AICD FOR NON-ISCHEMIC CARDIOMYOPATHY (NICM); CURRENT STATUS

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Last reviewed: October 2026

I SECONDARY PREVENTION (THE ABSOLUTE MANDATE)

- **Class I Recommendation:** Implantable Cardioverter-Defibrillator (ICD) therapy is indicated for patients with Non-Ischemic Cardiomyopathy (NICM) who have survived Sudden Cardiac Arrest (SCA) due to Ventricular Fibrillation (VF) or hemodynamically unstable sustained Ventricular Tachycardia (VT), provided they have an expected meaningful survival of **greater than 1 year**.

II PRIMARY PREVENTION: THE PARADIGM SHIFT AND LANDMARK EVIDENCE

- **The DANISH Trial (The Pivot Point):**
  - **Study Design:** Randomized patients with symptomatic NICM (LVEF 35 percent or less) to prophylactic ICD implantation versus optimal medical therapy.
  - **Primary Result:** Routine prophylactic ICD implantation **did not significantly reduce overall all-cause mortality** in the general NICM population.
  - **The Age Interaction Caveat:** A pre-specified subgroup analysis demonstrated a significant survival benefit in younger patients (**less than 68 years of age**), whereas older patients frequently died of non-arrhythmic pump failure or competing comorbidities.
  - **The Quadruple GDMT Mandate (Class I Prerequisite):**
  - **Mandatory Waiting Period:** A primary-prevention ICD should not be implanted until the patient has been treated with optimally titrated **Quadruple GDMT** (**ARNI, Beta-blocker, MRA, and SGLT2 inhibitor**) for a minimum of **3 to 6 months**.
  - **Rationale:** Contemporary quadruple therapy (particularly ARNI and SGLT2 inhibitors) induces substantial left ventricular reverse remodeling, frequently recovering the LVEF above the 35 percent threshold and eliminating the need for an ICD.

III THE CMR TIEBREAKER

- **Late Gadolinium Enhancement (LGE) as the Arrhythmogenic Substrate:** Because LVEF alone poorly predicts Sudden Cardiac Death (SCD) in NICM, **Cardiac Magnetic Resonance (CMR)** serves as the central risk-stratification tool by identifying macroscopic replacement fibrosis (LGE) that forms the anatomical substrate for re-entrant ventricular arrhythmias.
- **Guideline Integration:**
  - **Presence of Extensive LGE (Class IIa):** In patients with **LVEF below 50 percent**, ESC 2022 gives **Class IIa** when **2 or more risk factors** are present: unexplained syncope, **LGE on CMR**, inducible sustained monomorphic VT at PES, or a pathogenic **LMNA, PLN, FLNC or RBM20** variant.
  - **Absence of LGE:** Identifies a lower-risk cohort in whom primary-prevention ICD implantation may be deferred when LVEF is borderline.

IV GENOTYPE-GUIDED ICD THERAPY

- **Bypassing the LVEF <= 35% Threshold in High-Risk Genotypes:** In specific arrhythmogenic genetic cardiomyopathies, malignant ventricular arrhythmias occur early before severe systolic dysfunction develops, lowering the threshold for prophylactic ICD placement.
- **Lamin A/C (*LMNA*) Mutations:**
- **Phenotype:** High rates of conduction system disease (AV block) progressing rapidly to malignant VT/VF.
- **Guideline Recommendation (Class IIa):** Early prophylactic ICD is recommended if the patient has **2 or more risk factors** (**non-sustained VT, LVEF less than 45 percent, male sex, or non-missense mutation**), even when LVEF is above 35 percent (HRS 2019); ESC 2022/2023 uses the **LMNA risk calculator** (ICD if 5-year risk is 10 percent or more with NSVT, LVEF below 50 percent or AV conduction delay).
- **Filamin C (*FLNC*) and Phospholamban (*PLN*) Mutations:**
- **Phenotype:** Highly arrhythmogenic cardiomyopathy characterized by ring-like subepicardial LGE on CMR and frequent ventricular tachycardia.
- **Guideline Recommendation (Class IIa):** Prophylactic ICD is recommended if **LVEF is less than 45 percent** or if significant **LGE or non-sustained VT** is present.

Clinical / Genetic Scenario in NICM	Guideline Class	Key Qualifying Criteria
Secondary Prevention	**Class I**	Survivors of aborted SCA (VF) or hemodynamically unstable VT with >1 year expected survival
Primary Prevention (Standard LVEF <= 35%)	**Class I (AHA/ACC) / Class IIa (ESC)**	NYHA Class II–III, **LVEF <= 35%** despite **>= 3 months of Quadruple GDMT**, and >1 year survival
Primary Prevention (CMR / High-Risk Genotype)	**Class IIa**	Pathogenic ***LMNA, FLNC, PLN*, or *RBM20*** variant or **extensive CMR LGE**, even with **LVEF 35–45%**
Newly Diagnosed NICM (< 3 Months) or Refractory NYHA IV	**Class III (Harm)**	Within **first 3 months** of initial HF diagnosis (await GDMT recovery) or **NYHA IV** not eligible for CRT/LVAD/Transplant

V SUMMARY OF CURRENT GUIDELINE ALGORITHM

- **Class I / IIa (LVEF <= 35%):** Primary prevention in symptomatic NICM (NYHA Class II–III) with **LVEF 35 percent or less** after **at least 3 months of optimal quadruple GDMT** and expected survival greater than 1 year (Class IIa in ESC post-DANISH; Class I in AHA/ACC with shared decision-making incorporating age and CMR LGE).
- **Class IIa (Genotype and CMR Risk Modifiers):** Patients with high-risk pathogenic mutations (***LMNA, FLNC, PLN, RBM20***) or extensive mid-wall/epicardial LGE on CMR, even when LVEF is between 35 and 45 percent.
- **Class III (Harm):**
  - Implantation **within the first 3 months** of initial heart failure diagnosis prior to completing a trial of quadruple GDMT for LVEF recovery.
  - Implantation in **ambulatory NYHA Class IV** patients who are not candidates for Cardiac Resynchronization Therapy (CRT), Left Ventricular Assist Device (LVAD), or cardiac transplantation.

KEY REFERENCES

- **Køber L, Thune JJ, Nielsen JC, et al. (DANISH Investigators):** Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure, *New England Journal of Medicine*.
- **Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al.:** 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death, *European Heart Journal*.
- **Arbelo E, Protonotarios A, Gimeno JR, et al.:** 2023 ESC Guidelines for the management of cardiomyopathies, *European Heart Journal*.