Στρογυλό Τραπέζι

Ενδιαφέροντα περιστατικά με Πνευμονική Υπέρταση

Περιστατικό 2

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MEDICAL HISTORY

- Female 51 y.o
- Sickle Cell Disease with multiple episodes of ‘sickle-cell crisis’
- Functional asplenia (auto-infarction)
- Sickle-cell nephropathy with nephrotic-range proteinuria
- Dyspnea on effort since July/2017 deteriorated to WHO III.

Admission in a General Hospital due to dyspnea and lower limb oedema(Nov/2017)

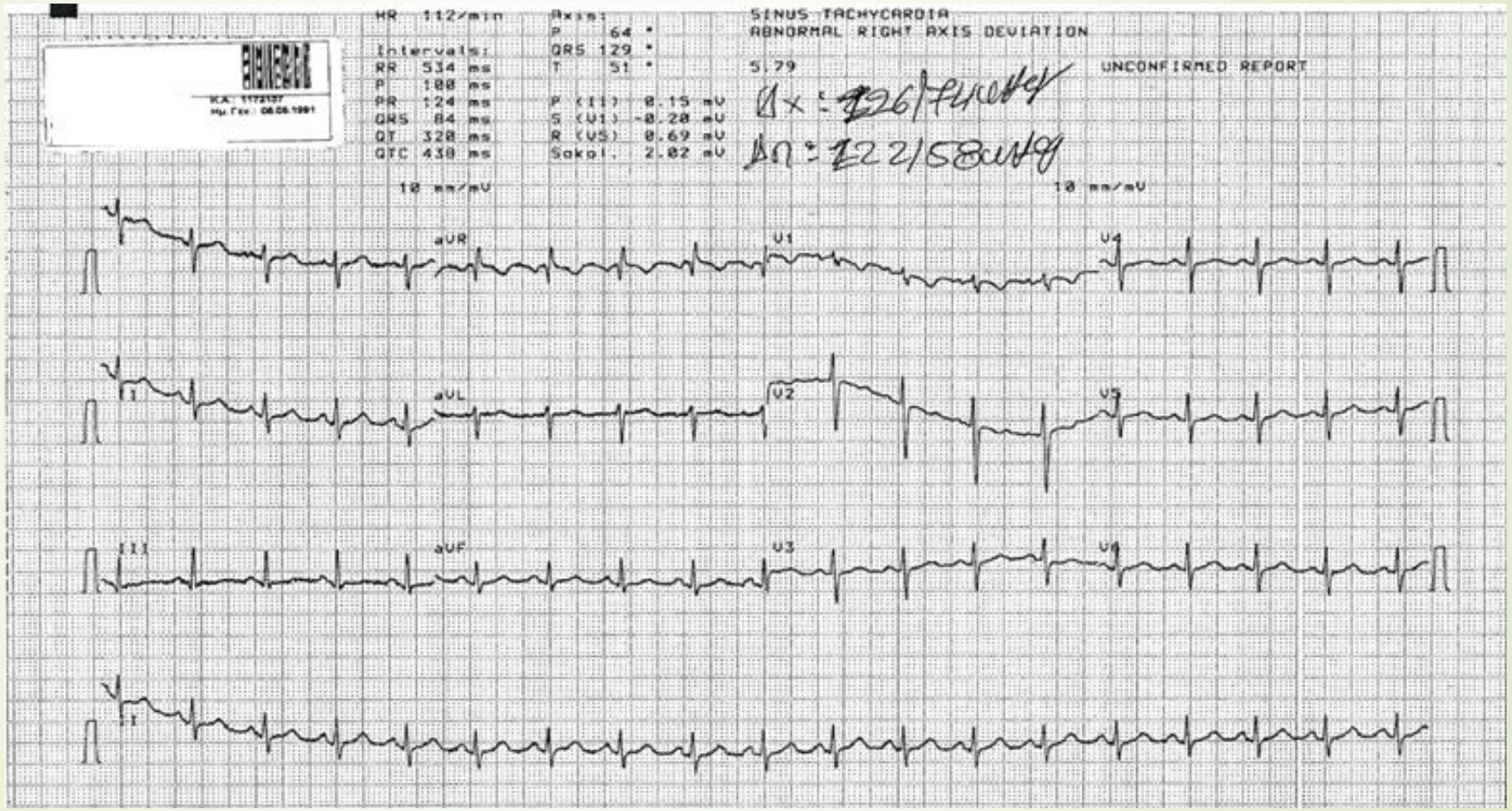
FINDINGS

- BP: 135/85, HR:98/1', SO2: 93%, Ht:30.4%, HB: 9.9 g/dl, WBC:8100, PLT: 383000, PO2:62 mmHg, PCO2:30 mmHg
- CTPA: bilateral pleural effusion, mosaic-like appearance, no visual thrombi or filling defects.
- ECHO: LVEF:60%, D-shape, RV dilatation, moderate TR, RVSP:65 mmHg
- RHC (11/2017): RA 11 mmHg, PA 62/23/38 mmHg, PCW 9 mmHg, CI 3.44 l/min/m^2, PVR 4.8 WU

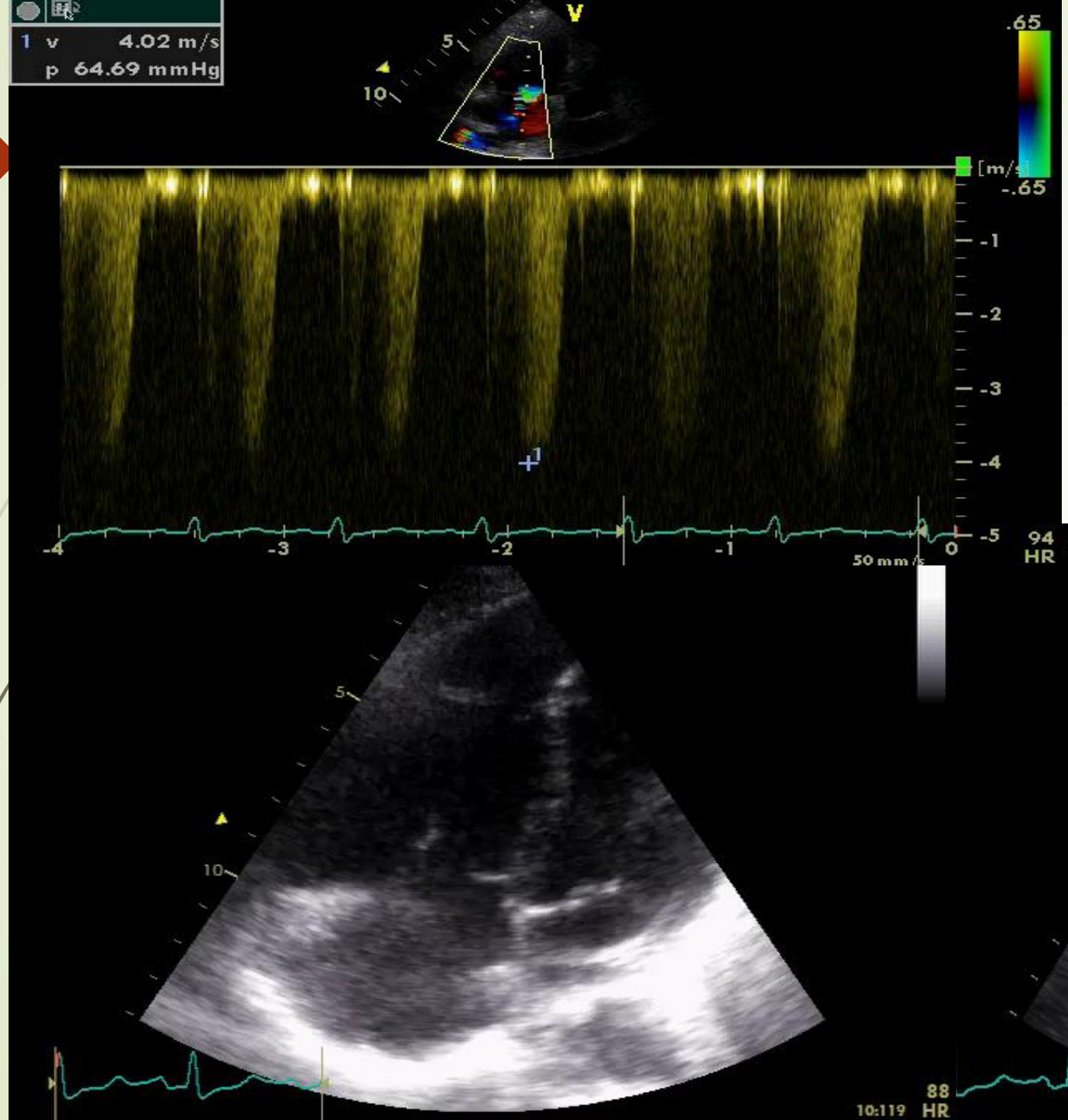
MEDICAL HISTORY

- Treatment with diuretics (slight improvement)
- Discharged after 4 days without specific treatment for PH
- Hydroxyurea, folic-acid, allopurinol, Diltiazem
- One month later significant deterioration to WHO IV
- Admission in OCSC

ECG


HR 112/min
Intervals:
RR 534 ms
P 100 ms
PR 124 ms
QRS 84 ms
QT 328 ms
QTC 430 ms
Axis:
P 64 °
QRS 129 °
T 51 °
P (I) 0.15 mV
S (V1) -0.20 mV
R (V5) 0.69 mV
Sokol. 2.02 mV
SINUS TACHYCARDIA
ABNORMAL RIGHT AXIS DEVIATION
5.79
UNCONFIRMED REPORT
10 mm/mV
10 mm/mV
aVR
V1
V4
aVL
V2
V5
III
aVF
V3
V6

Cardiac u/s

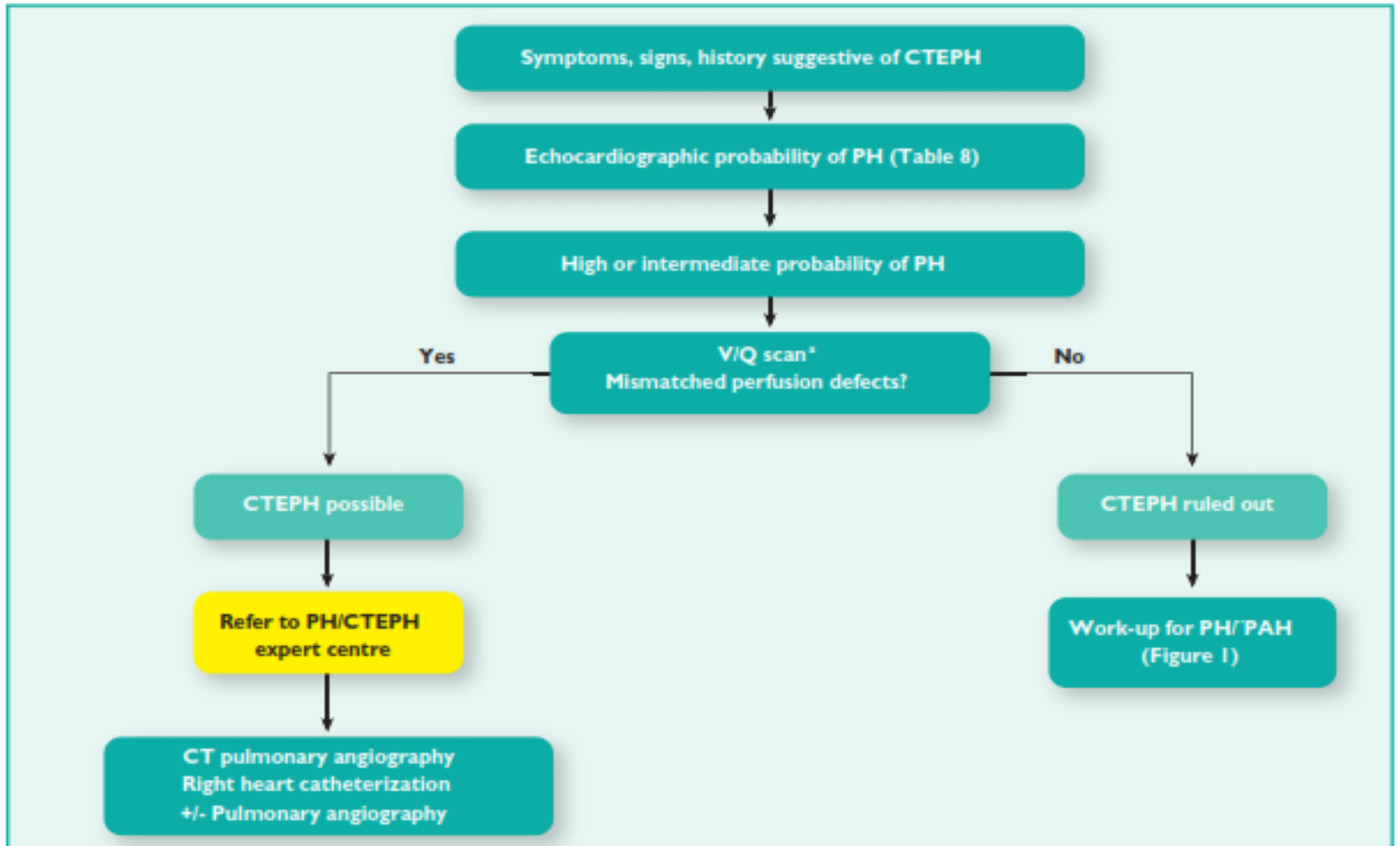

1 v 4.02 m/s
p 64.69 mmHg
.65
-.65
[m/s]
-1
-2
-3
-4
-5
-4
-3
-2
-1
0
50 mm/s
94
HR
88
10:119
HR
88
10:121
HR

Question 1

Which one should be the next step for the patient?

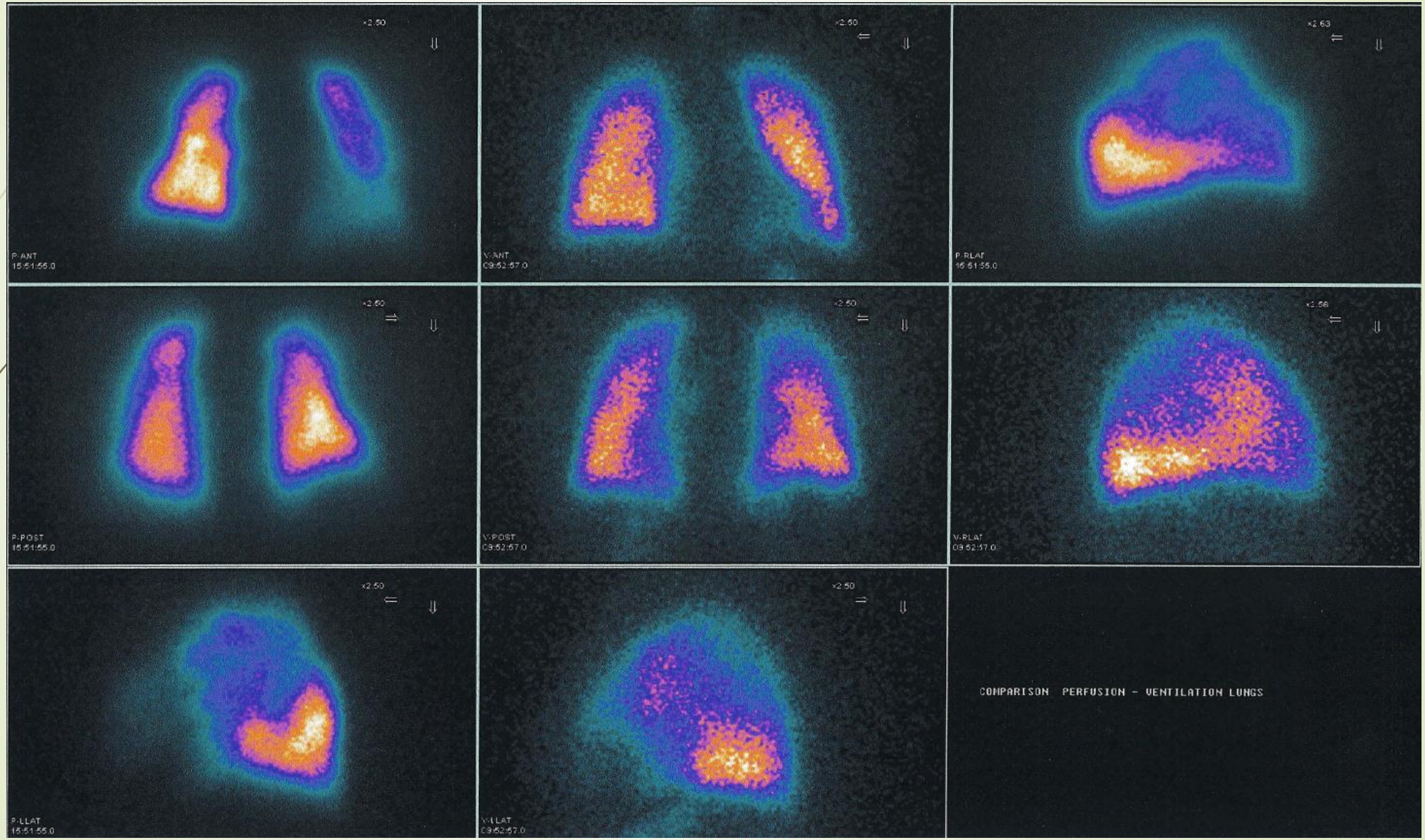
1. Initiation for specific PH-treatment
2. A HRCT for the lungs
3. V/Q scan
4. A new RHC

Diagnostic Algorithm for CTEPH

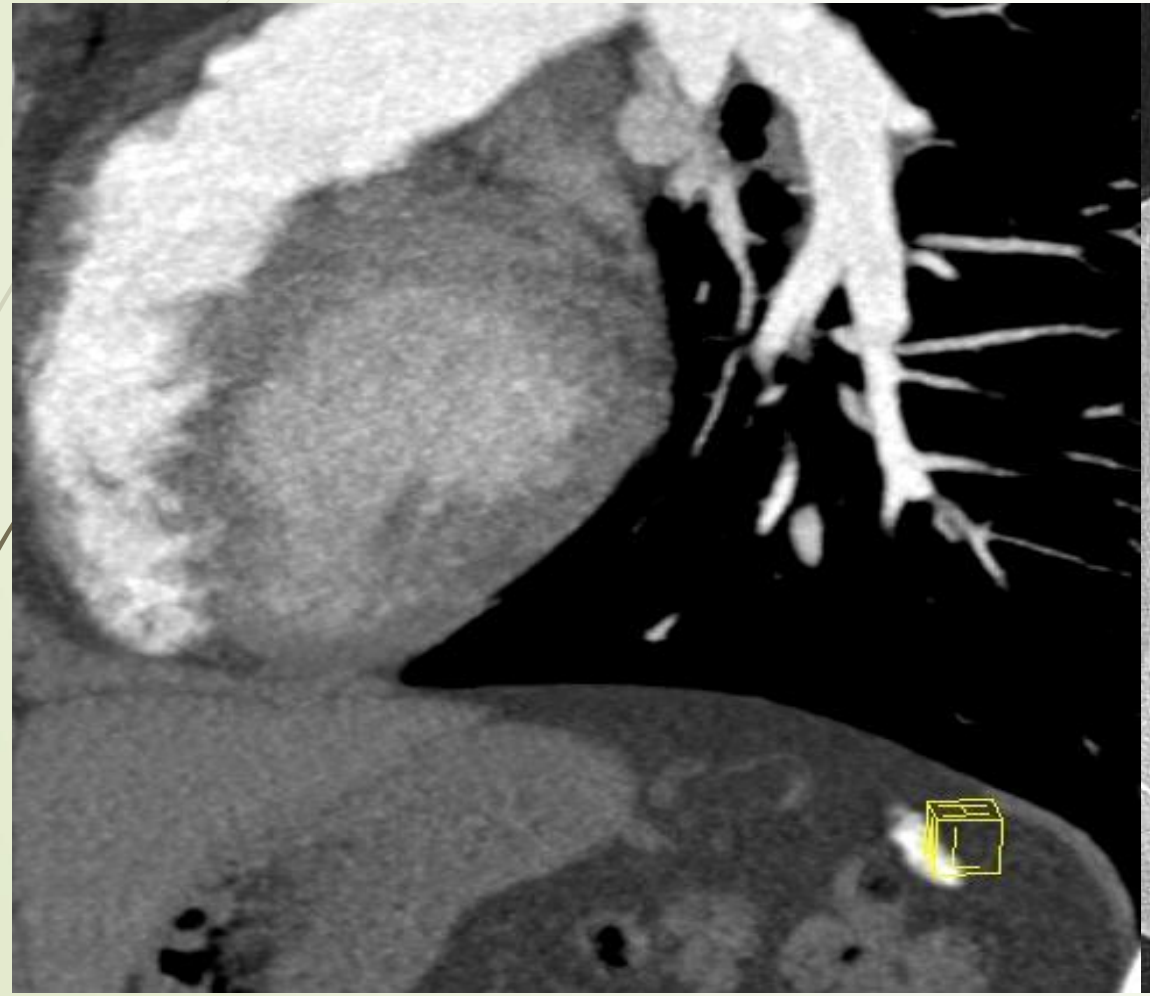


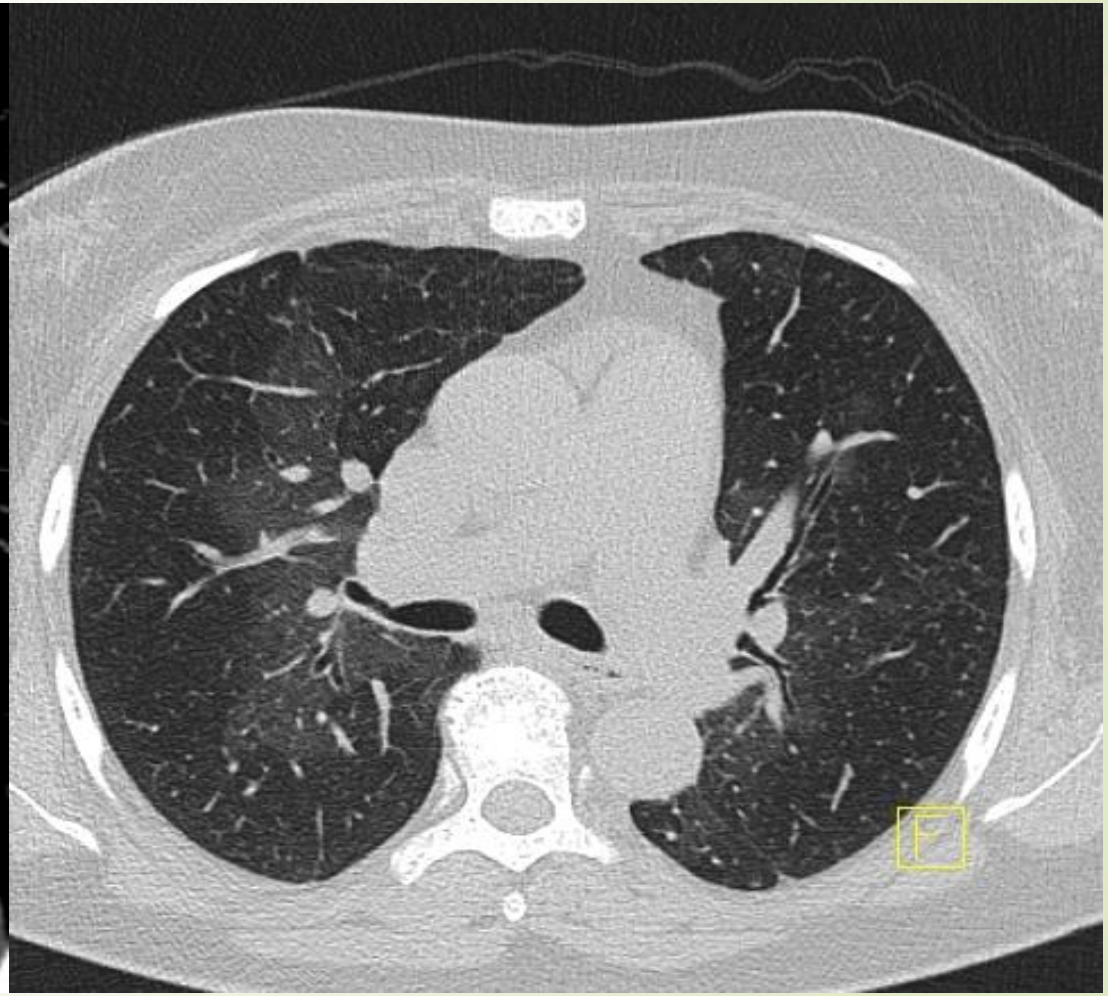
CT = computed thomography; CTEPH = chronic thromboembolic pulmonary hypertension; PAH = pulmonary arterial hypertension; PH = pulmonary hypertension; V/Q = ventilation/perfusion.
[a]CT pulmonary angiography alone may miss diagnosis of chronic thromboembolic pulmonary hypertension.

PERFUSION/VENTILATION SCAN



New CTPA





Right heart cath (8/1/2018)

- P.A : 79/33/56 mmHg
- RA: **18** mmHg
- PWP: 12 mmHg
- Ao : 130/83/99 mmHg
- SAO2: **72.5%** SPA **34.8%**
- CO: 3.88 l/min
- CI: 2.24 l/min/m^2
- PVR: 11.08 WU
- (HB 10.5 g/dl, NT-proBNP: 601 pg/ml)

Table 13 Risk assessment in pulmonary arterial hypertension

Determinants of prognosis[a] (estimated 1-year mortality)	Low risk <5%	Intermediate risk 5–10%	High risk >10%
Clinical signs of right heart failure	Absent	Absent	Present ✓ ●
Progression of symptoms	No	Slow	Rapid ✓ ●
Syncope	No	Occasional syncope[b]	Repeated syncope[c]
WHO functional class	I, II	III	IV ✓ ●
6MWD	>440 m	165–440 m	<165 m
Cardiopulmonary exercise testing	Peak VO_2 >15 ml/min/kg (>65% pred.) VE/VCO_2 slope <36	Peak VO_2 11–15 ml/min/kg (35–65% pred.) VE/VCO_2 slope 36–44.9	Peak VO_2 <11 ml/min/kg (<35% pred.) VE/VCO_2 ≥45
NT-proBNP plasma levels	BNP <50 ng/l NT-proBNP <300 ng/ml	BNP 50–300 ng/l ✓ ● NT-proBNP 300–1400 ng/l	BNP >300 ng/l NT-proBNP >1400 ng/l
Imaging (echocardiography, CMR imaging)	RA area <18 cm^2 No pericardial effusion	RA area 18–26 cm^2 ✓ ● No or minimal, pericardial effusion	RA area >26 cm^2 Pericardial effusion
Haemodynamics	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%

Simplified Risk stratification in PAH (Nice 2018)

Prognostic Criteria		Low Risk variables	Intermediate Risk variables	High Risk variables
A	WHO functional class	I, II	III	IV
B	6MWD	> 440 m	165-440 m	< 165 m
C	NT-proBNP/BNP plasma levels OR RAP	BNP < 50 ng/l NT-proBNP < 300 ng/l OR RAP < 8 mmHg	BNP 50-300 ng/l NT-proBNP 300-1400 ng/l OR RAP 8-14 mmHg	BNP > 300 ng/l NT-proBNP > 1400 ng/l OR RAP > 14 mmHg
D	CI OR SVO2	CI ≥ 2.5 l/min/m^2 OR SVO2 > 65%	CI 2.0-2.4 l/min/m^2 OR SVO2 60-65%	CI < 2.0 l/min/m^2 OR SVO2 < 60%

Simplified Risk stratification in PAH (Nice 2018)

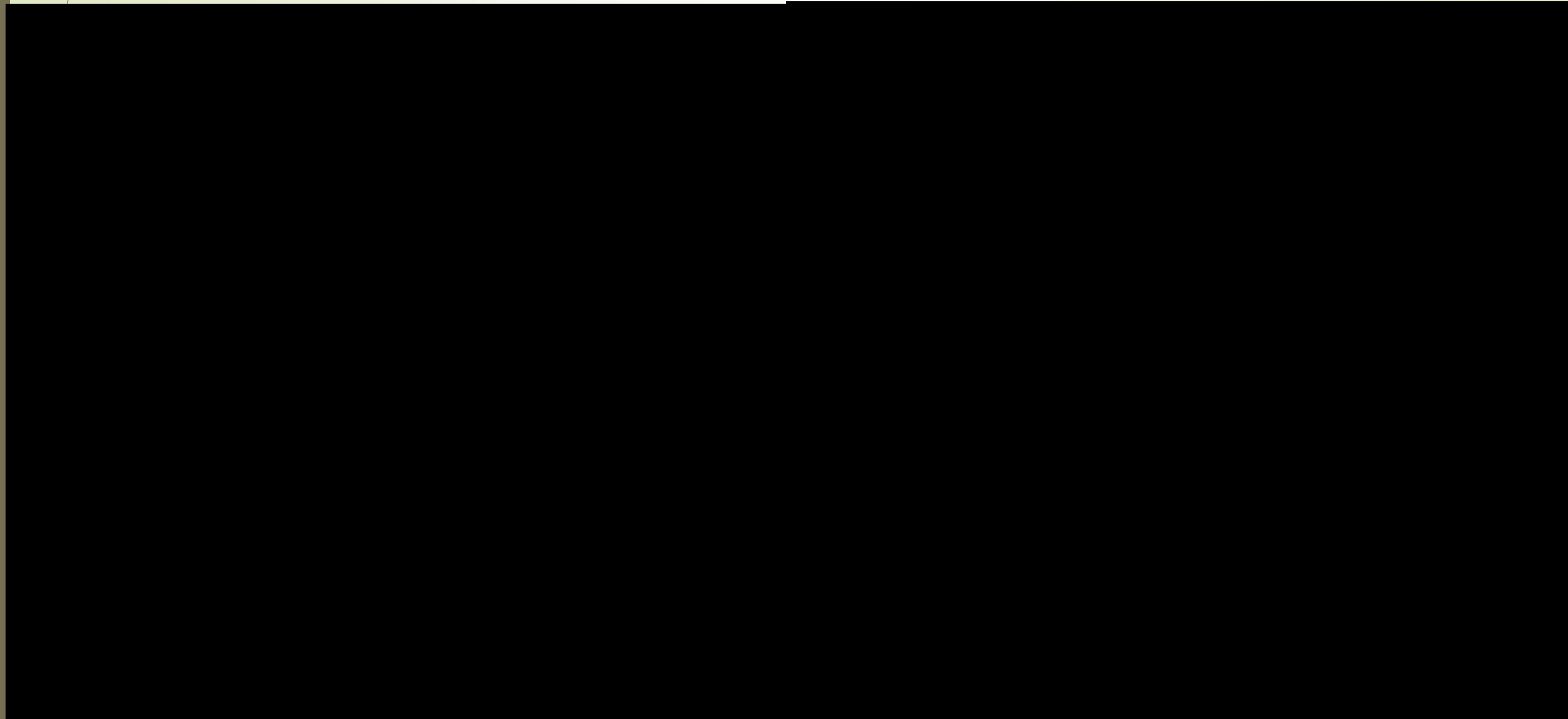
Low Risk	Intermediate Risk	High Risk
At least 3 low risk criteria and no high risk criteria	Definitions of low or high risk criteria not fulfilled	At least 2 high risk criteria including CI or SVO2

Simplified Risk stratification in PAH

Prognostic Criteria		Low Risk variables	Intermediate Risk variables	High Risk variables
A	WHO functional class	I, II	III	IV ✓ ●
B	6MWD	> 440 m	165-440 m	< 165 m
C	NT-proBNP/BNP plasma levels OR RAP	BNP < 50 ng/l NT-proBNP < 300 ng/l OR RAP < 8 mmHg	BNP 50-300 ng/l NT-proBNP 300-1400 ng/l OR RAP 8-14 mmHg	BNP > 300 ng/l NT-proBNP > 1400 ng/l OR RAP > 14 mmHg ✓ ●
D	CI OR SVO2	CI ≥ 2.5 l/min/m^2 OR SVO2 > 65%	CI 2.0-2.4 l/min/m^2 OR SVO2 60-65%	CI < 2.0 l/min/m^2 OR SVO2 < 60% ✓ ●

PULMONARY ANGIOGRAPHY

MULTIPLE SUB-SEGMENTAL AND VERY PERIPHERAL LESIONS



Question 2

Which one might be the best therapeutic strategy for the patient?

1. PEA
2. Specific PH-treatment
3. BPA
4. Continuation of conservative therapy
5. 2+3
6. 1+2

Question 3

In case of specific PH-therapy which one might be the best option for the patient?

1. Initial combination therapy
2. Drugs targeting the NO pathway (Riociguat, PDE5)
3. Initial monotherapy and sequential combination therapy
4. Prostacyclin analogues monotherapy

Management of patients with SCD

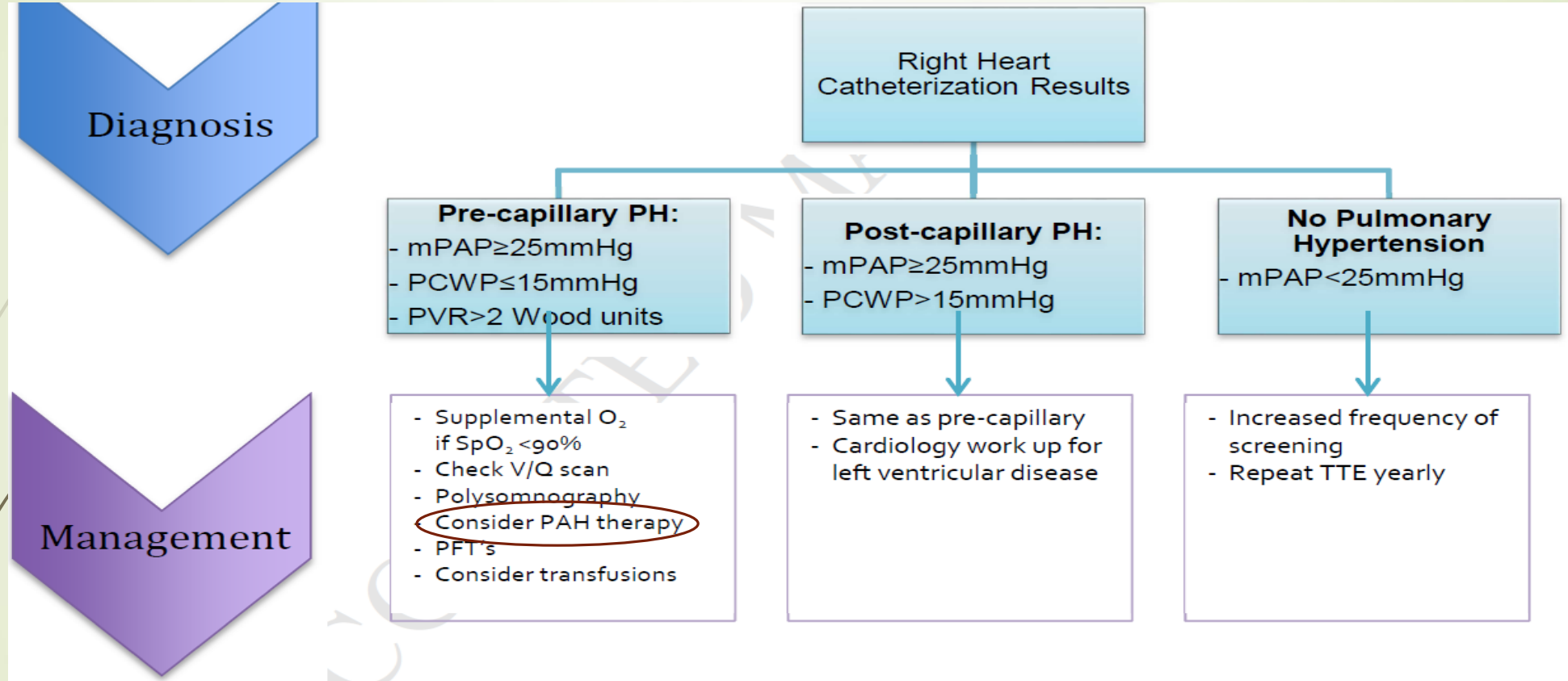


Figure 1. **Proposed algorithm for the evaluation and management of pulmonary hypertension in sickle cell disease.** 6-MWD = 6-Minute Walk Distance; SpO_2 = Saturation of oxygen on room air; TRV = Tricuspid Regurgitation; mPAP = Mean Pulmonary Artery Pressure; PAWP = Pulmonary Artery Wedge Pressure; PVR = Pulmonary Vascular Resistance; V/Q = Ventilation/Perfusion; PAH = Pulmonary Arterial Hypertension; PFT = Pulmonary Function Test; TTE = Tran-thoracic echocardiogram

Adapted from

1. *Klings ES, Machado RF, Barst RJ, Morris CR, Mubarak KK, Gordeuk VR, et al. An Official American Thoracic Society Clinical Practice Guideline: Diagnosis, Risk Stratification, and Management of Pulmonary Hypertension of Sickle Cell Disease. American Journal of Respiratory and Critical Care Medicine. 2014;189(6):727-40*

Am J Respir Crit Care Med. 2014 Mar 15;189(6):727-40. doi: 10.1164/rccm.201401-0065ST.

An official American Thoracic Society clinical practice guideline: diagnosis, risk stratification, and management of pulmonary hypertension of sickle cell disease.

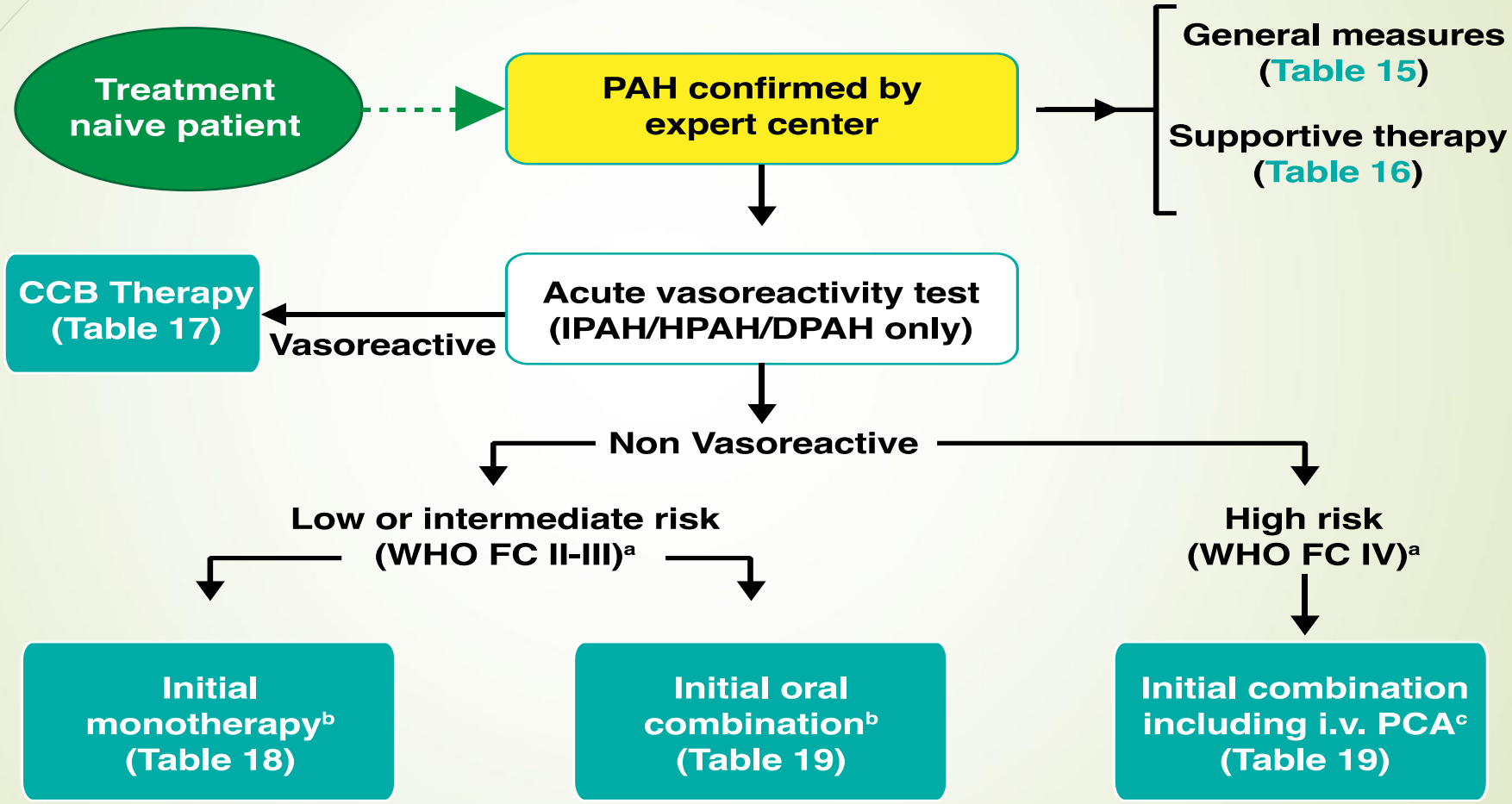
Klings ES, Machado RF, Barst RJ, Morris CR, Mubarak KK, Gordeuk VR, Kato GJ, Ataga KI, Gibbs JS, Castro O, Rosenzweig EB, Sood N, Hsu L, Wilson KC, Telen MJ, Decastro LM, Krishnamurti L, Steinberg MH, Badesch DB, Gladwin MT; American Thoracic Society Ad Hoc Committee on Pulmonary Hypertension of Sickle Cell Disease.

Recommendation: For patients with SCD who have an RHC-confirmed marked elevation of their pulmonary vascular resistance, a normal pulmonary artery wedge pressure, and related symptoms, we recommend *against* phosphodiesterase-5 inhibitor therapy as a first-line treatment (strong recommendation, moderate-quality evidence).

Remarks: The recommendation is based on the observation that phosphodiesterase-5 inhibitor therapy may increase the risk of hospitalization for vaso-occlusive crisis.

Values and preferences: This recommendation places a higher value on avoiding serious complications and a lower value on symptomatic and hemodynamic improvement.

2015 ESC/ERS guidelines treatment algorithm (PAH)



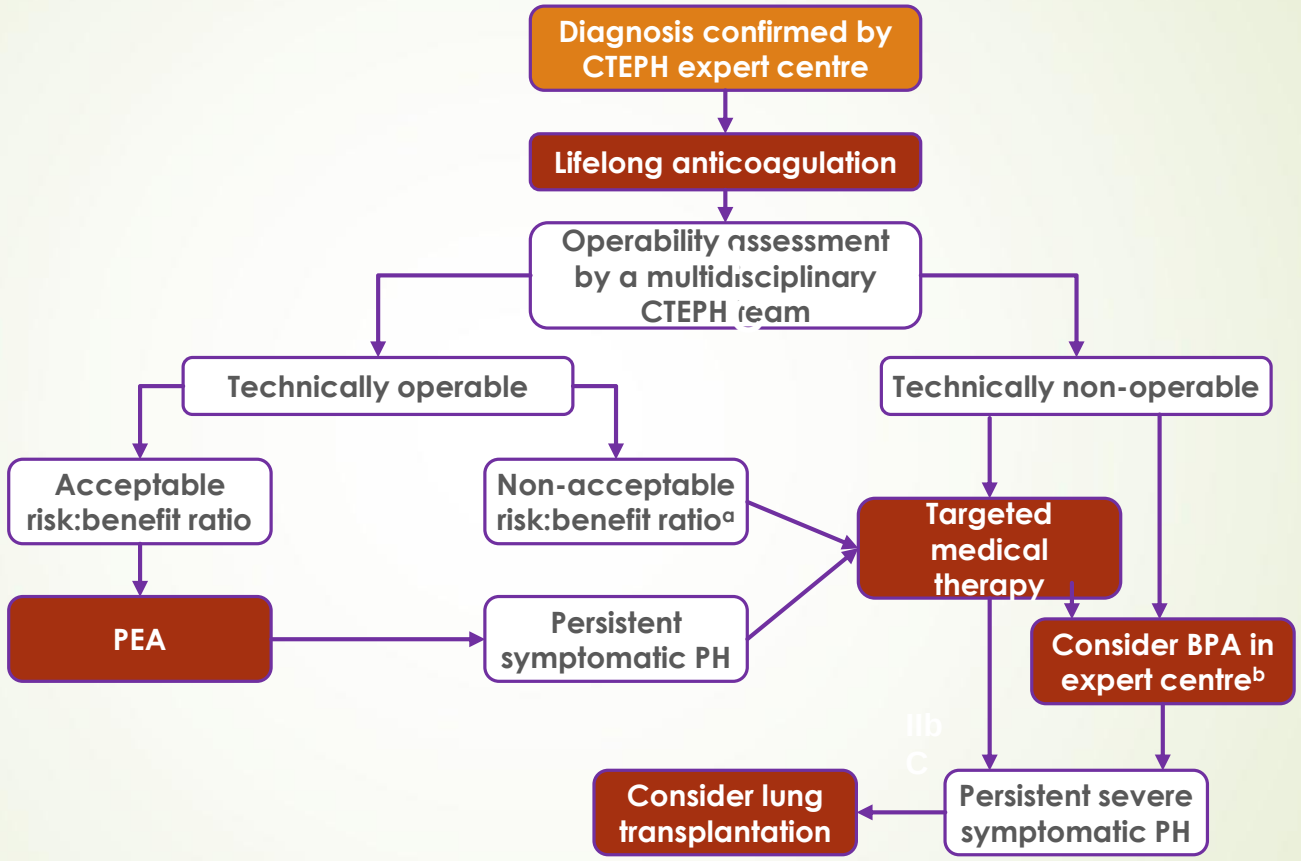
Galiè N, *et al. ESC/ERS Guidelines. Eur Respir J & Eur Heart J*. 2015.

TREATMENT

- Anticoagulants (Sintrom)
- Macitentan plus Selexipag (600µg bid)
- Diuretics
- Exchange blood transfusions
- Oxygene

- Significant improvement after 2 weeks
- Dyspnea WHO II-III
- 1 episode of sickle-cell crisis (mild)
- Consider BPA

Interventional BPA may be considered in patients who are technically non-operable or carry an unfavourable risk to benefit ratio for PEA



Galiè N, *et al. Eur Respir J* 2015; 46:903-75;
Galiè N, *et al. Eur Heart J* 2016; 37:67-119.

[a]Technically operable patients with non-acceptable risk/benefit ratio can also be considered for BPA.
[b]In some centres medical therapy and BPA are initiated concurrently.

BPA: balloon pulmonary angioplasty, PEA: pulmonary endarterectomy

RHC-BPA (12/2/2018)

- P.A : 49/19/30 mmHg
- RA: 8 mmHg
- PWP: 13 mmHg
- Ao : 124/75/91 mmHg
- SO2: 80% PA **58.5%**
- CO: 6.07 l/min
- CI: 3.51 l/min/m^2
- PVR: 3.2 WU
- (HB 11.1 g/dl, HR 94/min)

BPA in 7 lesions of RPA (RA1, RA2, RA3, RA4a, RA4b, RA5a, RA5b) with balloon 1.5X20mm & 2.0X20 mm

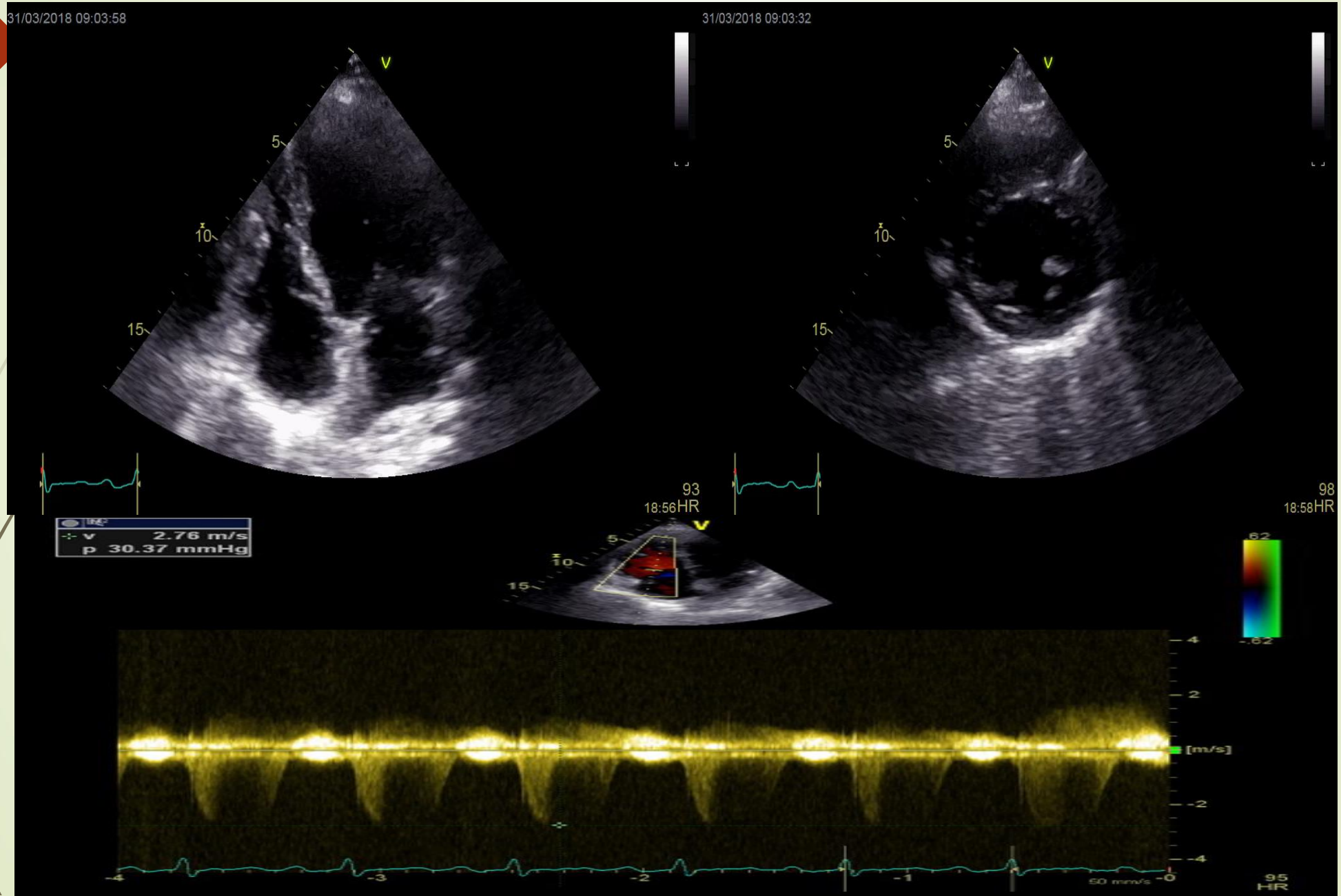
BALLOON PULMONARY ANGIOPLASTY

BALLOON PULMONARY ANGIOPLASTY

BALLOON PULMONARY ANGIOPLASTY

BALLOON PULMONARY ANGIOPLASTY

ΗΧΩΚΑΡΔΙΟΓΡΑΦΗΜΑ (4/2018)



OUTCOME (3 Months LATER)

- WHO I
- NT-proBNP: 130 pg/ml
- Call for a new BPA session

BUT

RHC (21/5/2018)

- P.A : 33/16/22 mmHg
- RA: 5 mmHg
- PWP: 10 mmHg
- Ao : 137/75/96 mmHg
- SO2: 94% SPA: 68%
- CO: 4.7 l/min (HR 71/min, Hb 11.5 g/dl)
- CI: 2.90 l/min/m^2
- PAR: 2.5 WU

RIGHT HEART CATH

	11/2017	1/2018	2/2018	5/2018
Rx	Conservative		Macitentan Selexipag	& BPA
RA	11	18	8	5
PA	62/23/38	79/33/56	49/19/30	33/16/22
CI	3.44	2.24	3.51	2.9
PVR	4.8	11.08	3.2	2.5
HR	98	104	94	71
SAO2	93%	72.5%	80%	94%
SPA	N/A	34.8%	58.5%	68%

Prognosis evaluation

	BASELINE	FOLLOW UP
Right Heart Failure	Yes	No
WHO	IV	I
NT pro BNP	601 ng/l	130ng/l
R.H.C.	RAP: 18 mmHg CI: 2.24 L/min/m^2	RAP: 5 mmHg CI: 2.9 L/min/m^2
SVO2	34.8%	68%

Conclusions

- The role of BPA may emerge as a valuable treatment option for SCD patients with CTEPH, especially when most of the disease are due to peripherally located thrombi

- As pulmonary hypertension causes significant morbidity and mortality in SCD, further studies would help to ascertain the benefit and efficacy of potential PAH-targeted therapies, and help to establish more definitive guidelines.

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