Classification of Cardiomyopathy

Chapter 266 | Part 6: Disorders of the Cardiovascular System

KEY CLINICAL POINTS

1. Cardiomyopathy is defined as primary disease of the heart muscle itself, excluding myocardial dysfunction resulting from other cardiovascular diseases (e.g., ischemic or valvular).
2. Traditional morphologic classification identifies three major phenotypes: Hypertrophic (HCM), Dilated (DCM), and Restrictive (RCM).
3. HCM diagnostic criteria: Septal thickness ≥15 mm in men, ≥13 mm in women; LVEF ≥ normal (usually >0.60); LV chamber volume ≤ normal.
4. DCM diagnostic criteria: LVEF ≤0.50 (typically ≤0.40) and/or LVEDV >112% of age/sex normal or LVEDD >95% predicted sex/height; persistent LVEF ≤0.30–0.35 is the threshold for primary prevention ICD.
5. RCM is a functional diagnosis based on moderate-to-severe diastolic dysfunction and/or elevated cardiac filling pressures.
6. Arrhythmogenic Cardiomyopathy (ACM) includes ACM-LV (dominant in LV, DCM phenotype) and ACM-RV (dominant in RV, also known as ARVC).
7. Left ventricular noncompaction (LVNC) is often assessed by a maximum ratio of noncompacted/compacted LV myocardium >2.3.
8. Several conditions can mimic HCM morphology, including storage diseases (GLA/Anderson-Fabry, PRKAG2, LAMP2/Danon's) and amyloidosis.
9. Significant regional variations exist in clinical presentation, comorbidity burden, and treatment response (e.g., spironolactone efficacy in the TOPCAT trial).
10. Congestive heart failure is a non-specific syndrome requiring thorough evaluation of underlying causes; it is not a diagnosis of cardiomyopathy itself.

1. DEFINITION & OVERVIEW

- **Core Definition:**

The term cardiomyopathy describes primary disease of the heart muscle itself, originally excluding myocardial dysfunction resulting from other cardiovascular disease.

- **Phenotypic Classification:**

- **Hypertrophic Cardiomyopathy (HCM):** Left ventricular wall thickness is increased (≥13–15 mm depending on context) and ejection fraction is normal or high.

- **Dilated Cardiomyopathy (DCM):** Defined when the left ventricular ejection fraction (LVEF) is ≤0.50, but most clinical presentations are with LVEF ≤0.40.

- **Restrictive Cardiomyopathy (RCM):** Typically presents with mildly decreased ejection fraction and variably increased wall thickness; defined more by evidence of abnormal diastolic physiology than morphology.

• **Arrhythmogenic Cardiomyopathy (ACM):** A fourth evolving phenotype with predominantly genetic causes characterized by life-threatening arrhythmias and abnormal right ventricular structure/function, with variable expression in the left ventricle.

• **Evolution of Phenotypes:**

• **DCM Dynamics:** May respond to therapy with 'reverse remodeling' (higher EF, smaller ventricles).

• **HCM Progression:** Evolves in ≈5% of patients to a reduced ejection fraction (HCM-rEF) with more restrictive physiology.

• **Mid-range LVEF:** Often represents a transition in DCM (deterioration from normal or improvement into remission). It also includes rare transitions to HCM with LV systolic dysfunction (LVEF <0.50) in patients with known HCM or positive genetic tests.

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2. EPIDEMIOLOGY

• **Regional Variations:**

• **Clinical Profiles:**

• **North America:** Higher comorbidity burden, higher rates of diabetes, prior coronary revascularization, and higher device use.

• **South America:** Lowest rates of comorbidities, revascularization, and device use.

• **Eastern Europe:** Patients with ADHF tend to be younger, with higher EFs and lower natriuretic peptide levels.

• **Trial Disparities:**

• **TOPCAT Trial:** Spironolactone was effective in the U.S. population but showed no difference in patients from Russia and contiguous territories.

• **Generalizability:** Geographic differences in baseline characteristics mean that therapeutic outcomes in Western Europe/U.S. may require verification in other regions.

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3. ETIOLOGY & PATHOPHYSIOLOGY

• **Genetic and Acquired Factors:**

• **Genetics:** Rapidly growing catalog of pathogenic genetic variants leading to heritable cardiomyopathies, often identifiable via new imaging before clinical disease.

• **Immune/Inflammatory Pathways:** Inherited immune response pathways contribute to infectious and noninfectious inflammation (myocarditis → cardiomyopathy).

• **Two-Hit Model:** Clinical expression of a genetic predisposition may be triggered by acquired conditions:

• Infections

• Toxic exposures

• Pregnancy

• Tachycardia

• **Storage Diseases:** Specific mutations (GLA/Anderson-Fabry, PRKAG2, LAMP2/Danon's) can mimic HCM morphology.

- **Clinical Distinction:** Congestive heart failure is a non-specific syndrome; it must be differentiated from specific cardiomyopathy etiologies.

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4. CLINICAL FEATURES

- **Primary Symptoms:**
- Exertion intolerance (breathlessness, fatigue).
- Arrhythmias as presenting events of unrecognized cardiomyopathy.
- **Complications:**
- Embolic events (atrial fibrillation or apical ventricular thrombi).
- **Congestion Syndrome:**
- Fluid retention and elevated left heart filling pressures → shortness of breath, orthopnea.
- **Right-Sided Failure:** Edema and abdominal symptoms due to elevated right-sided filling pressures.

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5. DIFFERENTIAL DIAGNOSIS

- **Morphological Mimickers (HCM):**
- Athlete's heart
- Severe chronic hypertension
- Aortic stenosis
- Amyloidosis (especially in older patients with asymmetric septal thickening)
- Storage diseases: GLA (Anderson-Fabry), PRKAG2, and LAMP2 (Danon's).
- **Structural/Inflammatory Mimickers:**
- Coronary artery disease or infarction.
- Primary valve disease.
- Cardiac sarcoidosis (can mimic ACM-RV with RV involvement, arrhythmias, and aneurysms).
- **Arrhythmia Differentiation:** Distinguishing PVC-related cardiomyopathy from genetic cardiomyopathy causing both arrhythmia and cardiomyopathy.

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6. INVESTIGATIONS & DIAGNOSIS

1. **Clinical Evaluation:** Detailed history/examination for cardiac, genetic, and systemic clues.
2. **Echocardiography:** Initial imaging to define morphology and function.
3. **Magnetic Resonance Imaging (MRI):**
   - Tissue characterization.
   - Late Gadolinium Enhancement (LGE) to identify fibrosis patterns.
   - T1 and T2 mapping for focal/diffuse inflammation.
4. **Diagnostic Criteria by Phenotype:**
   - **Hypertrophic Cardiomyopathy (HCM):**
   - Septal thickness: ≥15 mm (men), ≥13 mm (women).

- Special Case: 13–14 mm may be diagnostic in relatives of probands or those with positive genetic tests.
- LVEF: ≥ normal (usually >0.60).
- LV Chamber Volume: ≤ normal.
- **Dilated Cardiomyopathy (DCM):**
- Early Diagnosis: LVEF ≤0.50 and/or LVEDV >112% of age/sex normal or LVEDD >95% predicted sex/height.
- Therapy Threshold: LVEF ≤0.40.
- ICD Primary Prevention: Persistent LVEF ≤0.30–0.35.
- **Restrictive Cardiomyopathy (RCM):**
- Functional diagnosis based on moderate-severe diastolic dysfunction or elevated filling pressures.
- LVEF: Usually mildly reduced, occasionally normal.
- **Arrhythmogenic Cardiomyopathy (ACM):**
- **ACM-LV:** Morphologic criteria for DCM; tachyarrhythmias dominate before/without severe heart failure. ICD considered even if LVEF >0.35.
- **ACM-RV (ARVC):** Modified task force criteria (2010) including major/minor criteria.
- **Left Ventricular Noncompaction (LVNC):**
- Assessment: Maximum ratio of noncompacted/compacted LV myocardium >2.3.

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7. MANAGEMENT & TREATMENT

1. **Heart Failure Management:**
   - LVEF ≤0.40 is the threshold for traditionally recommended therapies for heart failure with low LVEF.
2. **Device Therapy (ICD):**
   - Standard: Persistent LVEF ≤0.30–0.35 for primary prevention.
   - ACM-LV: Primary prevention ICD considered even when LVEF >0.35.
3. **Clinical Monitoring:**
   - Monitor for 'reverse remodeling' in DCM patients.
   - Identify transition states (mid-range LVEF) to determine if progression or remission is occurring.
4. **Regional Adaptation:**
   - Adjust treatment based on regional prevalence of comorbidities and specific drug responses (e.g., spironolactone).

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8. PROGNOSIS & COMPLICATIONS

- **Arrhythmia Risk:**
- ACM-LV: Tachyarrhythmias often occur before heart failure.
- ACM-RV: High risk of life-threatening arrhythmias and RV structural damage.
- **Embolic Events:** Risk from atrial fibrillation or apical ventricular thrombi.
- **Congestion:** Development of pulmonary hypertension or right-sided heart failure.

9. SPECIAL CONSIDERATIONS

- **Pregnancy:** LVNC can occur in normal hearts or during pregnancy.
- **Athletic Hearts:** High prevalence of LVNC in athletes; must be distinguished from true cardiomyopathy.
- **Elderly Patients:** Must exclude amyloidosis when asymmetric septal thickening is present.
- **Geographic Variations:**
- South America: Lower rates of comorbidities and device use.
- Eastern Europe: Younger ADHF patients with higher EFs.

10. KEY PEARLS & CLINICAL TRAPS

- **Diagnostic Thresholds:**
- HCM: ≥15 mm (men), ≥13 mm (women).
- DCM: LVEF ≤0.50; ICD threshold ≤0.30–0.35.
- LVNC: Ratio >2.3.
- **Clinical Traps:**
- **Congestive Heart Failure:** It is a syndrome, not a diagnosis of cardiomyopathy.
- **Mid-range LVEF (0.40–0.50):** Represents a transition state in DCM or rare cases of HCM with systolic dysfunction.
- **Mimic Awareness:** Always exclude amyloidosis, aortic stenosis, and sarcoidosis when evaluating cardiomyopathy phenotypes.

REFERENCE TABLES

TABLE 266-1

Classification of Cardiomyopathies CARDIOMYOPATHY (CM) PHENOTYPE Hypertrophic cardiomyopathy (HCM) Septal thickness in...

CARDIOMYOPATHY (CM) PHENOTYPE	DIAGNOSTIC CRITERIA	OTHER MORPHOLOGY	COMMON CHALLENGES IN DIAGNOSIS
Hypertrophic cardiomyopathy (HCM) **Mid-range LVEF includes rare transition to HCM with LV systolic dysfunction (LVEF <0.50)**	Septal thickness in men ≥15 mm, ≥13 mm in women. 13–14 mm may be diagnostic in relatives of proband with known HCM or with positive genetic test. LVEF ≥ normal, usually >0.60 LV chamber volume ≤normal.	Patterns of LV hypertrophy (LVH) in HCM: • Asymmetric septal hypertrophy • Inverse (sigmoid pattern) septal hypertrophy • Concentric LVH • Apical hypertrophy	Distinction from athlete's heart and severe chronic hypertension The storage diseases of GLA (Anderson-Fabry), PRKAG2, and LAMP2 (Danon's), which can mimic HCM morphology Exclude aortic stenosis In older patients, exclude amyloidosis, which can also cause asymmetric septal thickening
	Functional diagnosis based on moderate-severe diastolic dysfunction and/or elevated cardiac filling pressures. Wall thickness often increased but can appear normal. LVEF usually mildly reduced, occasionally normal.	Usually marked atrial enlargement Although both ventricles affected, clinical right heart failure often dominates. Marked wall thickness suggests: • Amyloidosis • Inherited storage diseases • Inborn metabolic diseases	
Mid-range LVEF is often a transition in DCM, either deterioration from early DCM or improvement into DCM remission **LV dilated cardiomyopathy (DCM)**	• Early: LVEF ≤0.50 and/or LVEDV >112% normal for age/sex or LVEDD >95% predicted sex/height • LVEF ≤0.40: threshold for traditionally recommended therapies for heart failure with low LVEF • Persistent LVEF ≤0.30–0.35: threshold for primary prevention ICD	Can involve LV alone or with RV involvement either from primary cause or from secondary RV failure due to chronically elevated pulmonary artery pressures	Structural heart disease such as coronary artery disease or infarction from other cause, primary valve disease

CARDIOMYOPATHY (CM) PHENOTYPE	DIAGNOSTIC CRITERIA	OTHER MORPHOLOGY	COMMON CHALLENGES IN DIAGNOSIS
	Morphologic criteria generally those for DCM. Ventricular tachyarrhythmias dominate without or before severely reduced LVEF and heart failure. Primary prevention ICD considered even when LVEF >0.35.	Suggestive but not necessarily conclusive differences in patterns of late gadolinium enhancement between different variants Occasional ACM-LV with RCM phenotype	
Arrhythmogenic CM Dominant in RV (ACM-RV; also termed ARVC) Biventricular arrhythmogenic CM	Modified task force criteria from 2010 include combinations of major and minor criteria Ventricular arrhythmias and evidence of both ACM-RV and ACM-LV	Abnormal RV function or structure Biventricular ACM often diagnosed from LGE in ventricle with less involvement	Cardiac sarcoidosis can cause predominantly RV involvement with ventricular arrhythmias, RV wall motion abnormalities, aneurysms, and dilation
	Often assessed by maximum ratio of noncompacted/compacted LV myocardium >2.3 and other criteria	Can occur with HCM, DCM, some dystrophies, and other syndromic presentations	