Case presentation

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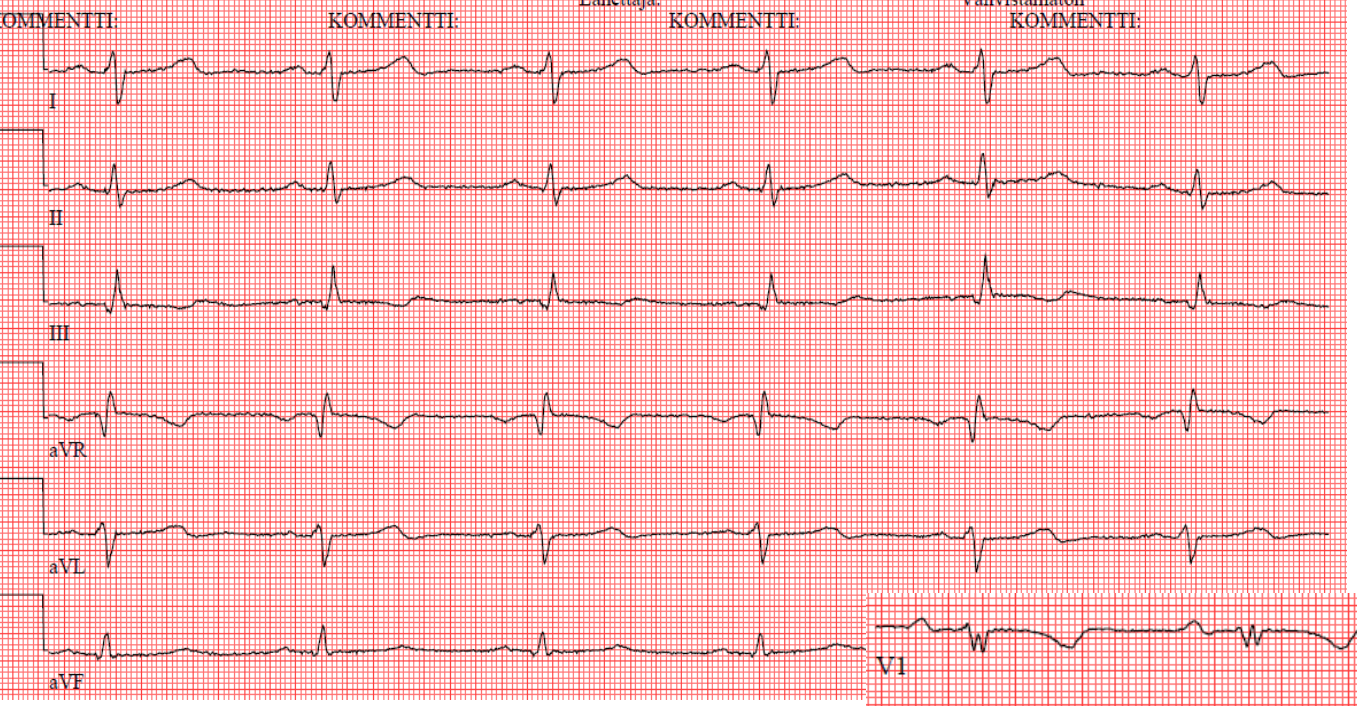
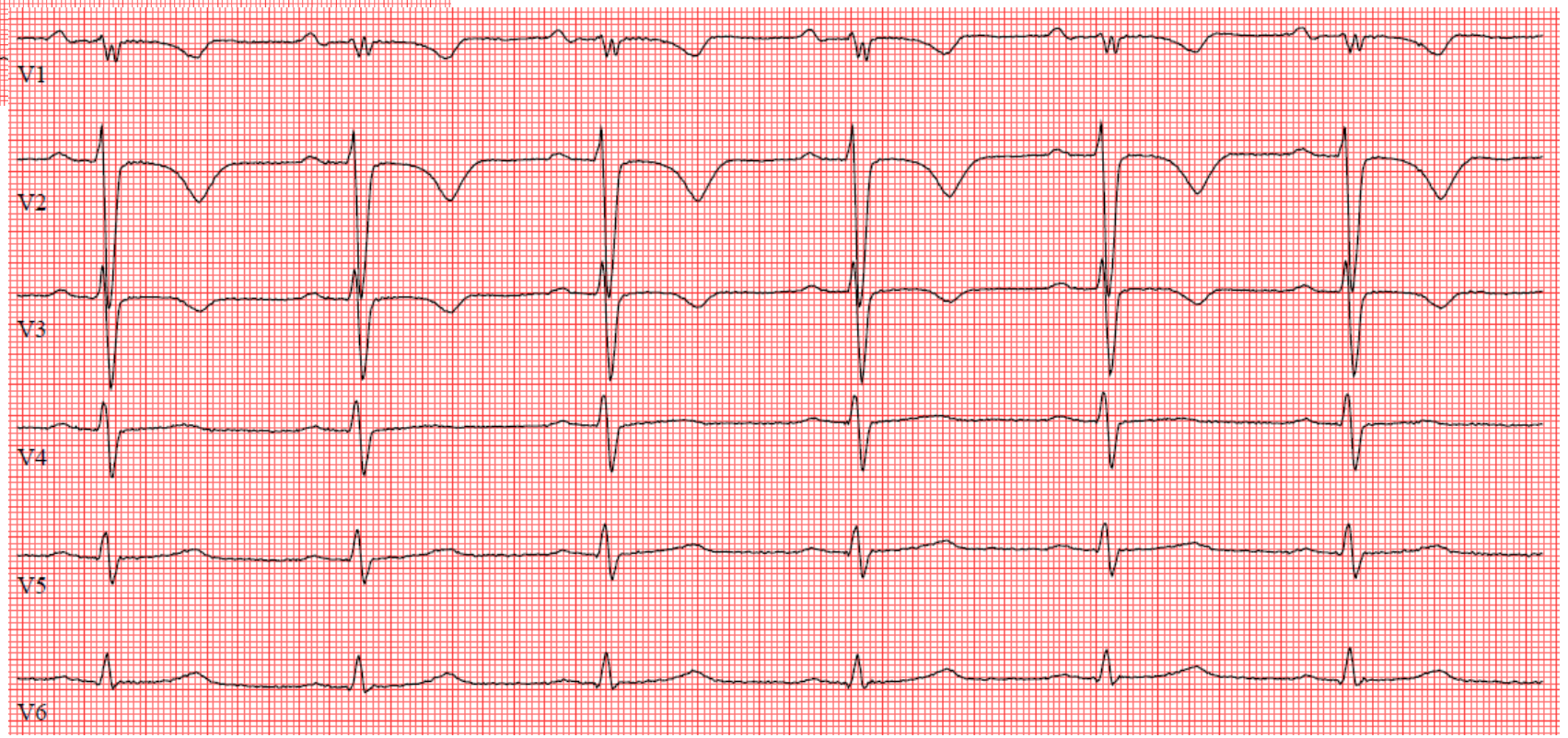
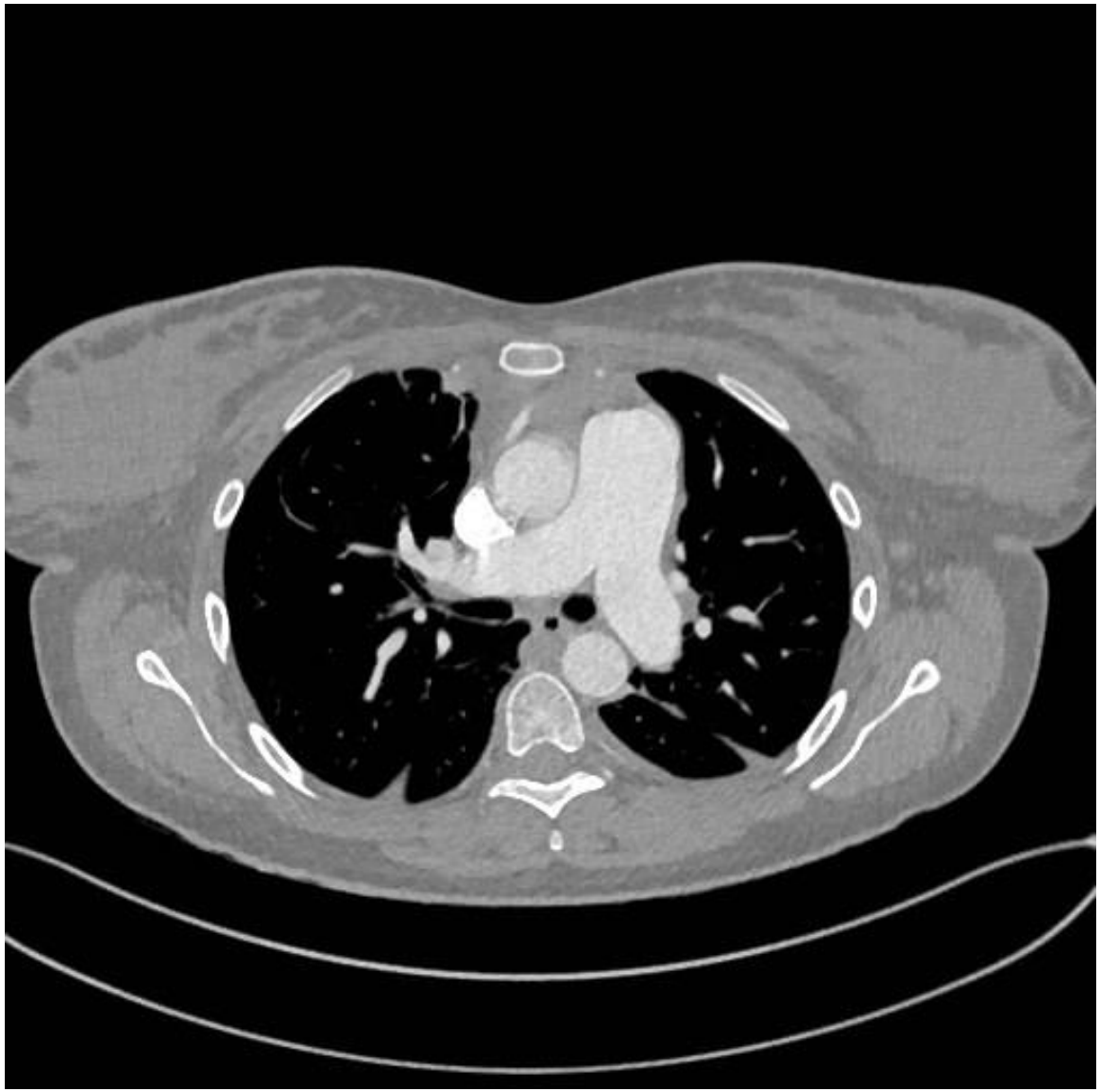
- 27y old woman, diagnosed earlier with depression (citalopram only medication)
- Her (twin) pregnancy was complicated with pre-eclampsy, she is admitted to hospital (labor ward) and eventually urgent ceasarean section is performed on week 35
- After the cesasarean section she shows signs of dyspnea and lowered oxygen saturation 90-93%

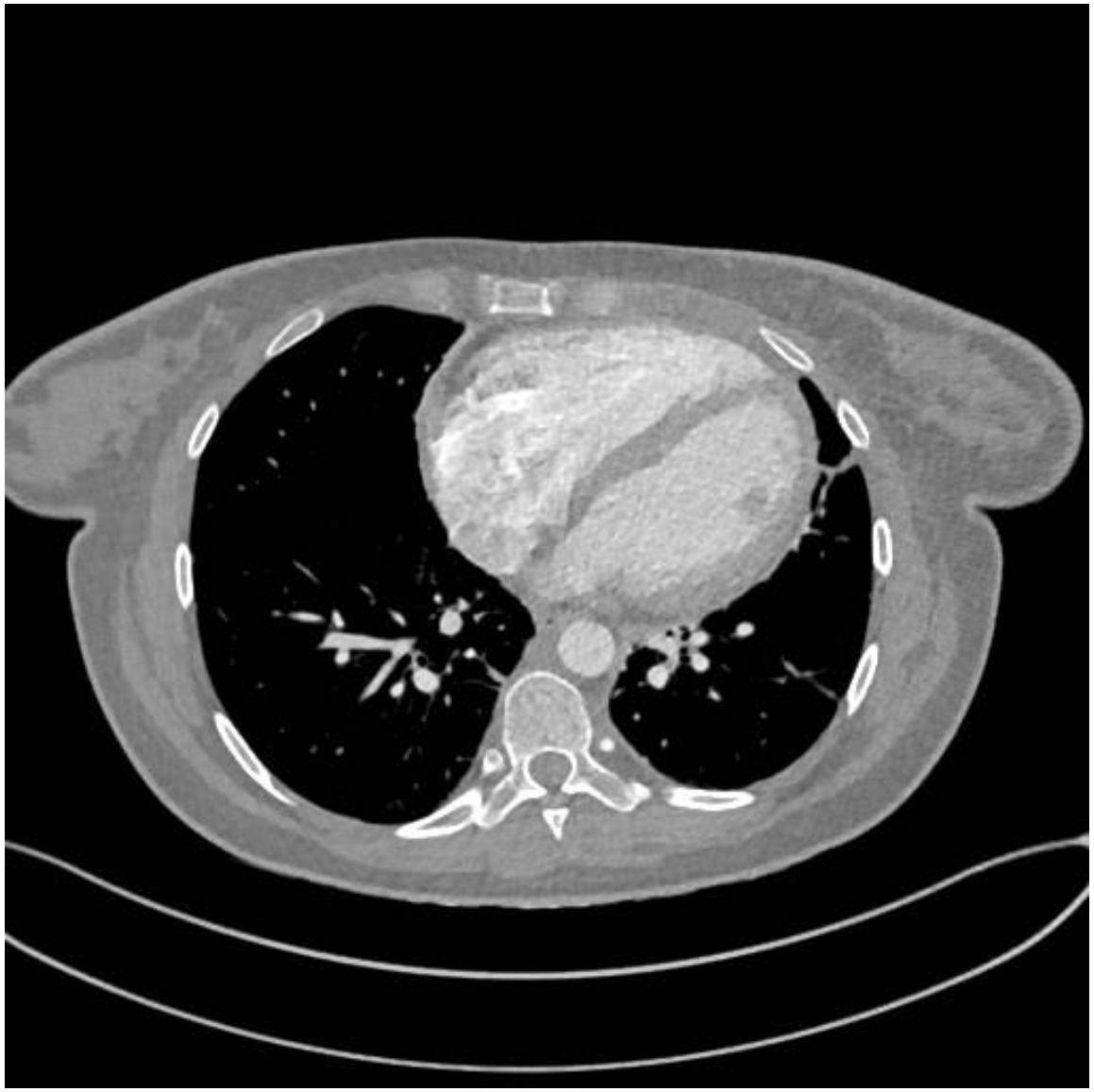
- Blood tests: normosytic anemia Hb 83g/l, leuc 8.8 E9/l, elevated proBNP 2000 ng/l, CRP 120 mg/l, hypoalbuminemia 17.6 g/l, D-dimer 2.8 mg/l
- Treatment with labetalol, antibiotic, later diuretic





RV-strain (T-wave inversion in right-sided precordial leads V1-V3)



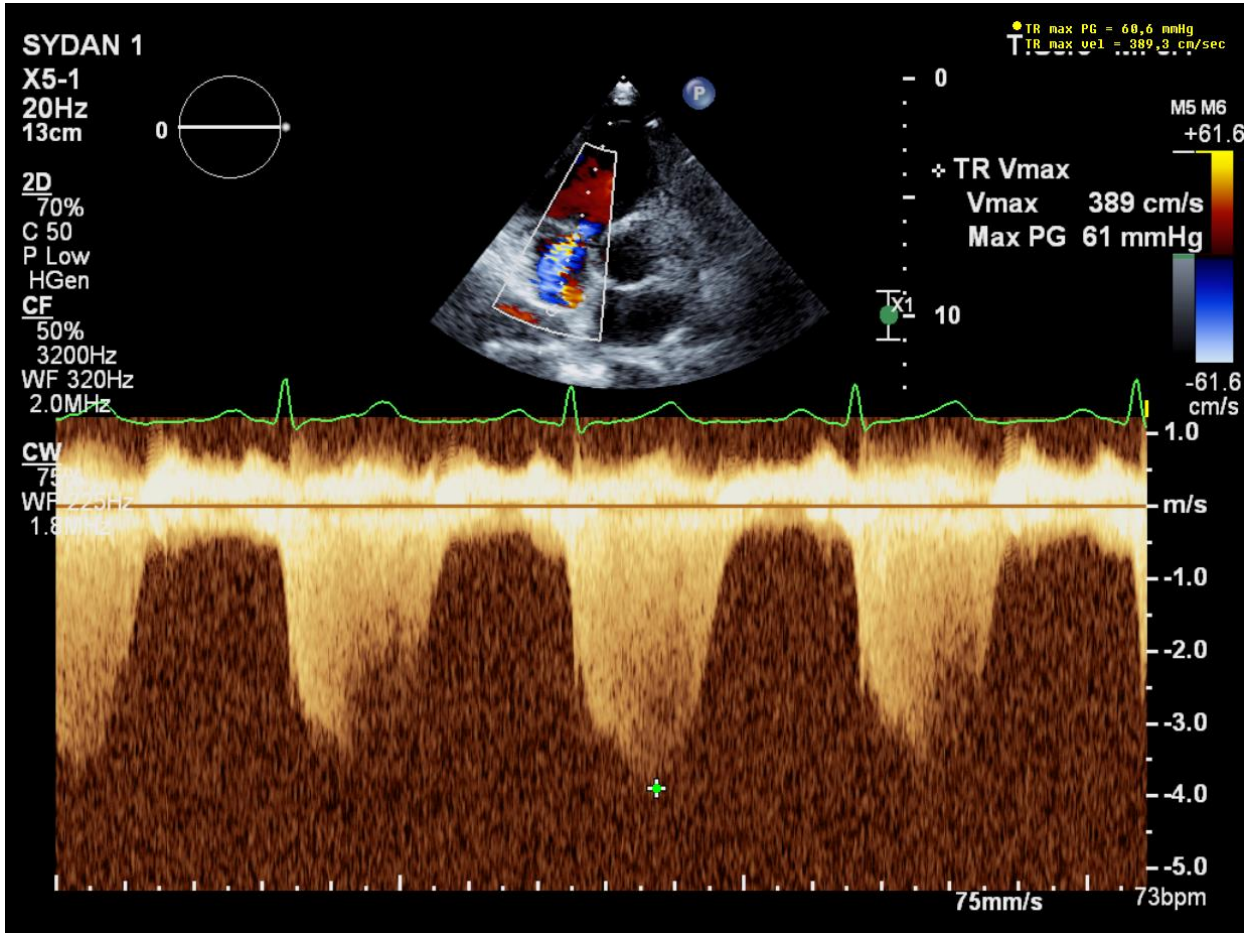


CT

- No signs of pulmonary embolism (PE)
- Enlarged pulmonary trunk, diameter 3.6cm
- Straightening of the interventricular septum
- Enlarged right atrium/ventricle
- Basal bilateral pleurar fluid/effusion, 1.8cm on the left and 1.5cm on the right side
- Slightly enlarged bilateral axillary lymph nodes, largest ones 1.-1.4cm

Echocardiogram

- Pulmonary trunk enlargement, RA and RV enlargment, straightening of IV septum, but normal RV-function and RV wall thickness was normal
- Basal septum was 12mm, lateral wall 8mm, the first ECHO showed signs of marginal pericardial fluid (at first also suspicion of also marginal lateral wall thickening and elevated filling pressures)
- Tricuspid regurgitation (TR) with substantial peak velocity/RV-RA gradient, indicating increased pulmonary arterial pressure
- Also pulmonary flow parameters indicative of elevated pulmonary artery pressure
- The latter ECHO showed normal LVEF, LVEDD, LA, normal diastolic function/LV filling pressures, no significant aortic/mitral valve disease
- MRI still showed mild septal hypertrophy, but no other clear signs inflammatory, other myocardial disease or congenital heart disease (CHD)



TR Vmax 3.89m/s (PH probability high if > 3.4 m/s)
TR systolic PG 61mmHg (4xTRV2)
TR PG = sRVP (= sPAP) – RAP (= CVP)
sPAP =TR PG + CVP
CVP estimated from IVC diameter and degree of collapse during inspiration/sniffing

Table 8A Echocardiographic probability of pulmonary hypertension in symptomatic patients with a suspicion of pulmonary hypertension

Peak tricuspid regurgitation velocity (m/s)	Presence of other echo 'PH signs'[a]	Echocardiographic probability of pulmonary hypertension
≤2.8 or not measurable	No	Low
≤2.8 or not measurable	Yes	Intermediate
2.9–3.4	No	
2.9–3.4	Yes	High
>3.4	Not required	

Right heart catetrisation (RHC) and vasoreactivity testing

- Why? Confirmation of PH, severity of PH, to clarify if the etiology is pre- or postcapillary PH and to guide treatment for certain PAH subtypes (vasoreactivity testing)
- mPAP 62/28/40mmHg, CO 4.15 l/min, PCWP 15mmHg, CVP 8mmHg, PVR 6.26 WU

- mPAP (mean pulmonary arterial pressure) 40mmHg is clearly elevated (≥25mmHg)
- PCWP (pulmonary capillary wedge pressure, a surrogate of filling pressure/LA pressure) within normal range (≤15mmHg)
- PVR (pulmonary vascular resistance) elevated = (PAPm – PCWP)/CO > 3WU

- Confirmation of PH (PAPm clearly ≥ 25mmHg), confirmation of increased PVR, but within normal range PCWP (left sided filling pressure), meaning that the cause of the elevated PH is increased PVR and not left heart disease (passive backward transmission of elevated LV filling pressures)
- No clear vasoreactivity to inhaled nitric oxygen (NO)
- Main conclusion: RHC confirmed precapillary PH

- medical history: no family history of PH, maybe signs of dyspnea/fatigue during exercise already years before, no prior severe illness or general symptoms
- status: mildly elevated body temperature (only 1 day >38C), dyspnea during walking, oxygen saturation (91-94%)
- The proteinuria and hypertension was normalized
- First lab tests on the cardiac ward: Hb 99 (MCV 88), leucopenia 2.0 E9/l, neutropenia 0.4-1.4 E9/l, lymphopenia 0.6-1.1 E9/l, elevation of CRP 29-66-33mg/l and ESR 121mm/h, slightly low C3 0.66 g/l, C4 0.1 g/l.
- Pleural puncture: Pf-prot elevated 59.7 (exudate), leuc 3895 (80% mononuclear), LD 163, no bacteria

PH etiology?

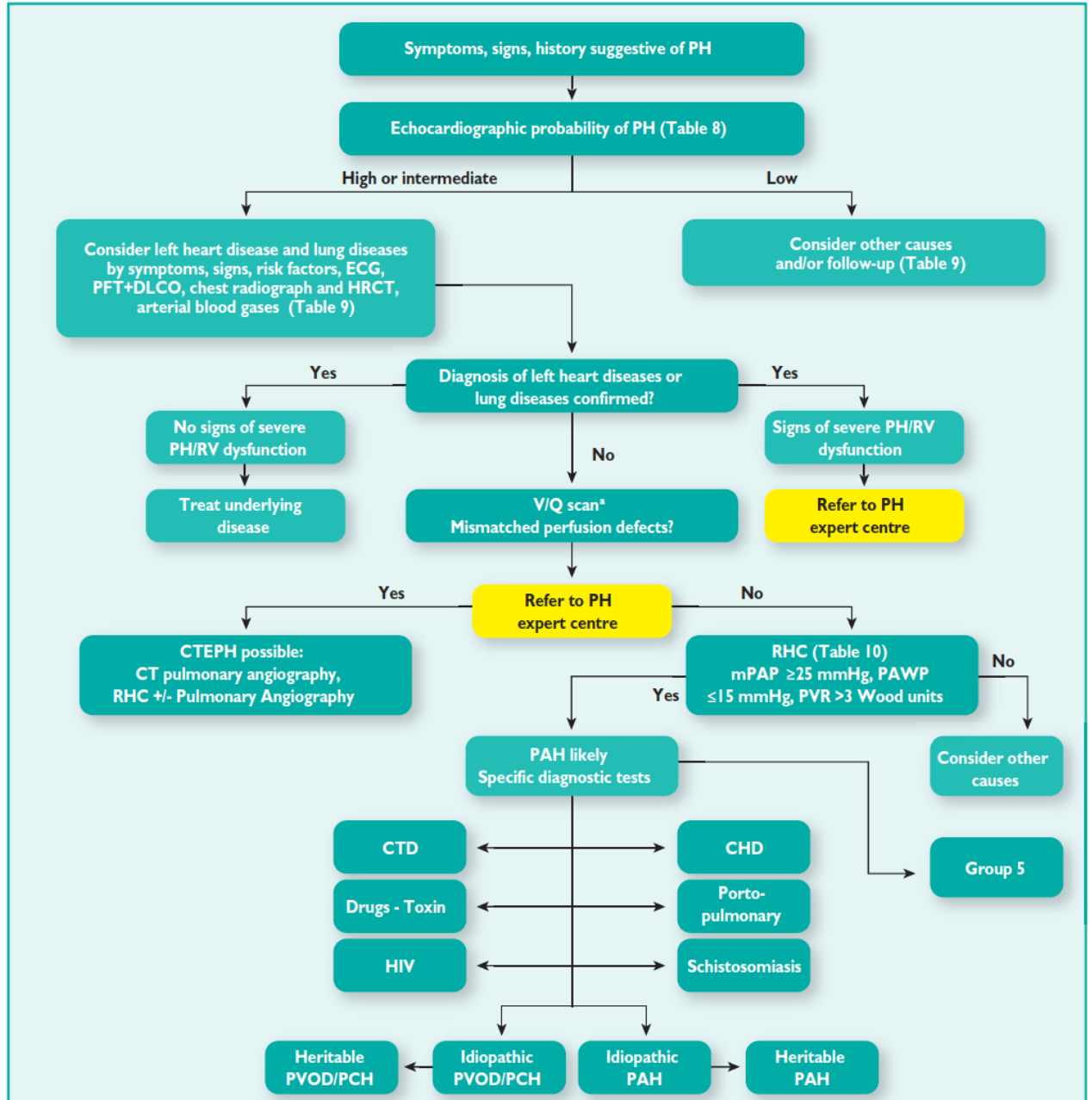
- 1. PAH (pulmonary arterial hypertension)
- 1.1. idiopatic (IPAH), 1.2. heritable (HPAH), 1.3 drugs and toxins induced (DPAH), 1.4 associated with (APAH): CTD, HIV, PoPH, CHD, Schistosomiasis
- 1’. PVOD and/or PCH (pulmonary veno-occlusive disease and pulmonary capillary hemangiomatosis), 1’’. (persistent PH of the newborn)
- 2. PH due to left heart disease (PH-LHD: HFrEF, HFpEF, valvular disease..)
- 3. PH due to lung diseases and/or hypoxia
- 4. CTEPH (thromboembolic)
- 5. PH with unclear/multifactoral mechanisms

- Class 2 is the only postcapillary PH, i.e. develops in response to a passive backward transmission of elevated left-sided filling pressures

- mild fever, normocytic anemia, leucopenia, elevation of inflammation parameters (CRP, ESR), low complement levels, exudative pleural effusion
- PAH
- Finally, a very high titer of speckled antinuclear antibody (ANA) pattern was verified (> 1:5000)
- Further analysis showed strong reaction of antibodies to Ribonucleoproteins RNP-70kD, RNP-A, RNP-C, to Sm-proteins (”Smith”) SmB, SmD and histone-proteins, but no antibodies to DNA, SSA/SSB, scleroderma-70 or sentromere. RF negative.

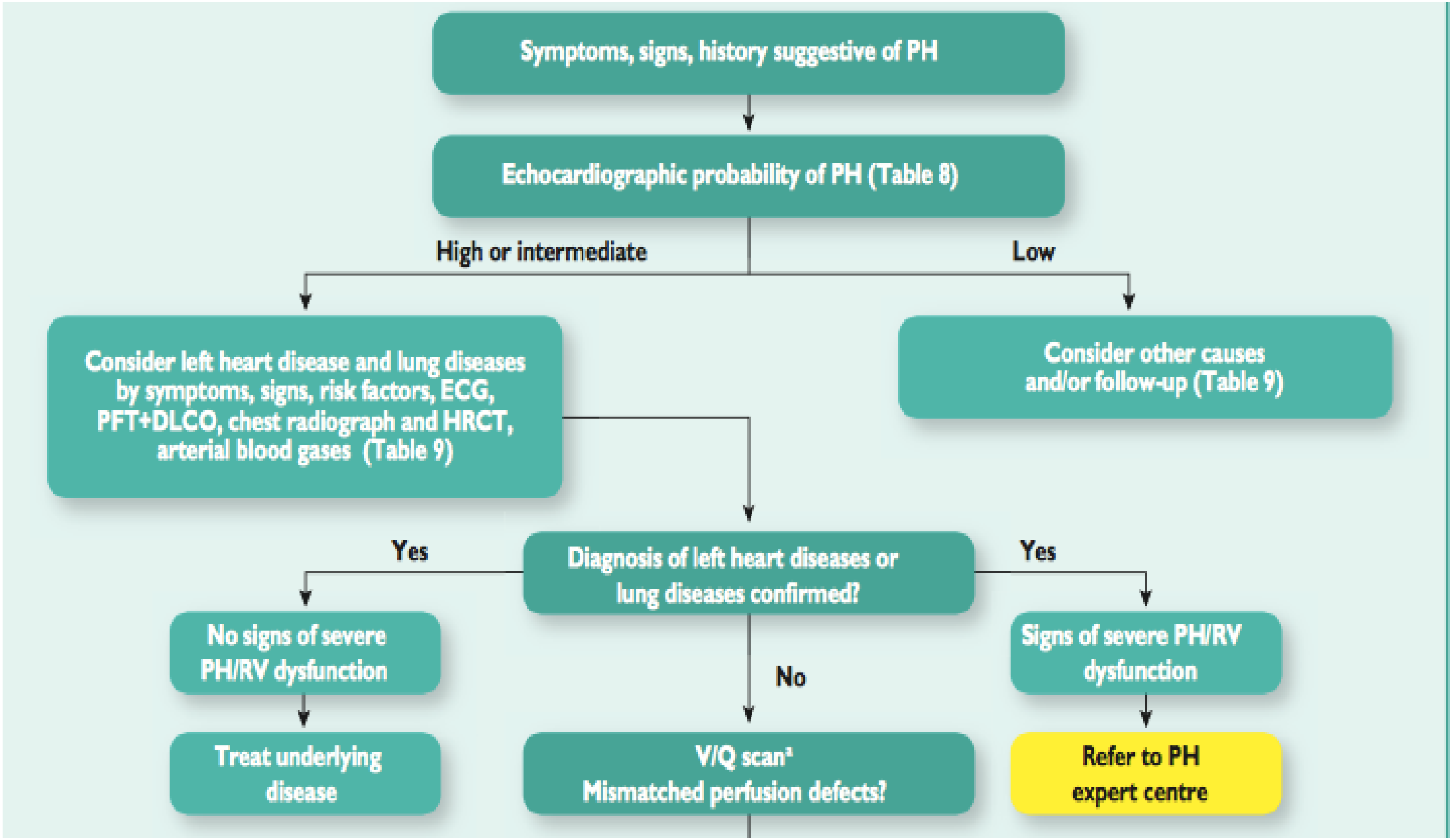
Final diagnosis (?) and treatment

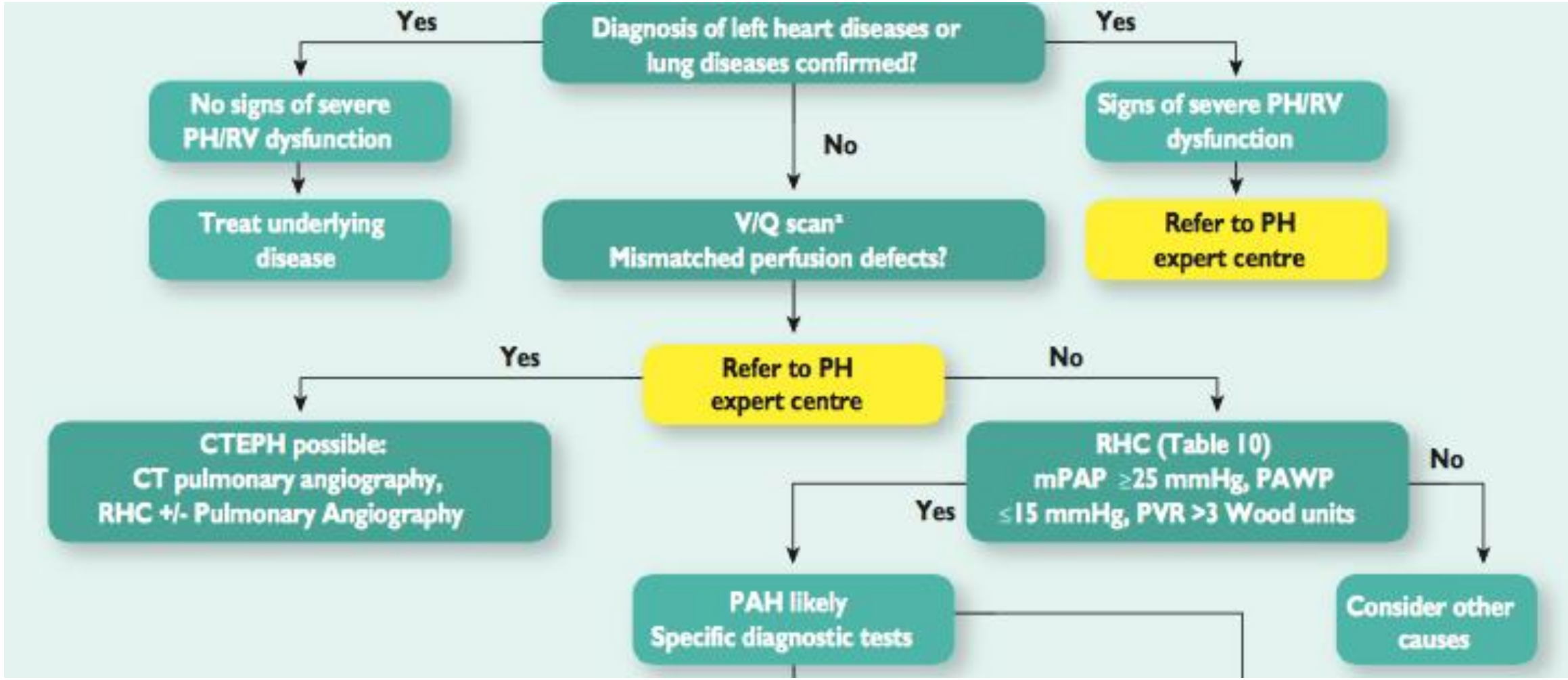
- A Rheumatologist was consulted: no clear symptoms or clinical findings of specific CTD: no skin- or joint symptoms, no Raynaud-symptom, no hair loss, no sicca- symptoms or signs of scleroderma/systemic sclerosis, no esophageal symptoms. Maybe some muscle weakness (CK and myoglobin was normal).
- Later nailfold videocapillaroscopy (to search for microvascular abnormalities related to CTD) was performed, but showed no clear signs of SSc
- MCTD was considered the most likely CTD-diagnosis (SLE possible), with manifestation of APAH, pleural effusion, enlarged lymph nodes, anemia, leucopenia, low complement levels and ANAAb pattern
- So the diagnosis was considered to be CTD associated PAH (APAH)
- Treatment for CTD was started with Prednisolon 30mg x1 (0.5mg/kg with tapering of 5mg/week) and hydroxychloroquine 100mg x1, with target dose of 300mg x1.
- Treatment of PAH was started with a combination of endotelin receptor antagonist (ERA) macitentan and PDE5-inhibitor sildenafil
- Treatment continued on the ward of pulmonary diseases and follow-up was arranged on the outpatient clinics of rheumatology, pulmonary diseases and cardiology



CHD = congenital heart diseases; CT = computed tomography; CTD = connective tissue disease; CTEPH = chronic thromboembolic pulmonary hypertension; DLCO = carbon monoxide diffusing capacity; ECG = electrocardiogram; HIV = Human immunodeficiency virus; HR-CT = high resolution CT; mPAP = mean pulmonary arterial pressure; PA = pulmonary angiography; PAH = pulmonary arterial hypertension; PAWP = pulmonary artery wedge pressure; PFT = pulmonary function tests; PH = pulmonary hypertension; PVOD/PCH = pulmonary veno-occlusive disease or pulmonary capillary hemangiomathosis; PVR = pulmonary vascular resistance; RHC = right heart catheterisation; RV = right ventricular; V/Q = ventilation/perfusion.

[a]CT pulmonary angiography alone may miss diagnosis of chronic thromboembolic pulmonary hypertension.


Symptoms, signs, history suggestive of PH
Echocardiographic probability of PH (Table 8)
High or intermediate
Low
Consider left heart disease and lung diseases by symptoms, signs, risk factors, ECG, PFT+DLCO, chest radiograph and HRCT, arterial blood gases (Table 9)
Consider other causes and/or follow-up (Table 9)
Diagnosis of left heart diseases or lung diseases confirmed?
Yes
Yes
No
No signs of severe PH/RV dysfunction
Signs of severe PH/RV dysfunction
Treat underlying disease
V/Q scan[a] Mismatched perfusion defects?
Refer to PH expert centre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Yes
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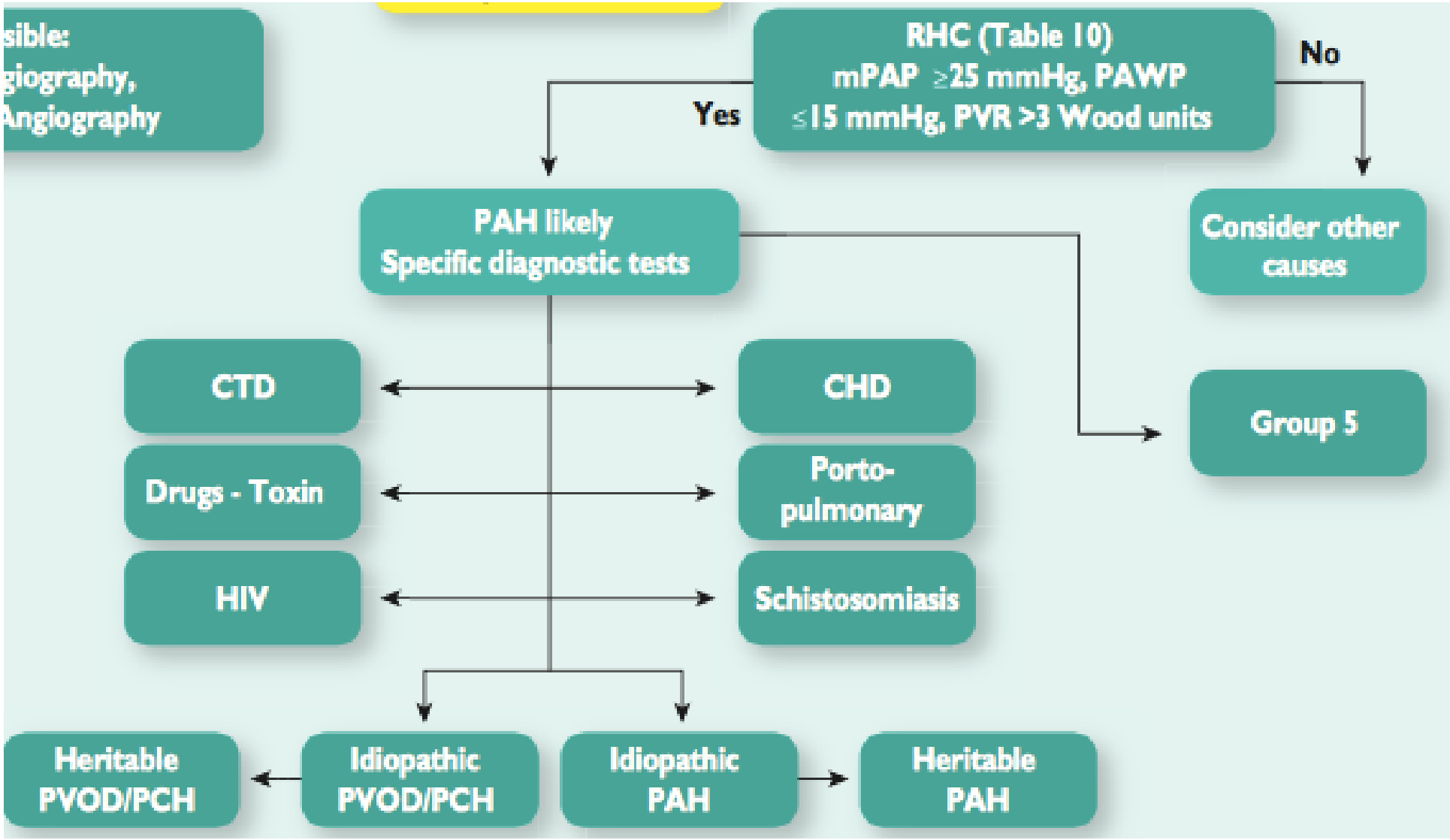
Signs of severe PH/RV dysfunction
Refer to PH expert centre
No
V/Q scan[a] Mismatched perfusion defects?
Yes
Refer to PH expert centre
CTEPH possible: CT pulmonary angiography, RHC +/- Pulmonary Angiography
No
RHC (Table 10) mPAP ≥25 mmHg, PAWP ≤15 mmHg, PVR >3 Wood units
Yes
PAH likely Specific diagnostic tests
No
Consider other causes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giography,
Angiography
RHC (Table 10)
mPAP ≥25 mmHg, PAWP
≤15 mmHg, PVR >3 Wood units
Yes
No
PAH likely
Specific diagnostic tests
Consider other causes
CTD
CHD
Group 5
Drugs - Toxin
Porto-pulmonary
HIV
Schistosomiasis
Heritable PVOD/PCH
Idiopathic PVOD/PCH
Idiopathic PAH
Heritable PAH