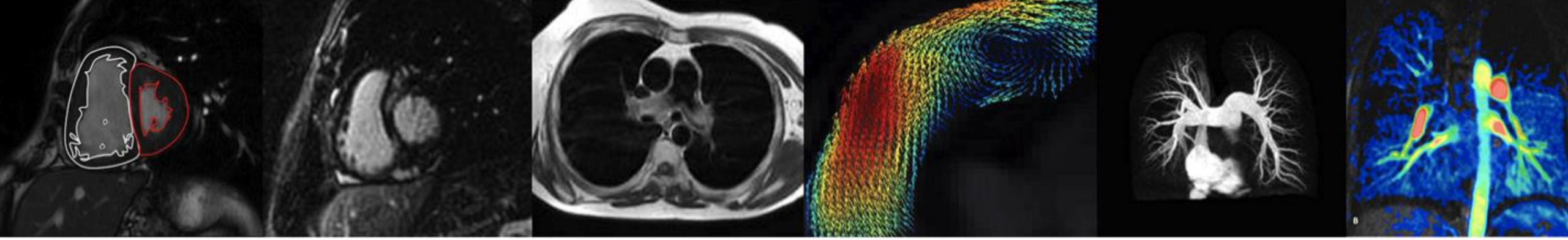

Unexplained Dyspnea: Could it be PAH?

Red Flags in Clinical Suspicion

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Mediclinic Airport Road Hospital

Abu Dhabi

A significant delay remains in PAH diagnosis

Time from symptom onset to diagnosis - little change over the past 15 years

Spain 2012[2] (*n*=866)
Mean: 42.0 months

Poland 2020[3] (*n*=50)
Median: 18.0 months

UK/Ireland 2012[1] (*n*=404)
Median: 18.0 months

UK 2019[9] (n=545)
20% of patients 3+ years

China 2011[4] (*n*=712)
Median: 36.7 months

USA 2012[8] (*n*=2635)
REVEAL:
Median: 12.8 months
Mean: 31 months

Australia 2013[5] (*n*=32)
Median: 44.0 months
Mean: 47.0 months

Saudi Arabia 2014[7] (*n*=107)
Mean: 27.8 months

Australia/NZ 2020[6] (*n*=2044)
Median: 14.4 months
Mean: 30.0 months

1. Ling Y, *et al. Am J Crit Care Med* 2012; 186:790-6; 2. Escribano-Subias P, *et al. Eur Resp J* 2012; 40:596-603; 3. Bylica J, *et al. Kardiol Pol* 2020; 25:750-2;
4. Jing Z-C, *et al. Am J Crit Care Med* 2011; 183:1723-9; 5. Strange G, *et al. Pulm Circ* 2013; 3:89-94; 6. Khou V, *et al. Respirology* 2020; 25:863-71;
7. Idrees MM, *et al. Ann Thorac Med* 2014; 9:209-15; 8. Benza RL, *et al. Chest* 2012; 142:448-56; 9. Armstrong I, *et al. BMC Pulm Med* 2019; 19:67.

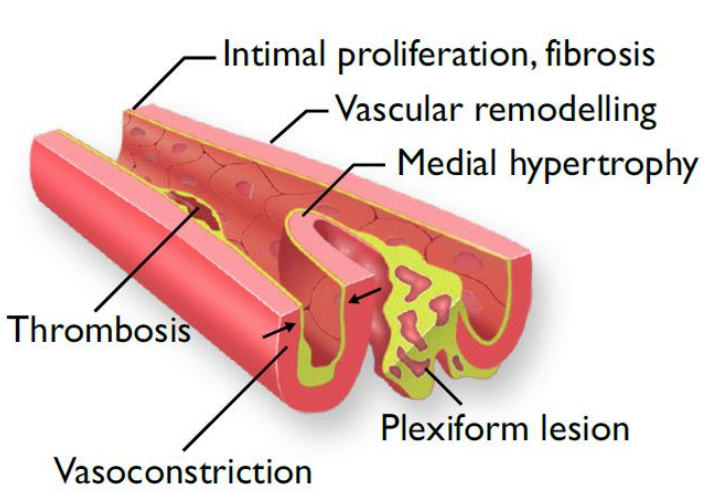
The diagnosis of PAH is often challenging due to non-specific symptoms and signs and presence of comorbidities

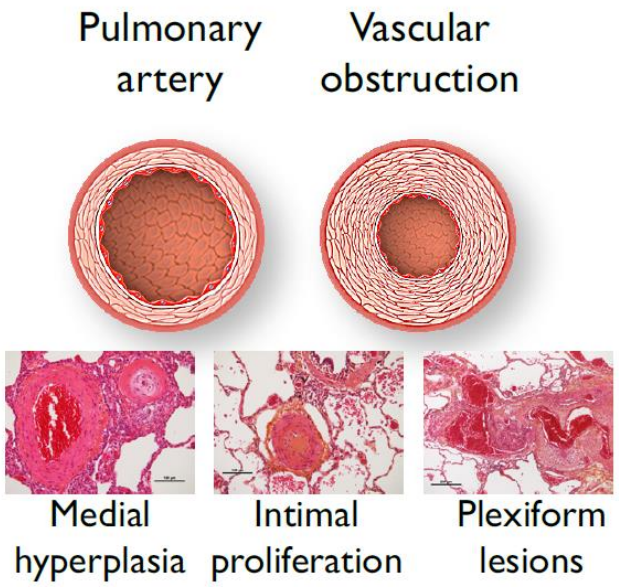
RED FLAG
DON'T ASSUME DYSPNEA IN YOUNG IS ONLY ASTHMA OR ANEMIA !!!

1. Humbert M, *et al. Eur Heart J* 2022; 00:1–114; 2. Armstrong I, *et al. BMJ Pulmonary Medicine* 2019; 19:67.

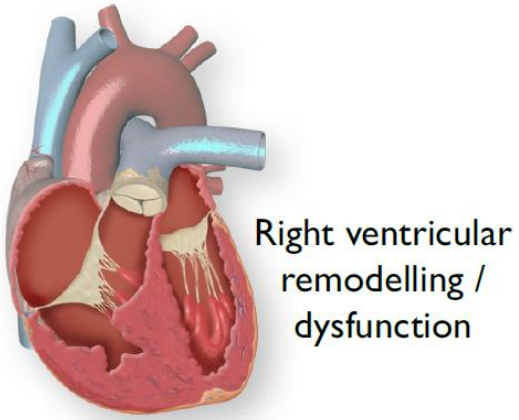
Silent disease progression and delays in diagnosis prevent timely disease management

Pulmonary Vasculopathy





Right Heart Failure

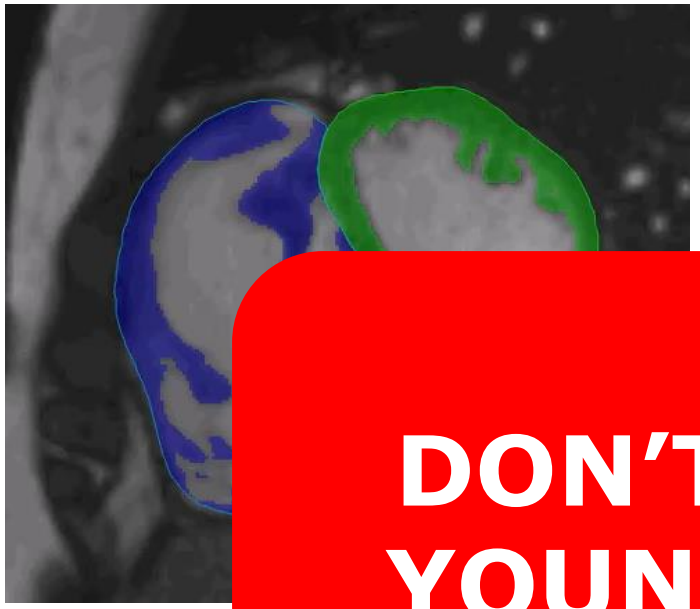


- Pathological changes to pulmonary vasculature lead to increased PVR and PAP[2,3], **forcing the right heart to work harder to maintain cardiac output[4]**
- As a consequence of increased afterload, **right heart undergoes adaptive compensatory changes, which become maladaptive over time as the disease progresses**[2-5]

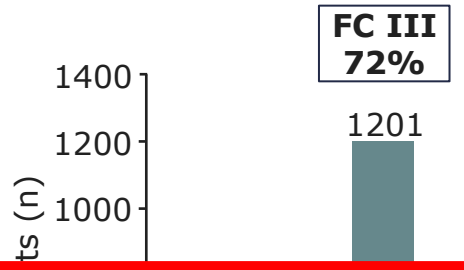
1. Image from Humbert M, *et al. Eur Heart J* 2022; 00:1–114; 2. Austin ED, *et al. Ann Am Thorac Soc* 2014; 11:S178-85; 3. Bogaard HJ, *et al. Chest* 2009; 135:794-804; 4. Swift AJ, *et al. Am J Respir Crit Care Med* 2017; 196:228-39; 5 Goh ZM, *et al. JACC Cardiovasc Imaging* 2021; 14:1271-2.

Delayed diagnosis disease is advanced with diagnostic delays negatively impacting on survival

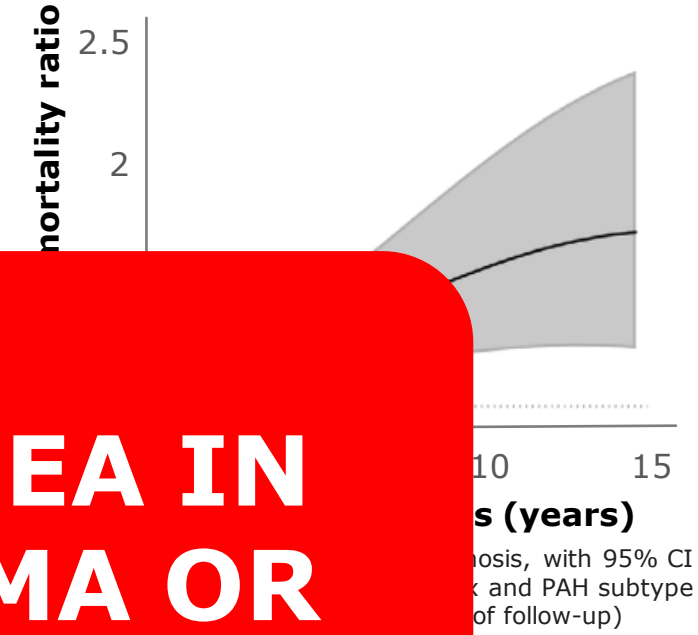
cMRI Cine Image short axis[1]



SPAHR Registry[2] (N = 1668)

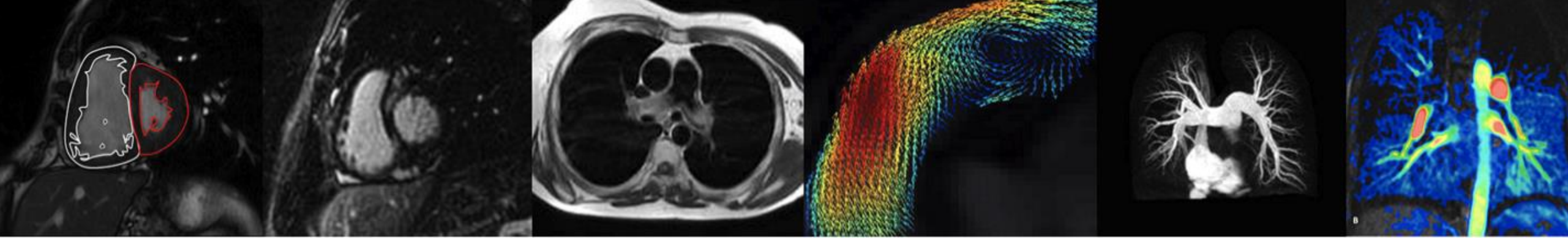


Diagnostic delays of 2 or 5 years increased mortality for PAH patients by 11% and 29%, respectively[3]



RED FLAG
DON'T ASSUME DYSPNEA IN YOUNG IS ONLY ASTHMA OR ANEMIA !!!

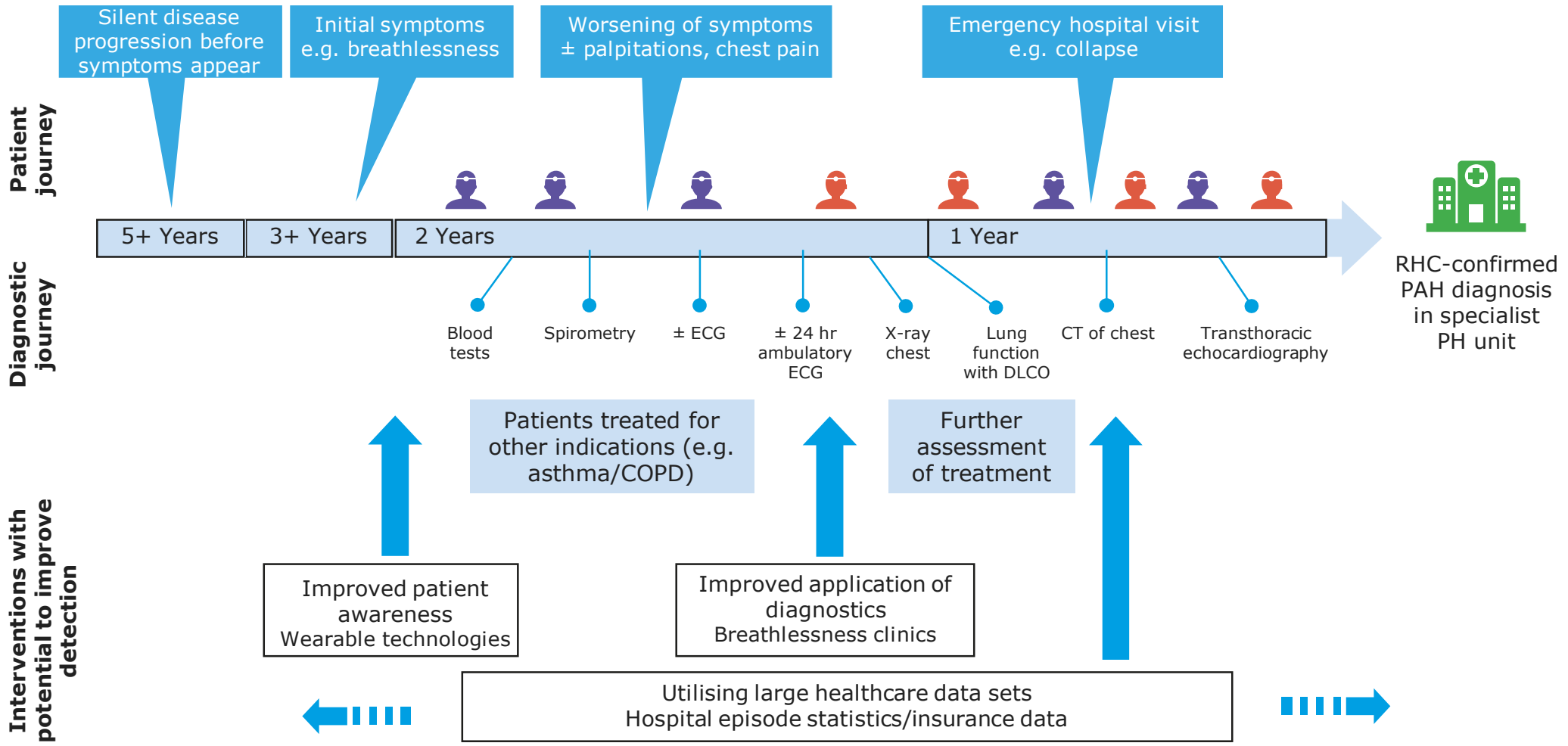
1. Video from speaker data on file; 2. Kjellström B, *et al.* Swedish Pulmonary Arterial Hypertension Registry Annual Report 2019;
3. Khou V, *et al. Respirology* 2020; 25:863-71



What Should We Do?

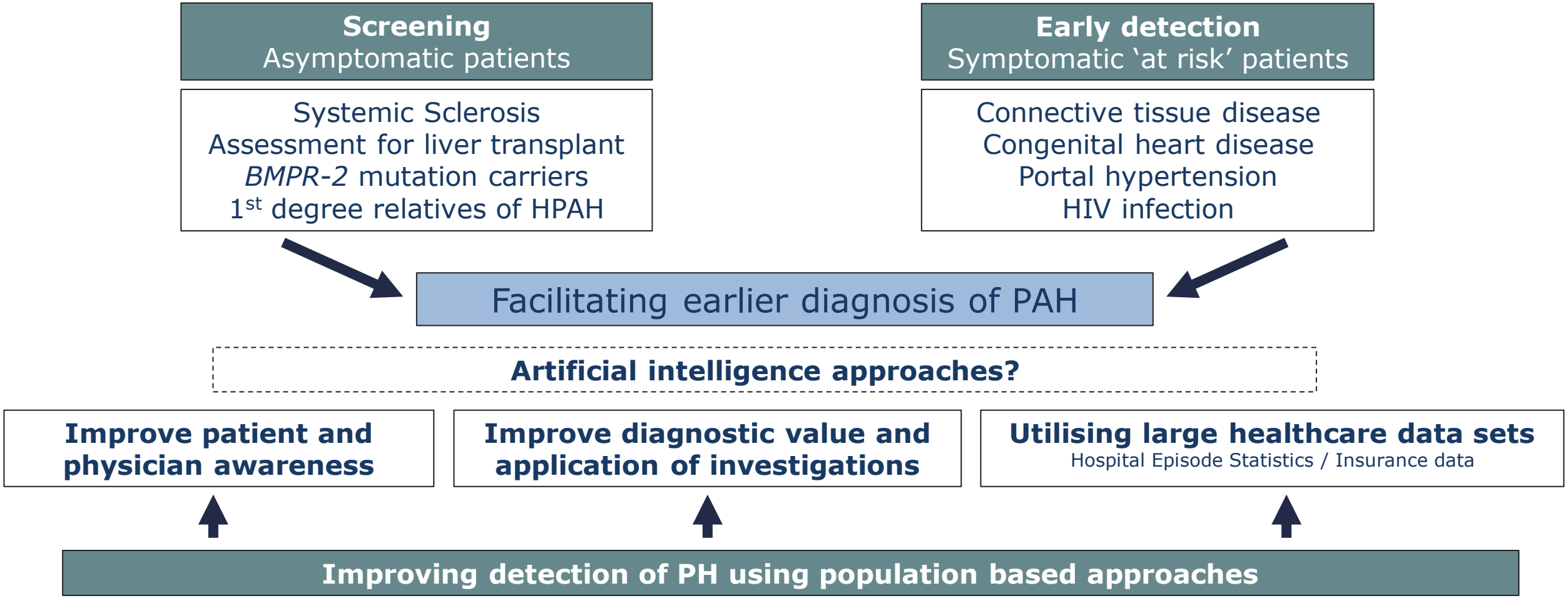
RED FLAG
DON’T ASSUME DYSPNEA IN YOUNG IS ONLY ASTHMA OR ANEMIA !!!

Improving the time to diagnosis: understanding the journey of a typical patient with PAH

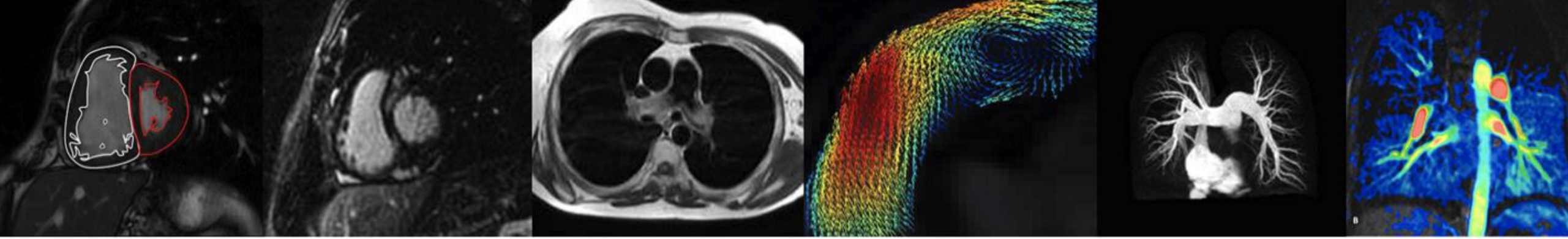


Kiely DG, *et al. Eur Heart J Suppl* 2019; 21:K9-K20.

Improve the time to diagnosis in PAH: Combine approaches



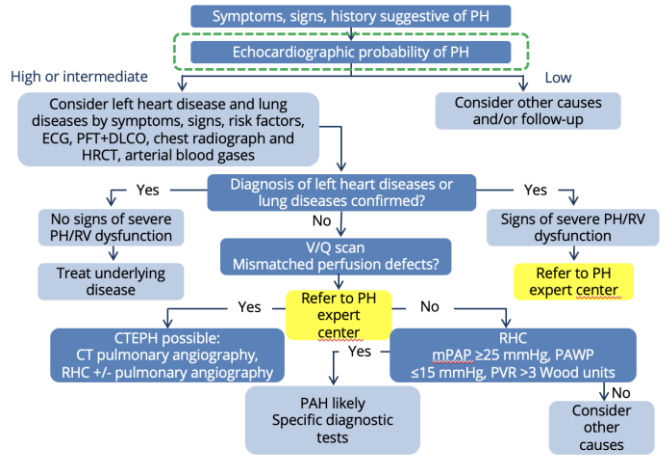
Kiely DG, *et al. Eur Heart J Suppl* 2019; 21:K9-K20.



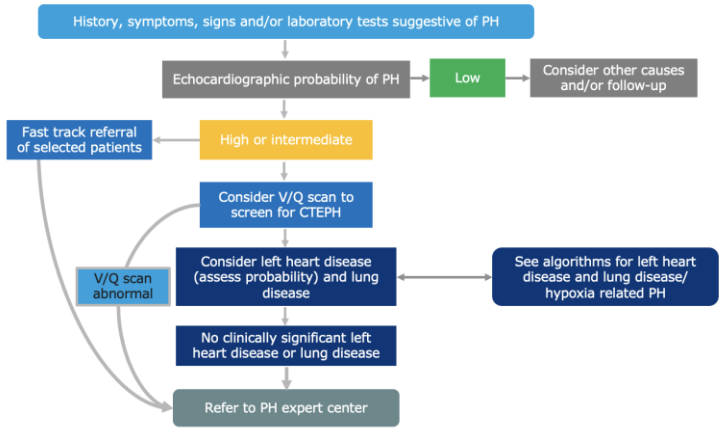
PH diagnostic algorithm ESC/ERS guidelines 2022

The evolution of diagnostic algorithms in PH

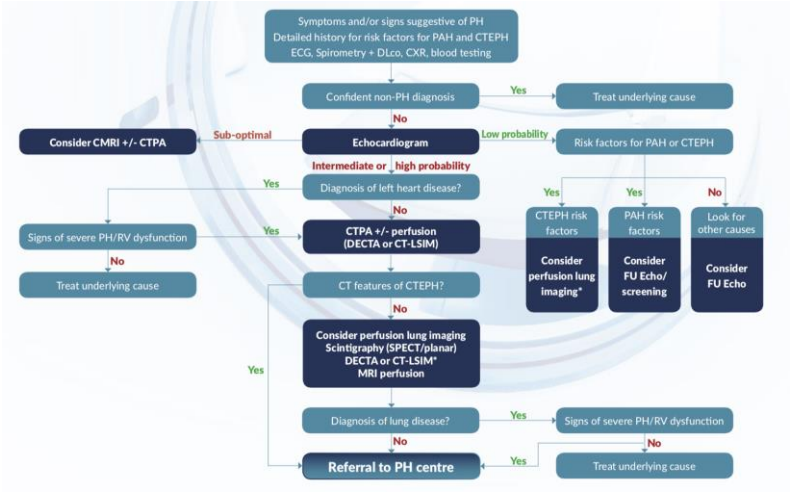
2015 ESC/ERS Guidelines[1]



2019 6th World Symposium[2]



2019 PVRI Diagnostic algorithm[3]



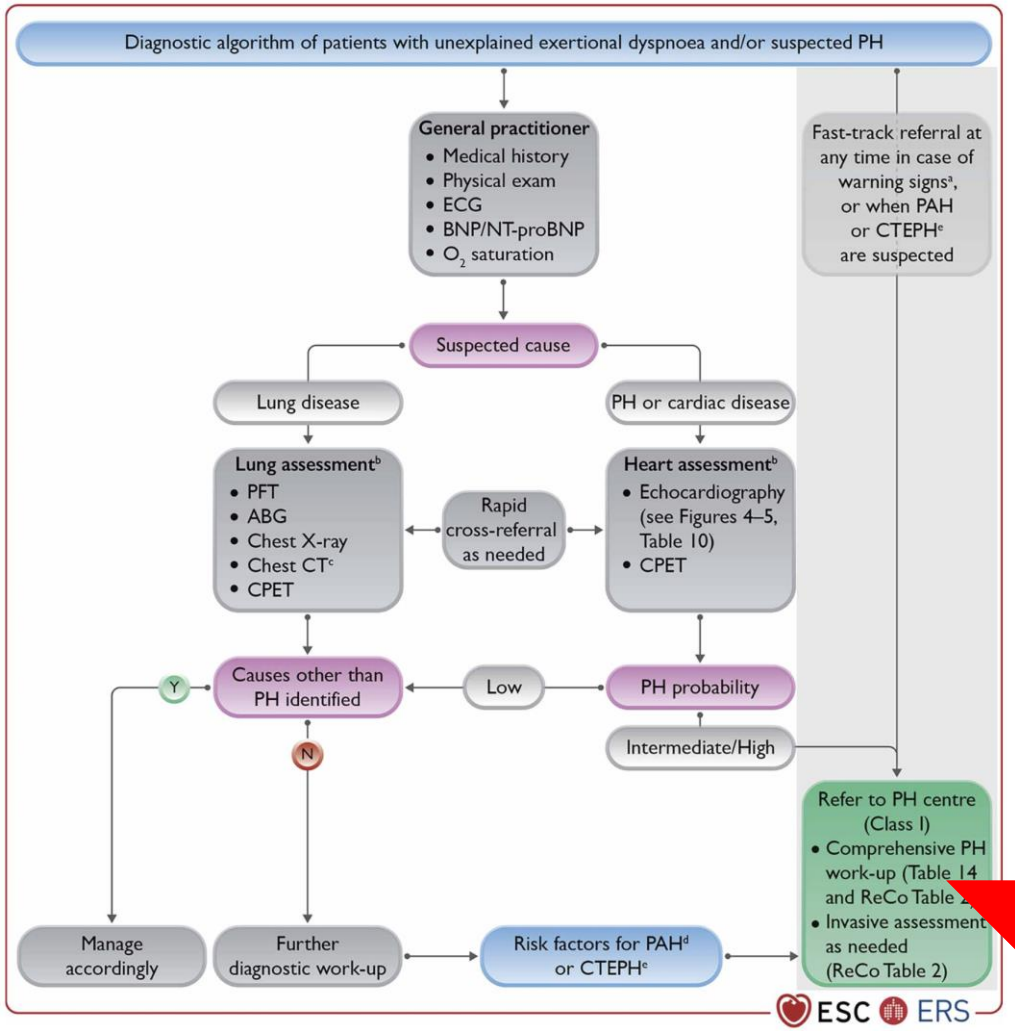
1. Galie N, *et al. Eur Heart J* 2016; 37: 67-119; 2. Frost A, *et al. Eur Respir J* 2019; 53:1801904; 3. Kiely DG, *et al. Pulm Circ* 2019; 9:2045894019841990.

Improving the detection of PH by adopting a multistep approach: ESC/ERS 2022 algorithm

STEP 1
Suspicion

STEP 2
Detection

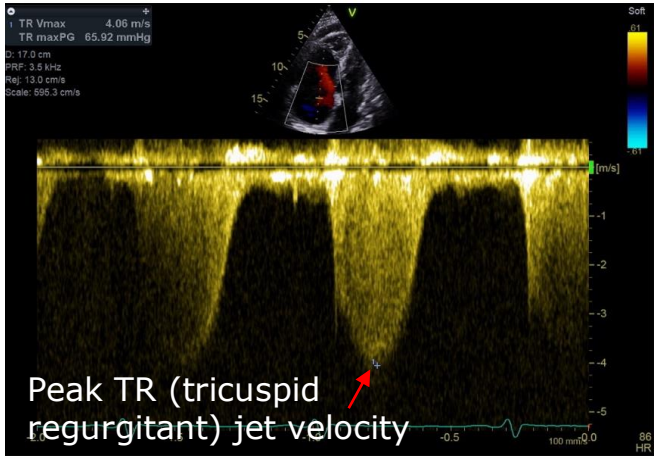
STEP 3
Confirmation

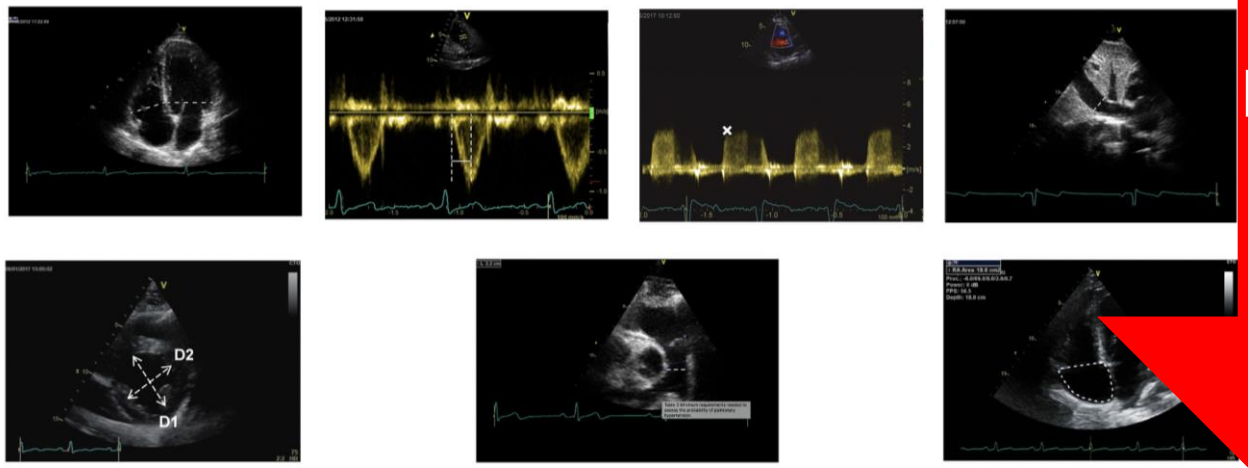


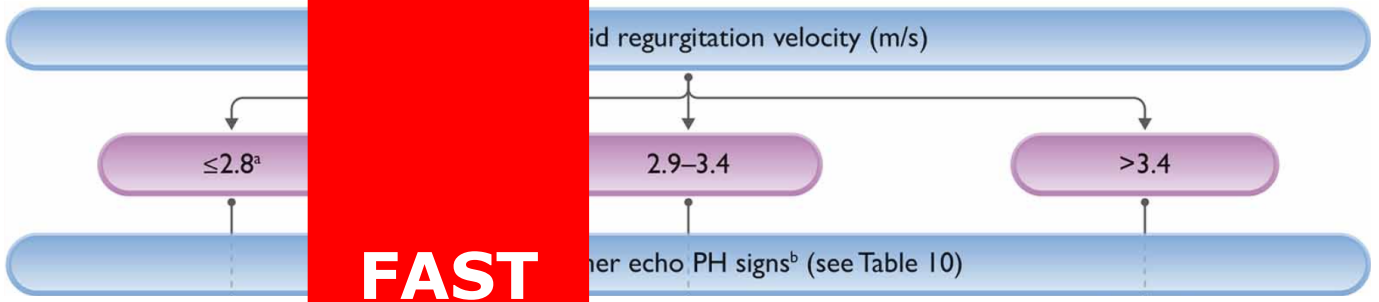
FAST TRACK REFER TO PH EXPERT

Humbert M, *et al. Eur Heart J* 2022; 00:1–114.

Echocardiography is recommended as first line imaging test if PH is suspected







FAST TRACK REFER TO PH EXPERT

A: The ventricles	B: Pulmonary artery	C: Inferior vena cava and RA
RV/LV basal diameter/ area ratio >1.0	RVOT AT <105 ms and/or mid-systolic notching	IVC diameter >21 mm with decreased inspiratory collapse (<50% with a sniff or <20% with quiet inspiration)
Flattening of the interventricular septum (LVEI >1.1 in systole and/or diastole)	Early diastolic pulmonary regurgitation velocity >2.2 m/s	RA area (end-systole) >18 cm^2
sPAP ratio 35 mm/mmHg	PA diameter >AR diameter	
	PA diameter >25 mm	

Humbert M, *et al. Eur Heart J* 2022; 00:1–114; Augustine D, *et al. Echo Res Pract* 2018; 5:G11-G24

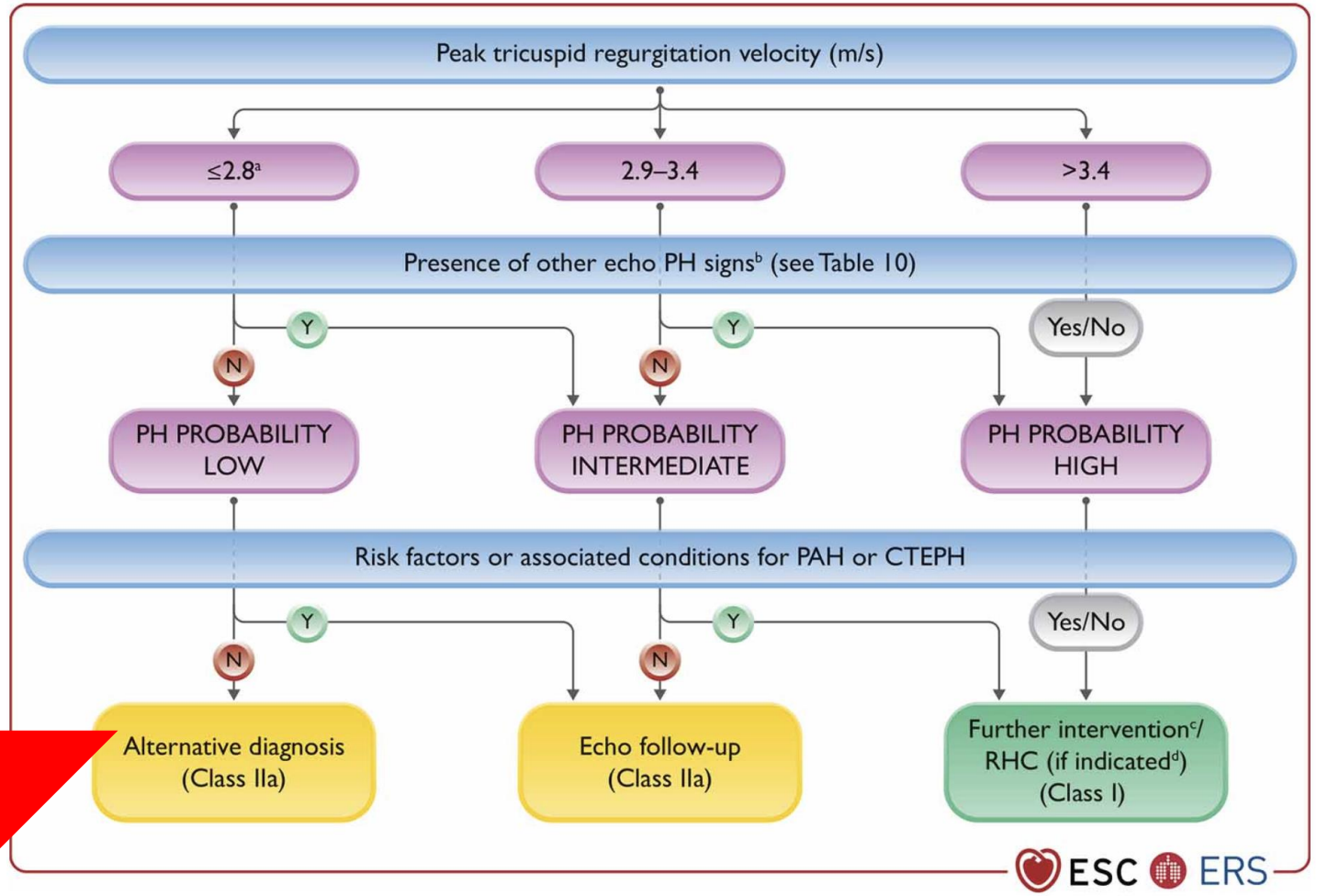
Using echocardiography probability to aid decisions for further assessment

Same thresho TRV as 2015 Guidelines

Presence of ot signs of PH

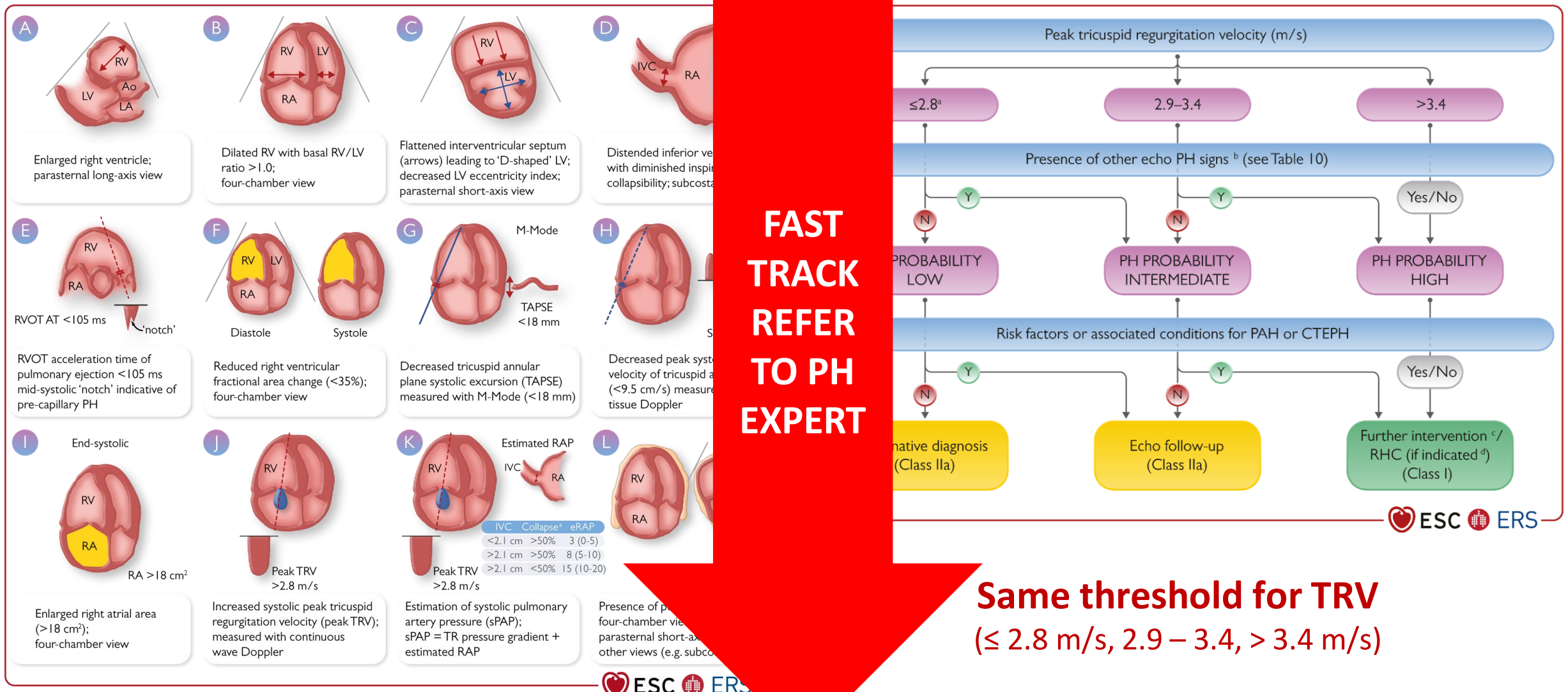
Risk factors t incorporated i assessment

FAST TRACK REFER TO PH EXPERT



Humbert M, *et al. Eur Heart J* 2022; 00:1–114.

Detection of Chronic PH by Echocardiography: 2022 ESC/ERS Guidelines for Pulmonary Hypertension



FAST TRACK REFER TO PH EXPERT

Same threshold for TRV

(≤ 2.8 m/s, 2.9 – 3.4, > 3.4 m/s)

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension (*European Heart Journal;* 2022 – doi: 10.1093/eurheartj/ehac237 and *European Respiratory Journal;* 2022 – doi: 10.1183/13993003.00879-2022)

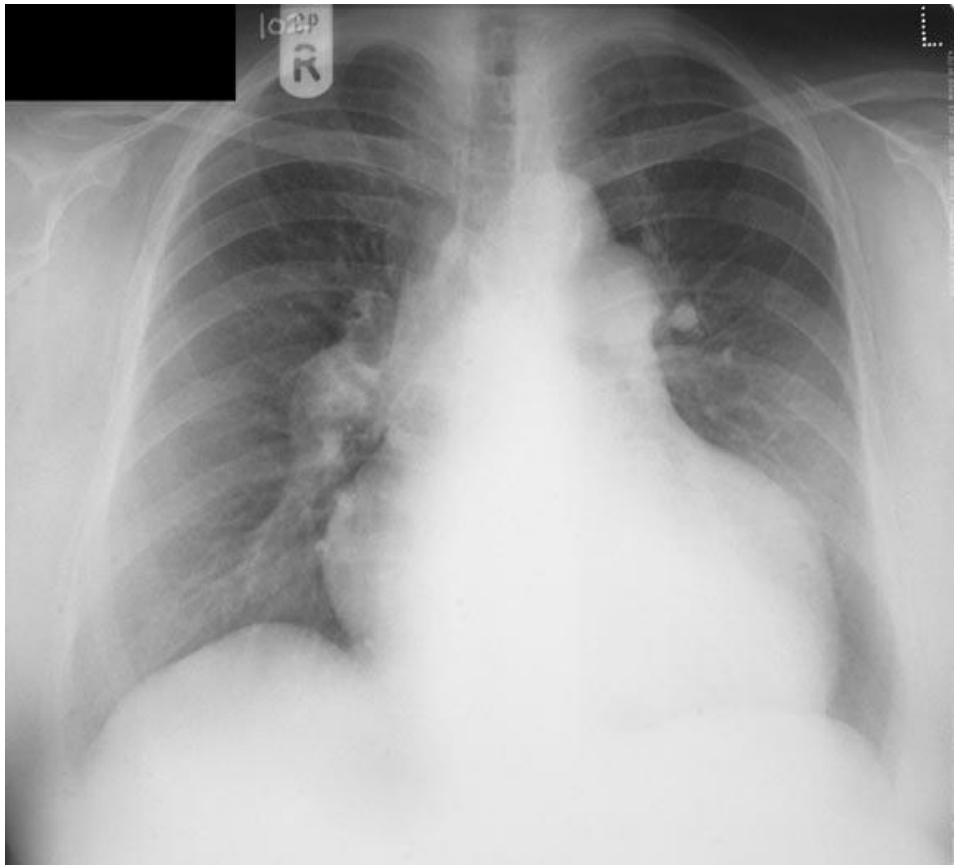
Detection of Chronic PH by Echocardiography: 2022 ESC/ERS Guidelines for Pulmonary Hypertension

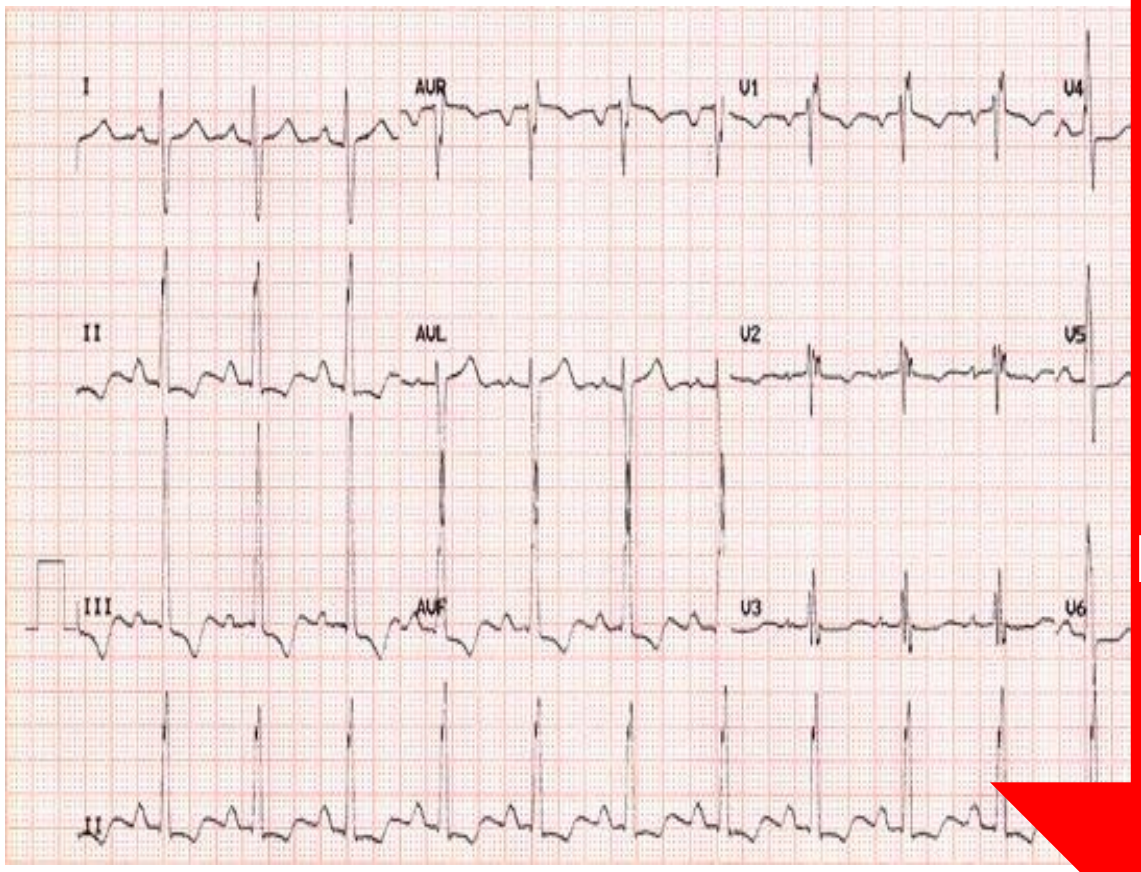
Additional echocardiographic signs suggestive of pulmonary hypertension

A: The ventricles	B: Pulmonary artery	C: Inferior vena cava and RA
RV/LV basal diameter/area ratio >1.0	RVOT AT <105 ms and/or mid-systolic notching	IVC diameter >21 mm with decreased inspiratory collapse (<50% with a sniff or <20% with quiet inspiration)
Flattening of the interventricular septum (LVEI >1.1 in systole and/or diastole)	Early diastolic pulmonary regurgitation velocity >2.2 m/s	RA area (end-systole) >18 cm^2
TAPSE/sPAP ratio <0.55 mm/mmHg	PA diameter > AR diameter PA diameter >25 mm	

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension (*European Heart Journal;* 2022 – doi: 10.1093/eurheartj/ehac237 and *European Respiratory Journal;* 2022 – doi: 10.1183/13993003.00879-2022)

CXR and ECG may suggest the diagnosis of pulmonary hypertension – ADD NT-PR0BNP !!!



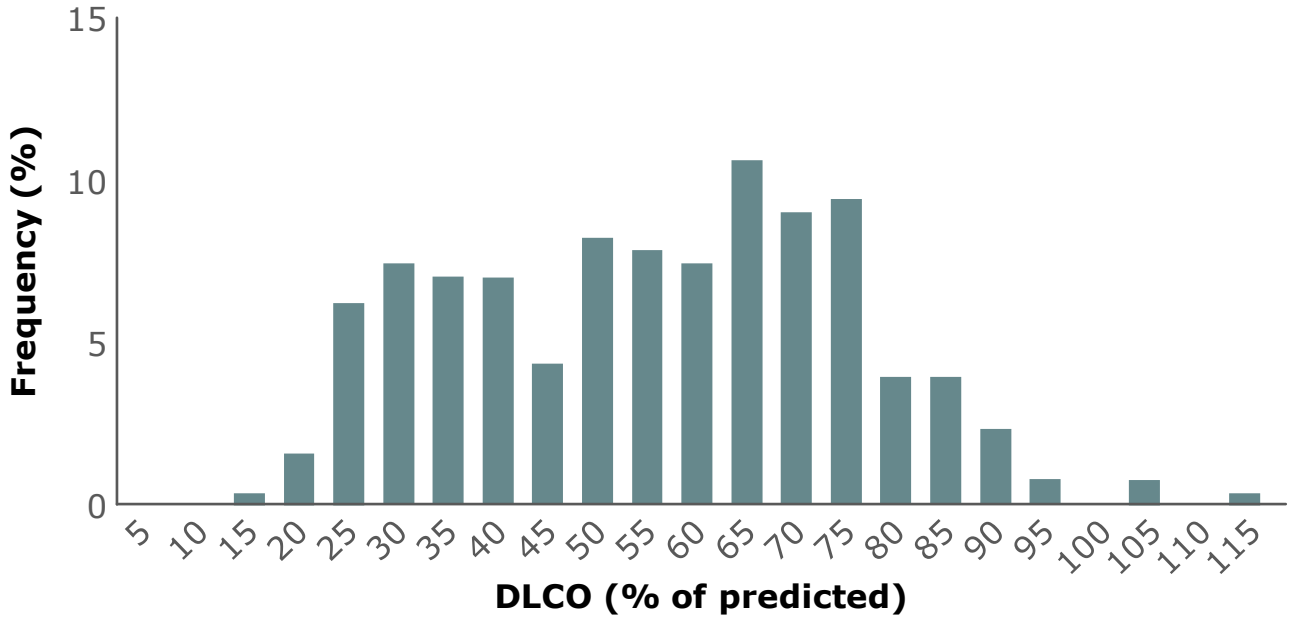


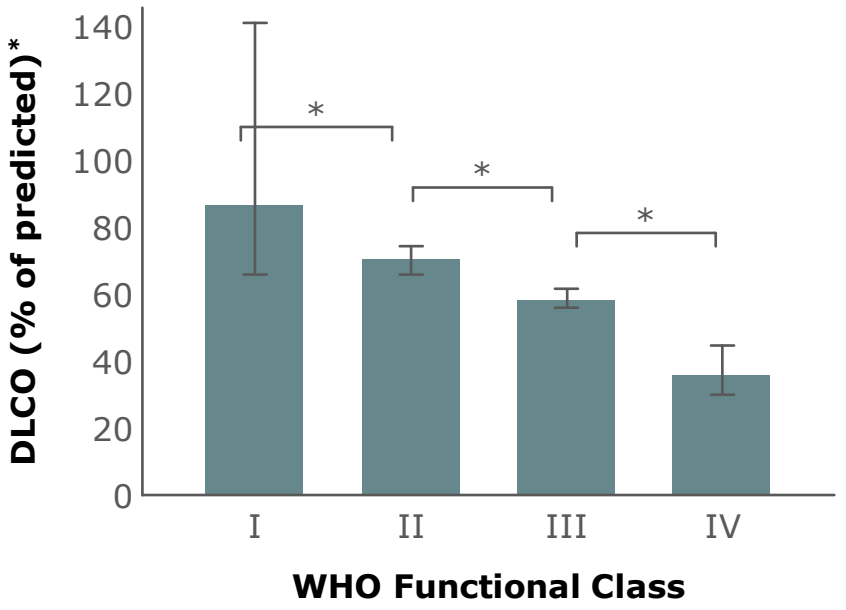
FAST TRACK REFER TO PH EXPERT

Humbert M, *et al. Eur Heart J* 2022; 00:1–114; Rich S, *et al. Ann Intern Med* 1987; 107:216–23.

Lung function testing with DLCO is recommended in the initial evaluation of patients with PH

Mildly reduced DLCO is common in classical IPAH and in PH correlates with disease severity



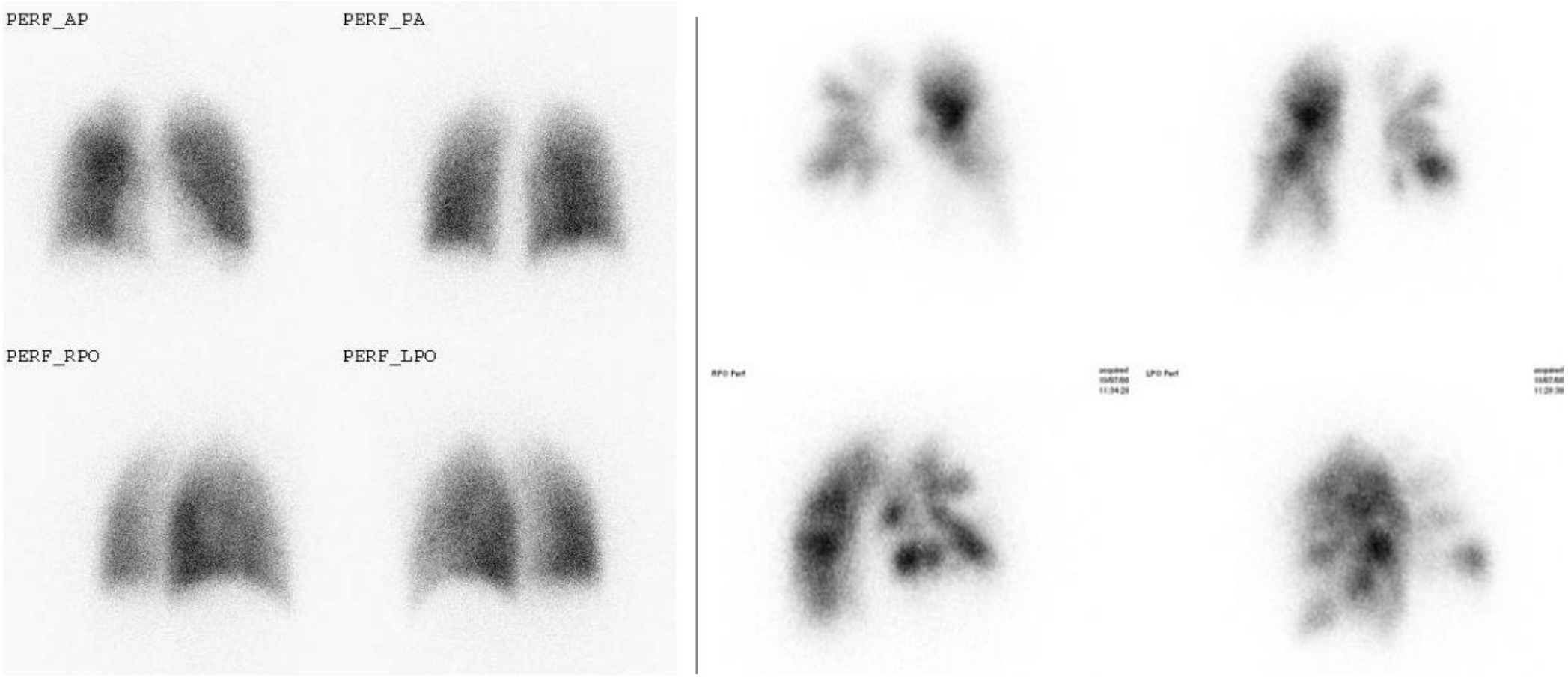


DLCO <45% should raise possibility of SSc or co-existing lung disease or PVOD

*Error bars are 95% CI. Dlco diffusion / transfer co-efficient for carbon monoxide; SSc systemic sclerosis; PVOD pulmonary veno-occlusive disease.

Humbert M, *et al. Eur Heart J* 2022; 00:1–114; Lewis RA, *et al. Eur Resp J* 2020; 55:2000041; Billings CG, *et al. Front Med* 2018; 5:1–10.

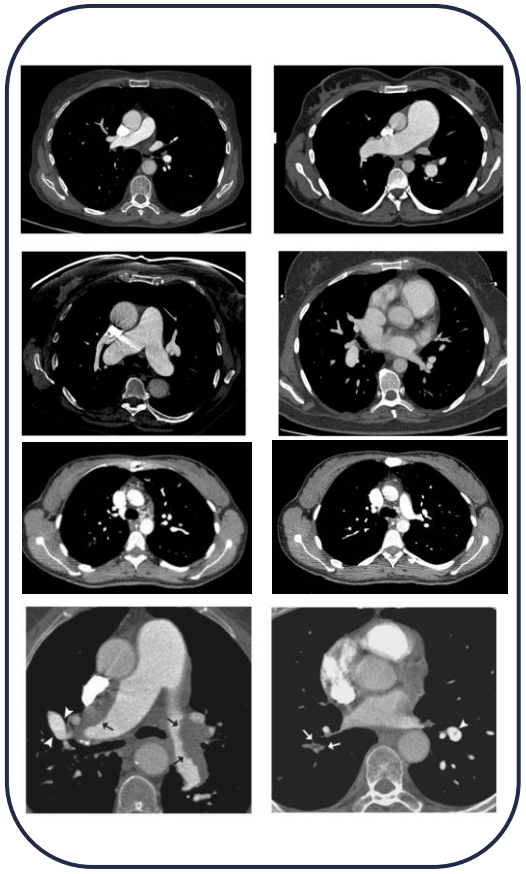
VQ or Q scanning is recommended to exclude CTEPH in unexplained PH (NOT CT PULMONARY ANGIO!!)



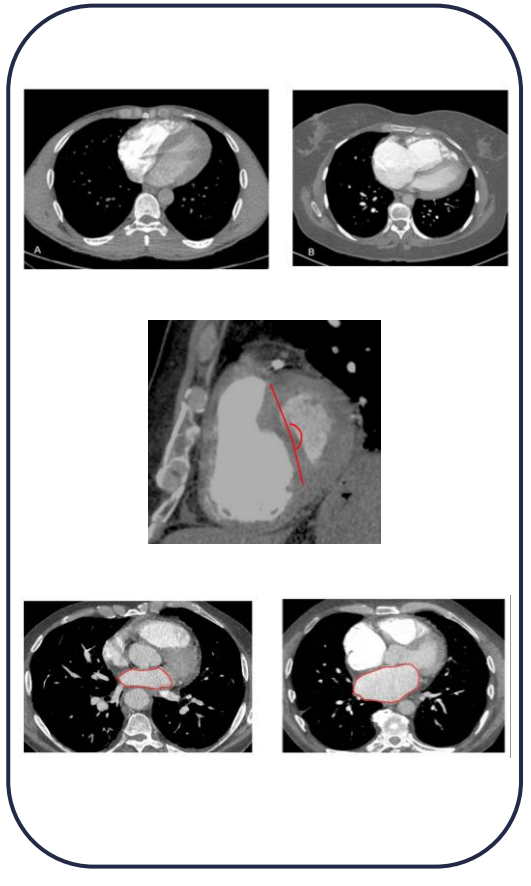
Tunariu N, *et al. J Nucl Med* 2007; 48:680-4; Humbert M, *et al. Eur Heart J* 2022; 00:1–114.

CT imaging in PH: Systematic approach

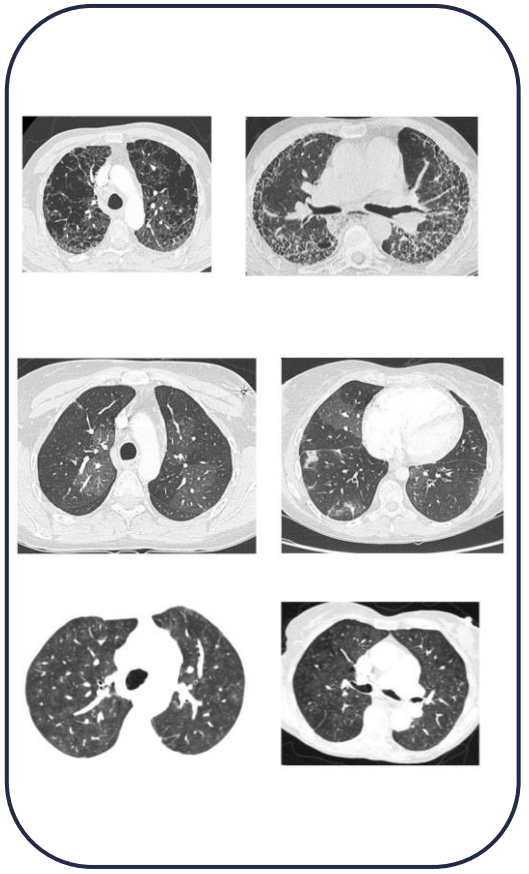
Vessels



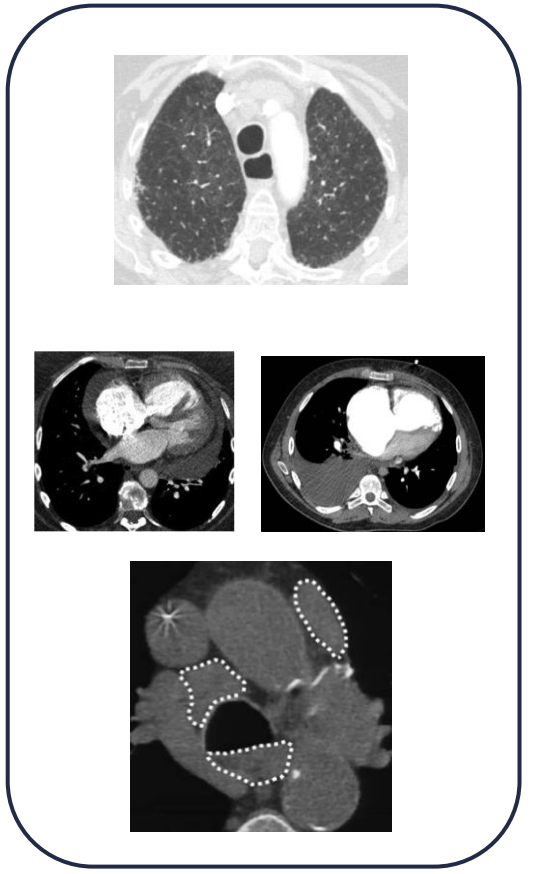
Cardiac chambers



Lungs



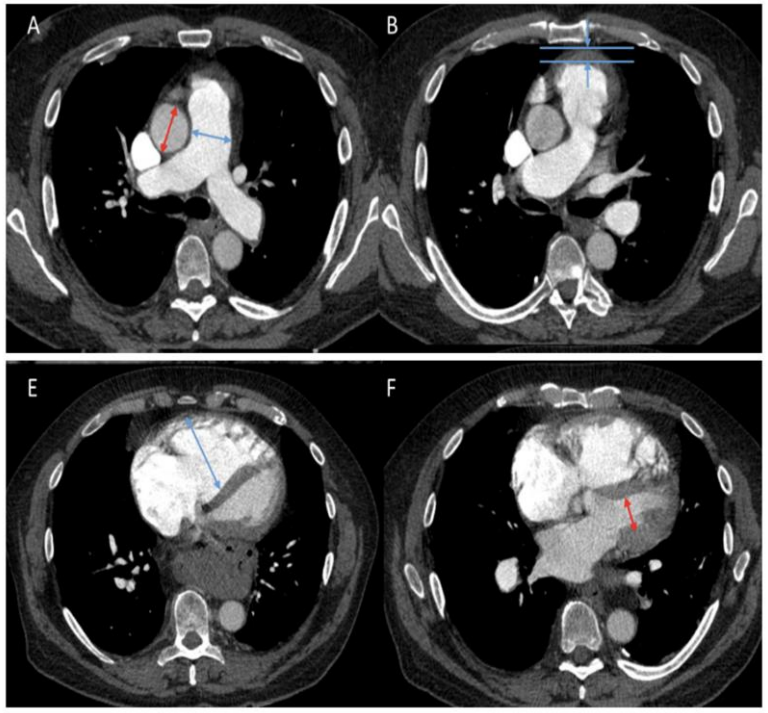
Mediastinum / other



Moore NR, *et al. Clin Radiol* 1988; 39:486-9, Devaraj A, *et al. Radiology* 2008; 249:1042-9; Condliffe R, *et al. Rheumatology* 2011; 50:1480-6; Lewis RA, *et al. Respirology* 2020; 25:1066-72; Castener E, *et al. Radiographics* 2009; 29:31-50; Swift AJ, *et al. Eur Radiol* 2020;30:4918-4929; Currie BJ, *et al. Int J Cardiol 2018; 260: 172-7;* Sherrick AD, et al. *Am J Roentgenol* 1997; 169:79-82; Kauczor HU, *et al. J Comput Assist Tomogr* 1994; 18:855-61.

Combining CT findings and integrating with the clinical picture

Probability of Pulmonary Hypertension

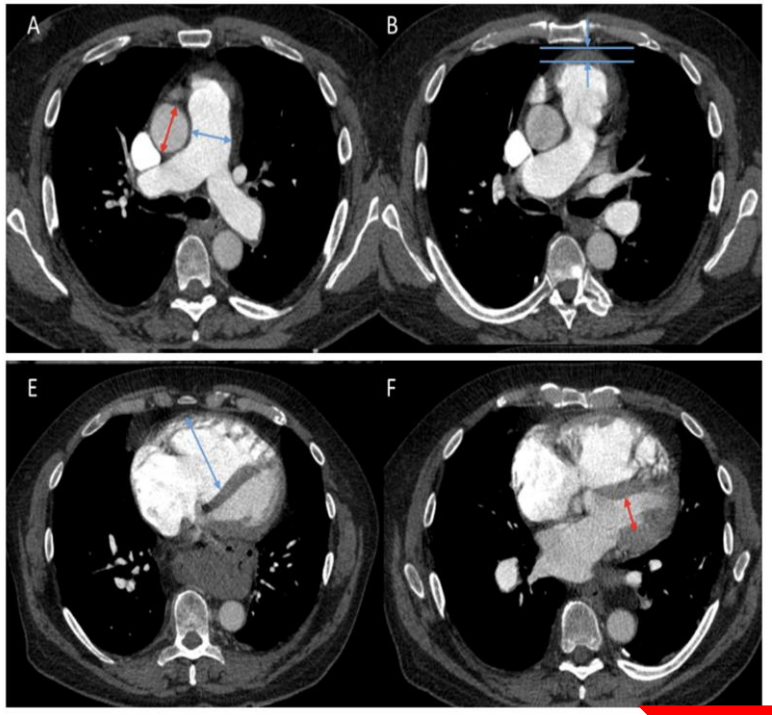


PA ≥30mm + RVOTH ≥6 mm and RV:LV ratio ≥1 highly predictive of PH

Swift AJ, *et al. Eur Radiol* 2020;30:4918-4929 Montani D, *et al. Eur Respir J* 2009; 33:189-200; Hadinnapola C, *et al. Circulation* 2017; 136:2022-33.

Combining CT findings and integrating with the clinical picture

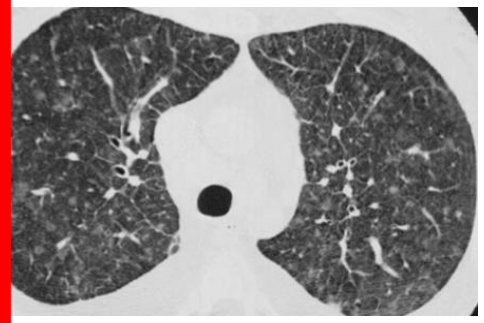
Probability of Pulmonary Hyperte

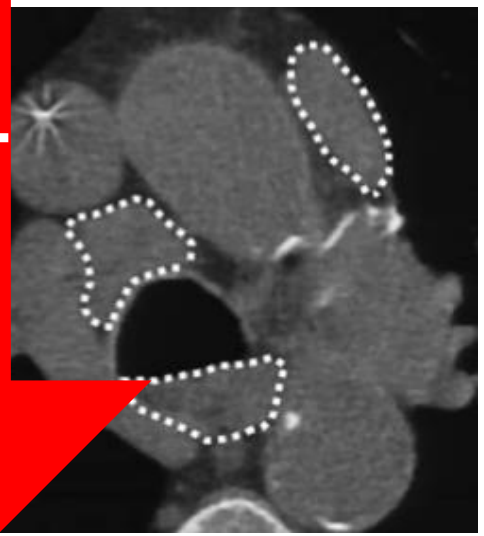


PA ≥30mm + RVOTH ≥6 mm and ratio ≥1 highly predictive of PH

FAST TRACK REFER TO PH EXPERT

ombining imaging data, physiology testing nd genetic testing





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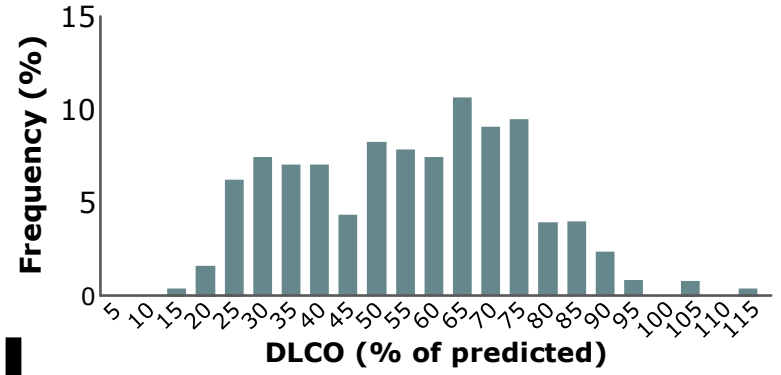
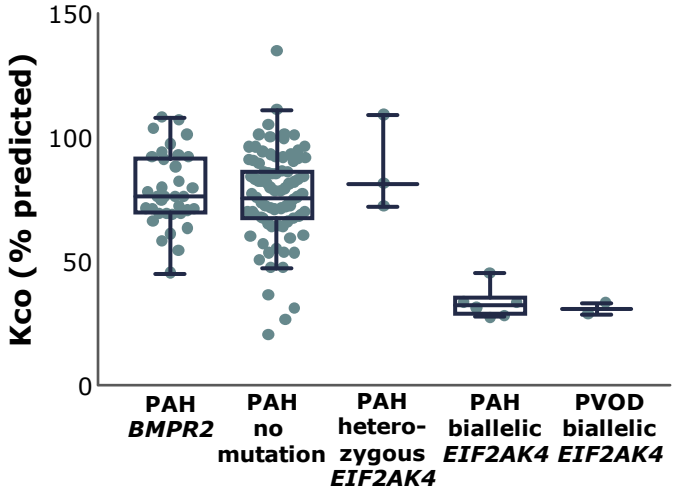
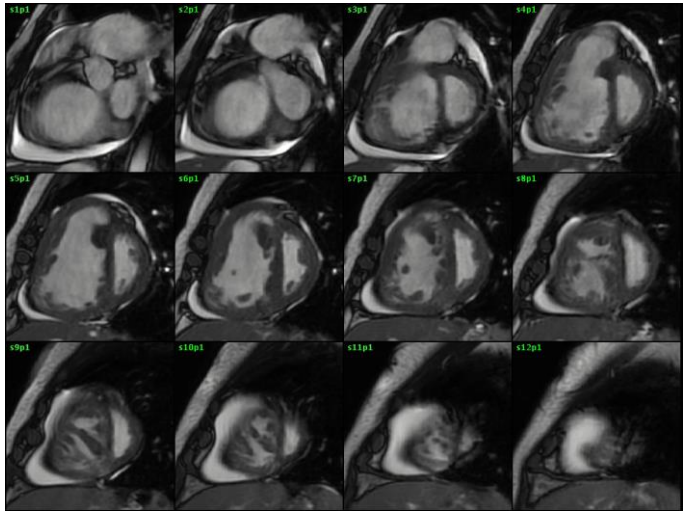
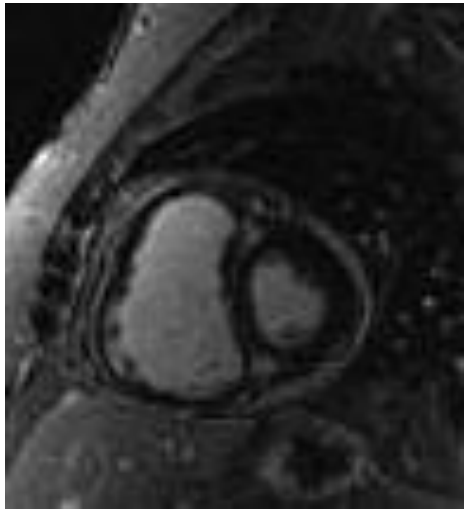
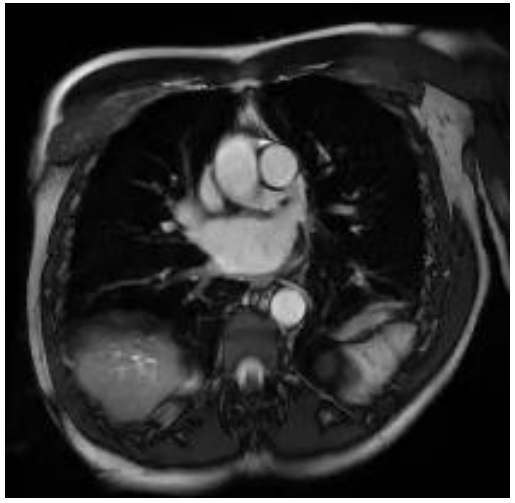
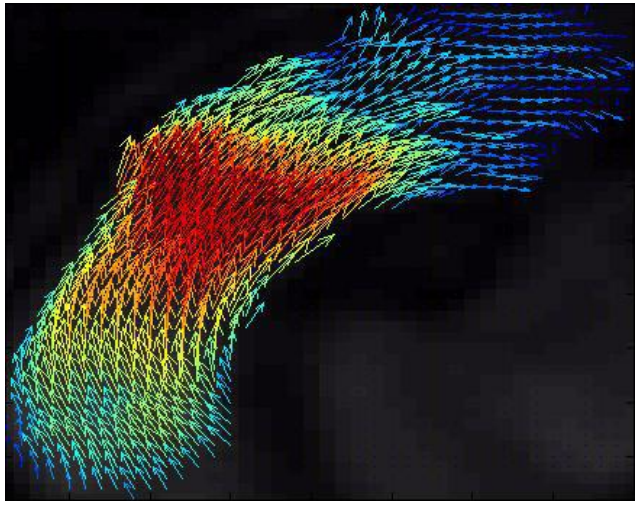
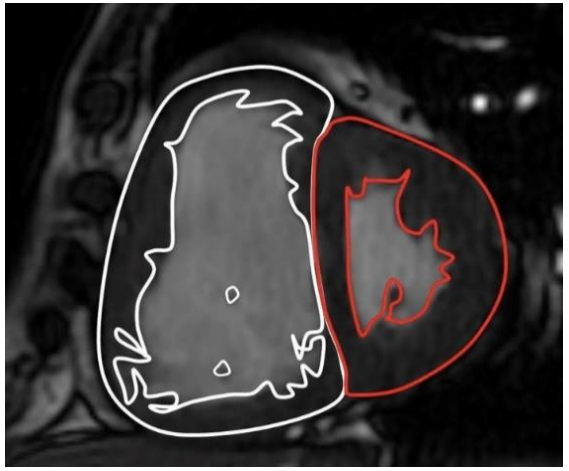
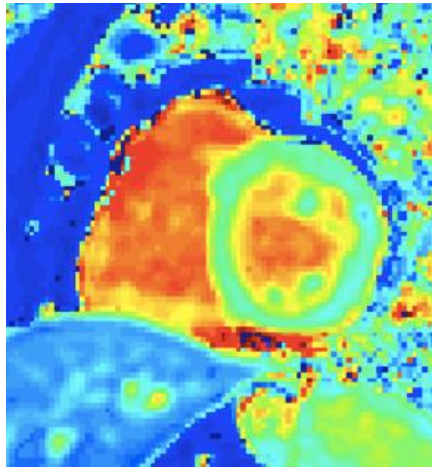
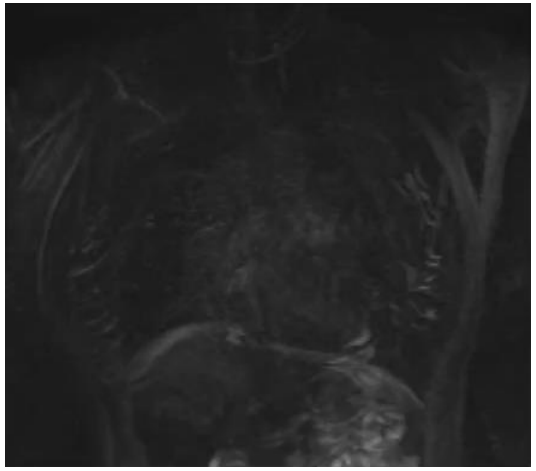
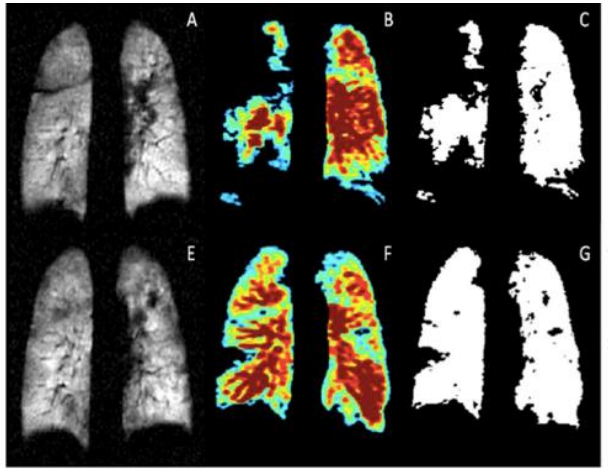
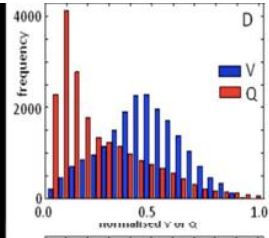


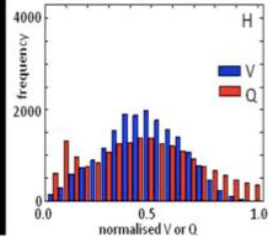


Swift AJ, *et al. Eur Radiol* 2020;30:4918-4929 Montani D, *et al. Eur Respir J* 2009 Hadinnapola C, *et al. Circulation* 2017; 136:2022-33; Kiely DG, *et al. Pulm Circ* 2019; 9:2045894019841990.

Emerging imaging modalities: MRI imaging provides a comprehensive cardiorespiratory assessment

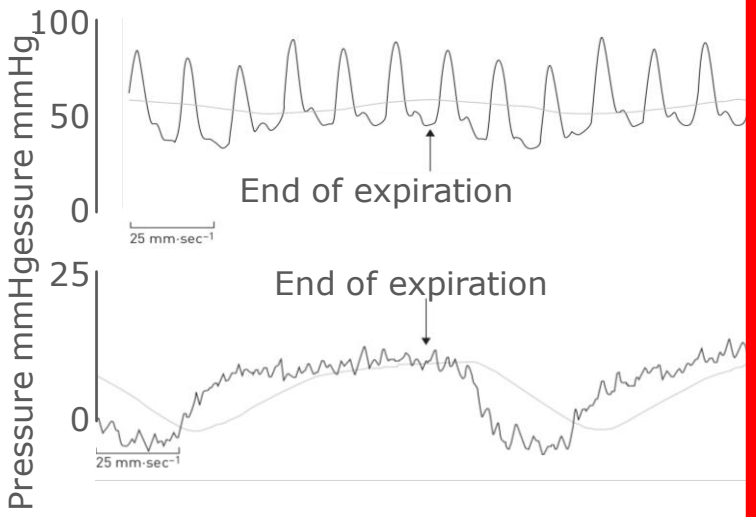













Van Wolferen SA, *et al. Eur Heart Journal* 2007; 28:1250-7; Van de Veerdonk MC, *et al. JACC* 2011; 58:2511-9; Saba T, *et al. Eur Resp J* 2001; 18:247; Swift AJ, *et al. Investigative Radiology* 2012; 47:571-7; Gan CT, *et al. Chest* 2007; 132:1906-12; McCann GP, *et al. Circulation* 2005;112:e268; Blyth KG, *et al. Eur Heart J* 2005; 26:1993-9; Sanz J, *et al. American Journal of Cardiology* 2007; 100:731-5*; Swift et al. JACC Cardiovasc imaging* 2017:1209-17, Swift AJ, *et al. Am J Crit Care Med* 2017; 196:228-39; Marshall H, *et al. Am J Respir Crit Care Med* 2014;190:e18-9; Swift AJ, *et al. J Cardiovasc Magn Reson* 2012; 14:40.

Confirming diagnosis of PH: RHC is the gold standard test for measurement of pulmonary artery pressure



Right heart catheterization: Best practice and

RHC is recommended to confirm the diagnosis of PH+ and to support treatment decisions

It is recommended that RHC be performed in experienced centres with a complete set o haemodynamic measurements

Vasoreactivity testing is recommended in patients with I/H/DPAH to detect patients wi treated with high does of CCBs[1]*

FAST TRACK REFER TO PH EXPERT

*Recommended that this be performed in PH specialist centers. + if it aids management decisions

1. Humbert M, *et al. Eur Heart J* 2022; 00:1–114; Rosenkranz S and Preston IR, *Eur Respir Rev* 2015; 24:642-52

2022 ESC/ERS Guidelines for Pulmonary Hypertension:

Mandatory Right Heart Catheterization

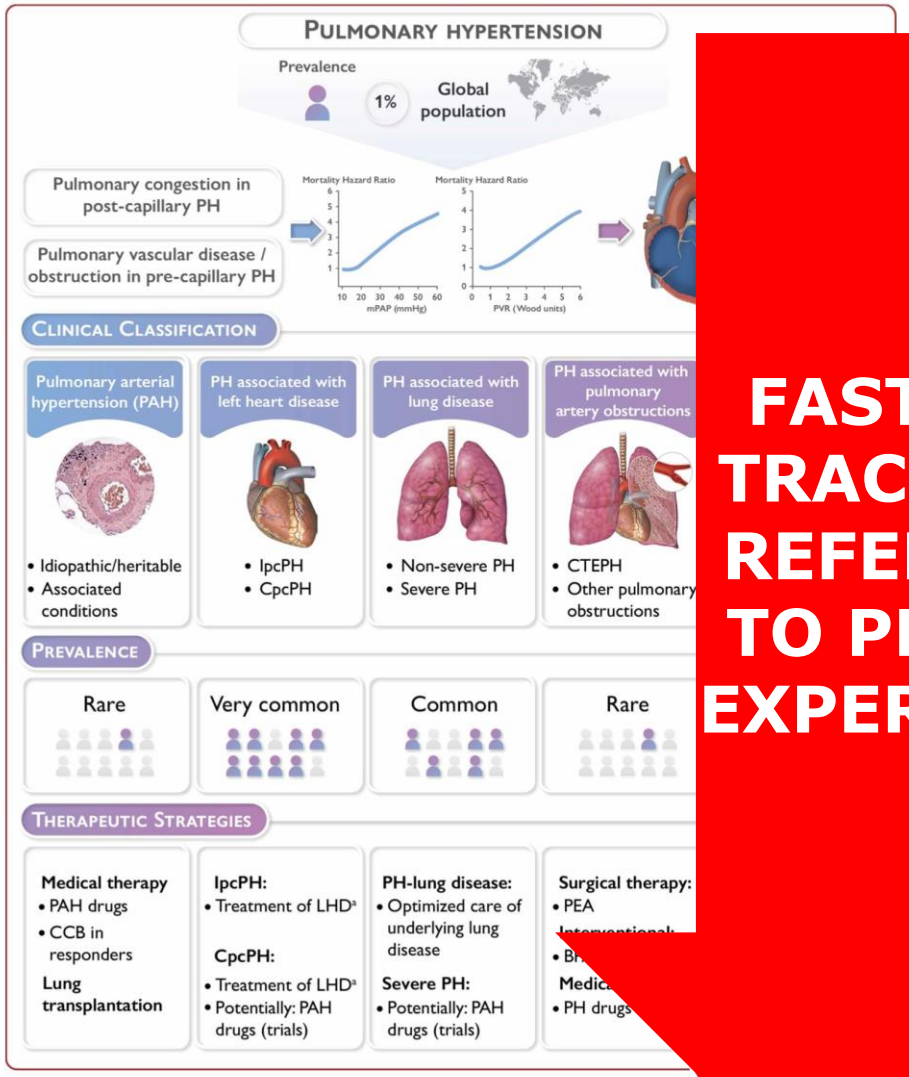
Recommendations	Class	Level
Right heart catheterizat		
RHC is recommended to	or CTEPH),	I	B
and to support treatme		
In patients with suspect	rm RHC in	I	C
experienced centres		
It is recommended that	amics, and	I	C
is performed following s		

Table 11 Haemodynamic measures obtained during right heart catheterization

Measured variables	Normal value
Right atrial pressure, mean (RAP)	2–6 mmHg
Pulmonary artery pressure, systolic (sPAP)	15–30 mmHg
Pulmonary artery pressure, diastolic (dPAP)	4–12 mmHg
Pulmonary artery pressure, mean (mPAP)	8–20 mmHg
Pulmonary arterial wedge pressure, mean (PAWP)	≤15 mmHg
Cardiac output (CO)	4–8 L/min
Mixed venous oxygen saturation (SvO_2)[a]	65–80%
Arterial oxygen saturation (SaO_2)	95–100%
Systemic blood pressure	120/80 mmHg
Calculated parameters	
Pulmonary vascular resistance (PVR)[b]	0.3–2.0 WU
Pulmonary vascular resistance index (PVRI)	3–3.5 WU·m^2
Total pulmonary resistance (TPR)[c]	<3 WU
Cardiac index (CI)	2.5–4.0 L/min·m^2
Stroke volume (SV)	60–100 mL
Stroke volume index (SVI)	33–47 mL/m^2
Pulmonary arterial compliance (PAC)[d]	>2.3 mL/mmHg

hypertension (*European Heart Journal;* 2022 –
doi: 10.1093/eurheartj/ehac237 and *European Respiratory Journal;* 2022 – doi: 10.1183/13993003.00879-2022)

Conclusion



FAST TRACK REFER TO PH EXPERT

- Despite advances in treatment significant delays to diagnosis exist
- Making the diagnosis of PH depends on systematically evaluating patients with breathlessness and screening high risk groups
- The likelihood, form and severity of PH can usually be established by combining investigations with clinical characteristics
- Algorithms provide a framework to improve diagnostic approaches and aid phenotyping
- Specialist PH centres can rapidly assess patients, make informed treatment decisions and provide support for patients and families

Humbert M, *et al. Eur Heart J* 2022; 00:1–114.

PULMONARY HYPERTENSION CLINIC

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