Pulmonary Arterial Hypertension

A Rare Presentation

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Dr. DY Patil Medical College Hospital and Research Centre, Pune

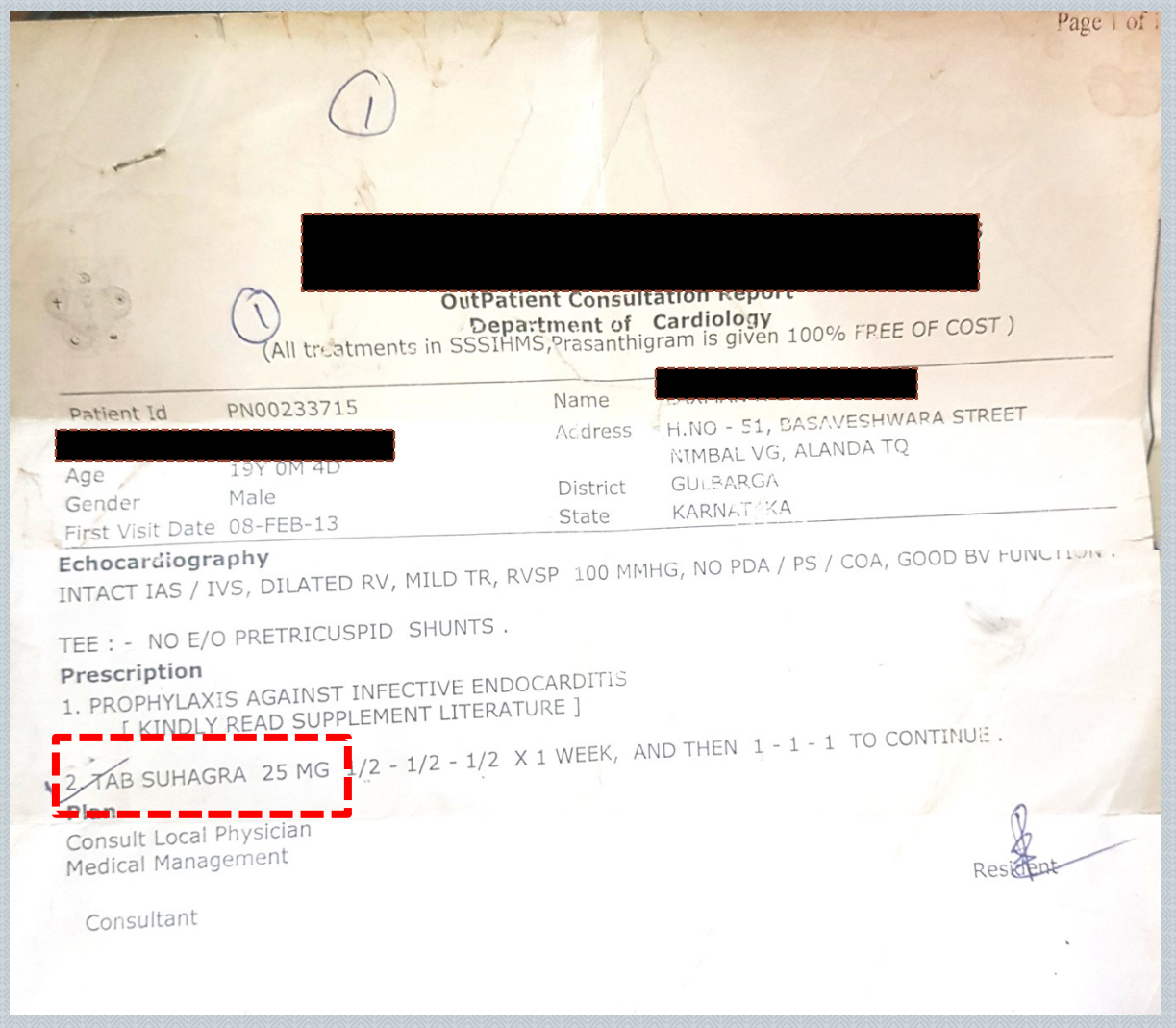
Clinical Course

24y/M, Resident of Solapur
Shop Owner; Non-Smoker

- **May, 2014 – Onset of illness**
- Presented with **streaky haemoptysis**
- No associated dyspnea, fever, chest pain, loss of wt
- He was worked up at a private hospital
- All hematological and biochemical parameters were normal

- CXR (PA) – labelled as Normal Study
- 2D-Echo revealed
- **RVSP – 100mm Hg**, severe PAH with mild TR

- Diagnosed as **Pulmonary Hypertension**



Page 1 of 1

[redacted]

OutPatient Consultation Report

Department of Cardiology

(All treatments in SSSIHMS,Prasanthigram is given 100% FREE OF COST)

Patient Id	PN00233715	Name	[redacted]
[redacted]		Address	H.NO - 51, BASAVESHWARA STREET NIMBAL VG, ALANDA TQ
Age	19Y 0M 4D		
Gender	Male	District	GULBARGA
First Visit Date	08-FEB-13	State	KARNATAKA

Echocardiography

INTACT IAS / IVS, DILATED RV, MILD TR, RVSP 100 MMHG, NO PDA / PS / COA, GOOD BV FUNCTION .

TEE : - NO E/O PRETRICUSPID SHUNTS .

Prescription

1. PROPHYLAXIS AGAINST INFECTIVE ENDOCARDITIS
   [KINDLY READ SUPPLEMENT LITERATURE]
2. TAB SUHAGRA 25 MG 1/2 - 1/2 - 1/2 X 1 WEEK, AND THEN 1 - 1 - 1 TO CONTINUE .

Plan

Consult Local Physician
Medical Management

Resident

Consultant

- Started on therapy with **T. Sildenafil!!!** (25mg) TID, by the treating physician.
- No other causes were ruled out/no relevant investigations were done, patient discharged

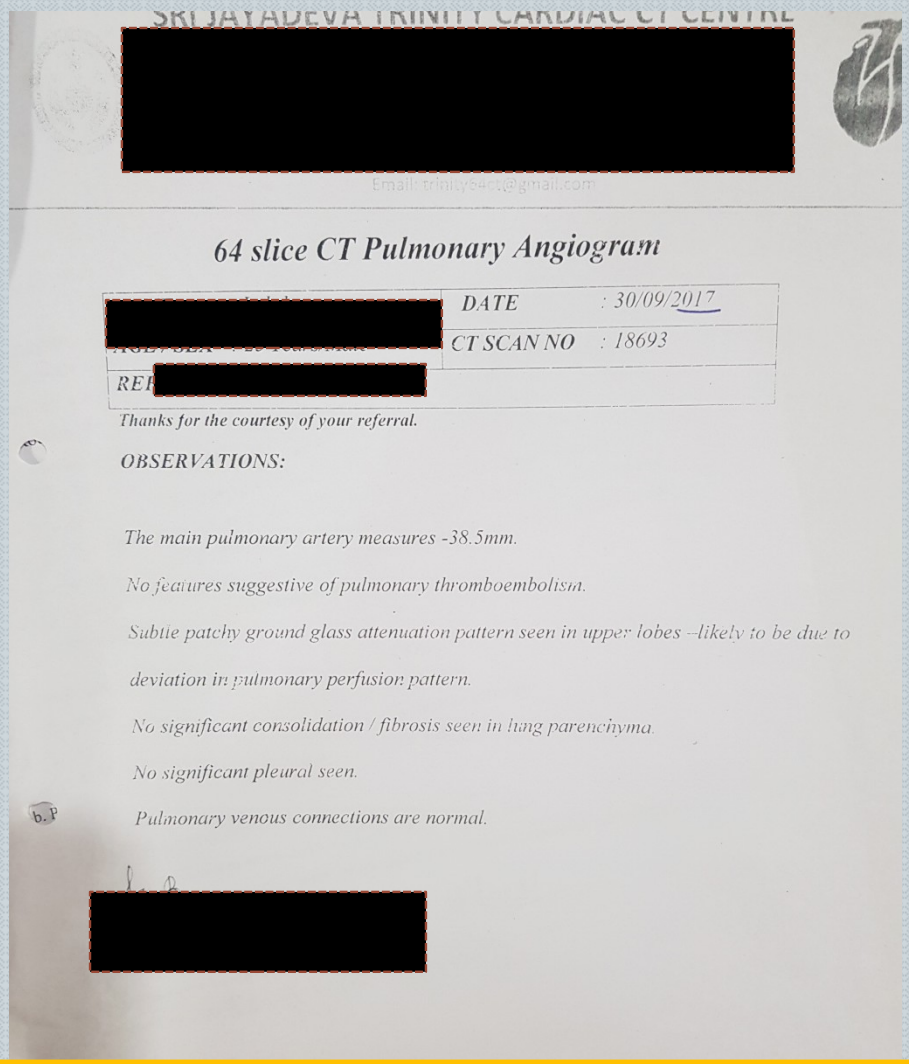
- Patient continued **T. Sildenafil** for 3 years, no further symptoms/follow up till

Sept, 2017

Patient presented, *again with streaky haemoptysis*, at a private hospital

Basic workup revealed normal parameters

CTPA – No features suggestive of pulmonary thromboembolism (film not available)



SRI JAYADEVA TRINITY CARDIAC CT CENTRE

[redacted]

Email: trinitycct@gmail.com

64 slice CT Pulmonary Angiogram

[redacted] DATE : 30/09/2017

CT SCAN NO : 18693

REF [redacted]

Thanks for the courtesy of your referral.

OBSERVATIONS:

The main pulmonary artery measures -38.5mm.

No features suggestive of pulmonary thromboembolism.

Subtle patchy ground glass attenuation pattern seen in upper lobes –likely to be due to deviation in pulmonary perfusion pattern.

No significant consolidation / fibrosis seen in lung parenchyma.

No significant pleural seen.

Pulmonary venous connections are normal.

[redacted]

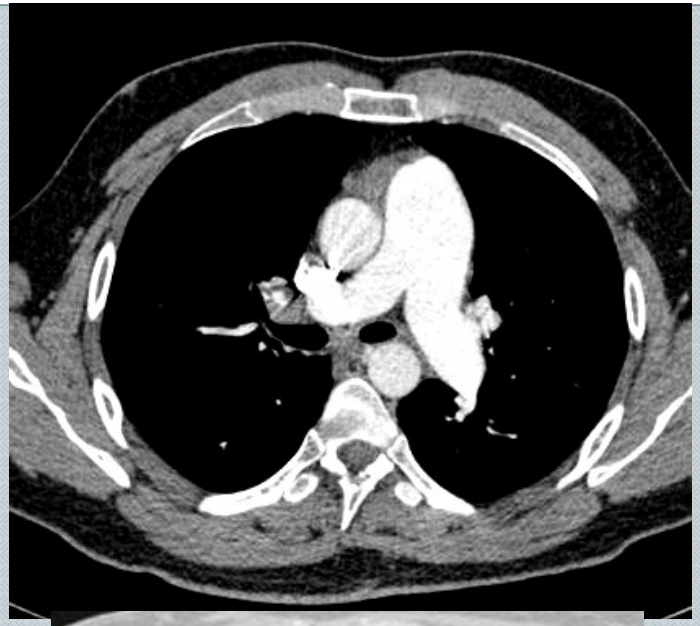
1. Dilation of Main Pulmonary Artery (38.5mm)
2. B/L upper lobe patchy ground glass attenuation pattern

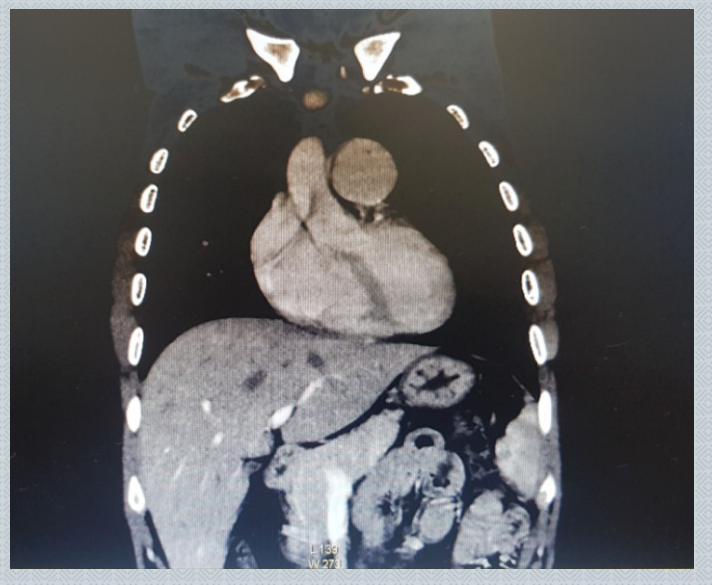
Patient was discharged without any change in treatment

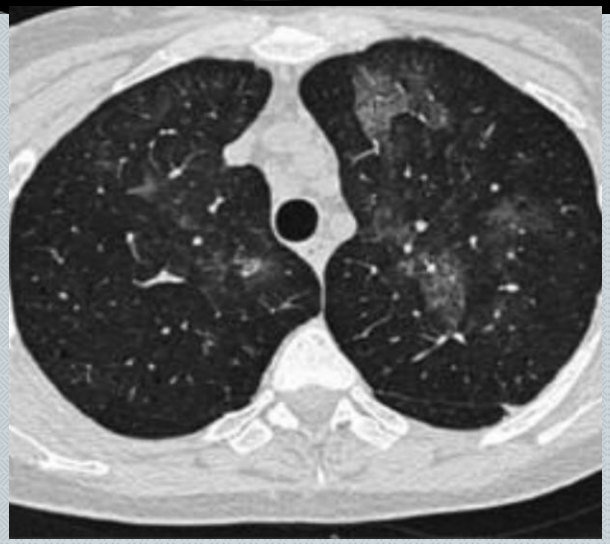
Aug, 2018

- Presented again to a private hospital with streaky haemoptysis and **breathlessness mMRC II**
- Haematological and Biochemical parameters were normal
- Trans-Esophageal Echocardiography done –
- **Dilated RV, RA, Main Pulmonary Artery, mild TR, Severe PAH, (RVSP-85mm Hg); LVEF 55%**

- CECT (thorax) – Ground Glass opacification in left upper lobe with dilated pulmonary trunk; No parenchymal abnormality detected







Patient N [redacted]
MRN
Age/Sex : 25Y/M

Requested By : Dr. C Dr Sagar C
Procedure Date : 25-08-2018 12:25
Hospital : NH-HEALTH CITY

CT – CHEST WITH INTRAVENOUS CONTRAST

[redacted]

FINDINGS:

There are multiple discrete areas of ground glass opacification in bilateral lungs, largest in subpleural aspect of left lower lobe medially (3.5x2.7cm).

There is mild associated septal thickening in the lungs bilaterally.

No mass lesion or bronchiectasis is seen.

Main pulmonary artery and branch pulmonary arteries are significantly dilated with MPA to aorta ratio >1.

No significant pleural thickening / fluid collection seen.

Mediastinal position and contents including the trachea and its bifurcation, thoracic aorta appear normal.

No definite mass lesions identified in the mediastinum / hilar regions. No significant lymph node enlargement identified.

The axillary and supraclavicular regions are normal. The bones of the thoracic cage and the vertebrae do not reveal significant abnormality. Superficial soft tissues of the chest wall appear normal.

Upper part of the liver, spleen and adrenals included in the study region show no obvious abnormality.

REMARKS:

- **Ground glass consolidation in left lower lobe. Likely secondary to alveolar haemorrhage.**
- **CT features of pulmonary artery hypertension with ground glass opacities in the lungs.**

- Discharged on **Tab Sildenafil (25mg) TID along with *T. Ambrisentan (5mg) OD***

Jan 2019

Admitted in our hospital with **4th episode of streaky haemoptysis along with breathlessness mMRC Grade II** x 4 days; admitted in Respiratory ICU

No H/O

- fever,
- chest pain,
- palpitations
- joint pains
- abdominal pain
- syncope
- limb swelling,
- wheeze
- other medications
- co-morbidities (HTN, DM etc)
- skin lesions
- significant family history
- addictions

On examination –

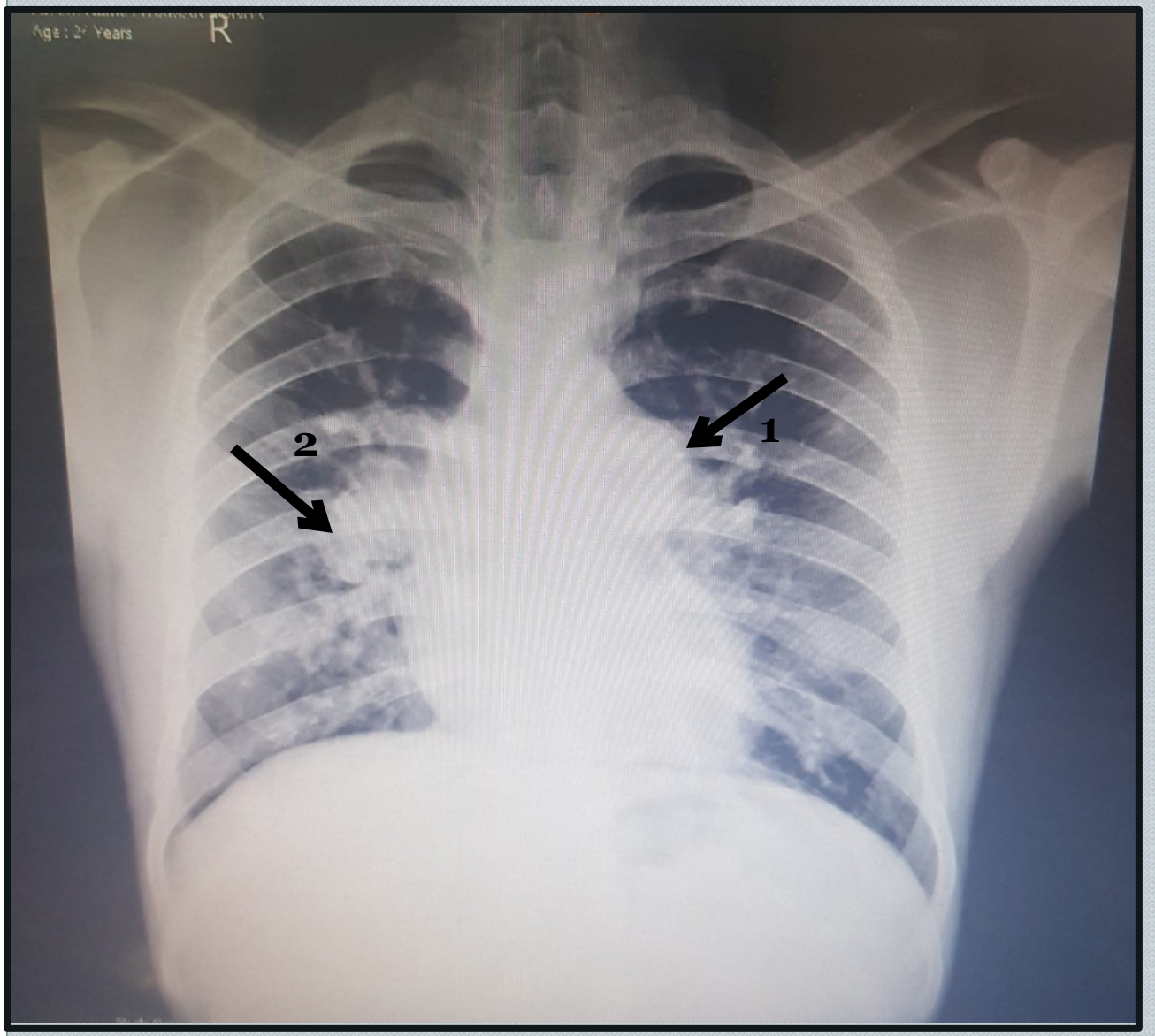
- PR – 98/min, regular; RR – 15/min;
  BP – 120/80 mmHg; SpO2 – 95% on room air

  JVP – not raised No palpable lymphadenopathy

- No Pallor, Pedal Oedema ,Clubbing
- BMI – 19.5kg/m^2
- Upper Resp Tract - NAD
- Resp. System – Left sided crackles (Supra and Infra-scapular area)
- **CVS – S1, S2 (loud P2), Ejection Systolic Murmur heard (pulmonary area)**

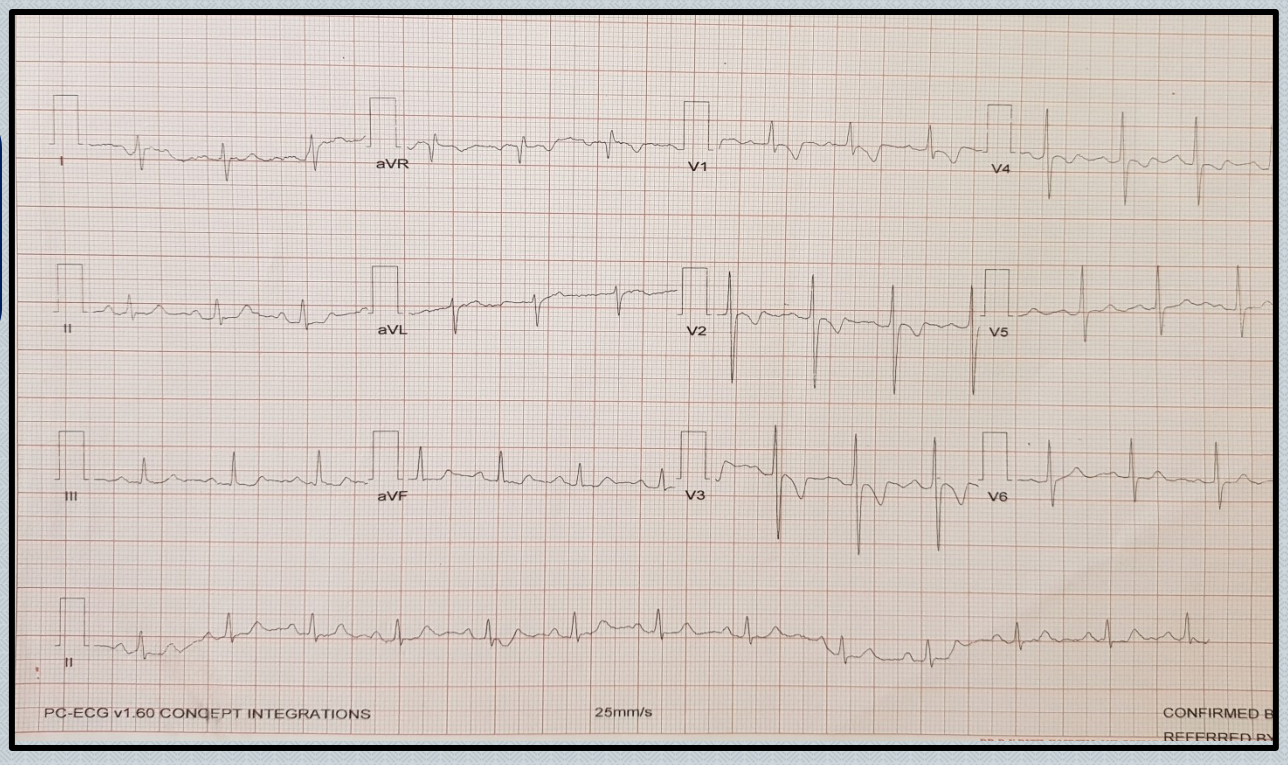
LAB

- **Hb - 15.7g%, TLC – 6600; Platelets – 2.4L**
- **RFT – WNL; LFT – WNL;**
- **PT/INR – 13.20/1.2;**
- **Thyroid function – WNL;**
- **Serology – Negative for HIV;**
- **NT – proBNP – 8.4pg/ml (Normal <29.4)**
- **RA/ANA – Negative;**



1. Prominent pulmonary conus
2. Enlarged pulmonary hila
3. No obvious parenchymal findings

- **ECG – T wave inversion seen in V1-V4**



- **2D-Echo – Dilated RA, RV; mild TR, Severe PAH (RVSP – 116mm Hg); LVEF-55%**

(no change from previous report)

6MWT – Distance walked – 420m
SpO2 (Pre) – 95%; (post) – 93% (no significant de-saturation)

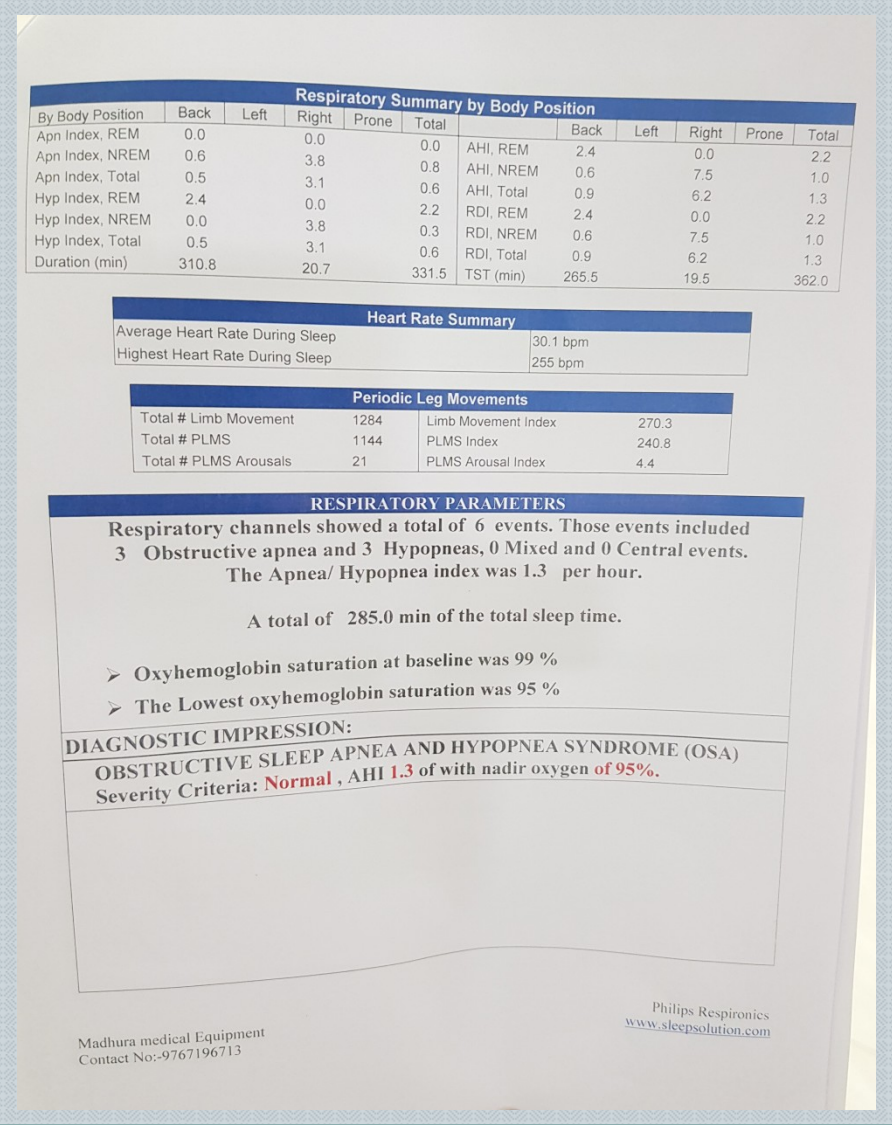
USG (Abdomen/Pelvis) – No significant abnormality detected

Colour doppler (both lower limbs) – No features suggestive of DVT

ABG- on Room Air – Mild Hypoxemia

pH – 7.418 PaO2 – 75.7
PaCO2 – 34.8 HCO3 – 21.8

Polysomnography – Normal study



Respiratory Summary by Body Position

By Body Position	Back	Left	Right	Prone	Total
Apn Index, REM	0.0		0.0		0.0
Apn Index, NREM	0.6		3.8		0.8
Apn Index, Total	0.5		3.1		0.6
Hyp Index, REM	2.4		0.0		2.2
Hyp Index, NREM	0.0		3.8		0.3
Hyp Index, Total	0.5		3.1		0.6
Duration (min)	310.8		20.7		331.5

	Back	Left	Right	Prone	Total
AHI, REM	2.4		0.0		2.2
AHI, NREM	0.6		7.5		1.0
AHI, Total	0.9		6.2		1.3
RDI, REM	2.4		0.0		2.2
RDI, NREM	0.6		7.5		1.0
RDI, Total	0.9		6.2		1.3
TST (min)	265.5		19.5		362.0

Heart Rate Summary

Average Heart Rate During Sleep	30.1 bpm
Highest Heart Rate During Sleep	255 bpm

Periodic Leg Movements

Total # Limb Movement	1284	Limb Movement Index	270.3
Total # PLMS	1144	PLMS Index	240.8
Total # PLMS Arousals	21	PLMS Arousal Index	4.4

RESPIRATORY PARAMETERS

Respiratory channels showed a total of 6 events. Those events included 3 Obstructive apnea and 3 Hypopneas, 0 Mixed and 0 Central events. The Apnea/ Hypopnea index was 1.3 per hour.

A total of 285.0 min of the total sleep time.

- Oxyhemoglobin saturation at baseline was 99 %
- The Lowest oxyhemoglobin saturation was 95 %

DIAGNOSTIC IMPRESSION:

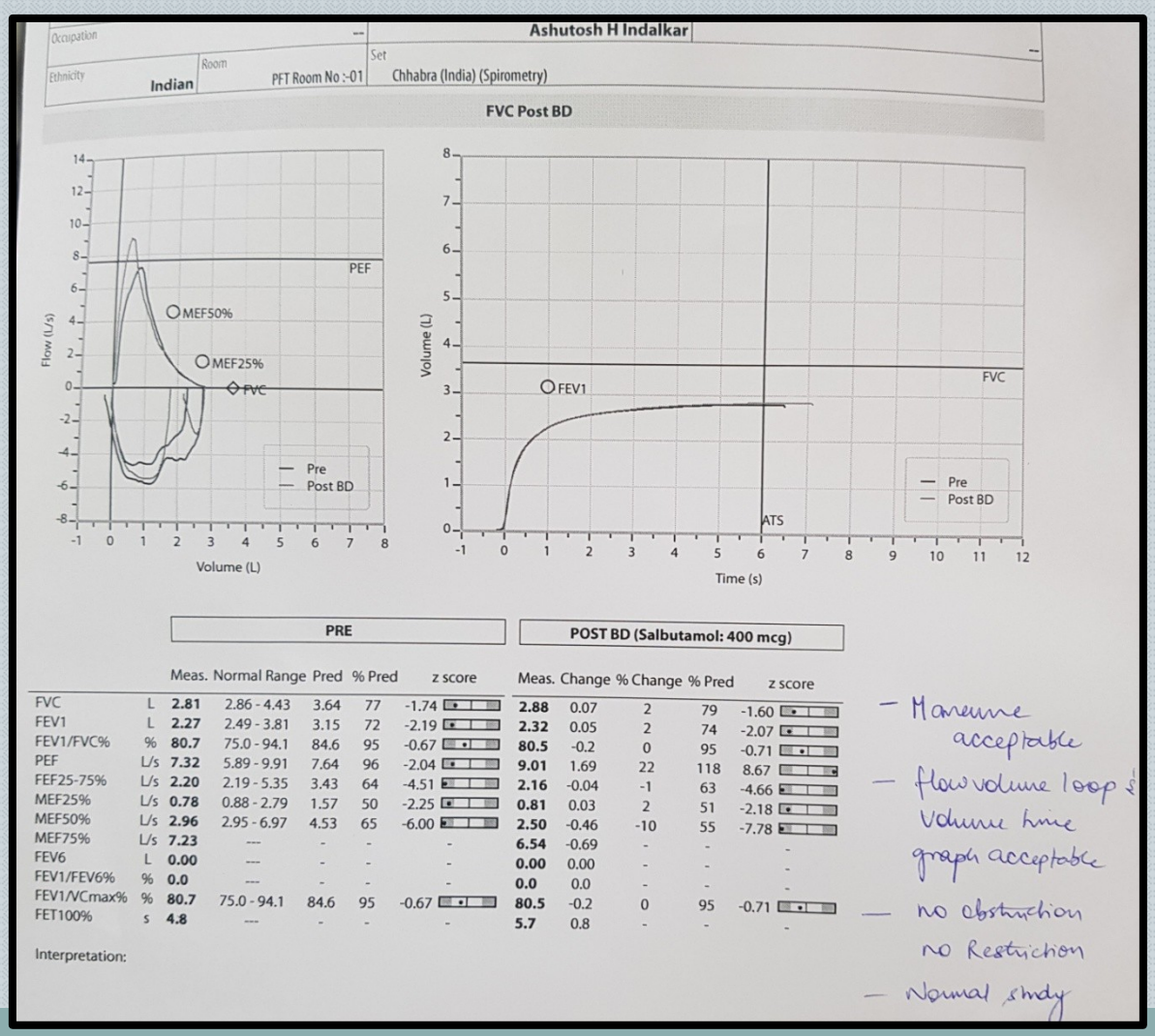
OBSTRUCTIVE SLEEP APNEA AND HYPOPNEA SYNDROME (OSA)
Severity Criteria: Normal , AHI 1.3 of with nadir oxygen of 95%.

Madhura medical Equipment
Contact No:-9767196713

Philips Respironics
www.sleepsolution.com

AHI- 1.3 (WNL)
No evidence of Obstructive Sleep Apnoea

Spirometry – Normal study, No obstruction/no restriction



Occupation --
Ethnicity Indian
Room PFT Room No :-01
Ashutosh H Indalkar
Set Chhabra (India) (Spirometry)

FVC Post BD

		PRE					POST BD (Salbutamol: 400 mcg)				
		Meas.	Normal Range	Pred	% Pred	z score	Meas.	Change	% Change	% Pred	z score
FVC	L	**2.81**	2.86 - 4.43	3.64	77	-1.74	**2.88**	0.07	2	79	-1.60
FEV1	L	**2.27**	2.49 - 3.81	3.15	72	-2.19	**2.32**	0.05	2	74	-2.07
FEV1/FVC%	%	**80.7**	75.0 - 94.1	84.6	95	-0.67	**80.5**	-0.2	0	95	-0.71
PEF	L/s	**7.32**	5.89 - 9.91	7.64	96	-2.04	**9.01**	1.69	22	118	8.67
FEF25-75%	L/s	**2.20**	2.19 - 5.35	3.43	64	-4.51	**2.16**	-0.04	-1	63	-4.66
MEF25%	L/s	**0.78**	0.88 - 2.79	1.57	50	-2.25	**0.81**	0.03	2	51	-2.18
MEF50%	L/s	**2.96**	2.95 - 6.97	4.53	65	-6.00	**2.50**	-0.46	-10	55	-7.78
MEF75%	L/s	**7.23**	---	-	-	-	**6.54**	-0.69	-	-	-
FEV6	L	**0.00**	---	-	-	-	**0.00**	0.00	-	-	-
FEV1/FEV6%	%	**0.0**	---	-	-	-	**0.0**	0.0	-	-	-
FEV1/VCmax%	%	**80.7**	75.0 - 94.1	84.6	95	-0.67	**80.5**	-0.2	0	95	-0.71
FET100%	s	**4.8**	---	-	-	-	**5.7**	0.8	-	-	-

Interpretation:

- Maneuver acceptable
- flow volume loop & Volume time graph acceptable
- no obstruction no Restriction
- Normal study

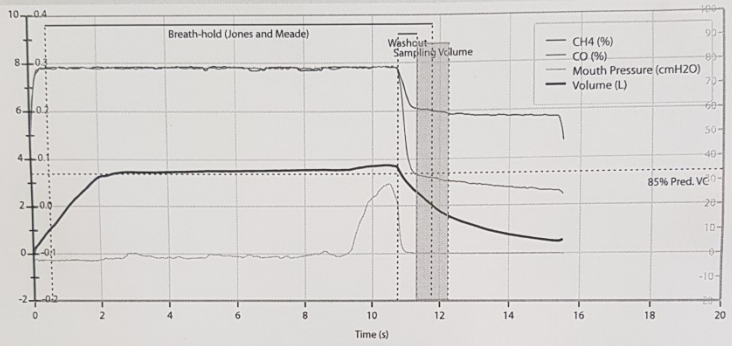
FEV_1 - 2.27 L (72%)
FEV_1/FVC – 80.7%
FVC – 2.81L (77%)

DLCO – Normal study

Ashutosh H Indalkar

Ethnic	Room	Set
Indian	--	ECCS extended (DLCO)

DLCO Single Breath



DLCO Results

		Meas.	Normal Range	Pred	% Pred	z score
DLCO	mL/min/mmHg	**31.51**	22.81 - 36.69	29.75	106	0.42
DLCO corr	mL/min/mmHg	**29.06**	22.81 - 36.69	29.75	98	-0.16
DLCO/VA	mL/min/mmHg/L	**2.74**	3.98 - 6.74	5.36	51	-3.11
VA	L	**10.60**	4.40 - 6.71	5.55	191	7.21
TLC(DLCO)	L	**10.73**	4.55 - 6.86	5.70	188	7.18
Hb	g/dL	**18.0**	---	-	-	-

DLCO Trials Results

(*) Best Trial		Trial 1 10:26 AM	Trial 2 10:29 AM (*)
DLCO	mL/min/mmHg	-	31.51
DLCO corr	mL/min/mmHg	-	29.06
DLCO/VA	mL/min/mmHg/L	-	6.62
VA	L	16.80	4.39
TLC(DLCO)	L	16.94	4.52
IV(DLCO)	L	2.95	3.33
DLCO 3eq	mL/min/mmHg	0.00	35.73
FiCO	%	0.294	0.294
FiCH4	%	0.291	0.294
FiO2	%	21.00	21.00
FaCO	%	-0.237	0.061
FaCH4	%	0.045	0.201
Sample Vol	mL	1019	1011
Washout Vol	mL	1056	1019
Breath Hold Time	s	11.12	11.24
Hb	g/dL	18.0	18.0

$DLCO_{corr}$ – 98%

All other causes of Pulmonary Hypertension were ruled out (i.e Pulmonary diseases, Cardiac abnormalities, DVT, HIV related, Connective tissue disorders, haematological disorders etc)

DIAGNOSIS

Idiopathic Pulmonary Arterial Hypertension

WHO Functional Class II

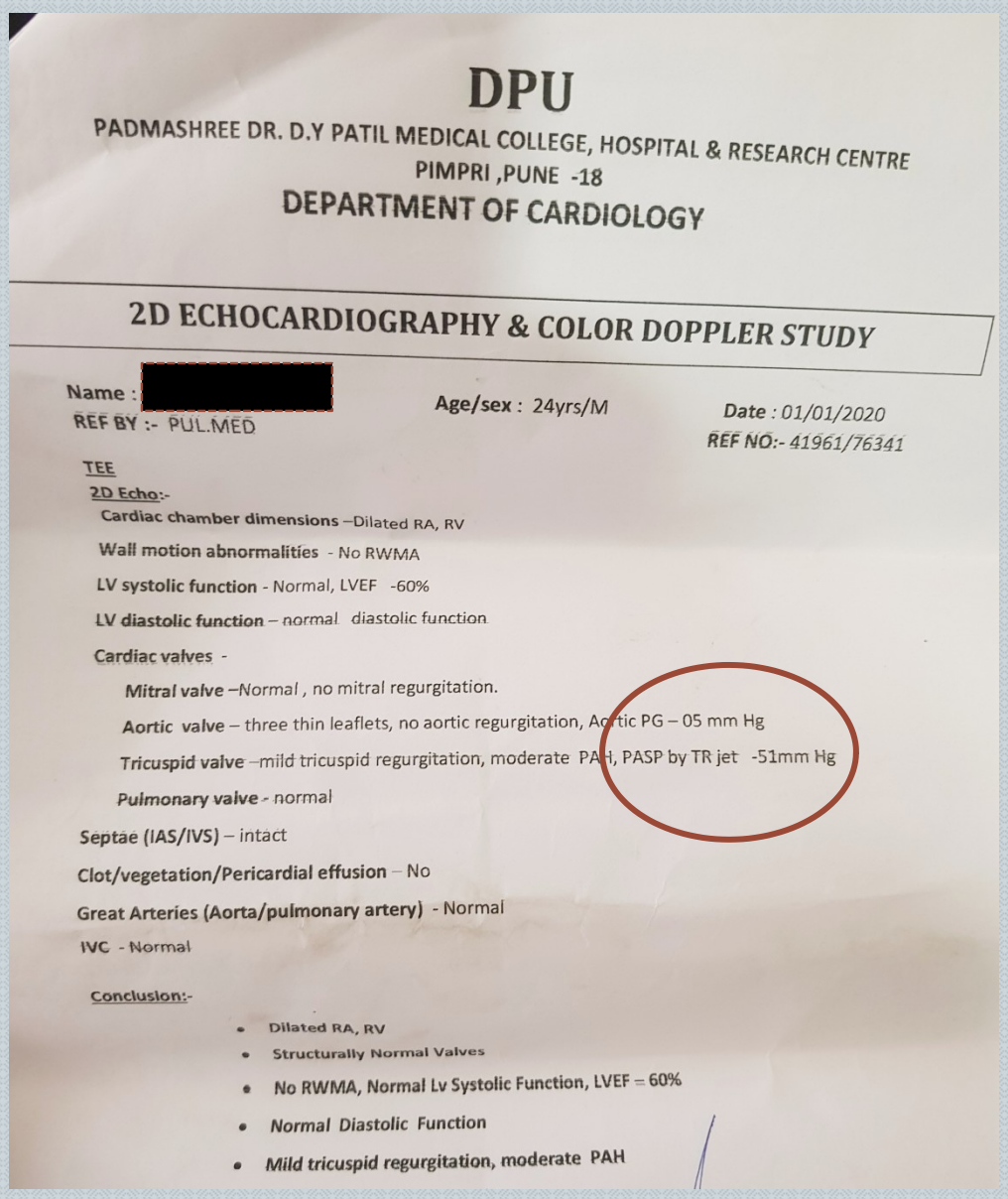
Discharged on

- **T. Ambrisentan+Tadalafil (5+20mg) OD**
- **T. Furosemide+Spironolactone (50mg) BD**
- **T. Digoxin (0.25mg) OD (5 days/week)**

(Sildenafil was replaced with Tadalafil as per latest guidelines)

- INJ. PNEUMOCOCCAL POLYSACCHARIDE VACCINE 23
- INFLUENZA VACCINE

GIVEN ON DISCHARGE



DPU

PADMASHREE DR. D.Y PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE
PIMPRI ,PUNE -18
DEPARTMENT OF CARDIOLOGY

2D ECHOCARDIOGRAPHY & COLOR DOPPLER STUDY

Name : [redacted]
REF BY :- PUL.MED

Age/sex : 24yrs/M

Date : 01/01/2020
REF NO:- 41961/76341

TEE

2D Echo:-

Cardiac chamber dimensions –Dilated RA, RV

Wall motion abnormalities - No RWMA

LV systolic function - Normal, LVEF -60%

LV diastolic function – normal diastolic function

Cardiac valves -

Mitral valve –Normal , no mitral regurgitation.

Aortic valve – three thin leaflets, no aortic regurgitation, Aortic PG – 05 mm Hg

Tricuspid valve –mild tricuspid regurgitation, moderate PAH, PASP by TR jet -51mm Hg

Pulmonary valve - normal

Septae (IAS/IVS) – intact

Clot/vegetation/Pericardial effusion – No

Great Arteries (Aorta/pulmonary artery) - Normal

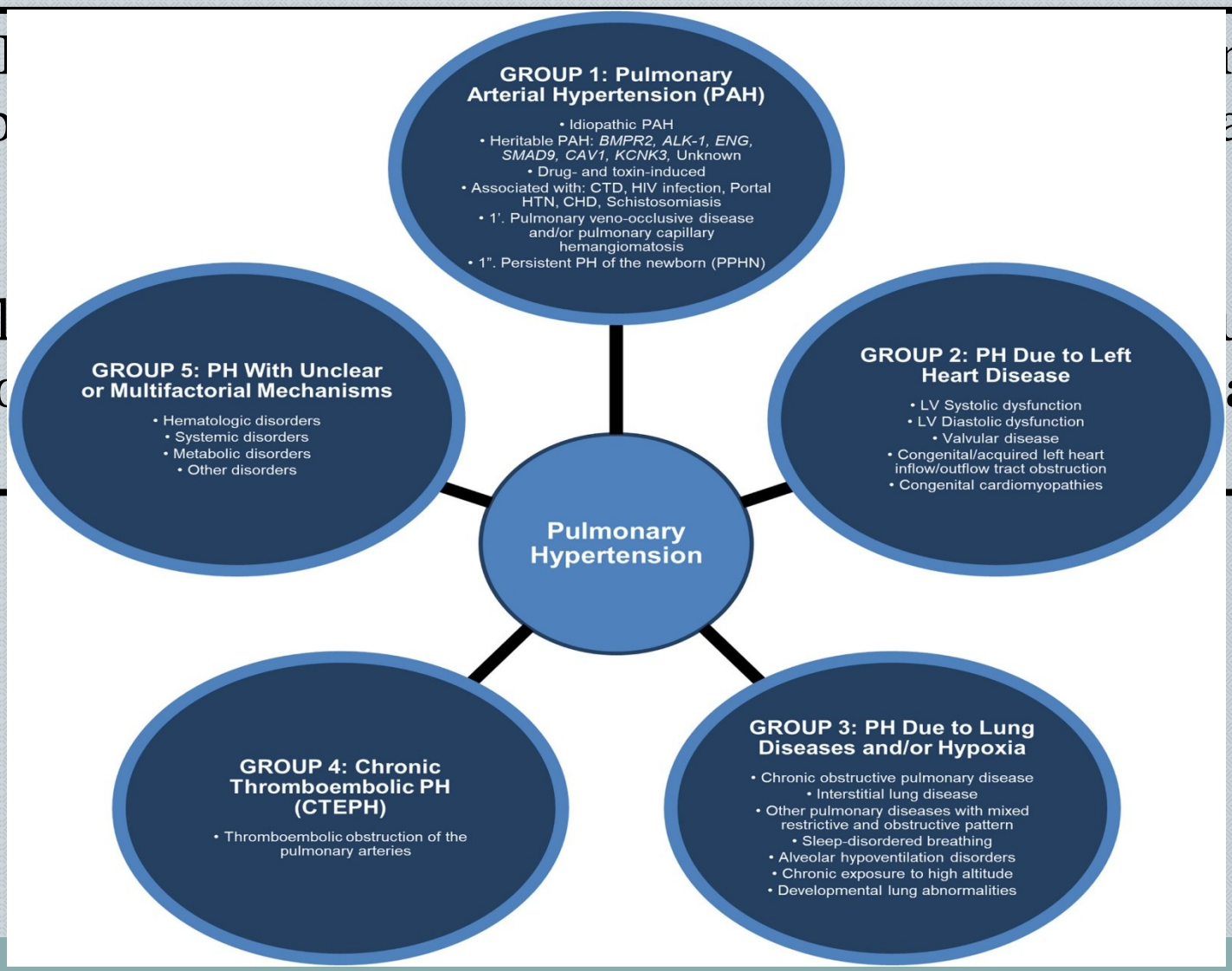
IVC - Normal

Conclusion:-

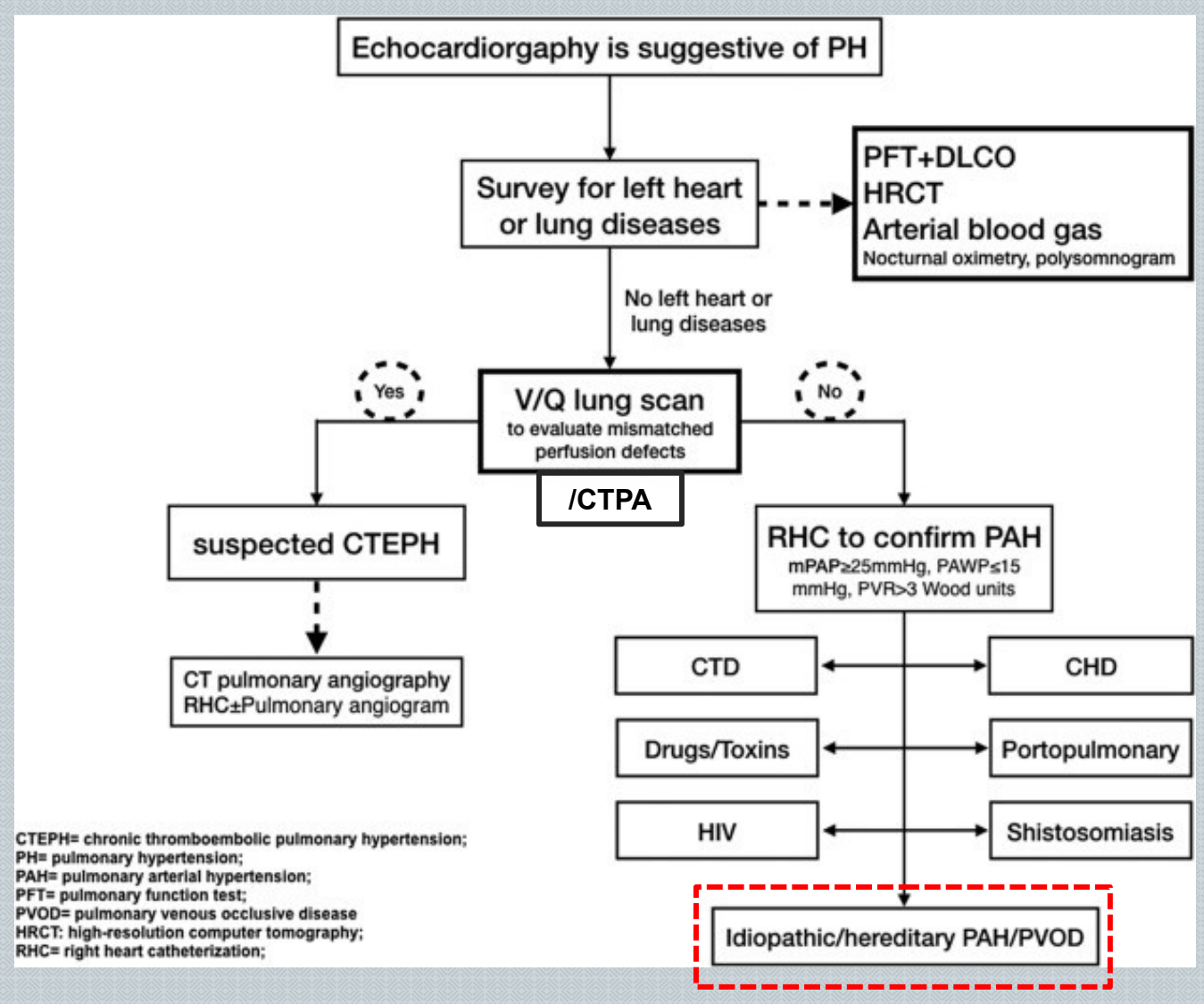
- Dilated RA, RV
- Structurally Normal Valves
- No RWMA, Normal Lv Systolic Function, LVEF = 60%
- Normal Diastolic Function
- Mild tricuspid regurgitation, moderate PAH

Patient is on regular follow up and as of TEE done in *January, 2020* - PASP = 51mm Hg, with a mild Tricuspid Regurgitation

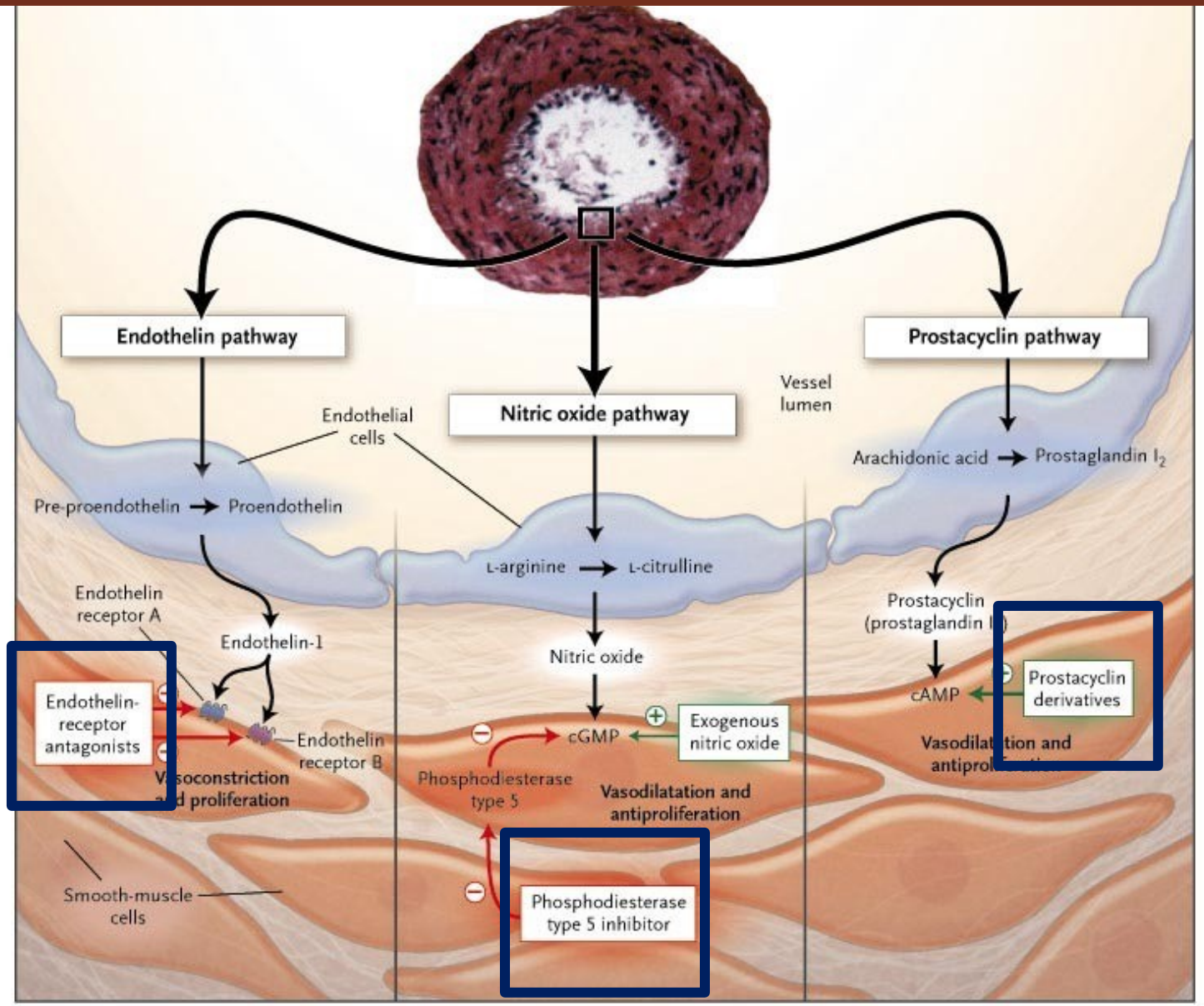
Discussion


GROUP 1: Pulmonary Arterial Hypertension (PAH)
• Idiopathic PAH
• Heritable PAH: BMPR2, ALK-1, ENG, SMAD9, CAV1, KCNK3, Unknown
• Drug- and toxin-induced
• Associated with: CTD, HIV infection, Portal HTN, CHD, Schistosomiasis
• 1'. Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis
• 1". Persistent PH of the newborn (PPHN)
GROUP 2: PH Due to Left Heart Disease
• LV Systolic dysfunction
• LV Diastolic dysfunction
• Valvular disease
• Congenital/acquired left heart inflow/outflow tract obstruction
• Congenital cardiomyopathies
GROUP 3: PH Due to Lung Diseases and/or Hypoxia
• Chronic obstructive pulmonary disease
• Interstitial lung disease
• Other pulmonary diseases with mixed restrictive and obstructive pattern
• Sleep-disordered breathing
• Alveolar hypoventilation disorders
• Chronic exposure to high altitude
• Developmental lung abnormalities
GROUP 4: Chronic Thromboembolic PH (CTEPH)
• Thromboembolic obstruction of the pulmonary arteries
GROUP 5: PH With Unclear or Multifactorial Mechanisms
• Hematologic disorders
• Systemic disorders
• Metabolic disorders
• Other disorders
Pulmonary Hypertension

WORK-UP

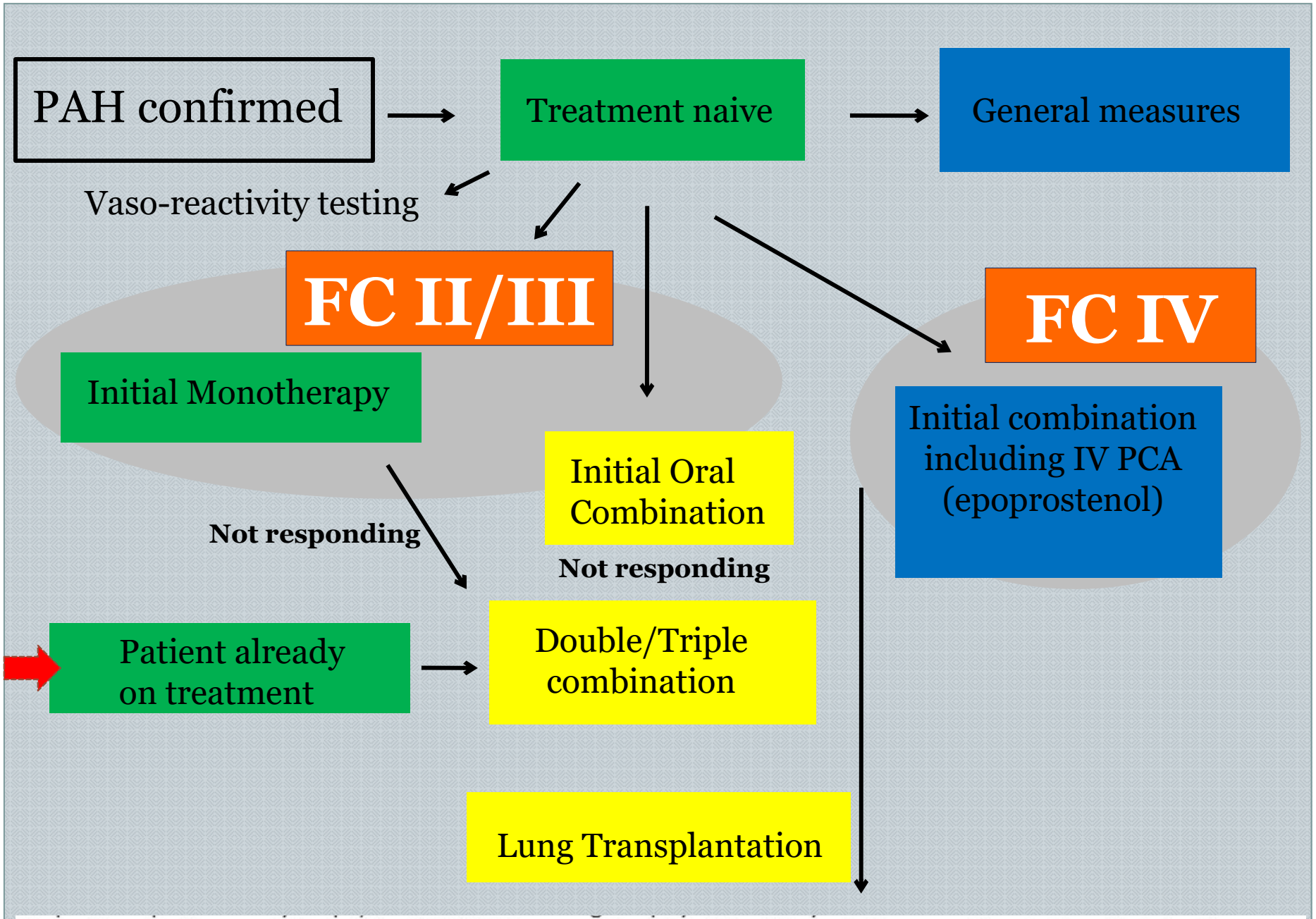

Echocardiorgaphy is suggestive of PH
Survey for left heart or lung diseases
PFT+DLCO
HRCT
Arterial blood gas
Nocturnal oximetry, polysomnogram
No left heart or lung diseases
Yes
V/Q lung scan
to evaluate mismatched perfusion defects
/CTPA
No
suspected CTEPH
CT pulmonary angiography
RHC±Pulmonary angiogram
RHC to confirm PAH
mPAP≥25mmHg, PAWP≤15 mmHg, PVR>3 Wood units
CTD
CHD
Drugs/Toxins
Portopulmonary
HIV
Shistosomiasis
Idiopathic/hereditary PAH/PVOD
CTEPH= chronic thromboembolic pulmonary hypertension;
PH= pulmonary hypertension;
PAH= pulmonary arterial hypertension;
PFT= pulmonary function test;
PVOD= pulmonary venous occlusive disease
HRCT: high-resolution computer tomography;
RHC= right heart catheterization;

MANAGEMENT


Endothelin pathway
Nitric oxide pathway
Prostacyclin pathway
Vessel lumen
Endothelial cells
Pre-proendothelin
Proendothelin
Arachidonic acid
Prostaglandin I2
L-arginine
L-citrulline
Endothelin receptor A
Endothelin-1
Endothelin-receptor antagonists
Endothelin receptor B
Nitric oxide
Prostacyclin (prostaglandin I2)
cAMP
Prostacyclin derivatives
Exogenous nitric oxide
cGMP
Phosphodiesterase type 5
Vasodilatation and antiproliferation
Smooth-muscle cells
Phosphodiesterase type 5 inhibitor

2015 ESC/ERS Guidelines:
Risk Assessment in PAH

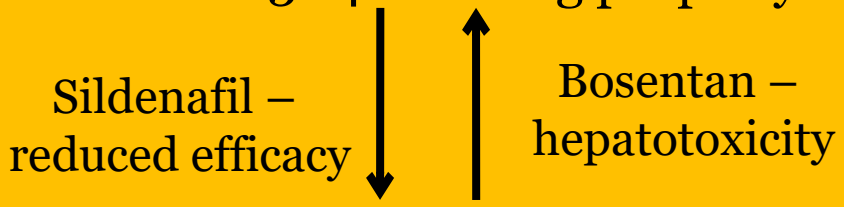
Determinants of prognosis[a] (estimated 1-year mortality)	Low risk <5%	Intermediate risk 5–10%	High risk >10%
Clinical signs of right heart failure	Absent	Absent	Present
Progression of symptoms	No	Slow	Rapid
Syncope	No	Occasional syncope[b]	Repeated syncope[c]
WHO functional class	I, II	III	IV
6MWD	>440 m	165–440 m	<165 m
Cardiopulmonary exercise testing	Peak VO_2 >15ml/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 slope ⩾45
NT-proBNP plasma levels	BNP <50 ng/l NT-proBNP <300 ng/l	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



Ambrisentan+Tadalafil vs Bosentan+Sildenafil

Sildenafil and Bosentan is a commonly used combination for PAH, however updates have advised for cautious use of these two drugs as –

1. Bosentan's CYP3A4 inducing property may lead to

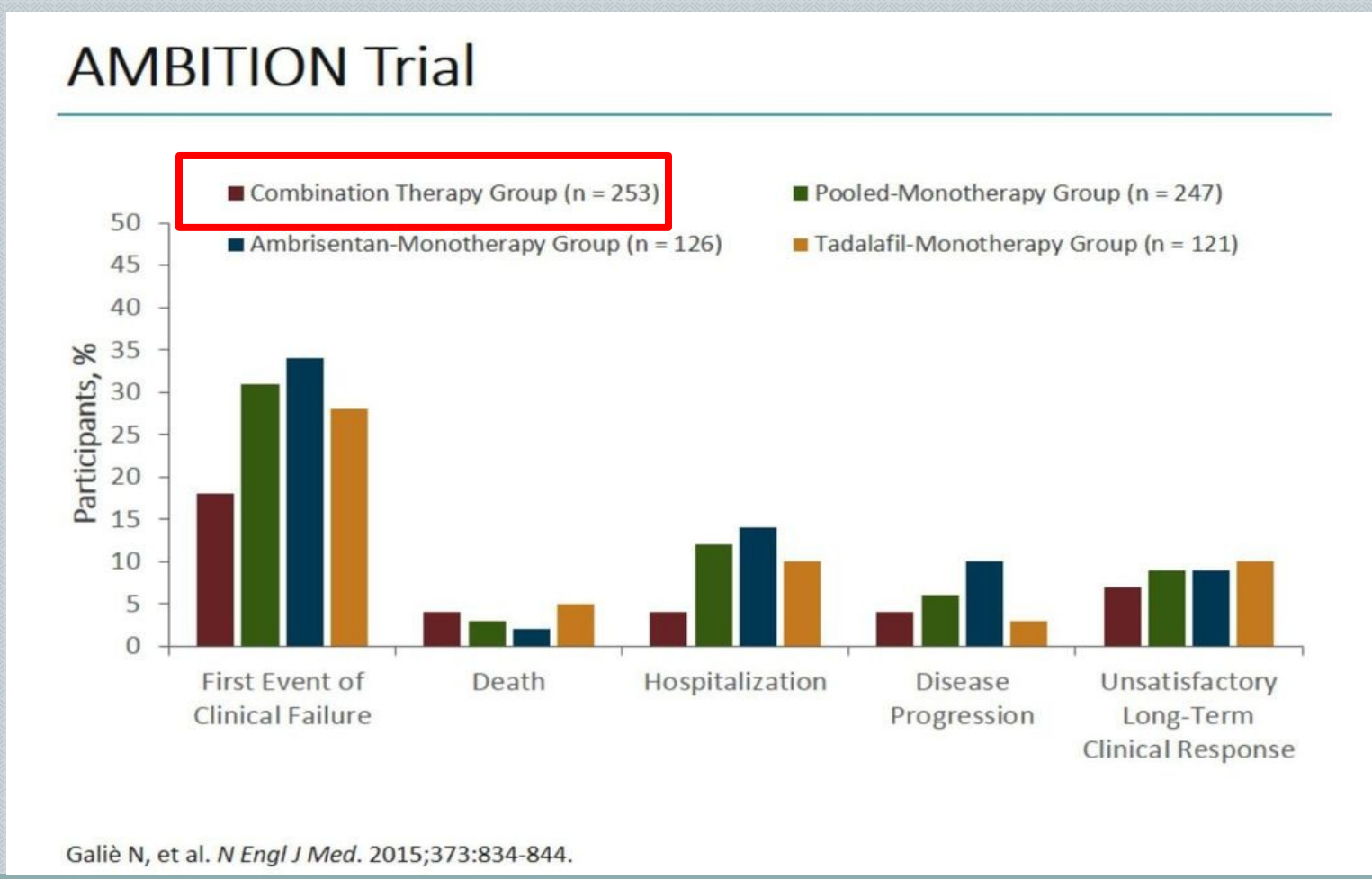


2. **COMPASS 2** (2014) - adding bosentan to sildenafil therapy was not superior to sildenafil monotherapy

McLaughlin et al, European Respiratory Journal 2015 46; 405-413

Sildenafil as a first line monotherapy is not recommended for PAH, and its combination with Ambrisentan as dual therapy over other drugs has not been proved adequately, either.

In the AMBITION trial of 2015, the risk of clinical failure was 50% lower among participants who received initial combination therapy with **Ambrisentan and Tadalafil** than among those who received monotherapy with either drug.



Galiè N, et al. *N Engl J Med*. 2015;373:834-844.

Recommendations	Class[a]	Level[b]
Diuretic treatment is recommended in PAH patients with signs of RV failure and fluid retention	I	C
Continuous long-term O_2 therapy is recommended in PAH patients when arterial blood O_2 pressure is consistently <8 kPa (60 mmHg)[d]	I	C
Oral anticoagulant treatment may be considered in patients with IPAH, HPAH and PAH due to use of anorexigens	IIb	C
Correction of anaemia and/or iron status may be considered in PAH patients	IIb	C
The use of angiotensin-converting enzyme inhibitors, angiotensin-2 receptor antagonists, beta-blockers and ivabradine is not recommended in patients with PAH unless required by co-morbidities (i.e. high blood pressure, coronary artery disease or left heart failure)	III	C

Diuretics and Digoxin, were added as part of supportive therapy, in view of the risk of decompensation and subsequent right heart failure.

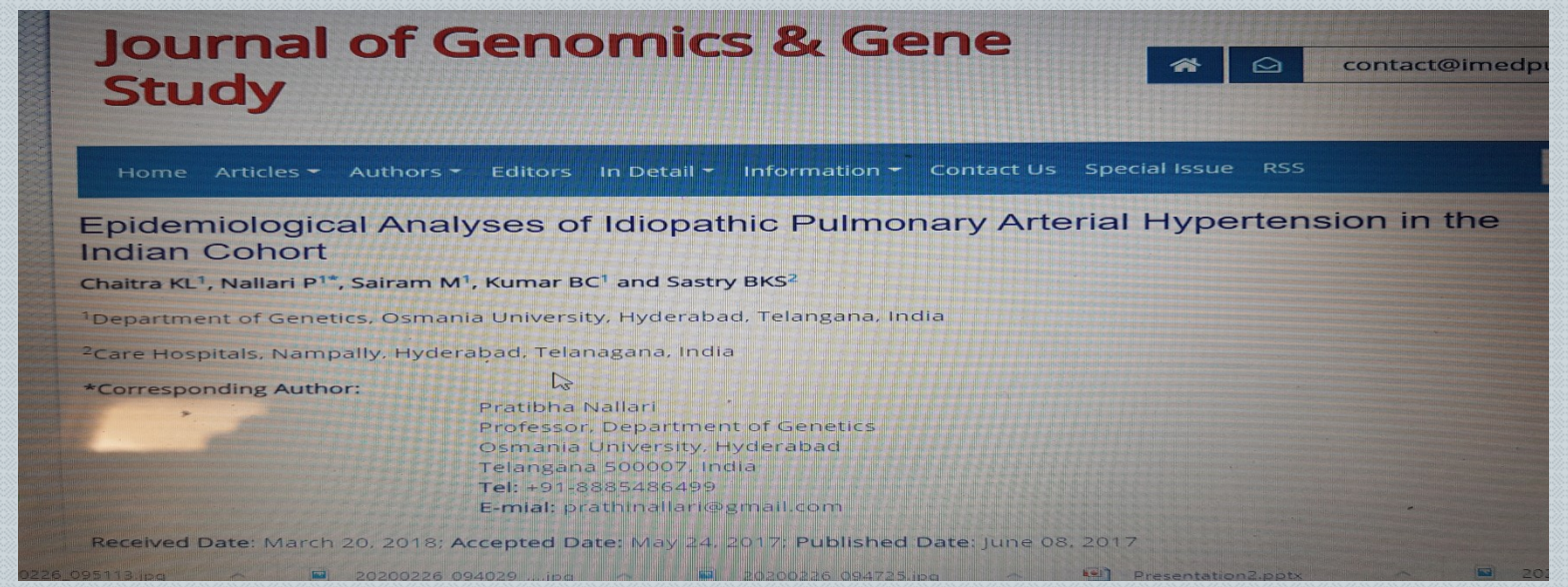
Oxygen, anticoagulants were avoided in view of the functional status of the patient, PaO2 at the time of presentation and complaints of hemoptysis.

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT), *European Heart Journal*, Volume 37, Issue 1, 1 January 2016, Pages 67–119, https://doi.org/10.1093/eurheartj/ehv317

A RARE PRESENTATION

1. Gender - 2:1 -9:1 female predilection

2. **Haemoptysis** - rare (<5%) symptom of PAH and presents variably.



Citation: Chaitra KL, Nallari P, Sairam M, Kumar BC, Sastry BKS (2018) Epidemiological Analyses of Idiopathic Pulmonary Arterial Hypertension in the Indian Cohort. J Genom Gene Study Vol.1 No.1:2

Follow Up

The frequency of follow-up testing should be 6 weeks at the time of initation of therapy and then 6 monthly with -

- **NT-proBNP**
- **six minute walk test (6MWT)**
- **2D ECHO with right heart catheterization (RHC)/TEE**
- **Troponin levels**
- **ABG**
- **iron status**
- **thyroid function**

Acknowledgements

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