ASSESSMENT OF REVERSIBILITY OF PAH

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I CLINICAL RATIONALE AND PATHOPHYSIOLOGICAL SPECTRUM

- **The Core Clinical Question:** In patients with Congenital Heart Disease and systemic-to-pulmonary shunts (ASD, VSD, PDA, AVSD) complicated by Pulmonary Arterial Hypertension (PAH-CHD), assessment of reversibility determines whether elevated **Pulmonary Vascular Resistance (PVR)** is driven by **reversible muscular vasoconstriction and medial hypertrophy (Heath-Edwards Grades I to III)** or **irreversible obliterative intimal fibrosis, plexiform lesions, and necrotizing arteritis (Heath-Edwards Grades IV to VI)**.
- **The Clinical Stakes:** Closing a shunt when PVR is still reversible halts pulmonary vascular disease and normalizes life expectancy; conversely, closing a shunt ("eliminating the RV pop-off safety valve") when PVR is irreversibly fixed precipitates **post-operative right ventricular failure, low cardiac output, and worse long-term survival than leaving the patient in Eisenmenger syndrome**.

II NON-INVASIVE CLUES OF REVERSIBILITY VS. IRREVERSIBILITY (CLINICAL, ECG, CXR, ECHO)

- **Bedside Clinical and Oximetry Clues:**
  - **Favors Reversibility (Left-to-Right Dominant Shunt):** Hyperdynamic precordium, displaced LV apex, preserved **loud holosystolic (VSD) or continuous (PDA) shunt murmur**, **apical diastolic flow rumble** (indicating Qp:Qs >2:1 across the mitral valve), and **resting and post-exercise (6MWT) SpO2 >= 95%** (in both upper and lower limbs).
  - **Favors Irreversibility (Bidirectional / Eisenmenger Shunt):** Quiet precordium with parasternal RV heave, palpable P2, **disappearance of the VSD/PDA shunt murmur**, high-pitched Graham Steell PR murmur, and **resting or exercise-induced arterial desaturation (SpO2 <90%) or differential toe cyanosis/clubbing**.
  - **12-Lead ECG and Chest Radiograph (CXR):**
  - **Favors Reversibility: Biventricular hypertrophy (BVH)** or isolated LV volume overload (tall R waves with deep narrow Q waves in V5–V6) on ECG; **cardiomegaly with pulmonary plethora** extending to the outer third of the lung fields on CXR.
  - **Favors Irreversibility:** Pure **Right Ventricular Hypertrophy (RVH)** with tall monophasic R in V1 and loss of lateral Q waves on ECG; **normal heart size with massive central PA aneurysmal dilatation and peripheral vascular "pruning"** (oligemic outer lung fields) on CXR.
  - **Transthoracic Echocardiography:**
  - **Favors Reversibility: Left Atrial and Left Ventricular enlargement** (confirming high pulmonary venous return), pure left-to-right color Doppler flow across the defect, and high-velocity shunt gradient.
  - **Favors Irreversibility:** Normal/small underfilled LA and LV with dilated hypertrophied RV, low-velocity bidirectional or right-to-left shunt flow across the defect, and interventricular septal flattening.

III INVASIVE HEMODYNAMIC CRITERIA ON RIGHT HEART CATHETERIZATION (ESC 2020 ACHD VS. PEDIATRIC INDEXED CRITERIA)

- **Adult Congenital Heart Disease (ESC 2020 ACHD Guidelines — Absolute PVR in Wood Units):**
  - **PVR less than 3 Wood Units (WU) with a Significant Shunt (Ventricular Volume Overload): Class I (Recommended)** for standard percutaneous or surgical shunt closure.
  - **PVR 3 to less than 5 WU with Qp:Qs > 1.5: Class IIa (Should Be Considered)** for closure when significant left-to-right shunting persists without exercise desaturation.
  - **PVR >= 5 WU:** Immediate standard closure is contraindicated (see **Treat-and-Repair** below for ASD vs. careful expert evaluation in VSD/PDA if Qp:Qs >1.5).
  - **Eisenmenger Physiology (PVR >= 5 WU with Qp:Qs < 1.5 or Right-to-Left Shunt): Class III (Harm — Strictly Contraindicated)**.
  - **Pediatric / Indexed PVR Criteria (AHA / Pediatric PH Consensus — PVRi in Wood Units·m2 and Rp/Rs Ratio):**
  - **PVRi < 4 WU·m2 and Rp/Rs < 0.3:** Safe for complete defect closure.
  - **PVRi 4 to 8 WU·m2 or Rp/Rs 0.3 to 0.5 ("The Grey Zone"):** Requires **Acute Vasoreactivity Testing (AVT)**, trial balloon occlusion, or targeted medical pretreatment (often repaired with a **fenestrated patch/device**).
  - **PVRi > 8 WU·m2 or Rp/Rs > 0.5 (Unresponsive to AVT):** High risk of irreversible PVOD; defect closure is generally contraindicated.

Assessment Domain	Favors Reversible PAH (Operable Shunt)	Borderline / "Grey Zone"	Favors Irreversible PVOD / Eisenmenger (Inoperable)
Resting & Exercise SpO2	**>=95%** at rest and on 6MWT (hands & feet)	Mild drop on peak exercise	**<90%** at rest or exercise; differential cyanosis/clubbing
CXR & ECG	Cardiomegaly + **plethora**; **BVH / LV volume overload** (qR in V5–V6)	Moderate cardiomegaly; BVH	Normal CT ratio + **peripheral pruning**; **pure RVH**
Echocardiography	**Dilated LA & LV**; pure L-to-R shunt	Predominant L-to-R with brief R-to-L	Small LA/LV; dilated RV; **bidirectional / R-to-L shunt**
ESC 2020 Adult PVR (WU)	**PVR < 3 WU** (significant shunt) — **Class I**	**PVR 3 to <5 WU** (Qp:Qs >1.5) — **Class IIa**	**PVR >= 5 WU** with Qp:Qs <1.5 / R-to-L — **Class III**
Pediatric Indexed PVRi (WU·m2)	**PVRi < 4 WU·m2** and **Rp/Rs < 0.3**	**PVRi 4–8 WU·m2** (Perform **AVT**)	**PVRi > 8 WU·m2** and **Rp/Rs > 0.5** despite AVT

IV ACUTE VASOREACTIVITY TESTING (AVT) AND TRIAL OCCLUSION IN THE CATH LAB

- **Important ESC 2020 Adult vs. Pediatric Nuance:** While the **2020 ESC ACHD Guidelines** note that acute vasodilator testing in *adults* has not been prospectively validated to predict late outcome and rely primarily on baseline PVR (<5 WU) and the **Treat-and-Repair** response, **AVT remains widely used in pediatric and Indian tertiary centers** for patients in the **PVRi 4 to 8 WU·m2 grey zone**:
- **Agents: Inhaled Nitric Oxide (10 to 40 ppm) + 100% Oxygen** (or inhaled Iloprost / IV Epoprostenol). When calculating Fick Qp during 100% O2 inhalation, **dissolved plasma O2 (0.003 x PO2)** must be included in the Fick denominator.
- **Pediatric Operability Criteria on AVT (Barst / Lopes Criteria):** A **greater than 20 percent decrease in PVRi and Rp/Rs**, achieving a **final PVRi less than 6 WU·m2** and a **final Rp/Rs ratio less than 0.3**, accompanied by an increase in Qp:Qs. (Note: These **shunt operability criteria** are distinct from the **Sitbon criteria** [mPAP drop >=10 mmHg to <=40 mmHg], which are used only in **Idiopathic PAH** to select Calcium Channel Blocker therapy.)
- **Trial Balloon / Device Occlusion in Large PDA or ASD:** Temporary 15-to-20-minute occlusion of a borderline **PDA** or **ASD** while recording simultaneous **PA and systemic aortic pressures**: a **>20 to 25 percent drop in PA pressure** (or PA/Ao systolic ratio falling <0.5) with **preserved systemic aortic pressure and cardiac output** supports closure (often using a **fenestrated device**).

V THE "TREAT-AND-REPAIR" STRATEGY AND THE INDIAN CONTEXT

- **"Treat-and-Repair" Protocol:** In patients presenting with baseline **PVR >= 5 WU** (or PVRi 6 to 8 WU·m2) who still exhibit a net left-to-right shunt, initiating **6 to 12 months of targeted PAH pharmacotherapy (Endothelin Receptor Antagonist [Bosentan/Macitentan] + PDE-5 Inhibitor [Sildenafil/Tadalafil])** followed by a **repeat RHC** allows **fenestrated defect closure** (creating a 4 to 6 mm unidirectional or calibrated pop-off) if PVR falls to **less than 5 WU** with **Qp:Qs greater than 1.5**, with lifelong continuation of PAH drugs post-closure.
- **Practical Considerations in the Indian Context:**
  - **Hydration and Altitude:** Ensure patients are normovolemic and free of acute lower respiratory infection or severe anemia prior to RHC, as dehydration and hypoxia falsely elevate PVR.
  - **Abandonment of Open Lung Biopsy:** Open lung biopsy for Heath-Edwards histological grading is **obsolete and not recommended** due to high perioperative mortality in PAH and non-uniform patchy distribution of plexiform lesions.

KEY REFERENCES

- **Baumgartner H, De Backer J, Babu-Narayan SV, et al.:** 2020 ESC Guidelines for the management of adult congenital heart disease, *European Heart Journal*, 2020.
- **Humbert M, Kovacs G, Hoeper MM, et al.:** 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension, *European Heart Journal*, 2022.
- **Lopes AA, O'Leary PW:** Measurement, interpretation and use of haemodynamic parameters in pulmonary hypertension associated with congenital cardiac disease, *Cardiology in the Young*, 2009.