CORONARY FLOW RESERVE (CFR) ASSESSMENT

Prepared by **Dr. Sidhartha Mullapudi**, DrNB (Cardiology), MD (General Medicine)
Last reviewed: October 2026

I OVERVIEW

- **Definition:** Coronary Flow Reserve (CFR) is the ratio of **maximal hyperemic myocardial blood flow** (during exercise or pharmacological vasodilation) to **resting myocardial blood flow**.
- **Integrated Scope:** Represents the integrated vasodilatory capacity of the **entire coronary arterial tree**, encompassing both the **epicardial conductance arteries** and the **microvascular resistance vessels** (pre-arterioles, arterioles, and capillaries).
- **Clinical Role:** In contemporary guidelines (ESC 2024 Chronic Coronary Syndromes Guidelines), CFR has transitioned from a research metric to a core clinical diagnostic parameter for phenotyping patients with **Angina/Ischemia with Non-Obstructive Coronary Arteries (ANOCA / INOCA)**.

II CORONARY AUTOREGULATION AND PHYSIOLOGY

- **Resting Autoregulation:** Under basal resting conditions, coronary arteriolar tone maintains high microvascular resistance so that resting coronary blood flow matches baseline myocardial oxygen demand (MVO2) across a wide range of perfusion pressures.
- **Hyperemic Reserve Capacity:** During maximal endothelium-independent pharmacological vasodilation (induced by intravenous **Adenosine** at 140 mcg/kg/min or intracoronary papaverine/adenosine), microvascular resistance drops to a minimum; a normal healthy coronary bed increases blood flow **3- to 5-fold above baseline (CFR >= 2.0 to 2.5)**.
- **Flow vs. Pressure (CFR vs. FFR):** Whereas **Fractional Flow Reserve (FFR)** is a pressure-derived ratio specific to the **epicardial artery** and largely independent of resting hemodynamics, **CFR** is a flow-derived ratio across the **epicardial + microvascular bed** and is directly influenced by resting heart rate, blood pressure, and ventricular contractility.

III MATHEMATICAL CALCULATION OF CFR BY MODALITY

- **Fundamental Theoretical Ratio:**
  - **Formula: CFR = Maximum Hyperemic Myocardial Blood Flow / Resting Myocardial Blood Flow**.
  - **Invasive Bolus Thermodilution (Pressure-Temperature Sensor Guidewire):**
  - **Formula: CFRthermo = Mean Transit Time at Rest (Tmn-rest) / Mean Transit Time at Hyperemia (Tmn-hyp)**.
  - **Technical Principle:** Because faster blood flow during hyperemia results in a *shorter* transit time for a 3-mL room-temperature saline bolus to travel down the coronary artery, **resting transit time (the larger number) is placed in the numerator** so that normal CFR exceeds 1.0 (and typically exceeds 2.0).
  - **Invasive Doppler Flow Velocity (Doppler-Tipped Guidewire):**
  - **Formula: CFRDoppler = Average Peak Velocity at Hyperemia (APVhyp) / Average Peak Velocity at Rest (APVrest)**.
  - **Technical Principle:** Because volumetric flow is directly proportional to flow velocity, **hyperemic velocity (the larger number) is placed in the numerator**.
  - **Non-Invasive Quantitative Positron Emission Tomography (Cardiac PET):**
  - **Formula: CFRPET (Myocardial Flow Reserve) = Hyperemic Myocardial Blood Flow (in mL/min/g) / Resting Myocardial Blood Flow (in mL/min/g)**.

Assessment Modality	Invasive vs. Non-Invasive	Calculation Formula	Key Advantage & Simultaneous Metrics
Bolus Thermodilution Wire	Invasive (Cath Lab)	**Tmn(Rest) / Tmn(Hyperemia)**	Simultaneous **FFR, CFR, & IMR** on a single pressure-temperature wire
Doppler Velocity Wire	Invasive (Cath Lab)	**APV(Hyperemia) / APV(Rest)**	Direct velocity measurement + **Hyperemic Microvascular Resistance (HMR)**
Quantitative Cardiac PET	**Non-Invasive Gold Standard**	**MBF(Hyperemia) / MBF(Rest) (mL/min/g)**	Absolute flow quantification across all three coronary territories
Transthoracic Doppler Echo / Stress CMR	Non-Invasive	Distal LAD peak diastolic velocity ratio / **MPRI**	Radiation-free, lower cost (Echo limited by acoustic window)

IV CLINICAL APPLICATIONS OF CFR

- **Diagnosing Coronary Microvascular Dysfunction (CMD) in ANOCA / INOCA:** In patients with anginal symptoms and unobstructed epicardial arteries (FFR > 0.80), a **CFR less than 2.0** (combined with an Index of Microcirculatory Resistance **[IMR] >= 25** or Hyperemic Microvascular Resistance **[HMR] >= 2.5 mmHg/cm/s**) confirms **Coronary Microvascular Dysfunction** and guides targeted therapy with beta-blockers, ACE inhibitors, statins, ranolazine, or nicorandil.
- **Discordant Epicardial Disease (FFR vs. CFR Discordance):** Integrating FFR and CFR distinguishes **focal epicardial stenosis with healthy microvasculature (Low FFR <=0.80 / Normal CFR >=2.0)**, which benefits from PCI, from **diffuse epicardial disease or severe microvascular disease (Normal FFR >0.80 / Low CFR <2.0)**, where stenting is ineffective and medical therapy is indicated.
- **Heart Failure with Preserved Ejection Fraction (HFpEF):** Impaired **CFR (< 2.0)** is present in up to 70 percent of patients with **HFpEF**, reflecting systemic endothelial inflammation and capillary rarefaction, and independently predicts HF hospitalization.

V LIMITATIONS AND TECHNICAL CHALLENGES

- **Sensitivity to Resting Hemodynamics:** Because resting blood flow is the denominator of the CFR equation, any condition that elevates **resting myocardial oxygen demand and resting flow**—such as **sinus tachycardia, systemic hypertension, Left Ventricular Hypertrophy (LVH), elevated LVEDP, or anemia**—mathematically lowers the calculated CFR even when maximal hyperemic flow is preserved (**Rate-Pressure Product-corrected resting flow** is used to adjust for this).
- **Lack of Epicardial vs. Microvascular Specificity in Isolation:** A low CFR alone cannot distinguish between a severe epicardial stenosis and primary microvascular disease unless paired with **FFR** (invasive) or regional perfusion defects (PET).
- **Technical Pitfalls in the Cath Lab:**
  - **Submaximal Hyperemia:** Caffeine or methylxanthine intake within **12 to 24 hours** competitively blocks adenosine A2A receptors, causing falsely low hyperemic flow and false-positive CFR results.
  - **Thermodilution Bolus Variability:** Requires the average of **at least 3 consistent rapid 3-mL room-temperature saline injections** with the guide catheter coaxial and disengaged from wedging.
  - **Doppler Signal Quality:** Requires careful wire-tip rotation to maintain a crisp spectral velocity envelope in the center of the vessel lumen.

VI LANDMARK EVIDENCE, GUIDELINES AND THE INDIAN CONTEXT

- **CorMicA Trial (*JACC* 2018) and ESC 2024 CCS Guidelines (Class I):** The **CorMicA Trial** proved that stratified medical therapy guided by invasive **CFR, IMR, and acetylcholine testing** significantly improves angina and quality of life in ANOCA patients, earning an upgraded **Class I (Level B)** recommendation for invasive coronary functional testing in persistently symptomatic ANOCA patients in the **2024 ESC Chronic Coronary Syndromes Guidelines**.
- **Application in the Indian Context:** Given the high prevalence of **Diabetes Mellitus** and microvascular disease in Indian patients presenting with angina and non-obstructive epicardial arteries, **Transthoracic Doppler Echocardiographic CFR of the distal LAD** serves as a practical, low-cost non-invasive screening tool in resource-limited settings prior to invasive wire-based testing.

KEY REFERENCES

- **Vrints C, Andreotti F, Koskinas KC, et al.:** 2024 ESC Guidelines for the management of chronic coronary syndromes, *European Heart Journal*, 2024.
- **Ford TJ, Stanley B, Good R, et al. (CorMicA Investigators):** Stratified Medical Therapy Using Invasive Coronary Function Testing in Angina: The CorMicA Trial, *Journal of the American College of Cardiology*, 2018.
- **Libby P, Bonow RO, Mann DL, Tomaselli GF, Bhatt DL, Solomon SD:** *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 12th Ed., Elsevier, 2022.