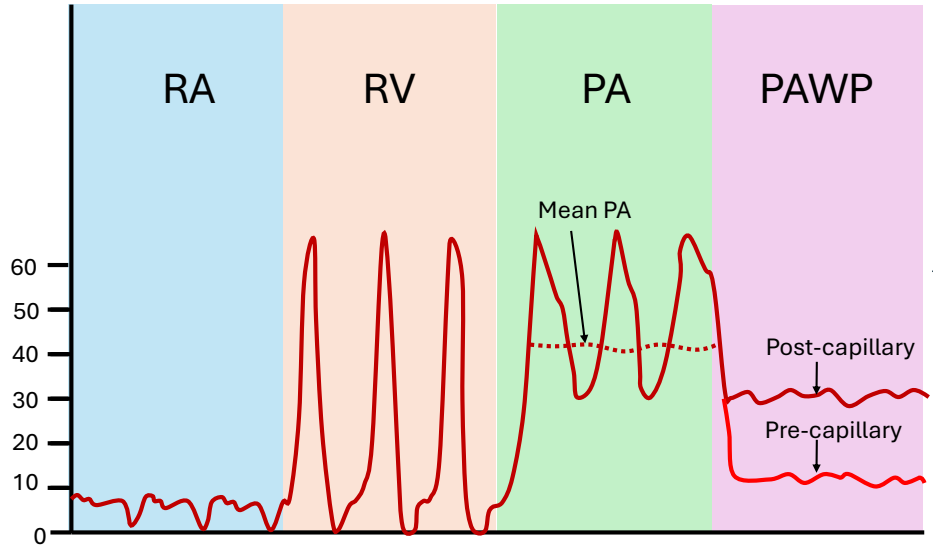
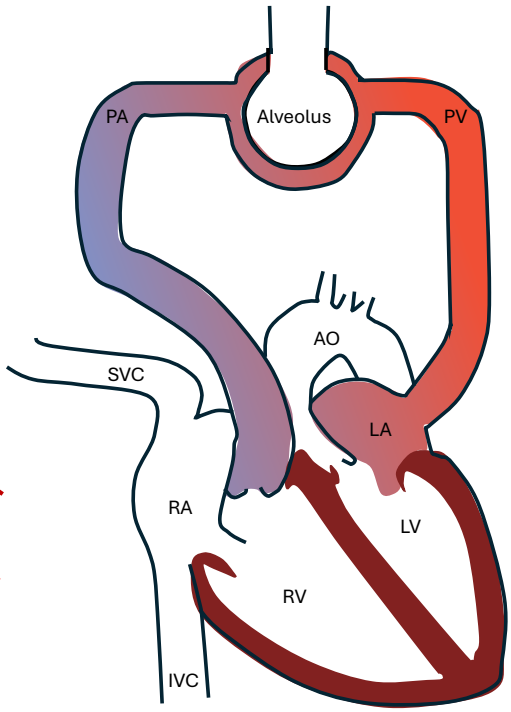
Pulmonary Hypertension

Zachary Fulkerson, MD, PhD

Definitions

- PH is a heterogenous syndrome and does not represent a single diagnosis
    - PH is defined by a mean PA pressure >20 mmHg
- Echocardiogram can aid in diagnosis though definitive diagnosis requires a right heart catheterization to directly measure the PA pressures
- An example of pressure tracings for a right heart catheterization is shown below
- PH can be organized a few different ways
    - Pre-capillary vs Post-capillary (see table below)
    - WHO Group
        - Group 1: Pulmonary arterial hypertension
        - Group 2: Pulmonary hypertension due to left sided disease
        - Group 3: Pulmonary hypertension due to chronic lung disease
        - Group 4: Pulmonary hypertension due to chronic thromboembolic disease
        - Group 4: Pulmonary hypertension from miscellaneous causes.





PH Classification

Parameter	Pre-Capillary PH	Post-Capillary PH	Combined (Mixed) PH
Mean Pulmonary Artery Pressure (mPAP)	>20 mmHg	>20 mmHg	>20 mmHg
Pulmonary Artery Wedge Pressure (PAWP)	≤15 mmHg	>15 mmHg	>15 mmHg
Pulmonary Vascular Resistance (PVR)	≥2 Wood Units (WU)	<2 Wood Units (WU) or normal	≥2 Wood Units (WU)
Common Causes	- Pulmonary arterial hypertension (PAH, WHO Group 1) - PH due to lung diseases (WHO Group 3) - Chronic thromboembolic PH (WHO Group 4) - PH with unclear/multifactorial mechanisms (WHO Group 5)	- Left heart disease (WHO Group 2, e.g., heart failure, valvular disease) - Venous obstruction or high-output states	- Left heart disease with secondary pulmonary vascular remodeling (WHO Group 2) - Heart failure with lung disease or PAH components - Complex multifactorial PH
Pathophysiology	Increased resistance in pulmonary arterioles, often due to vasoconstriction, remodeling, or obstruction	Backward transmission of elevated left atrial pressure into pulmonary circulation	Combination of elevated left atrial pressure and pulmonary arteriolar remodeling or resistance
Examples	Idiopathic PAH, connective tissue disease-associated PAH, COPD-related PH, CTEPH	Heart failure with preserved/reduced ejection fraction, mitral/aortic valve disease	Heart failure with preserved ejection fraction (HFpEF) with pulmonary vascular disease, severe aortic stenosis with PAH-like features

PH Severity

Variables (Est. 1 Yr Mortality)	Low Risk (<5%)	Intermediate Risk (5%–20%)	High Risk (>20%)
Point Value Per Variable	1	2	3
Signs of right HF	Absent	Absent	Present
Progression of symptoms	No	Slow	Rapid
Syncope	No	Occasional syncope	Repeated syncope
WHO-FC	I, II	III	IV
6MWD	>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	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 >0.32 mm/mmHg Minimal pericardial effusion	RA area >26 cm^2 TAPSE/sPAP >0.32 mm/mmHg Moderate–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 mm Hg CI ≥2.5 L/min/m^2 SVI >38 mL/m^2 SvO_2 >65%	RAP 8–14 mm Hg CI 2–2.4 L/min/m^2 SVI >31–38 mL/m^2 SvO_2 60%–65%	RAP >14 mm Hg CI <2 L/min/m^2 SVI <31 mL/m^2 SvO_2 <60%
Total Risk Score	Divide the sum of all variable scores by the number of variables entered and round to the nearest decimal		

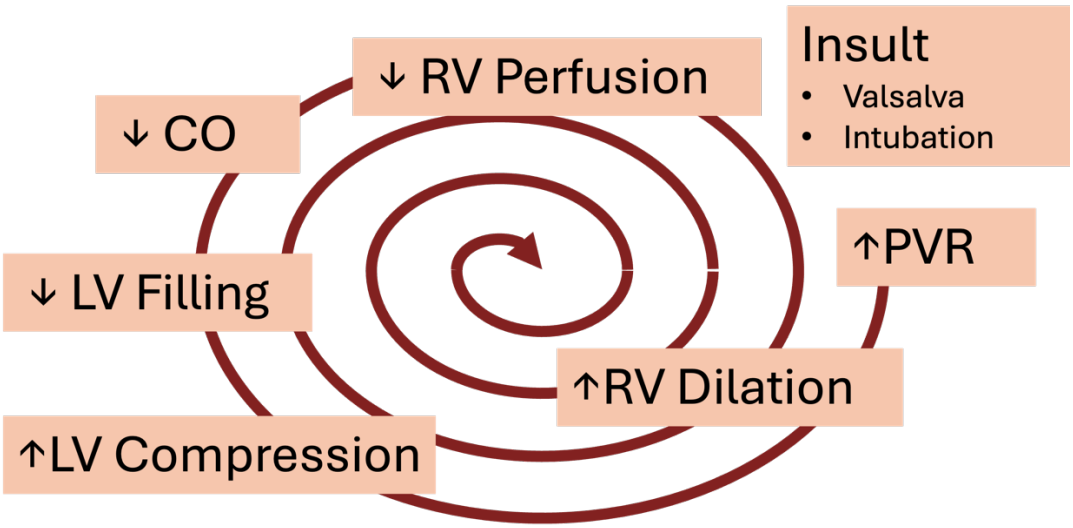
	Low Risk	Intermediate Risk	High Risk
Risk Score	1 to <1.5	1.5 to <2.5	2.5 to 3

PH Medications

Medication	Route of Administration	Half-Life	Common Side Effects
Prostacyclin Analogues and Receptor Agonists			
Epoprostenol	IV (continuous infusion)	2–5 minutes	Flushing, jaw pain, headache, nausea, diarrhea, hypotension, infusion site pain
Treprostinil	IV, SC (continuous infusion), Inhaled, Oral	4 hours (IV/SC), ~2–4 hours (oral)	Flushing, headache, nausea, diarrhea, jaw pain, infusion site pain (SC), cough (inhaled)
Iloprost	Inhaled	20–30 minutes	Cough, headache, flushing, jaw pain, nausea, throat irritation
Selexipag	Oral	0.8–2.5 hours (parent drug), 6–13 hours (active metabolite)	Headache, diarrhea, nausea, jaw pain, myalgia, flushing
Endothelin Receptor Antagonists (ERAs)			
Bosentan	Oral	~5 hours	Elevated liver enzymes, headache, nasal congestion, edema, anemia
Ambrisentan	Oral	9–15 hours	Peripheral edema, nasal congestion, headache, flushing, anemia
Macitentan	Oral	~16 hours (parent drug), ~48 hours (active metabolite)	Nasal congestion, headache, anemia, bronchitis, urinary tract infection
Phosphodiesterase-5 Inhibitors (PDE-5i) and Soluble Guanylate Cyclase Stimulators			
Sildenafil	Oral	4 hours	Headache, flushing, dyspepsia, nasal congestion, visual disturbances (e.g., blue tinge)
Tadalafil	Oral	17.5 hours	Headache, flushing, dyspepsia, back pain, myalgia, nasal congestion
Riociguat	Oral	7–12 hours	Hypotension, headache, dizziness, dyspepsia, nausea, diarrhea
Activin Signaling Inhibitors			
Sotatercept	Subcutaneous (every 3 weeks)	~23–27 days	Headache, epistaxis (nosebleeds), telangiectasia, dizziness, fatigue, injection site reactions, increased hemoglobin

Safety Concerns

PH Death Spiral



High Risk Activities

- Heavy weight training
- High intensity interval training (HIIT

Tips on Medications

- Some medications are CONTINUOUS infusions (either IV or SC)
- Know where your patient's insertion site is and where their tubing is.
- Work with your patient to prevent dislodgement
- **IV dislodgement is an EMERGENY**
- Know your patient's PH provider AND contact information
- Make sure emergency providers know which medications are CRITICAL
- Know who your GO-TO people are in your institution (pharmacy, physicians)