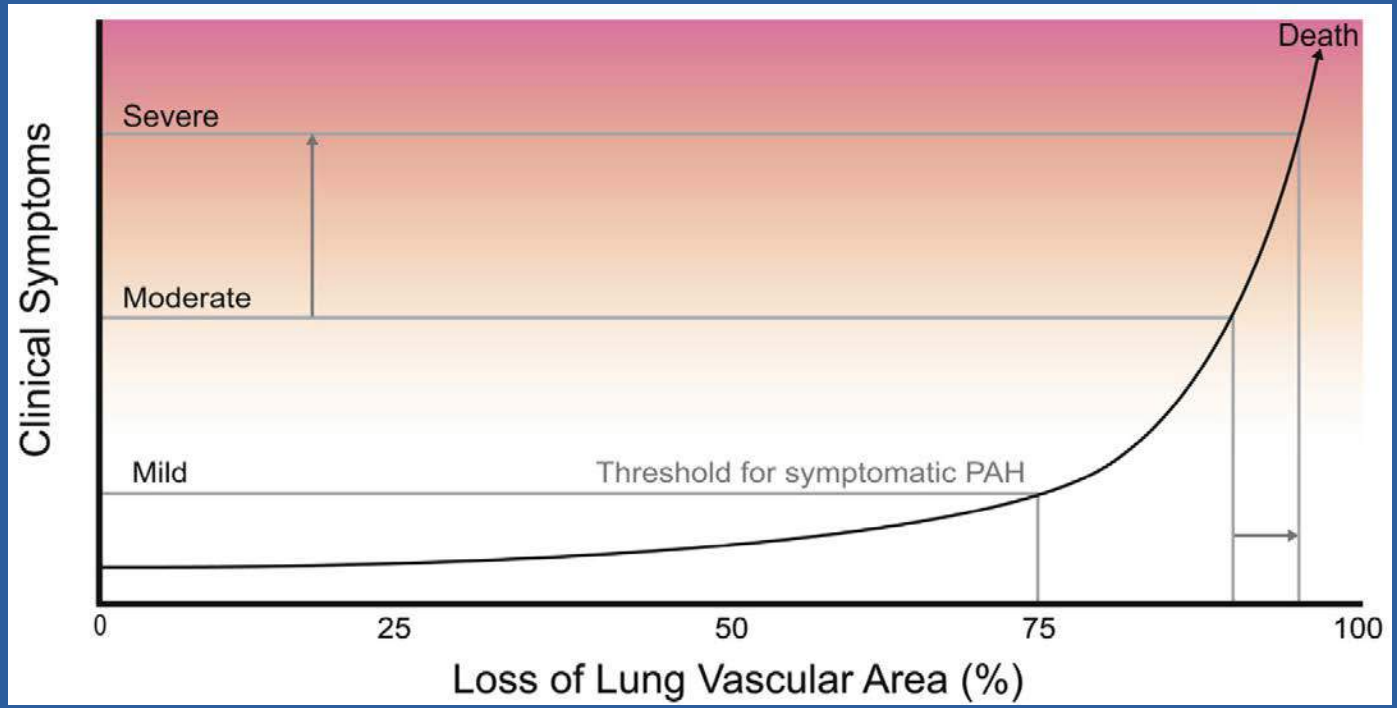
Courtesy of Brian Hanna, MD, PhD

Functional and structural vascular loss

Frank DB, et al.
in prep

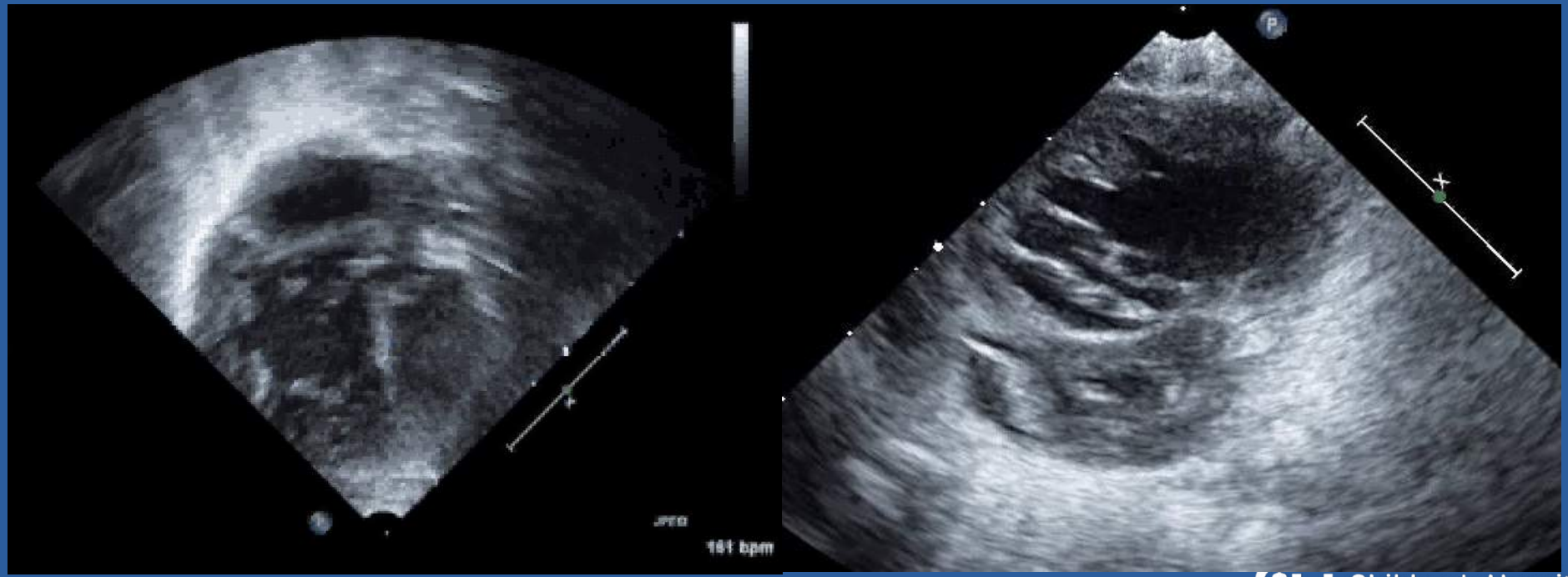


Vascular loss and clinical PH



Foster W, et al. *Can J Cardiol,* 2014

Pump failure



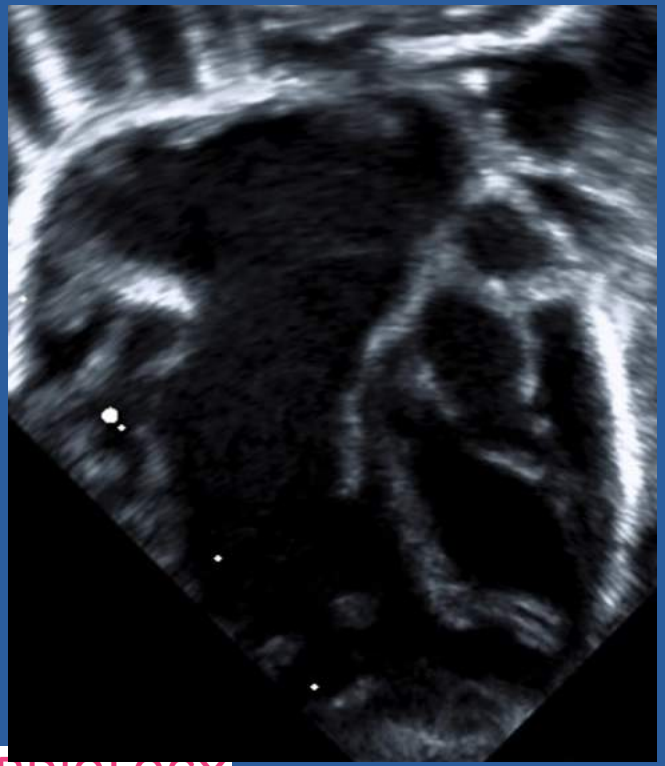
Case 1

- FT, IUGR, child multiple levels of left heart hypoplasia and obstruction, multiple VSDs difficult to close
- RV dysfunction requiring V-A ECMO
- Persistent shunt and over-circulation s/p PA banding
- OSA requiring nighttime CPAP
- GERD/aspiration s/p GT with later Nissen fundoplication
- Several early viral respiratory infections
- Left common pulmonary vein stenosis s/p angioplasty and stenting

Case 1

- Admissions for RV failure
- Malnutrition
- Sildenafil, bosentan, SQ treprostinil + supplemental O2
- Eventual VSD closure, PA band takedown, relief of PVS
- Moderate to severe LVOTO despite reintervention
- Weaned off SQ treprostinil to dual oral regimen
- Improved growth
- Lack of RV failure

Quiz 1:



How is this patient classified:

A. Group 1 PAH related to CHD of course!
B. Group 2 PH with left heart disease due to her LVOTO and PVS
C. Isn't there lung disease too?
D. I don't know - Why is the PH team talking about classification again? And did we get the sildenafil prior auth?

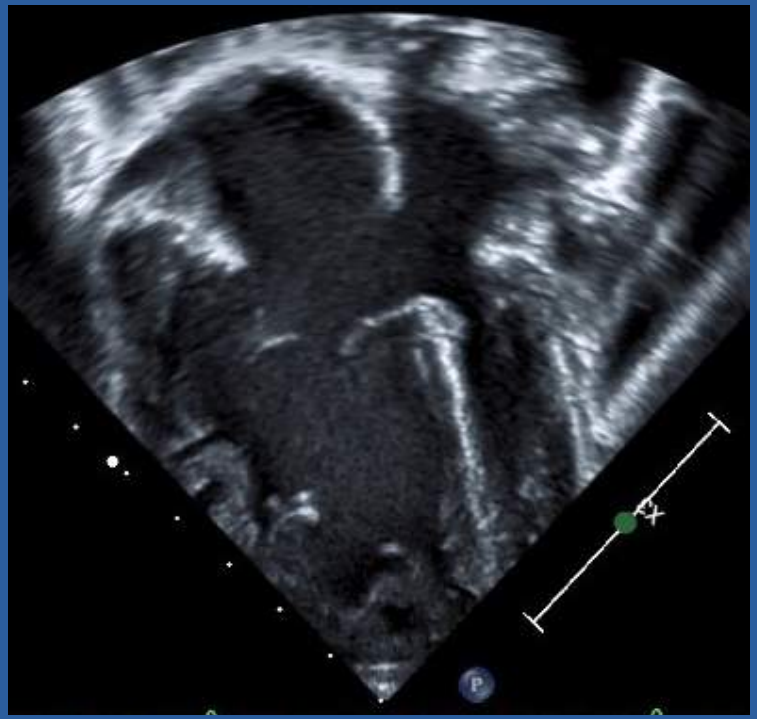
Case 2

- FT fraternal twin child with transitional AV canal defect
- Suprasystemic PH and RV failure at 18 months
- Cath: PAH with 2:1 shunt and elevated PVRi
- Ground glass opacities on chest CT c/f PVOD
- Treated with sildenafil, ambrisentan, and SQ treprostinil
- Heterozygous mutation in GDF2 which encodes BMP9, a ligand of the BMPR2 receptor
- Added tacrolimus

Case 2

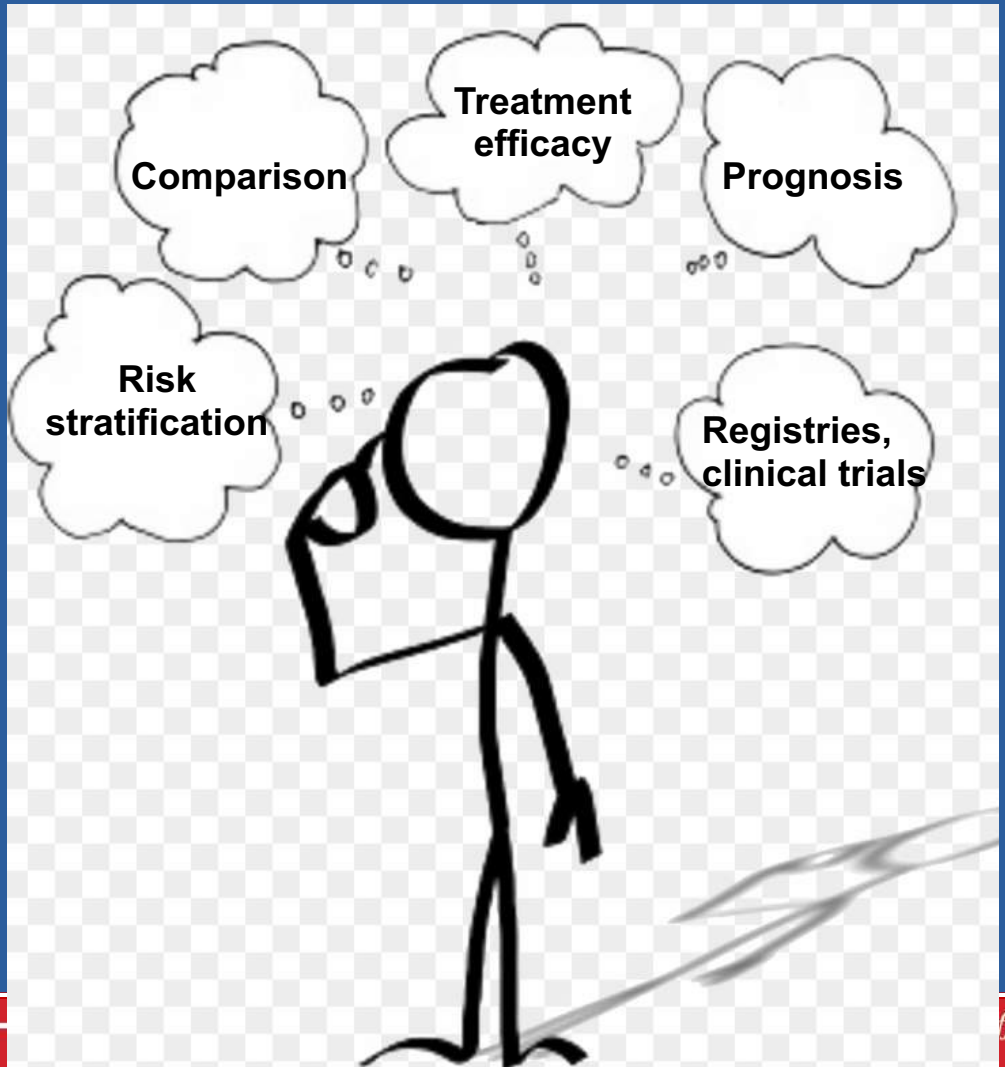
- Pulmonary edema requiring aggressive diuresis
- Severe malnutrition requiring NGT feeds
- Severe GERD/aspiration and GI distress
- Repeat cath with higher shunt and lower PVRi
- Fenestrated ASD + primary VSD closure, LAVV repair
- Frequent cellulitis at SQ sites
- Transition from SQ treprostinil to oral selexipag
- Tolerating diuretic weans
- Improved nutrition, activity, development

Quiz 2:



How is this patient classified:

A. Group 1 PAH related to CHD of course!
B. Group 1 Heritable PAH of course!
C. Should I worry about the ground glass opacities on chest CT?
D. I don't know - Why is the PH team talking about classification again? Are there concerns about increasing treprostinil?


Comparison
Treatment efficacy
Prognosis
Risk stratification
Registries, clinical trials

Maternal-fetal environment

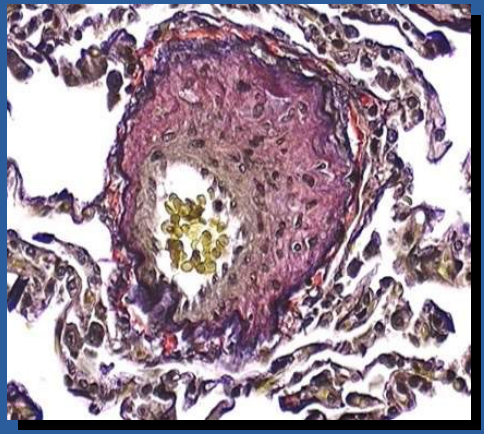
Genetics

Shunts

PH Classification

1. PAH
2. PH with left heart disease
3. PH associated with lung disease and/or hypoxia
4. PH due to pulmonary artery obstructions
5. PH with unclear and/or multifactorial mechanisms

Disruption of vascular signaling pathways



Left heart disease

Aspiration

OSA

Pediatric PH Risk Assessment

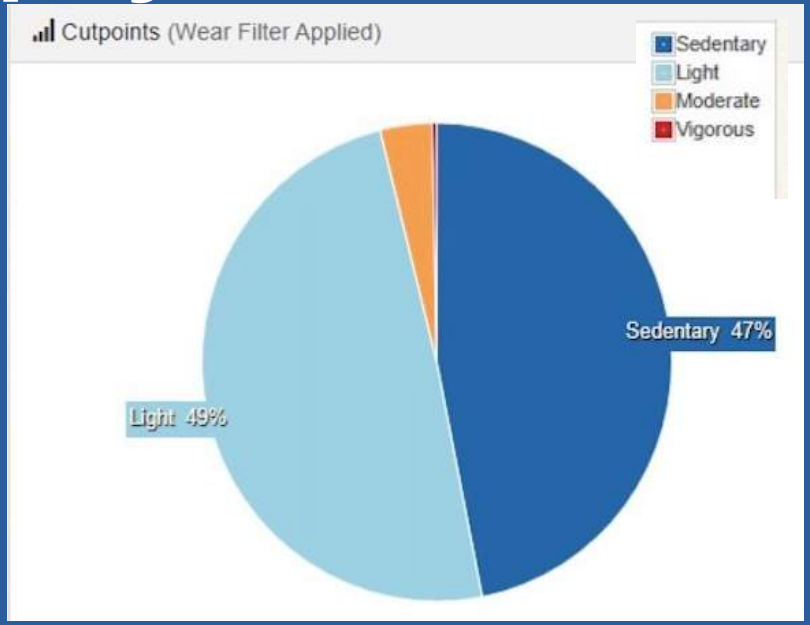
Lower Risk	Determinants of Risk	Higher Risk
No	Clinical evidence of RV failure	Yes
No	Progression of symptoms	Yes
No	Syncope	Yes
Normal (height, BMI)	Growth	Failure to thrive
I, II	WHO functional class	III, IV
Minimally elevated for age or not elevated	Serum NT-proBNP	Greatly elevated for age >1200 pg/mL (>1yr old) Rising NT-proBNP level
Minimal RA/RV enlargement No RV systolic dysfunction RV/LV e.s. ratio < 1 (PSAX) TAPSE normal (z > -2) S/D ratio <1.0 (TR jet) PAAT > 100 ms (>1yr old)	Echocardiography, CMR	Severe RA/RV enlargement RV systolic dysfunction RV/LV e.s. ratio >1.5 (PSAX) TAPSE ↓↓ (z < -3) S/D ratio >1.4 (TR jet) PAAT <70 ms (>1yr old) Pericardial effusion
CI >3.0 l/min/m^2 mRAP <10 mm Hg mPAP/mSAP <0.5 Acute vasoreactivity +	Invasive Hemodynamics	CI <2.5l/min/m^2 mRAP >15 mm Hg mPAP/mSAP >0.75 PVRi >15 WU · m^2

Hansmann, et al.

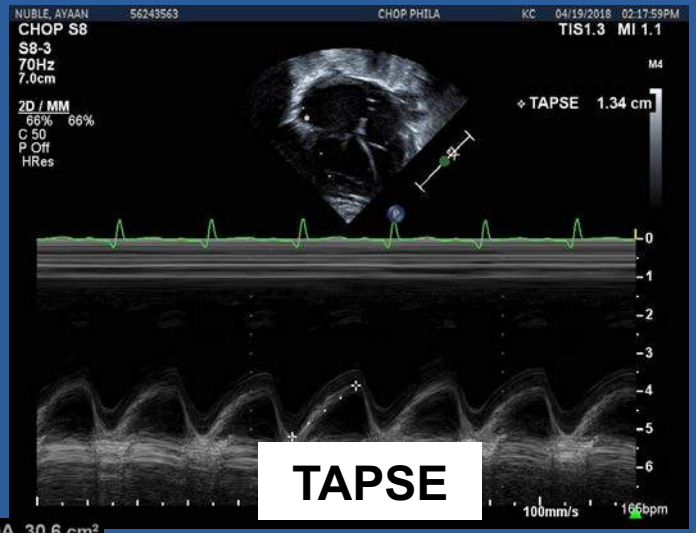
JHLT, 2019

Actigraphy

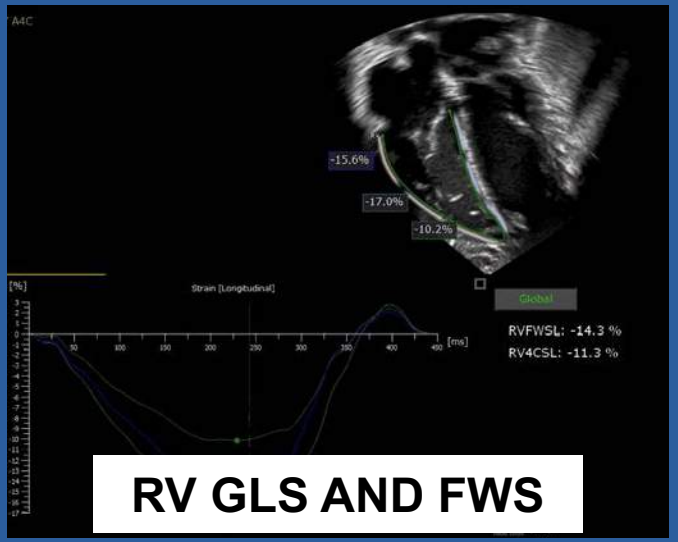

wGT3X-BT


Cutpoints (Wear Filter Applied)
Sedentary
Light
Moderate
Vigorous
Sedentary 47%
Light 49%

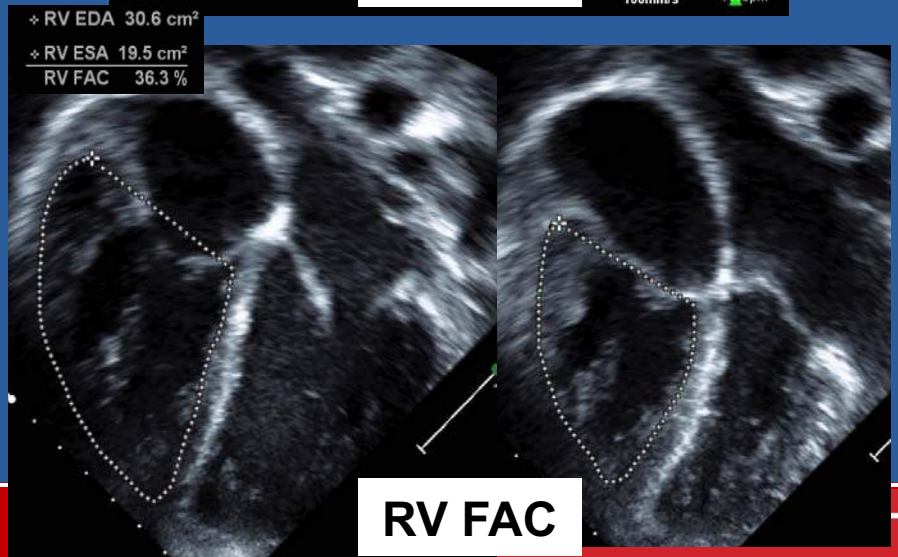

Steps
15000
10000
5000
0
10/26/2021
10/29/2021
11/01/2021
11/04/2021
11/07/2021
11/10/2021



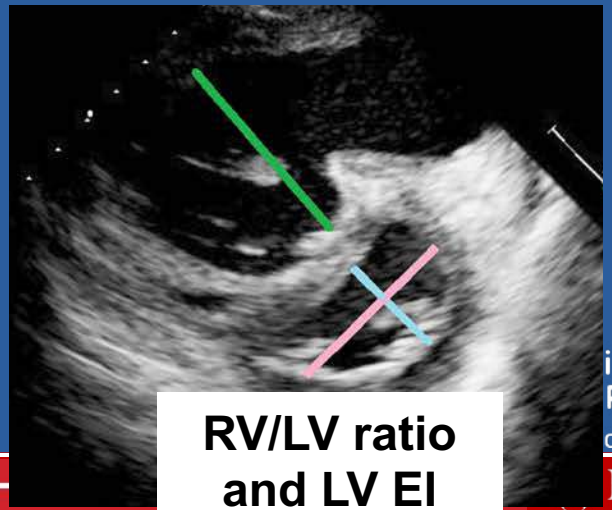
TAPSE



RV GLS AND FWS



RV FAC



RV/LV ratio and LV EI

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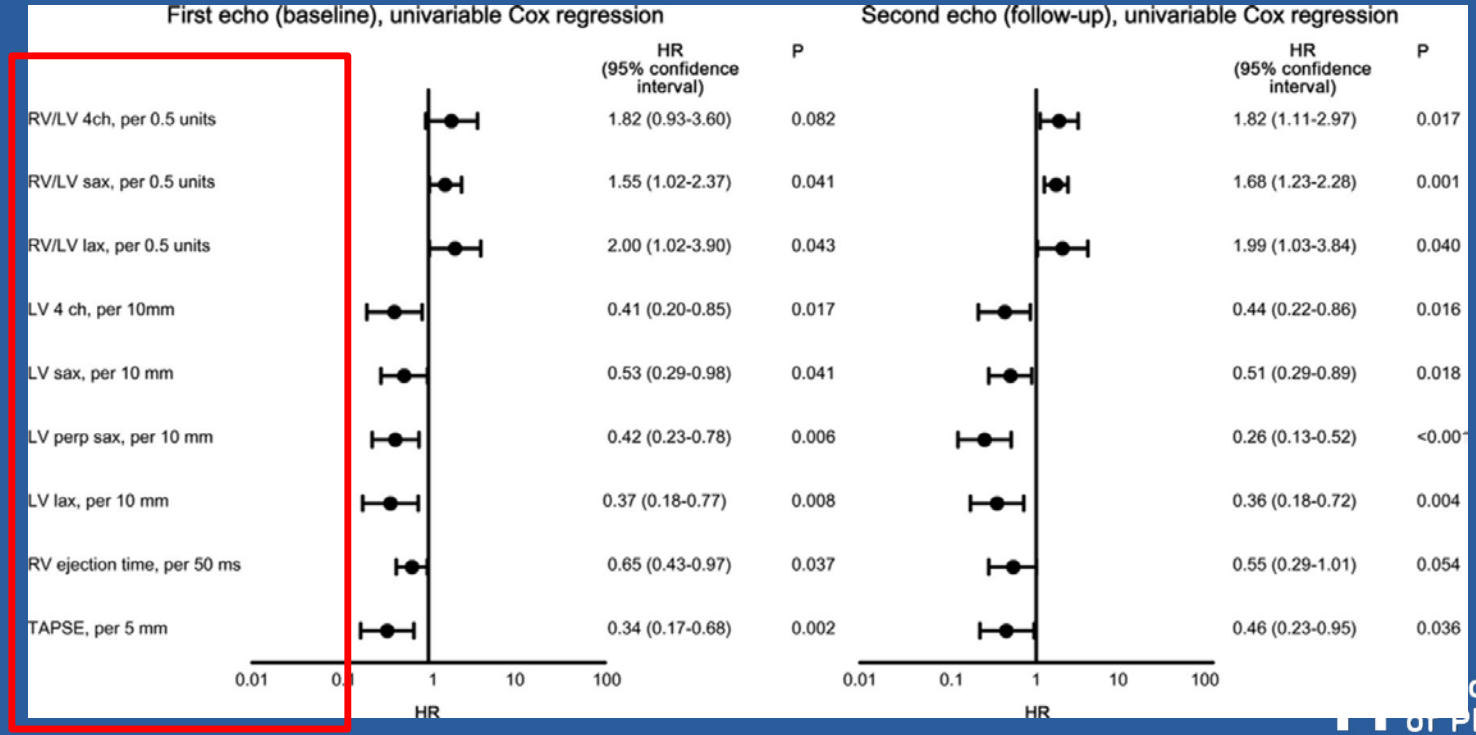
Echo parameters associated with death or transplant in PAH



Ploegstra, et al. *Circ Cardiovasc Imaging,* 2014.

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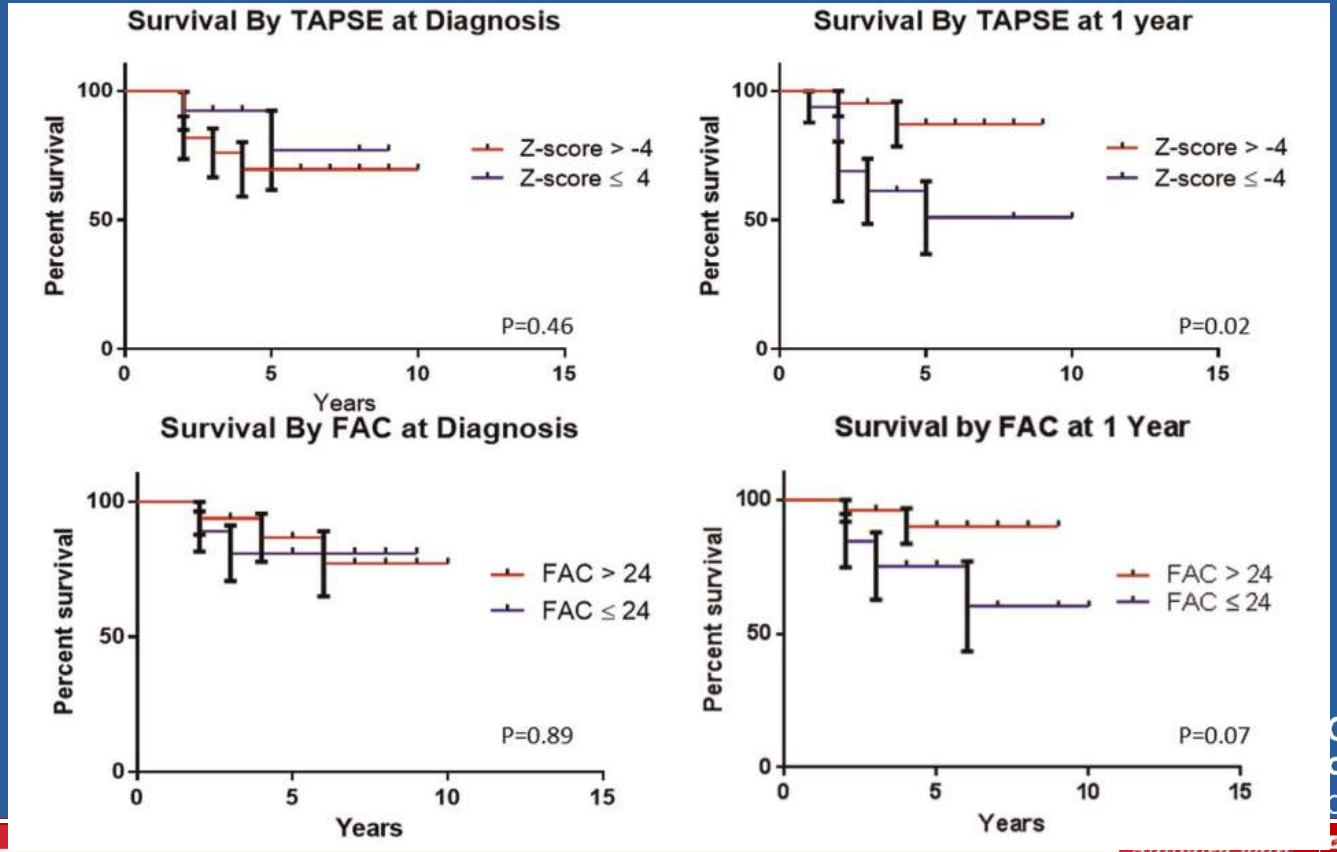
Decline in TAPSE and FAC predict outcome

IPAH (18)
PAH-CHD (25)
Lung dis (5)



Bitterman, et al. *JASE,* 2021

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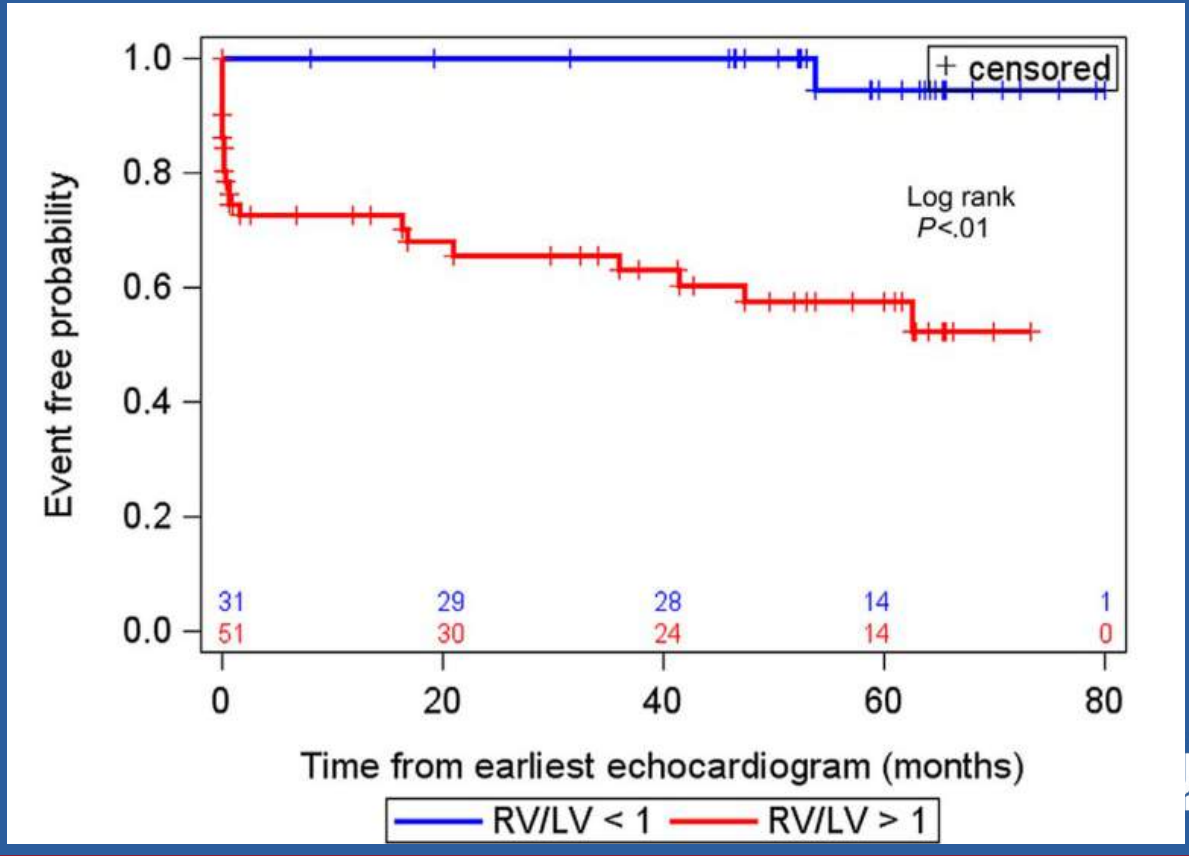
Adverse events with greater RV/LV

HR, 2.49 (95% CI, 1.92–3.24)



Every 0.1 unit increase in RV/LV, HR inc. 10%

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Jone et al. *JASE*, 2014

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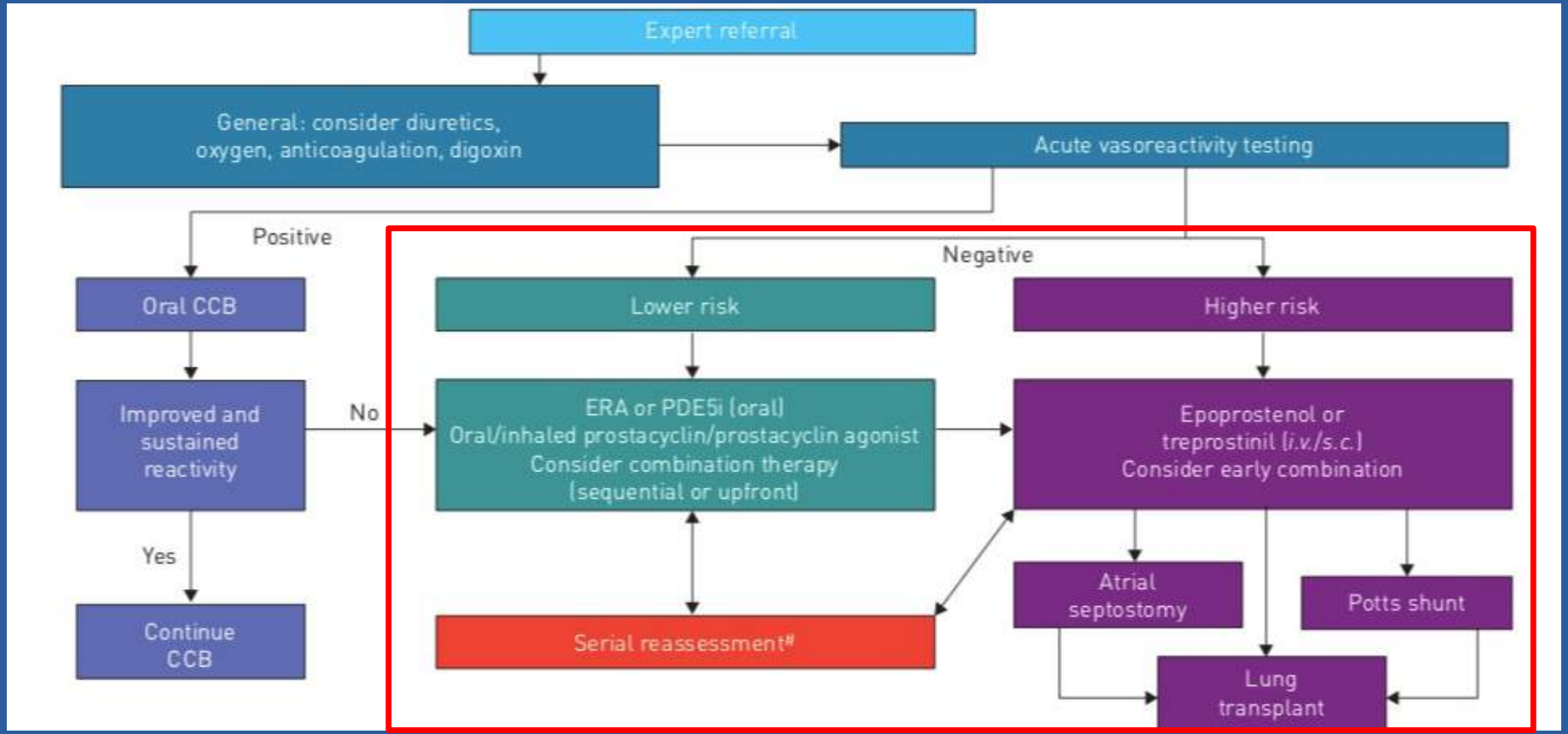
Treatment Algorithm



Abman, et al. *Circulation,* 2015

Final Thoughts

- Children with PH often overlap classifications
- Untreated PH ends in RV failure
- Survival for PAH-CHD varies by subtype
- Understanding patient risk factors and evidence of RV failure facilitates targeted treatment
- Novel clinical trial approaches are crucial to test new and existing therapies

It is not all the same!

Thank you