Pulmonary Hypertension:
Getting the Right Diagnosis and Knowing When to Refer

June 12, 2025

7:00 PM – 8:00 PM EDT

TOTAL CME

PATIENT CASE 1: LINDA

75-YEAR-OLD WOMAN

Case Description:

- Diabetes, hypertension, obesity, body mass index (BMI) 34
- Atrial fibrillation
- 2-year history of dyspnea
- Medication:
  - Dual antihypertensive therapy
  - Direct oral anticoagulant (DOAC) for atrial fibrillation

PATIENT CASE 1: LINDA

75-YEAR-OLD WOMAN

Case Description:

- Diabetes, hypertension, obesity, BMI 34
- Atrial fibrillation
- 2-year history of dyspnea
- Medication:
  - Dual antihypertensive therapy
  - DOAC for atrial fibrillation
- She presented to her primary care provider (PCP)
- On physical exam:
  - Hypertensive with 2+ lower extremity edema
  - Not on diuretics
- Echocardiogram:
  - Right ventricular systolic pressure (RVSP) of 45
  - Left atrial (LA) enlargement
  - Left ventricular hypertrophy (LVH)
  - Normal right ventricle (RV) size and function

PATIENT CASE 1: LINDA

75-YEAR-OLD WOMAN

Case Description:

- Diabetes, hypertension, obesity, BMI 34
- Atrial fibrillation
- 2-year history of dyspnea
- Medication:
  - Dual antihypertensive therapy
  - DOAC for atrial fibrillation

PCP is considering referral to a pulmonary hypertension (PH) center of excellence

- She presented to her PCP
- On physical exam:
  - Hypertensive with 2+ lower extremity edema
  - Not on diuretics
- Echocardiogram:
  - RVSP of 45
  - LA enlargement
  - LVH
  - Normal RV size and function

PATIENT CASE 1: LINDA

75-YEAR-OLD WOMAN

Case Description:

- Diabetes, hypertension, obesity, BMI 34
- Atrial fibrillation
- 2-year history of dyspnea
- Medication:
  - Dual antihypertensive therapy
  - DOAC for atrial fibrillation
- She presented to her PCP
- On physical exam:
  - Hypertensive with 2+ lower extremity edema
  - Not on diuretics
- Echocardiogram:
  - RVSP of 45
  - LA enlargement
  - LVH
  - Normal RV size and function

Case 1: Echocardiogram

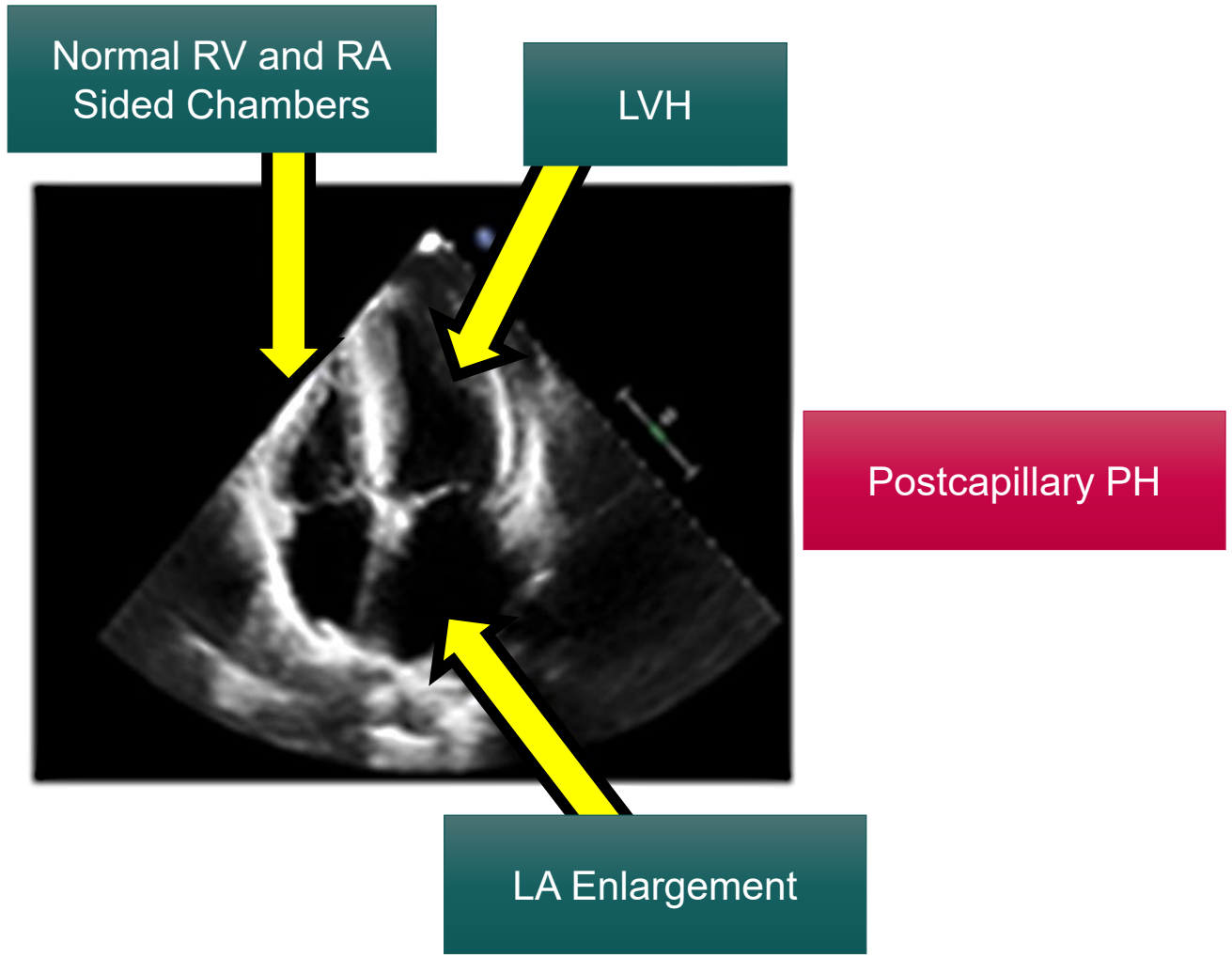
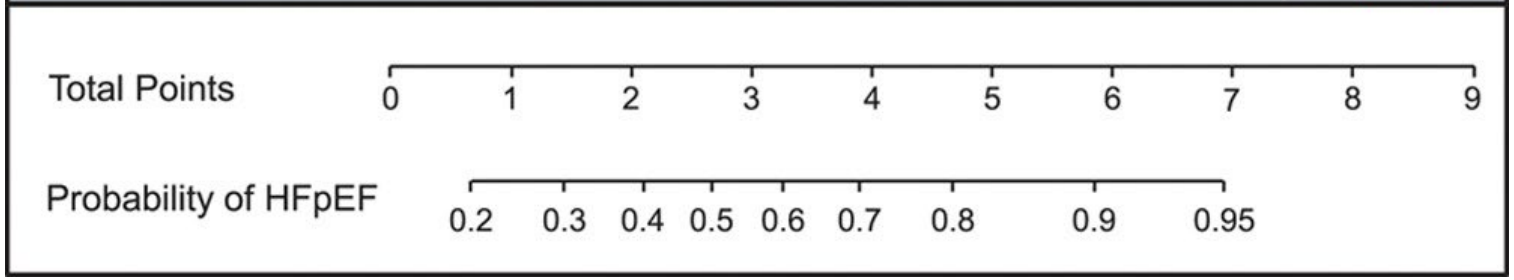


Image courtesy of faculty.

H_2FPEF Scoring System

	Clinical Variable	Values	Points
H_2	**H**eavy	BMI > 30 kg/m^2	2
	Hypertensive	2 or more antihypertensive medicines	1
F	Atrial **F**ibrillation	Paroxysmal or Persistent	3
P	**P**ulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
E	**E**lder	Age > 60 years	1
F	**F**illing Pressure	Doppler Echocardiographic E/e' > 9	1
H_2FPEF score			Sum (0-9)



HFpEF, heart failure with preserved ejection fraction.
Reddy YNV, et al. *Circulation*. 2018;138(9):861-870.

H_2FPEF and HFA-PEFF Scoring Systems

H_2FPEF Score

Comorbidity/Variable	Points
• Heavy (BMI>30 kg/m²)	2
• Hypertension (≥2 medications)	1
• Atrial Fibrillation	3
• Pulmonary Hypertension (Pulmonary Artery Pressure by echocardiography of >35mmHg)	1
• Age over 60 years	1
• Elevated Filling Pressures (E/e'>9 by echocardiography)	1

HFA-PEFF Score

Major (2 points)	Minor (1 point)
Functional Echocardiographic Parameters	
Septal e' <7 cm/sec Lateral e'<10 cm/sec Average E/e' ≥ 15 Tricuspid Regurgitation velocity >2.8 m/sec	Average E/e' ratio 9-14 Global Longitudinal strain <16%
Morphological Echocardiographic Parameters	
LA volume index >34ml/m2 LV mass index ≥ 149 m/m2 (m) or 122 g/m2 (w) and relative wall thickness >0.42	LA Volume index 29-34 ml/m2 LV mass index >115g/m2 (m) or >95 g/m2 (w) Relative wall thickness >0.42 LV wall thickness ≥ 12 mm
Biomarkers in Sinus Rhythm	
NT-pro BNP >220 pg/ml BNP>80 pg/ml	NT pro BNP 125-220 pg/ml BNP 35-80 pg/ml
Biomarkers in Atrial Fibrillation	
NT-pro BNP >660 pg/ml BNP>240 pg/ml	NT pro BNP 365-660 pg/ml BNP 105-240 pg/ml

BNP, B-type natriuretic peptide; HFA, Heart Failure Association; NT-proBNP, N-terminal pro-B-type natriuretic peptide.
Abramov D, Parwani P. *Front Cardiovasc Med*. 2021;8:665424.

Group 1 or Group 2 PAH?

- Scoring systems can be helpful
- Patients can straddle phenotypes
- Re-evaluate and treat any modifiable factors
- Determine if referral is appropriate

Linda is diagnosed as Group 2 PAH

Case 1: Group 2 PAH

Key Takeaways

- Ensure blood pressure (BP) is at target and patient is volume optimized
- Manage all underlying problems as best as possible
- Good partnerships with local PCP and local general cardiologist are critical

PATIENT CASE 2: EMILY

27-YEAR-OLD WOMAN

Case Description:

- No significant past medical history (PMH)
- Presents to her PCP with dyspnea on exertion
  - Began about 3 months ago
  - Seems to be getting worse, despite exercise & efforts at weight loss
- Echocardiogram:
  - RVSP of 45
  - RV enlargement, mild RV dysfunction
  - LA size is normal
  - Left ventricular ejection fraction (LVEF) 60%
- NT-proBNP is 1,000
- 6-minute walk test (6MWT) 350 m
  - Functional Class (FC) III
- Normal glomerular filtration rate (GFR)
- Systolic blood pressure (SBP) 120
- Heart rate (HR) 89

Case 2: Echocardiogram

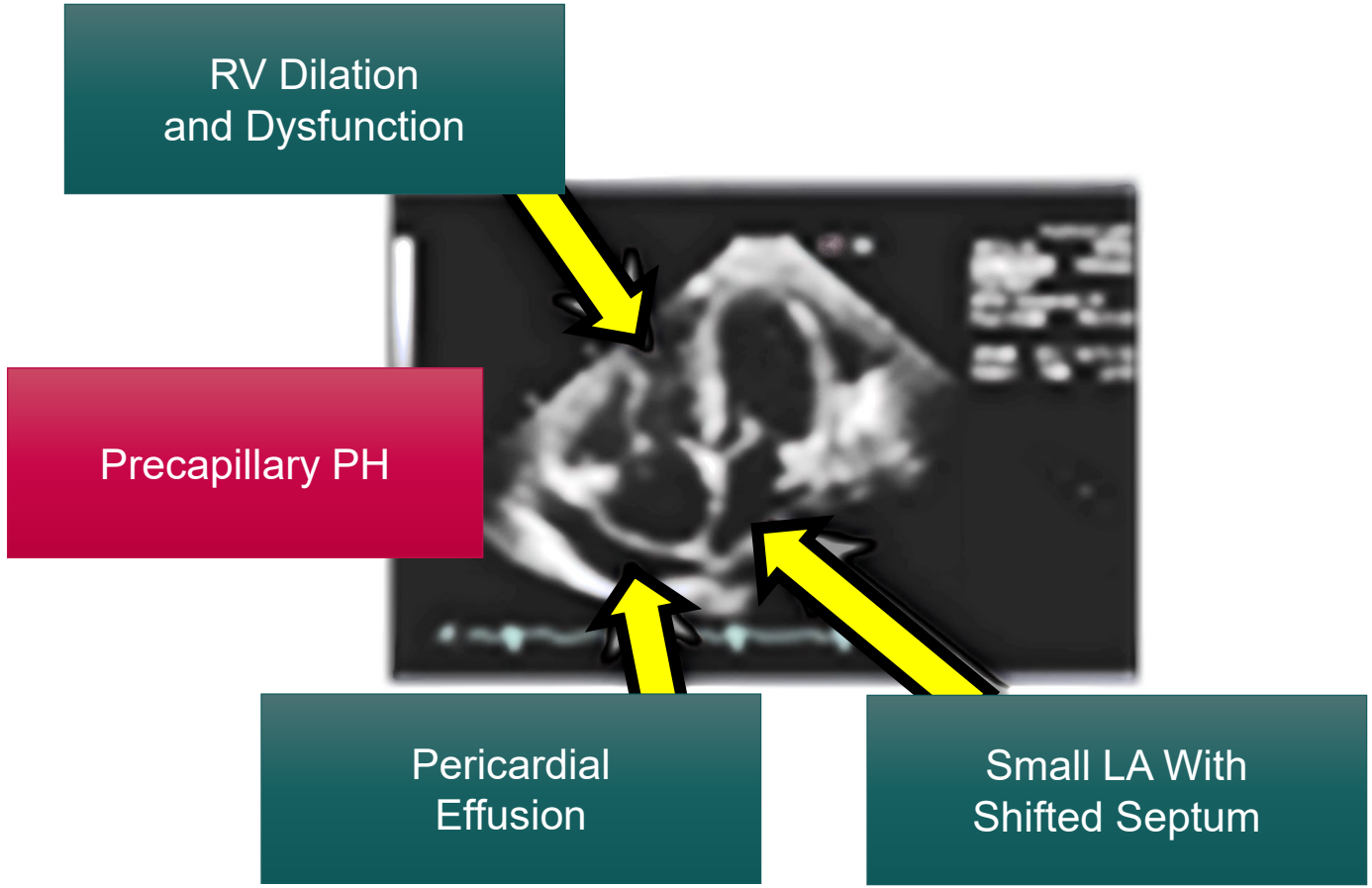


Image courtesy of faculty.

Case 2: Group 1 PAH

- Patient factors to consider:
  - Results of echocardiogram
  - Age and PMH

- Next steps:
  - Referral to a PH center and additional testing

Defining PAH for Patients

- Ask patients about their understanding of the condition
- Similar to a blood pressure in the arm, there is pressure in the vessels of the lungs
- When pressure in the lungs is high, it causes strain on the right side of the heart
- Leads to RV enlargement and dysfunction

Helping Patients Take an Active Role

- PH support materials and groups
- Medication support, as well as discussions about common side effects and management strategies
- Lifestyle changes support
  - Referring to a nutritionist
  - Counseling about staying active
  - Creating structured exercise programs

Helping Patients Take an Active Role

- Quality of life impact and emotional well-being
- Job considerations
- Social worker support and referral to mental well-being professional
- Pregnancy prevention and testing

Risk Score Calculators

REVEAL Lite 2 Risk Calculator

Directions: Select all variables that apply. **A minimum of 3 variables** are required to generate a score, where at least 2 are from most predictive values denoted **.

Step 1 Select at least 2 of the most predictive variables						Score
BNP (pg/mL)**	<50		50 to <200	200 to <800	≥800	
	–2		0	1	2	
OR						
NT-proBNP (pg/mL)**	<300		300 to <1100		≥1100	
	–2		0		2	
6MWT (m)**	≥440	320 to 440	<320 to 165	<165		
	–2	–1	0	1		
NYHA/WHO Functional Class**		I	II	III	IV	
		–1	0	1	2	
Step 2 Select additional variables.						
SBP (mm Hg)			SBP ≥110	SBP<110		
			0	1		
HR (BPM)			HR ≤96	HR >96		
			0	1		
eGFR < 60 mL/min/1.73m² or renal insufficiency			No	Yes		
			0	1		
				Step 3 Sum of above (min. 3 variables)		
						+6
					Step 4 Risk score	

	Low Risk	Intermediate Risk	High Risk
Risk Score	≤5	6–7	≥8

BPM, beats per minute; eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association; REVEAL, Registry to Evaluate Early and Long-Term PAH Disease Management; WHO, World Health Organization.
Benza RL, et al. *Chest*. 2021;159(1):337-346.

Risk Stratification Models

ESC/ERS

3-strata risk score

Comprehensive risk assessment in pulmonary arterial hypertension (three-strata model)			
Determinants of prognosis (estimated 1-year mortality)	**Low risk (<5%)**	**Intermediate risk (5–20%)**	**High risk (>20%)**
Clinical observations and modifiable variables			
Signs of right HF	Absent	Absent	Present
Progression of symptoms and clinical manifestations	No	Slow	Rapid
Syncope	No	Occasional syncope[a]	Repeated syncope[b]
WHO-FC	I, II	III	IV
6MWD[c]	>440 m	165–440 m	<165 m
CPET	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	Peak VO_2 <11 mL/min/kg (<35% pred.) VE/VCO_2 slope >44
Biomarkers: BNP or NT-proBNP[d]	BNP <50 ng/L NT-proBNP <300 ng/L	BNP 50–800 ng/L NT-proBNP 300–1100 ng/L	BNP >800 ng/L NT-proBNP >1100 ng/L
Echocardiography	RA area <18 cm^2 TAPSE/sPAP >0.32 mm/mmHg No pericardial effusion	RA area 18–26 cm^2 TAPSE/sPAP 0.19–0.32 mm/mmHg Minimal pericardial effusion	RA area >26 cm^2 TAPSE/sPAP <0.19 mm/mmHg Moderate or large pericardial effusion
cMRI[e]	RVEF >54% SVI >40 mL/m^2 RVESVI <42 mL/m^2	RVEF 37–54% SVI 26–40 mL/m^2 RVESVI 42–54 mL/m^2	RVEF <37% SVI <26 mL/m^2 RVESVI >54 mL/m^2
Haemodynamics	RAP <8 mmHg CI ⩾2.5 $L/min/m^2$ SVI >38 mL/m^2 SvO_2 >65%	RAP 8–14 mmHg CI 2.0–2.4 $L/min/m^2$ SVI 31–38 mL/m^2 SvO_2 60–65%	RAP >14 mmHg CI <2.0 $L/min/m^2$ SVI <31 mL/m^2 SvO_2 <60%

CI, cardiac index; cMRI, cardiac magnetic resonance imaging; CPET, cardiopulmonary exercise test; ESC, European Society of Cardiology; ERS, European Respiratory Society; HF, heart failure; RAP, right atrial pressure; RVEF, right ventricular ejection fraction; RVESVI, right ventricular end-systolic volume index; 6MWD, 6-minute walk distance; sPAP, systolic pulmonary arterial pressure; SVI, stroke volume index; SvO_2, venous oxygen saturation; TAPSE, tricuspid annular plane systolic excursion; VE/VCO_2, ventilatory equivalent for carbon dioxide; VO_2, volume oxygen.

Benza RL, et al. *Chest.* 2019;156(2):323-337. Benza RL, et al. *Chest.* 2021;159(1):337-346. Humbert M, et al. *Eur Respir J.* 2023;61(1):2200879.

Risk Stratification Models

ESC/ERS

3-strata risk score

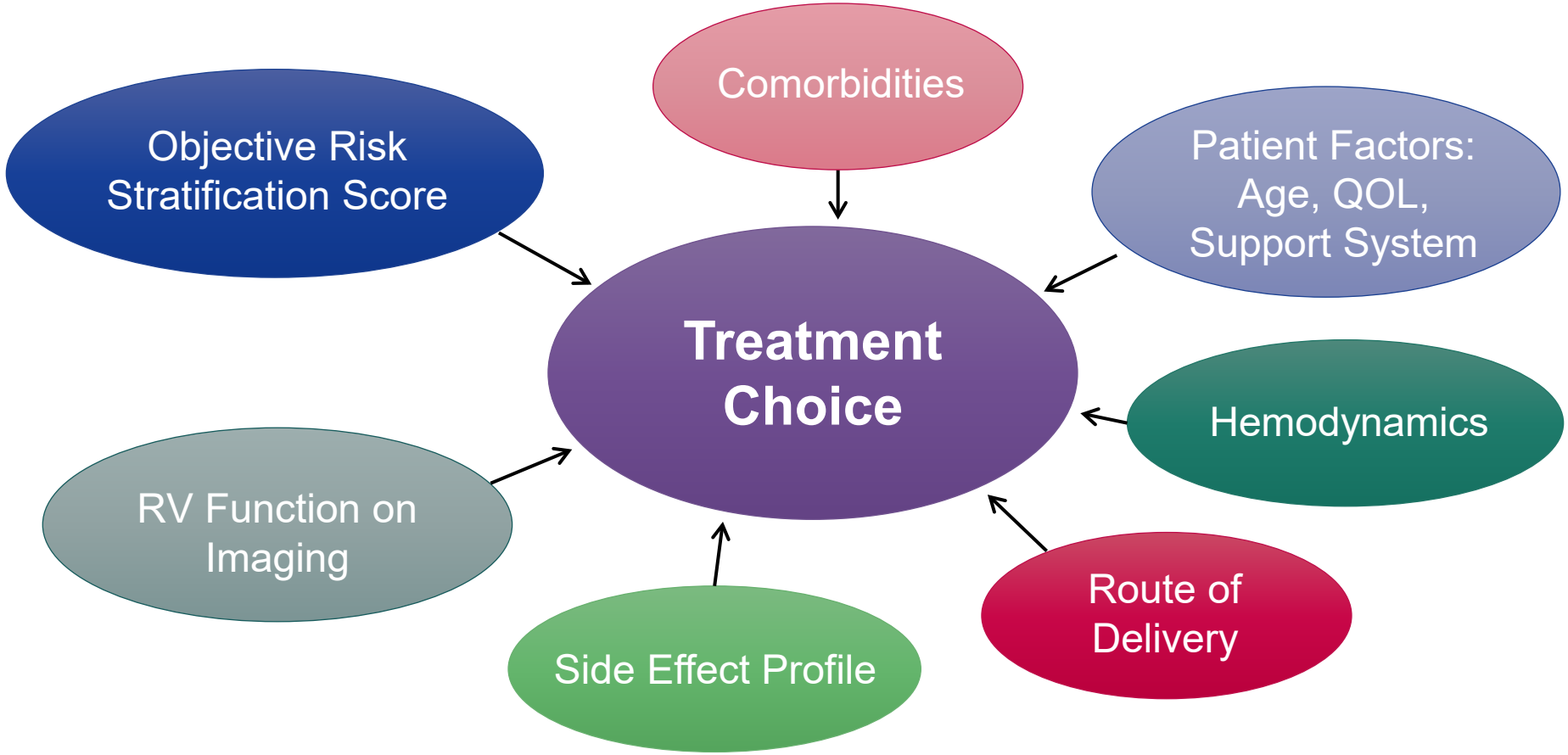
Comprehensive risk assessment in pulmonary arterial hypertension (three-strata model)			
Determinants of prognosis (estimated 1-year mortality)	**Low risk (<5%)**	**Intermediate risk (5–20%)**	**High risk (>20%)**
Clinical observations and modifiable variables			
Signs of right HF	Absent	Absent	Present
Progression of symptoms and clinical manifestations	No	Slow	Rapid
Syncope	No	Occasional syncope[a]	Repeated syncope[b]
WHO-FC	I, II	III	IV
6MWD[c]	>440 m	165–440 m	<165 m
CPET	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	Peak VO_2 <11 mL/min/kg (<35% pred.) VE/VCO_2 slope >44
Biomarkers: BNP or NT-proBNP[d]	BNP <50 ng/L NT-proBNP <300 ng/L	BNP 50–800 ng/L NT-proBNP 300–1100 ng/L	BNP >800 ng/L NT-proBNP >1100 ng/L
Echocardiography	RA area <18 cm^2 TAPSE/sPAP >0.32 mm/mmHg No pericardial effusion	RA area 18–26 cm^2 TAPSE/sPAP 0.19–0.32 mm/mmHg Minimal pericardial effusion	RA area >26 cm^2 TAPSE/sPAP <0.19 mm/mmHg Moderate or large pericardial effusion
cMRI[e]	RVEF >54% SVI >40 mL/m^2 RVESVI <42 mL/m^2	RVEF 37–54% SVI 26–40 mL/m^2 RVESVI 42–54 mL/m^2	RVEF <37% SVI <26 mL/m^2 RVESVI >54 mL/m^2
Haemodynamics	RAP <8 mmHg CI ⩾2.5 $L/min/m^2$ SVI >38 mL/m^2 SvO_2 >65%	RAP 8–14 mmHg CI 2.0–2.4 $L/min/m^2$ SVI 31–38 mL/m^2 SvO_2 60–65%	RAP >14 mmHg CI <2.0 $L/min/m^2$ SVI <31 mL/m^2 SvO_2 <60%

4-strata risk score

Variables used to calculate the simplified four-strata risk-assessment tool				
Determinants of prognosis	**Low risk**	**Intermediate–low risk**	**Intermediate–high risk**	**High risk**
Points assigned	1	2	3	4
WHO-FC	I or II[a]	-	III	IV
6MWD, m	>440	320–440	165–319	<165
BNP or NT-proBNP, ng/L	<50 <300	50–199 300–649	200–800 650–1100	>800 >1100

Benza RL, et al. *Chest*. 2019;156(2):323-337. Benza RL, et al. *Chest*. 2021;159(1):337-346. Humbert M, et al. *Eur Respir J*. 2023;61(1):2200879.

Factors Affecting Treatment Choice



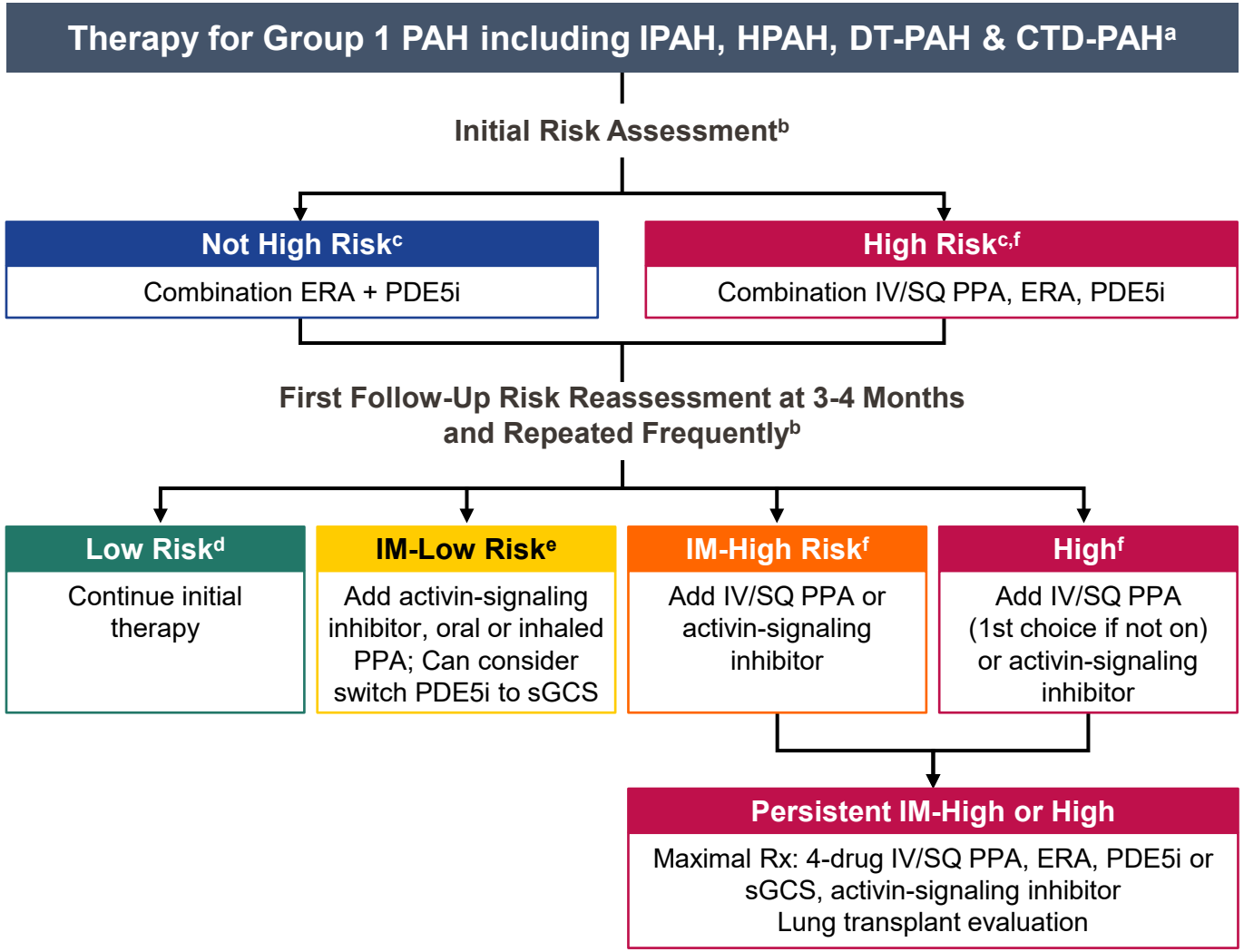
QOL, quality of life.

FDA-Approved Treatment Options

Endothelin receptor antagonist (ERA)	NO-cGMP pathway	Prostanoid - prostacyclin analog	Prostacyclin receptor agonist	Activin-signaling inhibitor	Combination NO-cGMP pathway/ERA
Bosentan PO	Sildenafil PO	Epoprostenol IV	Selexipag PO, IV	Sotatercept SQ	Tadalafil/ Macitentan PO
Ambrisentan PO	Tadalafil PO	Treprostinil IV, SQ, PO, Inh			
Macitentan PO	Riociguat PO	Iloprost Inh			

Inh, inhaled; IV, intravenous; NO-cGMP, nitric oxide-cyclic guanosine monophosphate; PO, by mouth; SQ, subcutaneous.

7th WSPH Treatment Algorithm



Treatment Algorithm Key Points

a. Treatment algorithm is intended for patients with confirmed group 1 PAH (phenotypically clear-cut, including ***mPAP ≥25 mmHg and PVR >3 Wood units*** and no significant response on acute vasoreactivity testing). Treatment nuances in PAH with complex phenotypes.

b. ***Risk assessment*** should be performed at baseline, within 3-4 months, and periodically thereafter, and using FC, 6MWD, and natriuretic peptides as a part of a validated risk calculator. Hemodynamics, RV imaging, and other measures should be used to supplement risk assessment.

c. ***Initial triple therapy*** with an IV/SQ PPA is recommended in high-risk patients and may be considered in non-high risk with severe hemodynamics and/or poor RV function.

d. Most ***low risk*** at follow-up patients should continue initial therapy.

e. Clinical trials with oral and inhaled treprostinil included ***only patients on monotherapy***, while studies of selexipag and sotatercept included patients on combination therapy.

f. ***Transplant referral*** should be considered for select high-risk patients **at diagnosis**, and for IM-high and high-risk patients at ***first*** or subsequent follow-up.

CTD, connective tissue disease; DT, drug and toxin; HPAH, hereditary PAH; IM, intermediate; IPAH, idiopathic PAH; mPAP, mean pulmonary artery pressure; PDE5i, phosphodiesterase-5 inhibitor; PPA, prostacyclin pathway agent; PVR, pulmonary vascular resistance; Rx, prescription; sGCS: soluble guanylyl cyclase stimulator; WSPH, World Symposium on Pulmonary Hypertension.

Chin KM, et al. *Eur Respir J*. 2024;64(4):2401325.

Achieving Low-Risk Status

- Initial therapy
  - Individual therapy vs dual therapy
  - Potential benefits of combination therapy:
    - May ease pill burden
    - Fewer prior authorizations, refills, and copays
- What does therapy look like after follow-up?

Talking Pregnancy Prevention With Your Patients

- PAH during pregnancy poses significant risks to mother and fetus
  - Potentially life-threatening
- Discuss pregnancy prevention early and often
- Certain therapies can be teratogenic
- Monthly pregnancy tests may be recommended
- Review options for birth control

Case 2: Group 1 PAH

Key Takeaways

- Group 2 patients can generally be managed in a cardiology practice rather than PH center
  - Seeing more Group 2 patients
  - But be on the lookout for Group 1 patients and refer them sooner rather than later
- Testing is important, but it may not provide all the information needed
  - Understand the differences of Group 1 and Group 2 echocardiogram findings

Case 2: Group 1 PAH

Key Takeaways

- Leverage your colleagues
- Employ risk assessment tools to help guide treatment decisions
- Aim for low risk, but goals should be individualized for the patient and their QOL

Case 2: Group 1 PAH

Key Takeaways

- Patient education
  - Can be extensive
  - May be ongoing
  - Will likely change over time
  - Should be patient-guided
- Many treatment options
  - Consider patient factors, such as pill burden
  - Educate around managing side effects
- Pregnancy prevention
  - Discuss early on
  - Review need for monthly tests

PAH Diagnosis, Management, and Referral

- Co-managing patients with PCPs and local specialists is key
- Group 2 patients and patients with comorbidities are becoming more common
- Be on the lookout for Group 1 patients and when to refer
- PH centers of excellence have key specialists and resources
- Risk assessment and appropriate escalation of therapy are important