Cardiomyopathy

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Interventional cardiologist & internist
**Definition:** A heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation and are due to a variety of causes that frequently are genetic. Cardiomyopathies either are confined to the heart or are part of generalized systemic disorders, often leading to cardiovascular death or progressive heart failure-related disability.

Figure 35.1 The clinical categories of inherited cardiomyopathies and their genetic basis.

The clinical entities hypertrophic cardiomyopathy and dilated cardiomyopathy share some disease genes with each other, as well as with restrictive cardiomyopathy and left ventricular noncompaction, which are less common. Arrhythmogenic right ventricular cardiomyopathy appears to be a genetically distinct category, although its clinical phenotype cannot always be easily distinguished from that of dilated cardiomyopathy. AMPK denotes AMP-activated protein kinase; GLA, α-galactosidase A; LAMP2, lysosomal-associated membrane protein 2; and TMEM43, transmembrane protein 43.

Dilated cardiomyopathy

**Definition:** Dilated cardiomyopathy (DCM) is characterized by left ventricular dilatation and systolic dysfunction in the absence of hypertension, coronary artery disease, valve disease, congenital heart disease, and other overloading conditions. Left ventricular diastolic dysfunction may coexist, and atrial dilation as well as right ventricular dilation and dysfunction can also develop.
MAJOR CAUSES OF DILATED CARDIOMYOPATHY:

Inflammatory Myocarditis:
Infective
Viral (coxsackie, adenovirus, HIV, hepatitis C)
Parasitic (T. 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 Peripartum
cardiomyopathy Transplant rejection
**Toxic:**
Alcohol
Catecholamines: amphetamines, cocaine Chemotherapeutic agents (anthracyclines, trastuzumab) Interferon
Other therapeutic agents (hydroxychloroquine, chloroquine)
Drugs of misuse (emetine, anabolic steroids)
Heavy metals: lead, mercury
Occupational exposure: hydrocarbons, arsenicals

**Metabolic:**
Nutritional deficiencies: thiamine, selenium, carnitine
Electrolyte deficiencies: calcium, phosphate, magnesium
Endocrinopathy
Thyroid disease
Pheochromocytoma
Diabetes Obesity Hemochromatosis
Inherited Metabolic Pathway Defects
**Familial:**
Skeletal and cardiac myopathy
Dystrophin-related dystrophy (Duchenne’s, Becker’s)
Mitochondrial myopathies (e.g., Kearns-Sayre syndrome)
Arrhythmogenic ventricular dysplasia
Hemochromatosis
Associated with other systemic diseases
Susceptibility to immune-mediated myocarditis

**Overlap with Nondilated Cardiomyopathy:**
“Minimally dilated cardiomyopathy” Hemochromatosis
Amyloidosis
Hypertrophic cardiomyopathy (“burned-out”)
“Idiopathic”
<table>
<thead>
<tr>
<th>Pathology</th>
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<tbody>
<tr>
<td><strong>• Cardiac dilatation</strong></td>
</tr>
<tr>
<td>– ? Adaptive – due to increased loading conditions</td>
</tr>
<tr>
<td>– Idiopathic DCM – maladaptive..</td>
</tr>
<tr>
<td><strong>• Myocellular hypertrophy and cell death</strong></td>
</tr>
<tr>
<td>– Cardiac hypertrophy – <strong>adaptive response</strong></td>
</tr>
<tr>
<td>increase in collagen content</td>
</tr>
<tr>
<td>preserves myocardial performance</td>
</tr>
<tr>
<td>– Cumulative loss of myofibrils and cardiac myocytes</td>
</tr>
<tr>
<td><strong>apoptosis, cellular necrosis decrease in the wall thickness</strong></td>
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</tbody>
</table>
• Extracellular matrix remodeling
  – Cardiac fibroblast proliferate
  – Mechanically stable cross linked collagen is degraded by metalloproteinases
  – Excess of poorly cross-linked collagen is deposited into interstitium
  – Increase myocardial mass, interstitial fibrosis, ventricular dilatation
MOLECULAR DEFECTS IN DILATED CARDIOMYOPATHY

GENES
- Lamin A/C
- δ-sarcoglycan
- Dystrophin
- Desmin
- Vinculin
- Titin
- Troponin-T
- α-tropomyosin
- β-myosin heavy chain
- Actin
- Mitochondrial DNA mutations

Fatkin D, et al. NEJM 1999;341
Clinical features

- Highest incidence in middle age
- Symptoms may be gradual in onset
- Acute presentation
  - Misdiagnosed as viral URTI in young adults
- Symptoms/Signs of heart failure
  - Pulmonary congestion (left heart failure) dyspnea (rest, exertional, nocturnal), orthopnea
  - Systemic congestion (right heart failure) edema, nausea, abdominal pain, nocturia
  - Low cardiac output
  - Hypotension, tachycardia, tachypnea
  - Fatigue and weakness
- Arrhythmia
  - Atrial fibrillation, conduction delays, sudden death
## Incidence of symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Incidence</th>
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<tbody>
<tr>
<td>Heart failure symptoms</td>
<td>75% - 85%</td>
</tr>
<tr>
<td>Anginal chest pain</td>
<td>8% - 20%</td>
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<tr>
<td>Emboli (systemic or pulmonary)</td>
<td>1% - 4%</td>
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<tr>
<td>Syncope</td>
<td>&lt;1%</td>
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<tr>
<td>Sudden cardiac death</td>
<td>&lt;1%</td>
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</table>
• Prevalence is 36 per 100,000 population
• Third most common cause of heart failure
• Most frequent cause of heart transplantation
• Complete recovery is rare
• 50% die within 2 yrs and 25% survive longer than 5 yrs
ECG

- Sinus tachycardia in presence of heart failure.
- Atrial and ventricular tachyarrhythmias
- Poor r wave progression
- Anterior q waves
- Intaventricular conduction defects –mostly LBBB
- Left atrial abnormality
- Hypertensive changes by voltage criteria not evident
Echocardiography

- Dilated chambers
- Left atrium is usually enlarged
- Left ventricle is enlarged. Normal 3.8—5.0cm
- Mitral and tricuspid regurgitation on doppler flow.
- Stress testing -- tachyarrhythmias
- Dobutamine stress echo helpful in assessing the clinical prognosis.
<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>INDICATIONS</th>
</tr>
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<tbody>
<tr>
<td>ACE Inhibitors</td>
<td>Symptomatic heart failure and asymptomatic LV dysfunction</td>
</tr>
<tr>
<td>ARBs</td>
<td>ACE intolerance</td>
</tr>
<tr>
<td>Hydralazine - nitrates</td>
<td>Volume overload</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Diuretic-induced depletion</td>
</tr>
<tr>
<td>Potassium/Magnesium</td>
<td>Symptomatic heart failure in addition to ACE inhibitor</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Persistent heart failure despite diuretics, ACE inhibitor</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Chronic or paroxysmal atrial fibrillation LV thrombus or prior embolic event</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Cardiac arrest; uncontrolled VT</td>
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<tr>
<td>ICD</td>
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Peripartum cardiomyopathy

• definition --- four criteria: three clinical and one echocardiographic –

1. Development of heart failure during last trimester of pregnancy or first six months post partum.

2. Absence of any identifiable cause for cardiac failure.

3. Absence of any recognizable heart disease prior to last trimester of pregnancy.

4. Echocardiographic criteria- Demonstrable echocardiographic proof of left ventricular systolic dysfunction. Ejection fraction less than 45%, left ventricular fractional shortening less than 30% or left ventricular end-diastolic dimension >2.7cm/m square of body surface area.
Hypertrophic cardiomyopathy

This is the most common form of cardiomyopathy, with a prevalence of approximately 100 per 100,000. It is characterized by inappropriate and elaborate left ventricular hypertrophy with mal-alignment of the myocardial fibres and myocardial fibrosis caused by mutation of genes encoding sarcomeric proteins. The hypertrophy may be generalized or confined largely to the interventricular septum or other regions.
### Pathogenesis

- Autosomal dominant with variable penetrance.
- Remaining are sporadic.
- Mutations are mostly missense.
- Mutations causing HCM found in genes encoding β MHC, cardiac TnT, α tropomyosin, myosin binding protein C.
The major abnormality of the heart in HCM -- excessive thickening of the muscle. Thickening usually begins during early adolescence and stops when growth has finished. Uncommon for thickening to progress after this age.

- Left ventricle almost always affected

- Hypertrophy is usually greatest in the septum, associated with obstruction to the flow of blood into the aorta.
• Asymmetric septal hypertrophy with obstruction to the outflow of blood from the heart may occur. The mitral valve touches the septum, blocking the outflow tract. Some blood is leaking back through the mitral valve causing mitral regurgitation.
• Extensive myocyte hypertrophy

• Myofiber disarray

• Interstitial and replacement fibrosis
Pathophysiology

- Impaired diastolic filling-----reduced stroke volume
- Reduced CO and increase in pulmonary venous pressure---exertional dyspneoa
- Diastolic dysfunction
  - Impaired diastolic filling, ↑ filling pressure
- Myocardial ischemia
- Mitral regurgitation
- Arrhythmias
Clinical features

• Asymptomatic
  – Echocardiographic finding only

• Symptomatic
  – Dyspnea in 90%
  – Harsh systolic ejection murmur
  – Angina pectoris in 75%
  – Fatigue, pre-syncope, syncope, ↑ risk of SCD
  – Palpitation, paroxysmal nocturnal dyspnea, CHF, dizziness
  – Atrial fibrillation, thromboembolism
## Physical Findings

<table>
<thead>
<tr>
<th>With outflow obstruction Arterial pulses</th>
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<tbody>
<tr>
<td>Rapid rise - with bisferiens contour Double or triple apical impulses may be palpable</td>
</tr>
<tr>
<td>– Outward systolic thrust - ventricular contraction</td>
</tr>
<tr>
<td>– Presystolic accentuated atrial contraction</td>
</tr>
<tr>
<td>Medium-pitch ESM at the lower left sternal border and apex</td>
</tr>
<tr>
<td>&gt;30 mm Hg</td>
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<table>
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<tr>
<th>Without subaortic gradients Subtle -</th>
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<tbody>
<tr>
<td>with no or soft systolic murmur Forceful apical impulse</td>
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ECG

Abnormal - >90% of pts & >75% of asymptomatic relatives
- Increased voltages consistent with LV hypertrophy
- ST-T changes - marked T wave inversion in the lateral precordial leads
- Left atrial enlargement
- Deep and narrow Q waves
- Diminished R waves in the lateral precordial leads.

Normal ECG - 5% of pts
- Less severe phenotype and favorable course
- Not predictive of future sudden death

Increased voltages
- Weakly correlated with the magnitude of LV hypertrophy
- Do not distinguish the obstructive and nonobstructive forms
Holter

- Supraventricular tachycardia (46 percent)
- Premature ventricular contractions (43 percent)
- Nonsustained ventricular tachycardia (26 percent)
- Atrial fibrillation (25 to 30 percent)
- Preexcitation has also been associated with HCM
Serum C-terminal propeptide of type I procollagen (PICP)

Elevated levels PICP indicated increased myocardial collagen synthesis in sarcomere-mutation carriers without overt disease.

Profibrotic state preceded left ventricular hypertrophy or fibrosis visible on MRI.
ECHOCARDIOGRAPHY

- Diffuse hypertrophy of the ventricular septum and anterolateral free wall (70% to 75%)
- Basal septal hypertrophy (10% to 15%)
- Concentric hypertrophy (5%)
- Apical hypertrophy (<5%)
- Hypertrophy of the lateral wall (1% to 2%)
- Mitral annulus velocity, Ea - status of myocardial relaxation - reduced in most patients with HCM
Mimicking Hypertrophic Cardiomyopathy

- Chronic hypertension
- RV hypertrophy
- Cardiac amyloidosis
- Athlete's heart
- Phaeochromocytoma
- Long-term haemodialysis
- Fabry disease
- Friedreich ataxia.

Apical hypertrophy - apical cavity obliteration caused by hypereosinophilic syndrome or noncompaction.
## Athlete's Heart Vs Hypertrophic Cardiomyopathy

<table>
<thead>
<tr>
<th><strong>HCM</strong></th>
<th><strong>Athletic heart</strong></th>
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<tbody>
<tr>
<td>• Can be asymmetric</td>
<td>• Concentric &amp; regresses</td>
</tr>
<tr>
<td>• Wall thickness: &gt; 15 mm</td>
<td>• &lt; 15 mm</td>
</tr>
<tr>
<td>• LA: &gt; 40 mm</td>
<td>• &lt; 40 mm</td>
</tr>
<tr>
<td>• LVEDD: &lt; 45 mm</td>
<td>• &gt; 45 mm</td>
</tr>
<tr>
<td>• Diastolic function: always abnormal</td>
<td>• Normal</td>
</tr>
</tbody>
</table>
CMR (Cardiovascular magnetic resonance imaging)

- More accurate than echo
- Can detect 6% more hypertrophy
- Accurate measurement of thickness
- Should be done in
  -- Poor echo window
  -- Discrepancy between Clinical findings / ECG / Echo
Increased LV mass index – not sensitive – 20% HCM normal

Better differentiation between physiological & pathological LVH

- End-diastolic wall thickness–to–cavity volume ratio < 0.15 mm/mL/m²

- Lack of LGE(late gadolinium enhancement) of the ventricular myocardium
CMR - Poor Prognostic factors

• Markedly elevated LV mass index (men > 91 g/m²; women > 69 g/m²) was sensitive (100%)
• Maximal wall thickness of more than 30 mm was specific (91%) for cardiac deaths
• Right ventricular (RV) hypertrophy
• Myocardial edema by T2-weighted imaging
• LGE (Late gadolinium enhancement) has been associated with
  – Ventricular arrhythmias
  – Progressive ventricular dilation
MANAGEMENT
General guidelines

- Screening all first-degree relatives is recommended
- Echocardiography
- Children & participating in competitive athletics Every 12 to 18 months
- Adults no competitive athletics - every 5 years
- Counseled against engaging in competitive athletics
- Maintain hydration
Sudden Death & Risk stratification

- Primary ventricular tachycardia and ventricular fibrillation
- Adolescents and young adults <30 to 35 years of age
- Most common cause of Athletic field deaths
- Death most commonly occur at rest
High Risk

Primary prevention
one or more of the following
1. Family history of one or more premature HCM-related deaths, particularly if sudden and multiple
2. Unexplained syncope, especially if recent and in the young
3. Hypotensive or attenuated blood pressure response to exercise
4. Multiple, repetitive (or prolonged) NSVT on Holter
5. Massive LVH (wall thickness, $\geq 30$ mm), particularly in young patients

Secondary prevention
1. Prior cardiac arrest
2. Sustained ventricular tachycardia
Potential arbitrators

- When level of risk judged - ambiguous on the basis of conventional markers

1. CMR - delayed enhancement
2. Thin-walled akinetic LV apical aneurysms
3. End-stage phase
4. Percutaneous alcohol septal ablation

- Very limited prognostic significance can be attributed to specific HCM-causing mutations
### Prevention of SCD

- ICD implantation – as primary prevention following cardiac arrest.
  - as secondary prevention if one or more high risk factors.

- Empirical pharmacological therapy with amiodarone is now obsolete.
Medical Treatment

- Empirical & highly variable
  - **Beta blockers**
  - Slowing heart rate
  - Reducing force of LV contraction
  - Augmenting ventricular filling and relaxation
  - Decreasing myocardial oxygen consumption
  - Long-acting preparations - propranolol, atenolol, metoprolol or nadolol
  - Blunt LV outflow gradient triggered by physiologic exercise.
  - Target resting heart rate - 60 beats/min
  - May require up to 400 mg equivalent of metoprolol
Verapamil

- Improves symptoms and exercise capacity (patients without marked obstruction to LV outflow)
- Beneficial effect on ventricular relaxation and filling
- Better angina control than beta blocker
- Hemodynamic deterioration with CCB agents - lowering of the afterload in the presence of severe outflow tract gradients and high diastolic filling pressures
**Disopyramide** *(sodium channel blocker)*

Negative inotropic effect decreases the gradient and improve symptoms.

Concomitant beta blockade may be important to prevent rapid atrioventricular node conduction.

Between 300 and 600 mg/d

The corrected QT interval must be monitored.

Anticholinergic side effects in older patients

Diuretic agents may be judiciously administered.

Either beta blockers or verapamil initially.

No advantage by combinations of BB & CCB.

Disopyramide may be combined with BB or CCB.
<table>
<thead>
<tr>
<th>Agent</th>
<th>Mechanisms of Action</th>
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<tr>
<td>Perhexiline</td>
<td>CPT₁/CPT₂ inhibition</td>
</tr>
<tr>
<td></td>
<td>NAD(P)H oxidase inhibition</td>
</tr>
<tr>
<td></td>
<td>NO potentiation</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>CPT₁ inhibition</td>
</tr>
<tr>
<td></td>
<td>β-Adrenoceptor blockade</td>
</tr>
<tr>
<td>Trimetazidine</td>
<td>PFOX inhibition</td>
</tr>
<tr>
<td></td>
<td>? CPT₁ inhibition</td>
</tr>
<tr>
<td>Ranolazine</td>
<td>PFOX inhibition</td>
</tr>
<tr>
<td></td>
<td>? Late Na⁺ current inhibition</td>
</tr>
<tr>
<td>Metformin</td>
<td>AMPK stimulation</td>
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</table>
Surgical myectomy

1. Drug-refractory heart failure symptoms
2. NYHA Classes III (Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea) & IV (Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases).
3. LV outflow obstruction
   - Rest - gradient ≥ 30 mm Hg
   - Physiologic exercise - gradient ≥ 50 mm Hg

Transaortic resection of muscle from the proximal to midseptal region. Operative mortality <1 percent

Maintain long-lasting improvement in symptoms and exercise capacity Mortality may be improved after septal myectomy
• Objective measurements of exercise capacity did not differ significantly.
• Overall decrease in outflow tract gradient (25 to 40 percent of baseline)
• Role of dual-chamber pacing - patients at high risk for other therapeutic modalities.
• Candidates for dual-chamber pacing
  – Significant bradycardia in which pacing may allow an increased dosage of medication
  – Patients who need ICD as a primary treatment
Alcohol Septal Ablation

- Outflow tract gradient is reduced from a mean of 60 to 70 mm of mercury often to <20 mm of mercury
- 80–85 % symptomatic improvement
- Complications
  - complete heart block < 10 %
  - coronary dissections
  - large myocardial infarctions
  - ventricular septal defects
  - myocardial perforations
  - ventricular fibrillation
In this rare condition, ventricular filling is impaired because the ventricles are ‘stiff’.
This leads to high atrial pressures with atrial hypertrophy, dilatation and later, atrial fibrillation.
## CAUSES

### Myocardial
- Idiopathic cardiomyopathy *
- Familial cardiomyopathy
- Scleroderma
- Pseudoxanthoma elasticum
- Diabetic cardiomyopathy
- Infiltrative
- Amyloidosis *
- Sarcoidosis *
- Gaucher’s disease
- Mucopolysaccharidoses
- Fatty infiltration
- Storage diseases
- Fabry’s disease
- Iron overload cardiomyopathy

### Endomyocardial
- Endomyocardial fibrosis * Radiation *
- Cardiotoxicity of anthracyclines *
- Hypereosinophilic syndrome
- Carcinoid heart disease Metastatic cancers
- Drugs causing fibrous endocarditis (serotonin, methysergide, ergotamine, mercurial agents, busulfan)

* the most common conditions.
Morphology

- Ventricles are of normal size
- Cavities are not dilated
- Myocardium is firm and non compliant
- Bialtrial dilatation is common
- Patchy/diffuse interstitial fibrosis
Clinical manifestations

- Symptoms of right and left heart failure

- Echo-Doppler
  - Abnormal mitral inflow pattern
  - Prominent E wave (rapid diastolic filling)
    - Almost invariably progresses to congestive heart failure, 10% survive for 10 yrs
• Cardiac enlargement without ventricular dilatation
• Ventricular walls are thickened and rubbery
• Amyloid deposition is most prominent in interstitial, perivascular and endocardial regions.
Arrhythmogenic right ventricular cardiomyopathy

- Inherited disease of cardiac muscle
- RVF, rhythm disturbances, ventricular tachycardia, fibrillation
- Rt ventricular wall is thinned, extensive fatty infiltration and fibrosis
- Autosomal dominant inheritance
Takotsubo
~ Stress Cardiomyopathy
• Also called “transient apical ballooning” and stress cardiomyopathy.
• It is a reversible cardiomyopathy featuring symptoms and signs of acute myocardial infarction without demonstrable coronary artery stenosis or spasm, in which the heart takes on the appearance of a Japanese octopus fishing pot called a ‘takot-subo’.
Takatsubo = Octopus trap
Comparison
• It is characterized by transient systolic ventricular dysfunction with regional wall motion abnormalities beyond a single vascular territory and in the absence of significant epicardial coronary artery obstruction.

• Often, there is an acute emotional or physical stress or immediately preceding the presentation. Classical apical ballooning is seen on ventriculography or echo.
• Catecholamine excess and cardiotoxicity is the most compelling putative mechanism.
• The long-term prognosis is excellent but serious complications including cardiogenic shock and arrhythmias may occur acutely.
• Supportive treatment is the mainstay of therapy.
Clinical presentation

- The clinical presentation of TTC is often identical to acute myocardial infarction (AMI).
- Most patients with TTC present with typical anginal chest pain, dyspnea, ischemic changes on electrocardiogram (ECG), and elevated cardiac markers, whereas syncope and out-of-hospital cardiac arrest are rare.
- Emotional stress, such as news of the death of a family member, divorce, or public speaking, is implicated as the trigger in approximately two-thirds of patients.
A few concepts about the pathophysiology of TTC

1) Multivessel coronary artery spasm
2) ACS with reperfusion injury
3) Impaired cardiac microvascular function
4) Impaired myocardial fatty acid metabolism
5) Endogenous catecholamine-induced myocardial stunning and microinfarction
ECG AND CARDIAC BIOMARKERS

• The most common abnormality on the ECG is ST elevation and T-wave inversion in the precordial leads, resembling acute AMI.

• Several ECG criteria have been proposed to differentiate TTC from acute myocardial infarction.

• The absence of q waves, reciprocal changes, ST segment elevation in V1 with sum of ST elevation in V4-6 greater than that in V1-V3 as well as ST depressions in a VR have been shown to discriminate between the two diseases with high sensitivity and specificity.
• More extensive ST elevation in inferior leads were seen more frequently in TTC compared with AMI.

• Evolutionary changes on ECG often occur two to three days after initial symptoms and presentation, with resolution of ST elevation, followed by diffuse and deep T-wave inversion, prolongation of QT interval.

• Pathologic q waves may be observed initially but rarely persist.

• T-wave inversion and QT-prolongation may persist for three to four months.
• Modest elevation of cardiac biomarkers is often observed in TTC.

• But the cardiac troponin levels in TTC are much less than that typically observed in acute STEMI and are out of proportions to the extensive wall motion abnormalities and hemodynamic compromise.

• Troponin T levels are typically < 5ng/ml.
• Due to the dramatic clinical presentation and high suspicion for acute MI, most patients undergo emergent coronary angiography.
• Typical findings in TTC are normal epicardial coronaries, mild non-obstructive atherosclerosis, or rarely coexistent coronary artery disease.
• Therefore, **TTC is a diagnosis of exclusion which can only be made after coronary angiography**.
• It should be on the differential diagnosis in any post-menopausal women over 50 years old presenting with chest pain and ischemic ECG changes particularly in the setting of emotional stress.
• Furthermore it should also be considered in critically ill patients with sudden hemodynamic compromise and/or heart failure.
**Ventriculography** reveals apical ballooning, with characteristic sparing of the basal segments and akinesis of the mid and apical left ventricle.

However, variants of this pattern have been described including midventricular ballooning or basal and midventricular akinesis with apical sparing (inverted Takotsubo).

In patients with typical TTC, the wall motion abnormality usually extends beyond the distribution of a single coronary artery.
• **Echocardiography** can detect and measure the degree of LVOT obstruction and associated systolic motion of the anterior mitral valve (SAM) and significant mitral regurgitation.

• LVOT obstruction is reported to occur in 25% patients and can have a major impact on acute management.

• In patients with hemodynamic compromise and shock, inotropes would worsen this situation and B - blockers and pure vasopressor pharmacologic or mechanical support may be needed.

LVOT=Left Ventricular Outflow Tract
• **Cardiac MRI** may reveal the absence of delayed gadolinium hyperenhancement.
• This is specific to TTC and can help differentiate it from myocarditis and acute myocardial infarction in which delayed hyperenhancement is present.
• Takotsubo cardiomyopathy has an excellent prognosis, with full and early recovery in virtually all patients.
• The majority of patients have normalization of LVEF within a week and all patients by 4-8 weeks.
• In-hospital mortality is low (0-8%) ; it may be increased in those with underlying conditions.
• Long-term survival is similar to the general population.
• Although TTC has a favorable prognosis, several acute complications should be anticipated.
1) Congestive heart failure is documented in 3-46%.
2) Hypotension and shock are rare in 4%.
3) Systemic thromboembolism is reported in 5%.
4) LVOT obstruction has been seen in 20-25% of patients, but symptomatic obstruction is uncommon.
5) Arrhythmias, including atrial fibrillation, are presents in 10-26% of cases, but fatal arrhythmias such as ventricular fibrillation are rare.

LVOT=Left Ventricular Outflow Tract
Takotsubo cardiomyopathy is a temporary condition and hence the goals of treatment are usually conservative, supportive care.

The therapy is guided by the patient’s clinical presentation and hemodynamic status.

Despite the supposed causative role of catecholamines in the disorder, patients who present in cardiogenic shock, and in the absence of LVOT obstruction, may be treated with inotropes.
• Alternatively patients may derive further benefit from mechanical hemodynamic support with intra-aortic balloon pump or rarely, left ventricular assist devices.

• If LVOT obstruction is present with cardiogenic shock, inotropes should be avoided and phenylphrine is the pressor agent of choice often combined with betablockade.
• Most experts advocate guideline-directed medical therapy for patients with left ventricular dysfunction.

• This includes cardioselective beta-blockers and ACE inhibitor for a short period of time (3-6 months).

• Full anticoagulation is usually reserved for those with documented ventricular thrombus or evidence of embolic events.