LEFT VENTRICULAR NON-COMPACTION (LVNC)

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I DEFINITION, NOMENCLATURE SHIFT AND PATHOPHYSIOLOGY (ESC 2023 CARDIOMYOPATHY GUIDELINES)

- **Traditional Definition vs. 2023 ESC Paradigm Shift ("Excessive Trabeculation"):** Historically termed **Left Ventricular Non-Compaction (LVNC)** and attributed to an arrest of embryological myocardial compaction between weeks 5 and 8 of gestation, the **2023 ESC Guidelines for the Management of Cardiomyopathies** officially recommend replacing the term "LVNC" with **"Hypertrabeculation" or "Excessive Trabeculation"**. Modern developmental biology demonstrates that compact and trabecular layers grow via differential proliferation rather than simple "compaction" of pre-existing trabeculae, and excessive trabeculation in adults is most commonly either a **phenotypic trait accompanying an underlying Dilated (DCM), Nondilated LV (NDLVC), or Hypertrophic (HCM) Cardiomyopathy**, or a **reversible physiological adaptation to chronic preload/afterload increase** (pregnancy, vigorous athletic training, sickle cell/chronic anemia).
- **Morphological Characteristics:** Bi-layered myocardial appearance consisting of a **thin compacted (C) epicardial layer** and a **thick non-compacted (NC) endocardial layer** composed of prominent muscular trabeculations and deep intertrabecular recesses that communicate directly with the **left ventricular cavity** (and have **no communication with the epicardial coronary circulation**), predominantly affecting the **LV apex, mid-lateral, and mid-inferior walls**.
- **Genetic Architecture:** Highly heterogeneous; sarcomeric gene variants—most commonly **MYH7** (most frequent in isolated excessive trabeculation), **MYBPC3**, **TTN (Titin)**, and **ACTC1**—account for the majority of familial cases. Crucially, **arrhythmogenic high-risk genotypes**—including **LMNA, SCN5A, RBM20, FLNC, and DES**—must be identified because they carry a high risk of malignant arrhythmias and conduction block independent of trabeculation extent, while **X-linked TAFAZZIN (TAZ)** mutations cause pediatric **Barth Syndrome** (LV hypertrabeculation/DCM + neutropenia + skeletal myopathy + 3-methylglutaconic aciduria) and **MIB1 / NOTCH** pathway variants link hypertrabeculation with congenital heart defects (Ebstein anomaly, BAV, VSD).

II CLINICAL PRESENTATION AND THE CLASSIC TRIAD

- **Spectrum of Presentation:** Ranges from completely asymptomatic individuals detected incidentally on imaging or family screening to severe neonatal/adult cardiomyopathy.
- **Classic Clinical Complication Triad:**
  - **Heart Failure (Systolic and Diastolic Dysfunction):** Progressive **HFrEF** (from subendocardial hypoperfusion and sarcomeric dysfunction) and **diastolic dysfunction** (abnormal relaxation and restriction caused by extensive spongy trabecular mass).
  - **Atrial and Ventricular Arrhythmias / Sudden Cardiac Death (SCD): Atrial Fibrillation** (10 to 25 percent), bundle branch blocks, WPW pre-excitation (especially in pediatric/Ebstein overlap), and **Ventricular Tachycardia (VT) / SCD**.
  - **Systemic Thromboembolism:** Sluggish swirling blood flow within deep intertrabecular recesses (especially when accompanied by **LV systolic dysfunction or Atrial Fibrillation**) predisposes to LV mural/recess thrombi, **ischemic stroke, transient ischemic attack, or systemic mesenteric/renal embolism**.

III MULTIMODALITY DIAGNOSTIC CRITERIA

- **Diagnostic Caveat:** Because isolated imaging ratios have a high false-positive rate in healthy populations, diagnosis requires combining morphological cut-offs with clinical phenotype (LVEF, family history, genetics, or CMR fibrosis).

A Transthoracic Echocardiography Criteria (Contrast Echo Enhances Recess Visualization)

- **Jenni Criteria (2001 — Most Widely Used Echo Standard):** Measured in the parasternal short-axis view at **end-systole**: (1) Bilayered myocardium with a **Non-Compacted to Compacted (NC/C) ratio greater than 2.0 at end-systole**; (2) Predominant localization in the mid-lateral, apical, and mid-inferior segments; (3) **Color Doppler evidence of deep perfused intertrabecular recesses** communicating with the LV cavity; and (4) Absence of coexisting cardiac structural abnormalities.
- **Chin Criteria (1990):** Ratio of the distance from the epicardial surface to the trough of the trabecular recess (**X**) divided by the distance from the epicardial surface to the peak of the trabeculation (**Y**) of **0.5 or less** at **end-diastole** at the LV apex.
- **Stöllberger Criteria (2002):** More than **three prominent trabeculations** protruding from the LV wall apical to the papillary muscles, visible in a single image plane at end-diastole, with intertrabecular spaces perfused from the ventricular cavity on color Doppler.

B Cardiac Magnetic Resonance (CMR) Criteria (Reference Standard for Tissue Characterization)

- **Petersen Criteria (2005):** Measured on long-axis cine views (excluding the true apical cap, segment 17) at **end-diastole**: **Non-Compacted to Compacted (NC/C) thickness ratio greater than 2.3 at end-diastole**.
- **Jacquier Volumetric Criteria (2010): Trabeculated LV myocardial mass greater than 20 percent of the global LV mass** at end-diastole (more reproducible than single-point linear thickness ratios).

Diagnostic Criterion	Modality & Cardiac Phase	Quantitative Cut-off	Key Clinical Feature / Limitation
Jenni Criteria (2001)	**2D Echo (Short-Axis)** at **End-Systole**	**NC / C ratio > 2.0**	Requires Color Doppler flow in deep recesses from LV cavity; most specific echo rule
Chin Criteria (1990)	**2D Echo** at **End-Diastole**	**X / Y ratio <= 0.5**	Trough-to-epicardium (X) vs. peak-to-epicardium (Y) at apex
Petersen Criteria (2005)	**Cardiac MRI (Long-Axis)** at **End-Diastole**	**NC / C ratio > 2.3**	High sensitivity; high false-positive rate (43% of **MESA** participants had at least one segment above 2.3)
Jacquier Criteria (2010)	**Cardiac MRI (Short-Axis Stack)** at **End-Diastole**	**Trabeculated LV mass > 20% of total LV mass**	Volumetric quantification of global trabecular burden

IV MANAGEMENT STRATEGIES (ESC 2023 CARDIOMYOPATHY / HRS 2019 GUIDELINES)

- **Phenotype-Directed Heart Failure Therapy:** Management follows standard **DCM / HFrEF Guideline-Directed Medical Therapy (GDMT)** when systolic dysfunction is present—combining **ARNI (Sacubitril/Valsartan) or ACEi/ARB, Beta-Blockers, MRAs, and SGLT2 Inhibitors**, plus **Cardiac Resynchronization Therapy (CRT)** when LVEF is 35 percent or less with LBBB. Asymptomatic individuals with **isolated hypertrabeculation, normal LVEF, no LGE on CMR, and negative family/genetic history require reassurance and do not require medical therapy or sports restriction**.
- **Arrhythmia and Sudden Cardiac Death (SCD) Prevention:**
  - **Secondary Prevention (Class I): ICD implantation** is recommended in survivors of cardiac arrest or sustained VT with hemodynamic compromise.
  - **Primary Prevention:** Guided by the underlying cardiomyopathy phenotype (**LVEF 35 percent or less** despite 3 months of optimal GDMT), **presence of extensive Late Gadolinium Enhancement (LGE) on CMR**, unexplained syncope, or **high-risk pathogenic variants (LMNA, FLNC, PLN, DSP, RBM20, SCN5A)** (where genotype-specific risk calculators guide early ICD placement even with LVEF greater than 35 percent).
  - **Thromboembolism Prophylaxis (Oral Anticoagulation — Warfarin or DOACs):**
  - **Class I Indications:** Mandatory in patients with excessive trabeculation/LVNC who have **Atrial Fibrillation**, a **prior thromboembolic event (stroke/TIA/systemic embolism)**, or a **documented intracavitary/intertrabecular LV thrombus** (evaluated via **contrast echocardiography** or **early/late gadolinium CMR**).
  - **Class IIb Consideration:** May be considered in patients with **severe LV systolic dysfunction (LVEF less than 30 to 35 percent)** in sinus rhythm when accompanied by extensive deep recesses or hypercoagulable states, though routine anticoagulation for isolated hypertrabeculation with normal LVEF and sinus rhythm is **not** indicated.

V LANDMARK EVIDENCE: PROGNOSIS IS DRIVEN BY LVEF AND LGE, NOT TRABECULATION ALONE

- **MESA Study (Zemrak et al., *JACC* 2014):** In 2,742 asymptomatic Multi-Ethnic Study of Atherosclerosis participants without baseline heart disease, **43 percent met Petersen CMR criteria (NC/C greater than 2.3) in at least one myocardial segment**, yet trabeculation extent was **not associated with deterioration in LV volumes or LVEF over 9.5 years of follow-up**—proving that isolated hypertrabeculation in healthy individuals is a benign anatomical variant.
- **Multicenter CMR Outcome Meta-Analyses (Andreini et al., *JACC* 2016; Grigoratos et al., *JACC Cardiovasc Imaging* 2019):** Demonstrated that in patients fulfilling imaging criteria for LVNC, **the extent of non-compacted myocardium (NC/C ratio or trabeculated mass) does NOT independently predict mortality or MACE**; instead, adverse prognosis is dictated entirely by **reduced LVEF** and the presence of **myocardial fibrosis (LGE on CMR)**.Patients with **preserved LVEF (50 percent or greater) and no LGE on CMR** have an event rate virtually identical to the general population.

VI PRACTICAL CONSIDERATIONS IN THE INDIAN CLINICAL CONTEXT

- **Avoiding Over-Diagnosis in Physiological High-Preload States:** In India, **chronic severe iron-deficiency or hemolytic anemia**, **pregnancy**, and **athletic training** frequently induce reversible left ventricular hypertrabeculation meeting Petersen or Jenni cut-offs. Labeling such individuals with “LVNC cardiomyopathy” causes unnecessary anxiety and inappropriate anticoagulation; **normal LVEF, normal GLS, and absence of LGE on CMR** confirm a benign adaptive phenotype.
- **Contrast Echocardiography in Resource-Limited Settings:** When CMR is unavailable, administering an intravenous **Ultrasound Enhancing Agent (echo contrast)** (or agitated saline/blood contrast where commercial microbubbles are costly) is essential both to clearly delineate the endocardial border of deep apical recesses and to exclude **apical intertrabecular thrombi** vs. **Apical Hypertrophic Cardiomyopathy** or **Left Ventricular Endomyocardial Fibrosis (LV-EMF)**.
- **Family Cascade Screening and Pediatric Syndromes:** When true cardiomyopathy with hypertrabeculation is diagnosed, **clinical and echocardiographic screening of first-degree relatives** (Class I) and targeted **Next-Generation Sequencing (NGS)** panels (including sarcomeric genes, high-risk arrhythmic genes, and **TAFAZZIN** in male infants with neutropenia/aciduria) are recommended.

KEY REFERENCES

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- **Petersen SE, Selvanayagam JB, Wiesmann F, et al.:** Left ventricular non-compaction: insights from cardiovascular magnetic resonance imaging, *Journal of the American College of Cardiology*, 2005.
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