# EXERCISE TESTING IN NON-ATHEROSCLEROTIC HEART DISEASE

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## I OVERVIEW AND CORE PRINCIPLE

- **Shifting the Diagnostic Paradigm:** While exercise stress testing (Treadmill Exercise Testing [TMT], Bicycle Ergometry, Stress Echocardiography, and Cardiopulmonary Exercise Testing [CPET]) is classically performed to detect epicardial coronary artery disease, it is a cornerstone functional modality in **Valvular Heart Disease (VHD)**, **Cardiomyopathies (HCM, DCM)**, **Heart Failure**, **Congenital Heart Disease**, and **Inherited Arrhythmia Syndromes**.
- **Primary Diagnostic Targets:** In non-atherosclerotic heart disease, interpretation shifts away from isolated ST-segment depression toward **unmasking occult symptoms** in ostensibly "asymptomatic" patients who have subconsciously restricted their daily lifestyle, quantifying **objective functional capacity (METs or Peak VO2)**, evaluating the **hemodynamic blood pressure response**, measuring **dynamic valvular/LVOT gradients and exercise pulmonary pressures**, and provoking **exercise-induced arrhythmias**.

## II CLINICAL APPLICATIONS AND GUIDELINE INDICATIONS

### A Asymptomatic Severe Valvular Heart Disease (2020 ACC/AHA & 2021 ESC/EACTS VHD Guidelines)

- **Asymptomatic Severe Aortic Stenosis (Class IIa; Symptomatic Severe AS is an Absolute Contraindication [Class III]):** Supervised exercise testing is safe and recommended in **asymptomatic** severe AS to confirm true absence of symptoms:
- **If Exercise Provokes Symptoms (angina, dyspnea, dizziness/syncope):** The patient is reclassified as **symptomatic severe AS**, triggering a **Class I indication for Aortic Valve Replacement (SAVR/TAVR)**.
- **If Exercise Unmasks an Abnormal Blood Pressure Response:** A **fall in systolic BP of 10 mmHg or more from baseline to peak exercise** (ACC/AHA 2020) or a fall below baseline (ESC 2021) during exercise, or a marked decrease in exercise tolerance below age/sex norms, is a **Class IIa indication for AVR**.
- **Chronic Primary and Secondary Mitral Regurgitation (Class IIa):** Exercise Doppler echocardiography unmasks subclinical functional limitation, worsens dynamic MR severity, assesses **Left Ventricular Contractile Reserve** (failure of LVEF to increase by at least 4 percent or GLS by 2 percent), and detects exercise-induced pulmonary hypertension (**exercise PASP greater than 60 mmHg**), guiding early mitral repair.
- **Rheumatic Mitral Stenosis (Class I for Discordant Symptoms):** In patients who appear asymptomatic despite severe MS (MVA 1.5 cm2 or less) or who have marked exertion-induced dyspnea despite moderate resting MS (MVA greater than 1.5 cm2), **exercise Doppler echocardiography** assesses the rise in **mean transmitral gradient (to greater than 15 mmHg on exercise)** and **PASP (to greater than 60 mmHg)** to guide **Percutaneous Transvenous Mitral Commissurotomy (PTMC)**.

### B Hypertrophic Cardiomyopathy (HCM) (2024 AHA/ACC & 2023 ESC Cardiomyopathy Guidelines)

- **Unmasking Latent LVOT Obstruction (Class I):** Approximately one-third of HCM patients have non-obstructive resting gradients (less than 30 mmHg) that increase to **30 mmHg or greater (or 50 mmHg or greater, the threshold for invasive septal reduction or myosin inhibitor therapy)** only during **exercise stress echocardiography** (physiological upright exercise is strongly preferred over dobutamine, which is non-physiological in HCM).
- **Sudden Cardiac Death (SCD) Risk Stratification (Class IIa):** An **abnormal blood pressure response to exercise**—defined as failure of systolic BP to increase by at least **20 mmHg** from rest to peak exercise, or a **drop in systolic BP of greater than 20 mmHg** from peak pressure during exercise—occurs in 20 to 25 percent of HCM patients (due to subendocardial ischemia and inappropriate vagal/baroreceptor vasodilation) and serves as a prognostic risk marker in patients aged 40 years or younger, alongside exercise-induced **Non-Sustained Ventricular Tachycardia (NSVT)**.

### C Chronic Heart Failure and Cardiac Transplantation Timing (CPET — Class I)

- **Cardiopulmonary Exercise Testing (CPET) Thresholds:** Simultaneous gas-exchange analysis during maximal exercise is the **Class I reference standard** for selecting candidates for **Heart Transplantation** or **Left Ventricular Assist Device (LVAD)** implantation:
- **Peak VO2 (Oxygen Consumption): Peak VO2 of 14 mL/kg/min or less** (in patients intolerant of beta-blockers) or **12 mL/kg/min or less** (in patients on **beta-blockers**, per the **ISHLT 2016** listing criteria) indicates severe functional impairment warranting transplant listing (provided the **Respiratory Exchange Ratio [RER = VCO2/VO2] is greater than 1.05 to 1.10**, confirming maximal patient effort).
- **Young and Obese Patients:** In young patients (under 50 years) and women, a **Peak VO2 less than 50 percent of predicted** is used; in obese patients (BMI greater than 30 kg/m2), **VE/VCO2 slope (ventilatory efficiency slope) greater than 35** or Peak VO2 adjusted to lean body mass (less than 19 mL/kg/min) is more accurate, especially when accompanied by **Exercise Oscillatory Ventilation (EOV)**.

### D Congenital Heart Disease and Channelopathies / Arrhythmias

- **Adult Congenital Heart Disease (ACHD):** Serial CPET tracks objective decline in **repaired Tetralogy of Fallot** and **Fontan circulation**, and unmasks exercise-induced arterial desaturation (right-to-left shunting) or exertional arrhythmias before sports clearance.
- **Channelopathies and Conduction Disease:** Exercise testing is **Class I diagnostic** in **Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)** (provoking bidirectional or polymorphic VT as heart rate exceeds 110 to 120 bpm) and **Long QT Syndrome (LQTS)** (maladaptive QTc prolongation at **4 minutes into recovery of 480 ms or greater** in LQT1), and differentiates benign **AV nodal (supra-Hisian)** block (which **improves** during exercise due to sympathetic vagolysis) from malignant **infranodal (His-Purkinje)** block (which **worsens** during exercise tachycardia).

| Disease Condition | Primary Exercise Modality | Key Diagnostic / Actionable Threshold |
|---|---|---|
| **Asymptomatic Severe Aortic Stenosis** | Symptom-limited TMT / Stress Echo | Provoked symptoms (**Class I** for AVR); SBP fall of >=10 mmHg from baseline (**Class IIa** for AVR) |
| **Hypertrophic Cardiomyopathy (HCM)** | Exercise Stress Echocardiography | Provoked **LVOT gradient >=50 mmHg** (Class I); **Abnormal BP response** (failure to rise >=20 mmHg or drop >20 mmHg) |
| **Rheumatic Mitral Stenosis (Discordant)** | Supine Bicycle / Treadmill Echo | Exercise **mean mitral gradient >15 mmHg** or **exercise PASP >60 mmHg** favors PTMC |
| **Advanced HFrEF (Transplant Listing)** | Cardiopulmonary Exercise Test (CPET) | **Peak VO2 <=12 mL/kg/min** (on beta-blocker) or **<=14 mL/kg/min** (off beta-blocker); **VE/VCO2 slope >35** (with RER >1.05) |
| **CPVT & Congenital LQTS** | Standard / Sprint Exercise ECG | Bidirectional/polymorphic VT in **CPVT**; **4-minute recovery QTc >=480 ms** in **LQTS** |

## III LIMITATIONS AND TECHNICAL PITFALLS

- **Baseline Repolarization Abnormalities (Poor ECG Specificity):** In patients with **Left Ventricular Hypertrophy (LVH)** with strain (AS, HCM, hypertension), **Right Ventricular Hypertrophy**, **Left Bundle Branch Block (LBBB)**, **Right Bundle Branch Block**, **Wolff-Parkinson-White (WPW) pre-excitation**, or **Digoxin therapy**, exercise-induced ST-segment depression occurs in over 50 percent of patients **without** epicardial coronary artery disease (due to subendocardial supply-demand mismatch and secondary repolarization changes), rendering the ECG uninterpretable for obstructive CAD.
- **Hemodynamic Hazard in Unstable Outflow Obstruction:** Performing an unsupervised or aggressive stress test in **symptomatic** severe AS, decompensated heart failure, or severe PAH can precipitate acute **exertional syncope, ventricular fibrillation, or hemodynamic collapse**.
- **Submaximal Effort Confounding:** Orthopedic limitations, frailty, or poor motivation can lead to premature test termination before achieving diagnostic hemodynamic stress (confirmed on CPET when **RER is less than 1.05**).

## IV ABSOLUTE INDICATIONS FOR TEST TERMINATION

- **Drop in Systolic Blood Pressure:** A decrease in systolic blood pressure of **greater than 10 mmHg below baseline** despite an increase in workload, or any progressive fall in systolic BP in AS or HCM.
- **Limiting Clinical Symptoms:** Development of angina, disproportionate dyspnea, dizziness, near-syncope, ataxia, pallor, or cyanosis.
- **Malignant Arrhythmias:** Sustained ventricular tachycardia, frequent polymorphic PVCs/couplets, bidirectional VT, or exercise-induced second- or third-degree AV block.

## V PRACTICAL CONSIDERATIONS IN THE INDIAN CLINICAL CONTEXT

- **Unmasking "Sedentary Masking" in Rheumatic Mitral Stenosis:** Many young Indian patients (particularly women) with moderate-to-severe **Rheumatic Mitral Stenosis** subconsciously curtail household physical exertion and deny dyspnea at rest. Supine bicycle or treadmill **exercise Doppler echocardiography** (or dynamic bedside leg-raising/squatting) rapidly unmasks a steep jump in transmitral mean gradient (above 15 mmHg) and pulmonary artery systolic pressure (above 60 mmHg), establishing the indication for **PTMC**.
- **Protocol Selection (Modified Bruce, Naughton, or Ramp Protocols):** Because many chronically ill or deconditioned Indian patients cannot tolerate the steep 3-MET increments of the standard **Bruce Protocol** (terminating prematurely at 2 to 3 minutes due to leg fatigue), gentler protocols with 1-to-2 MET stages—such as the **Modified Bruce**, **Naughton**, or continuous **Ramp Protocol**—are preferred to achieve an optimal 8-to-12-minute test duration.

KEY REFERENCES


- **Otto CM, Nishimura RA, Bonow RO, et al.:** 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease, *Circulation*, 2021.
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- **Guazzi M, Adams V, Conraads V, et al.:** EACPR/AHA Scientific Statement: Clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations, *Circulation*, 2012.