ADVANCES IN MANAGEMENT OF CTEPH

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I INTRODUCTION AND DIAGNOSTIC ADVANCES

- **Definition:** Chronic Thromboembolic Pulmonary Hypertension (CTEPH) is a progressive Group 4 Pulmonary Hypertension characterized by organized fibrotic thromboemboli in the pulmonary arteries and a secondary microvascular arteriopathy.
- **Hemodynamic Criteria:** Mean pulmonary artery pressure (mPAP) **greater than 20 mmHg**, pulmonary arterial wedge pressure (PAWP) **15 mmHg or less**, and pulmonary vascular resistance (PVR) **greater than 2 Wood Units** after 3 or more months of effective anticoagulation.
- **Imaging Advances:** While planar V/Q scan remains the **Class I** screening tool, **Dual-Energy CT (DECT)** and **3D V/Q SPECT** have emerged as advanced modalities to map the pulmonary tree and assess segmental operability without invasive angiography.

II SURGICAL ADVANCES: REFINING THE GOLD STANDARD

- **Surgical Technique: Pulmonary Endarterectomy (PEA)** performed under **Deep Hypothermic Circulatory Arrest (DHCA)** enables surgeons to dissect the fibrotic intimal layer down to the sub-segmental level, expanding the boundaries of operability.
- **Clinical Evidence:** Data from the **International CTEPH Registry** show that in high-volume expert centers, operative mortality has fallen to less than 5 percent, with sustained reductions in PVR.
- **Guideline Recommendation: Class I, LOE B** for all patients with anatomically accessible (operable) CTEPH.

III INTERVENTIONAL ADVANCES: THE CATH-LAB REVOLUTION

- **Balloon Pulmonary Angioplasty (BPA):** Uses coronary or peripheral balloons to crack and dilate organized fibrotic webs in distal, surgically inaccessible branches over 4 to 6 staged sessions.
- **The Landmark Evidence (RACE Trial):** Compared BPA versus Riociguat in inoperable CTEPH and demonstrated that BPA provides superior hemodynamic improvements (reduction in PVR) compared to medical therapy, though it carries a higher upfront risk of **Reperfusion Pulmonary Edema (RPE)**.
- **Guideline Recommendation: Class I, LOE B** for technically inoperable CTEPH or persistent/recurrent PH after PEA.

IV PHARMACOLOGICAL ADVANCES: TARGETING THE MICROVASCULATURE

A Soluble Guanylate Cyclase (sGC) Stimulators

- **Mechanism (Riociguat):** Directly sensitizes sGC to endogenous nitric oxide and stimulates the receptor independently of NO, causing pulmonary vasodilation.
- **Landmark Trials (CHEST-1 and CHEST-2):** Demonstrated significant improvements in 6-minute walk distance (6MWD) and PVR.
- **Guideline Recommendation: Class I, LOE B** as the approved drug for inoperable CTEPH or persistent/recurrent PH post-PEA.

B Endothelin Receptor Antagonists (ERAs)

- **Landmark Evidence (MERIT-1 Trial):** Showed that adding **Macitentan** significantly improves PVR in inoperable CTEPH patients, supporting combination medical therapy.
- **Guideline Recommendation: Class IIb, LOE B** for symptomatic inoperable patients.

C Subcutaneous Prostacyclins

- **Landmark Evidence (CTREPH Trial):** Demonstrated the efficacy of subcutaneous **Treprostinil** in severe inoperable CTEPH, providing a rescue option for WHO Functional Class III/IV patients.

Modality / Agent	Target Pathology	Landmark Trial / Registry	Guideline Status
Pulmonary Endarterectomy (PEA)	Proximal / segmental fibrotic thromboemboli	**International CTEPH Registry**	**Class I, LOE B** for operable CTEPH
Balloon Pulmonary Angioplasty (BPA)	Distal, surgically inaccessible webs	**RACE Trial**	**Class I, LOE B** for inoperable or persistent post-PEA PH
Riociguat (sGC Stimulator)	Secondary distal microvascular arteriopathy	**CHEST-1 & CHEST-2 Trials**	**Class I, LOE B** for inoperable or persistent post-PEA PH
Macitentan (ERA)	Microvascular remodeling	**MERIT-1 Trial**	**Class IIb, LOE B** in symptomatic inoperable CTEPH
Subcutaneous Treprostinil	Severe microvascular disease (WHO FC III/IV)	**CTREPH Trial**	Rescue therapy in severe inoperable CTEPH

V THE PARADIGM SHIFT AND THE INDIAN CLINICAL CONTEXT

- **The Multimodal CTEPH Heart Team (Class I, LOE C):** CTEPH management has shifted from a binary operable-versus-inoperable approach to a hybrid multimodal paradigm where a single patient may undergo PEA for proximal clots, followed by BPA for residual distal webs, and lifelong Riociguat for microvascular disease.
- **Diagnostic Mimics in the Indian Context:** In the Indian subcontinent, **Fibrosing Mediastinitis (post-Tuberculosis)** and **Takayasu Arteritis** frequently mimic CTEPH on imaging; detailed clinical history and DECT are essential to rule these out before attempting PEA or BPA.
- **BPA Accessibility:** Because expert PEA surgical centers are concentrated in a few major metropolitan cities, BPA serves as an important frontline intervention in Tier-1 catheterization laboratories across India for patients who cannot access open-heart surgery.

KEY REFERENCES

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