MANAGEMENT OF ACUTE PERICARDITIS AND ITS COMPLICATIONS

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I DIAGNOSTIC CRITERIA AND TRIAGE (ESC 2015 / ESC 2025 GUIDELINES)

- **ESC Diagnostic "2-out-of-4" Criteria:** The 2025 ESC Guidelines introduce the overarching framework of **Inflammatory Myopericardial Syndrome (IMPS)**. A clinical diagnosis of acute pericarditis requires at least **2 of the following 4 criteria**:
- **Pericarditic Chest Pain (greater than 85 to 90 percent):** Sharp, retrosternal, pleuritic pain that worsens on inspiration or supine posture and improves on sitting up and leaning forward.
- **Pericardial Friction Rub (33 percent or less):** Superficial, triphasic scratchy/leathery sound best heard with the diaphragm at the left lower sternal border during end-expiration while leaning forward.
- **Electrocardiographic Changes (up to 60 percent):** New widespread **concave (saddle-shaped) ST-segment elevation** and/or **PR-segment depression** across multiple coronary territories (with reciprocal **ST-depression and PR-elevation in lead aVR**).
- **Pericardial Effusion (up to 60 percent):** New or worsening pericardial effusion on transthoracic echocardiography.
- **Supportive Inflammatory and Imaging Criteria:** Elevated **C-Reactive Protein (CRP)** / ESR / leukocytosis and evidence of pericardial inflammation on **Cardiac MRI (pericardial thickening, T2-STIR edema, and Late Gadolinium Enhancement [LGE])** or CT.
- **High-Risk Triage Phenotype (Class I Indication for Hospital Admission and Etiological Workup):** Patients lacking any risk factors are safely managed as outpatients; hospital admission is **mandatory (Class I)** if any **Major** or **Minor** predictor of poor prognosis is present:
- **Major Risk Predictors: High fever (greater than 38 degrees C)**, **subacute onset** (symptoms developing insidiously over days to weeks), **large pericardial effusion** (diastolic echo-free space greater than 20 mm), **cardiac tamponade**, or **failure to respond within 7 days** of aspirin/NSAID therapy.
- **Minor Risk Predictors: Myopericarditis** (elevated troponin), **immunodepression**, **trauma**, or **oral anticoagulant therapy**.

II PHARMACOLOGICAL MANAGEMENT (FIRST-, SECOND-, AND THIRD-LINE)

- **First-Line Dual Anti-Inflammatory Therapy (Class I, Level A):** High-dose **Aspirin or an NSAID** combined with **Colchicine** (plus a proton pump inhibitor for gastroprotection) and **exercise restriction**.
- **Aspirin or Ibuprofen: Aspirin 750 to 1000 mg every 8 hours** (preferred in post-MI / Dressler syndrome or concomitant CAD/antiplatelet indication) or **Ibuprofen 600 mg every 8 hours** for 1 to 2 weeks. Taper gradually (by 250 to 500 mg of Aspirin or 200 to 400 mg of Ibuprofen every 1 to 2 weeks) **only after complete resolution of symptoms and normalization of CRP**.
- **Weight-Adjusted Colchicine (Class I, Level A):** Administered without a loading dose as **0.5 mg once daily** (for body weight **less than 70 kg**) or **0.5 mg twice daily** (for body weight **70 kg or greater**) for **3 months** in an acute first episode (and **at least 6 months** in recurrent pericarditis).
- **Second-Line Therapy — Low-Dose Corticosteroids (Class IIa for Specific Indications; Routine Use is Class III):** Strictly avoided as routine first-line therapy because steroids promote viral replication and double the risk of chronic recurrence. Reserved for true contraindications to Aspirin/NSAIDs (severe renal failure, active peptic ulcer, pregnancy past 20 weeks), autoimmune disease, or incomplete response to NSAID + Colchicine. Use **low-to-moderate dose Prednisone (0.2 to 0.5 mg/kg/day)** rather than high doses (1.0 mg/kg/day), with an extremely slow taper (e.g., 1 to 2.5 mg every 2 to 6 weeks once Prednisone is below 15 mg/day) guided by CRP.
- **Targeted Third-Line Biologics — Anti-Interleukin-1 (IL-1) Agents (ESC 2025 Upgraded Role):** Recommended for **corticosteroid-dependent, colchicine-resistant recurrent pericarditis** exhibiting an **inflammatory phenotype (elevated CRP and/or severe pericardial LGE on CMR)**: **Anakinra** (1 to 2 mg/kg/day up to 100 mg/day SC daily; **AIRTRIP Trial**) or **Rilonacept** (320 mg SC loading, then 160 mg SC weekly; **RHAPSODY Trial**), or **Intravenous Immunoglobulin (IVIG) / Azathioprine**.

Drug Class & Agent	Standard Adult Dosing	Treatment Duration	Tapering & Monitoring Rule
Aspirin (First-Line)	**750–1000 mg every 8 hours**	1–2 weeks at full dose	Taper by 250–500 mg every 1–2 wk **only after symptom resolution + normal CRP**
Ibuprofen (First-Line)	**600 mg every 8 hours**	1–2 weeks at full dose	Taper by 200–400 mg every 1–2 wk **after normal CRP**; add PPI
Colchicine (Class I Add-on)	**0.5 mg OD (<70 kg)** or **0.5 mg BD (>=70 kg)**	**3 months** (Acute); **>=6 months** (Recurrent)	Halves recurrence rate; reduce dose / avoid in severe CKD or CYP3A4/P-gp inhibitors
Prednisone (Second-Line)	**0.2–0.5 mg/kg/day** (low dose)	Until symptoms resolve & CRP normalizes	Slow taper (2.5 mg every 2–4 wk above 15 mg/d; 1–2.5 mg every 2–6 wk below 15 mg/d)
Rilonacept / Anakinra (IL-1 Blockers)	Rilonacept 160 mg/wk SC; Anakinra 100 mg/d SC	>=6–12 months before very gradual weaning	Allows rapid withdrawal of corticosteroids in inflammatory recurrent pericarditis (**RHAPSODY / AIRTRIP**)

III MANAGEMENT OF LIFE-THREATENING COMPLICATIONS

A Cardiac Tamponade (Emergency Intervention)

- **Immediate Stabilization:** Cautious intravenous fluid resuscitation is indicated **only** in hypovolemic tamponade; avoid volume overloading euvolemic patients and **avoid positive-pressure mechanical ventilation**, which acutely reduces right heart preload and precipitates cardiac arrest.
- **Definitive Management (Class I):** Urgent **echocardiography- or fluoroscopy-guided Pericardiocentesis** with prolonged indwelling pigtail catheter drainage (until 24-hour drainage is less than 25 to 30 mL) and concurrent anti-inflammatory therapy.
- **Indications for Surgical Drainage / Pericardial Window (Class I):** Tamponade complicating **Acute Type A Aortic Dissection** or **ventricular free-wall rupture** (where percutaneous pericardiocentesis is contraindicated unless performed in a hybrid OR with controlled minimal aspiration to restore pulse while prepping for sternotomy), recent **penetrating chest trauma**, or **purulent / loculated effusions**.

B Myopericarditis and Perimyocarditis (Overlapping IMPS)

- **Diagnosis:** Clinical acute pericarditis accompanied by **elevated high-sensitivity cardiac troponin (hs-cTnI or hs-cTnT)** and confirmed by **Cardiac MRI** (2018 Revised Lake Louise Criteria showing subepicardial/mid-myocardial T2 edema and non-ischemic LGE alongside pericardial inflammation). **Myopericarditis** has preserved LVEF without wall motion abnormalities; **Perimyocarditis** has focal or global LV systolic dysfunction.
- **Management (Class I):** Mandatory **hospitalization** for continuous ECG monitoring, exclusion of acute coronary syndrome (via CCTA or invasive angiography if risk factors exist), and reduced-duration anti-inflammatory therapy strictly to control chest pain (as experimental myocarditis models suggest high-dose NSAIDs may enhance myocardial inflammation; Colchicine remains safe and useful).
- **Exercise Restriction (Class I):** Complete abstinence from competitive sports and moderate-to-high-intensity physical training for **3 to 6 months** whenever myocardial involvement is documented (vs. 1 to 3 months until CRP/ECG/Echo normalization in isolated pericarditis).

C Transition to Constrictive Pericarditis (Transient vs. Permanent)

- **Transient Effusive-Constrictive Pericarditis (10 to 15 percent of Cases):** Constrictive hemodynamics (respiratory ventricular interdependence, septal bounce, hepatic vein expiratory diastolic flow reversal, and annulus reversus on tissue Doppler) occurring during subacute inflammation. Identified by **elevated CRP and marked pericardial T2 edema + vivid pericardial LGE on CMR**; resolves completely with **2 to 3 months (up to 3 to 6 months per ESC 2025) of intensive medical anti-inflammatory therapy** (NSAIDs, colchicine, steroids, or anti-IL-1 biologics) without surgery.
- **Permanent Chronic Constrictive Pericarditis:** Fibrotic, non-compliant, often calcified pericardium with burnt-out inflammation (normal CRP, absent edema/LGE on CMR) and persistent NYHA Class III–IV right heart failure despite 3 to 6 months of medical therapy; definitive treatment is **Surgical Complete ("Phrenic-to-Phrenic") Pericardiectomy (Class I)**.

IV PREVENTION OF RECURRENCE AND LANDMARK TRIAL EVIDENCE

- **COPE (2005) and ICAP (2013) Trials (First Acute Episode):** Proved that adding weight-adjusted **Colchicine for 3 months** to Aspirin/NSAIDs halves the rate of incessant or recurrent pericarditis from **37.5 percent to 16.7 percent (NNT = 4 to 5)** and reduces symptom persistence at 72 hours.
- **CORE (2005), CORP (2011), and CORP-2 (2014) Trials (Recurrent Pericarditis):** Proved that **6 months of Colchicine** halves subsequent recurrences in both first and multiple recurrent pericarditis.
- **AIRTRIP (2016) and RHAPSODY (2021) Trials (Biologics): RHAPSODY** (*NEJM* 2021) demonstrated that **Rilonacept** (IL-1alpha/beta trap) resolved acute flares within 5 days and reduced pericarditis recurrence by **96 percent (HR 0.04; 7 percent vs. 74 percent recurrence)** while enabling complete discontinuation of corticosteroids.

V PRACTICAL CONSIDERATIONS IN THE INDIAN CLINICAL CONTEXT

- **The Tuberculous Pericarditis Mandate:** While idiopathic/viral etiology accounts for 80 to 85 percent of acute pericarditis in Western countries (carrying a less than 1 percent risk of progression to constriction), **Mycobacterium tuberculosis** accounts for **50 to 70 percent of large pericardial effusions and constrictive pericarditis in India** (carrying a **20 to 30 percent risk of progression to constriction** despite anti-tubercular therapy).
- **Diagnostic Workup:** Pericardial fluid analysis must include **Adenosine Deaminase (ADA 40 U/L or greater)**, **Xpert MTB/RIF Ultra**, liquid mycobacterial culture, and unstimulated **Interferon-gamma (IFN-gamma)**. **Empirical corticosteroids must never be started for presumed idiopathic pericarditis in an Indian patient before excluding TB**.
- **Adjunctive Steroids in Confirmed TB Pericarditis (IMPI Trial, *NEJM* 2014):** In **HIV-negative** patients with tuberculous pericarditis at high risk of constriction (large effusion/fibrinous strands), a 6-week tapering course of adjunctive oral Prednisolone added to four-drug ATT may be considered (**Class IIb**) because the **IMPI Trial** showed a **44 percent reduction in progression to constrictive pericarditis** (4.4 percent vs. 7.8 percent), whereas steroids are **contraindicated (Class III) in HIV-positive patients** due to increased HIV-associated malignancy.
- **Uremic vs. Dialysis-Associated Pericarditis:** In end-stage renal disease, **Colchicine is contraindicated** (due to severe neuro-myotoxicity and cytopenias) and NSAIDs carry high GI bleeding risk with poor efficacy; definitive treatment is **initiation or intensification of heparin-free daily hemodialysis for 7 to 14 days**, with pericardiocentesis reserved for tamponade or non-responders.

KEY REFERENCES

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- **Klein AL, Imazio M, Cremer P, et al. (RHAPSODY Investigators):** Phase 3 Trial of Interleukin-1 Trap Rilonacept in Recurrent Pericarditis, *New England Journal of Medicine*, 2021.