Dilated Cardiomyopathies

Chapter 269 | Part 6: Disorders of the Cardiovascular System

KEY CLINICAL POINTS

1. Alcoholic cardiomyopathy requires cessation of alcohol; threshold is 3–4 ounces (≥60–80 g) of pure ethanol daily for ≥5 years, though women may develop it with lower amounts.
2. Peripartum cardiomyopathy (PPCM) recovery to LVEF ≥0.50 occurs in 50–80% of cases within 6 months; recovery is less likely if LVEF <0.35 or marked dilation is present.
3. Anthracycline cardiotoxicity management includes beta-adrenergic blockade and RAAS inhibition; dexrazoxane may prevent toxicity, but consensus on timing is lacking.
4. Takotsubo syndrome (stress-induced cardiomyopathy) typically resolves within days to weeks; recurrence occurs in 10% of patients at an estimated rate of 2%/year.
5. Checkpoint inhibitor myocarditis requires immediate high-dose glucocorticoids; outcomes are improving with earlier recognition and therapy.
6. Hemochromatosis diagnosis is made primarily by MRI iron quantitation; phlebotomy is the management for early disease to remove iron.
7. Trastuzumab cardiomyopathy may persist in about a third of affected patients and can progress to clinical heart failure and death.
8. PPCM anticoagulation is typically prescribed for the first 6 weeks postpartum if LVEF <0.35 or marked dilation is present due to thrombus risk.
9. TTN truncating mutations are found in ~15% of PPCM cases and are associated with lower rates of recovered systolic function.
10. Vaccine-induced myocarditis risk after COVID-19 vaccines is estimated at 1/100,000 doses, increasing to 2–3/100,000 for recipients aged 18–39 years.

1. DEFINITION & OVERVIEW

- **Definition:** Dilated cardiomyopathy (DCM) is characterized by decreased left ventricular systolic function, typically with increased left ventricular dimensions, although dilation may be minimal in some cases.
- **Pathophysiology of Progression:**
  - Myocyte death occurs early; remaining myocytes develop hypertrophy in response to increased wall stress.
  - Neurohormonal factors stimulate deleterious secondary responses contributing to disease progression.
  - Dynamic remodeling of the interstitial scaffolding affects diastolic function and ventricular dilation.
- **Complications of Dilation:**
  - Mitral regurgitation: Commonly develops as the ventricle dilates and the valvular apparatus is distorted; often moderate to severe in advanced heart failure.

– Right Ventricular (RV) Involvement: May result from initial injury or later due to secondary pulmonary hypertension and mechanical interactions with the failing LV.

- **Recovery Potential:**
  – Approximately one-third of patients with recent-onset cardiomyopathy (absent coronary artery disease) show substantial spontaneous recovery to normal ejection fraction.
  – Partial recovery to LVEF >0.40 is common in chronic DCM during therapy with neurohormonal modulation, cardiac resynchronization therapy for left bundle branch block, and diuretics.

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2. EPIDEMIOLOGY

- **Alcohol-Related Epidemiology:**
  – Prevalence: Similar between men and women with alcoholism.
  – Clinical Presentation: Significantly more hospital admissions in men than women.
  – Detection: LV dysfunction found in ~1/3 of asymptomatic patients with alcoholism.
  – Threshold for Cardiomyopathy: 3–4 ounces (≥60–80 g) of pure ethanol daily for ≥5 years; women may develop it with lower amounts.
  – Binge drinking: Frequent binge drinking may be sufficient to cause cardiomyopathy.
- **Peripartum Cardiomyopathy (PPCM) Epidemiology:**
  – Incidence: 1:1000 to 1:4000 deliveries in the United States.
  – Risk Factors: Fourfold higher risk in black women; recovery of normal LVEF is slower and less likely in black women than white women.
  – Mortality: One-year mortality rates range from 4% to 11% in the US; up to twofold higher in Africa.

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3. ETIOLOGY & PATHOPHYSIOLOGY

- **General Etiology:**
  – Multiple causes including myocarditis, genetic variants, toxic agents, and metabolic disorders (Table 269-1).
- **Inflammatory Myocarditis:**
  – Infective: Viral (coxsackie, adenovirus, COVID-19, HIV); Parasitic (Trypanosoma cruzi—Chagas' disease, trypanosomiasis, toxoplasmosis); Bacterial (diphtheria); Spirochetal (Borrelia burgdorferi—Lyme disease); Rickettsial (Q fever); Fungal.
  – Noninfective: Granulomatous inflammatory disease; Sarcoidosis; Giant cell myocarditis; Eosinophilic myocarditis; Polymyositis, dermatomyositis; Collagen vascular disease; Checkpoint inhibitor chemotherapy; Transplant rejection.
- **Toxic Causes:**
  – Alcohol; Catecholamines (amphetamines, cocaine); Chemotherapeutic agents (anthracyclines, trastuzumab); Interferon; Other therapeutic agents (hydroxychloroquine, chloroquine); Drugs of misuse (testosterone and other anabolic steroids, emetine); Heavy metals (lead, mercury); Occupational exposure (hydrocarbons, arsenicals).
- **Metabolic Causes:**
  – Nutritional deficiencies: thiamine, selenium, carnitine.
  – Electrolyte deficiencies: calcium, phosphate, magnesium.
  – Endocrinopathy: Thyroid disease, Pheochromocytoma, Diabetes mellitus, Obesity, Hemochromatosis.
  – Inherited metabolic pathway defects; Familial cardiomyopathies.

- **Miscellaneous Causes:**
  - Arrhythmogenic ventricular cardiomyopathy; Peripartum cardiomyopathy; Left ventricular noncompaction; Tachycardia-related cardiomyopathy; Supraventricular arrhythmias with uncontrolled rate; High burden of premature ventricular complexes or NSVT.

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4. CLINICAL FEATURES

- **General Presentation:**
  - Pulmonary edema, hypotension, and chest pain with ECG changes mimicking acute infarction.
  - LV dysfunction extends beyond a specific coronary artery distribution; typically resolves in days to weeks (in Takotsubo).
- **Peripartum Cardiomyopathy (PPCM):**
  - Timing: Most cases present within the first week after delivery.
  - Symptoms: Increasing edema and dyspnea as urine output fails to keep up with fluid mobilization.
  - Complications: Risk of pulmonary emboli or coronary artery dissection must be excluded.
- **Takotsubo Syndrome:**
  - Presentation: Often triggered by intense emotional/physical stress; characterized by apical ballooning.
  - Resolution: Dysfunction typically resolves within days to weeks.
- **Metabolic & Nutritional Conditions:**
  - Beriberi (Thiamine): Thiamine deficiency → heart failure; prompt recovery with thiamine repletion.
  - Carnitine: Abnormalities cause dilated/restrictive cardiomyopathy (common in children).
  - Selenium: Deficiency causes Keshan's disease.
  - Calcium: Chronic deficiency (e.g., hypoparathyroidism) → severe heart failure; responds to calcium repletion.
  - Phosphate: Hypophosphatemia during starvation or early refeeding.
  - Obesity: Associated with impaired excretion of volume load; weight reduction often improves EF.
- **Special Conditions:**
  - Pheochromocytoma: Often presents with postural hypotension; requires alpha-adrenergic receptor antagonists and surgical extirpation.
  - Renal Artery Stenosis: High renin states → modest depression in ejection fraction with little or no ventricular dilation; manifests as flash pulmonary edema due to sudden shifts in vascular tone.

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5. DIFFERENTIAL DIAGNOSIS

- **Alcohol vs. Genetic Cardiomyopathy:**
  - Alcohol cardiomyopathy is a diagnosis of exclusion.
  - Note: TTN truncating mutations found in ~15% of patients with presumed alcohol cardiomyopathy.
- **Takotsubo vs. Acute MI:**
  - Distinction: Takotsubo resolves in days/weeks; MI does not.
  - Distribution: Takotsubo dysfunction extends beyond a single coronary artery distribution.
  - Rule-out: Coronary angiography required to rule out acute coronary occlusion.
- **Hemochromatosis:**
  - Identification: Systemic iron overload causing cardiac siderosis.
  - Differentiation: Distinguished from other cardiomyopathies by MRI iron quantitation.

6. DIAGNOSTIC APPROACH

1. **General Diagnostic Pathway:**
   - Echocardiography: Initial assessment of LVEF and myocardial dimension.
   - Coronary Angiography: Performed if Takotsubo is suspected to rule out acute coronary occlusion.
   - Cardiac MRI: Used for quantifying iron stores (Hemochromatosis) or identifying apical ballooning/edema (Takotsubo).
   - Genetic Testing: Consider for TTN mutations in PPCM cases.
2. **Specific Diagnostic Criteria:**
   - **PPCM:**
     - Clinical presentation of heart failure/congestion within first week post-delivery.
     - Assessment of LVEF and myocardial dilation.
   - **Hemochromatosis:**
     - MRI iron quantitation (primary diagnostic modality).
   - **Takotsubo Syndrome:**
     - ECG changes mimicking infarction.
     - Cardiac MRI showing apical ballooning/edema without necrosis.
1. **General Management of DCM:**
   - Guideline-directed medical therapies (GDMT).
   - Beta-adrenergic antagonists.
   - Mineralocorticoid receptor antagonists.
   - Diuretics for fluid management.
   - Electrolyte repletion.
2. **Specific Management Protocols:**
   - **Anthracycline Cardiotoxicity:**
     - Beta-adrenergic blockade.
     - RAAS inhibition.
   - **Peripartum Cardiomyopathy (PPCM):**
     - Anticoagulation: Prescribed for first 6 weeks postpartum if LVEF <0.35 or marked dilation is present.
   - **Takotsubo Syndrome:**
     - Supportive management; resolution typically occurs in days to weeks.
   - **Hemochromatosis:**
     - Phlebotomy: Primary management for early disease to remove iron.
   - **Pheochromocytoma:**
     - Alpha-adrenergic receptor antagonists.
     - Surgical extirpation (definitive therapy).

8. PROGNOSIS & COMPLICATIONS

- **PPCM Prognosis:**
  - Recovery to LVEF ≥0.50: 50–80% of cases within 6 months.
  - Risk Factors for Poor Recovery: LVEF <0.35 at 6 weeks post-delivery; TTN truncating mutations.

- **Takotsubo Prognosis:**
  - Resolution: Typically occurs in days to weeks.
  - Recurrence: ~10% of patients (estimated rate of 2%/year).
- **Hemochromatosis Progression:**
  - Can progress to clinical heart failure and death if not managed.

9. SPECIAL CONSIDERATIONS

- **Pregnancy & Breastfeeding:**
  - PPCM: Requires exclusion of pulmonary emboli and coronary artery dissection.
- **Pediatric Considerations:**
  - Carnitine metabolism defects (dilated/restrictive cardiomyopathy).
  - Selenium deficiency (Keshan's disease).
- **Nutritional Deficiencies:**
  - Beriberi (Thiamine): High-output to low-output progression; prompt recovery with thiamine.
  - Calcium: Severe heart failure in hypoparathyroidism or intestinal dysfunction; responds to calcium repletion.
  - Phosphate: Hypophosphatemia during starvation/refeeding.

10. KEY PEARLS & CLINICAL TRAPS

- **Alcohol Threshold:** 3–4 oz (≥60–80 g) daily for ≥5 years is the standard metric.
  - Note: Women may develop cardiomyopathy with lower amounts.
  - Note: Frequent binge drinking may be sufficient.
- **Takotsubo Distinction:** Look for apical ballooning and resolution within weeks to differentiate from MI.
  - Recurrence rate: 10% of patients (2%/year).
- **Hemochromatosis Diagnosis:** Primarily MRI; phlebotomy is the management for early disease.
- **PPCM Timing:** Most cases present within the first week after delivery.
  - Anticoagulation threshold: LVEF <0.35 or marked dilation.
- **Checkpoint Inhibitors:** Require immediate high-dose glucocorticoids for myocarditis.
- **Vaccine Myocarditis:** Risk is 1/100,000 (general) and 2–3/100,000 (ages 18–39).

REFERENCE TABLES

TABLE 269-1

Major Causes of Dilated Cardiomyopathy (with Common Examples) Inflammatory Myocarditis (see Chap. 268) Infective

- Inflammatory Myocarditis (see Chap. 268)
- Infective
- Viral (coxsackie,a adenovirus,a COVID-19, HIV)
- Parasitic (Trypanosoma cruzi—Chagas' disease, trypanosomiasis, toxoplasmosis)
- Bacterial (diphtheria)
- Spirochetal (Borrelia burgdorferi—Lyme disease)

- Rickettsial (Q fever)
- Fungal (with systemic infection)
- Noninfective
- Granulomatous inflammatory disease
- Sarcoidosis
- Giant cell myocarditis
- Eosinophilic myocarditis
- Polymyositis, dermatomyositis
- Collagen vascular disease
- Checkpoint inhibitor chemotherapy
- Transplant rejection
- Toxic
- Alcohol
- Catecholamines: amphetamines, cocaine
- Chemotherapeutic agents (anthracyclines, trastuzumab)
- Interferon
- Other therapeutic agents (hydroxychloroquine, chloroquine)
- Drugs of misuse (testosterone and other anabolic steroids emetine)
- Heavy metals: lead, mercury
- Occupational exposure: hydrocarbons, arsenicals
- Metabolica
- Nutritional deficiencies: thiamine, selenium, carnitine
- Electrolyte deficiencies: calcium, phosphate, magnesium
- Endocrinopathy
- Thyroid disease
- Pheochromocytoma
- Diabetes mellitus
- Obesity
- Hemochromatosis Inherited metabolic pathway defects (see Chap. 267)
- Familiala (see Table 267-1)
- Cardiomyopathies without extracardiac involvement Cardiomyopathy with skeletal myopathy, for example:
- Dystrophin-related dystrophy (Duchenne's, Becker's)
- Mitochondrial myopathies (e.g., Kearns-Sayre syndrome)
- Hemochromatosis
- Susceptibility to immune-mediated myocarditis Associated with other systemic diseases
- Miscellaneous (Shared Elements of Above Etiologies)
- Arrhythmogenic ventricular cardiomyopathy Peripartum cardiomyopathy
- Left ventricular noncompactiona
- Tachycardia-related cardiomyopathy
- Supraventricular arrhythmias with uncontrolled rate

• Very frequent nonsustained ventricular tachycardia or high burden of premature ventricular complexes