Team Medicine

heart failure I

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■ Important notes ■ doctor notes/team notes

Definition:

Heart failure (HF) is a complex clinical syndrome can result from:

- Structural or functional cardiac disorder.
- Impairs the ability of the ventricle to **fill** with or **eject** blood
- Inability of the heart to pump blood at an output sufficient to meet the body's demands.

Heart failure is characterized by: imp

- Signs and symptoms of intravascular and interstitial **volume overload** (congestion) and/or manifestations of **inadequate tissue perfusion**.

Pathophysiology: (Davidson)

Starling's Law: cardiac output is a function of the:

- preload: volume and pressure of blood in the ventricle after diastole
- afterload: the volume and pressure of blood in the ventricle during systole
- cardiac contractility

✗ Fall in cardiac output ➔ activates counter-regulatory neurohormonal mechanisms that maintain cardiac output but if prolonged could lead to deleterious effects.

neurohormonal mechanisms: because of low perfusion of the kidneys

Renin-Angiotensin-Aldosterone Stimulation ➔ vasoconstriction, salt and water retention. Hypotension causes sympathetic nervous system activation ➔ initially maintain cardiac output by increasing cardiac contractility, heart rate and peripheral vasoconstriction.

Prolonged sympathetic activation leads to cardiac myocyte apoptosis, hypertrophy and focal myocardial necrosis.

✗ Further fall in cardiac output could intensify neurohormonal stimulation and thus initiates a vicious cycle and increase in peripheral vascular resistance.

Common Causes of HF:

- Coronary artery disease - most common
- Hypertension - uncontrolled hypertension
- Valvular heart disease
- Dilated cardiomyopathy
- Cor-pulmonale

Heart failure may result from an acute insult to cardiac function, such as a large myocardial infarction, valvular disease, myocarditis, and cardiogenic shock.
More commonly, from a chronic process

- Dilated Cardiomyopathy "heart muscle diseases of unknown cause": Diseases of the myocardium associated with cardiac dysfunction. dr called it (dilated cardiomyopathy)

Classification:

- **Dilated cardiomyopathy (DCM)**
- **Hypertrophic cardiomyopathy (HCM)**
- **Restrictive cardiomyopathy (RCM)**
- Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D)
- Unclassified cardiomyopathies

A: Dilated Cardiomyopathy:

- Dilated cardiomyopathy is characterized by ventricular dilation and impaired contractile performance, which may involve the left or both ventricles
- May develop as a consequence of prior myocarditis or as a result of a recognized toxin, infection, predisposing cardiovascular disease (e.g., hypertension, ischemic or valvular heart disease
- When no cause or associated disease is identified, dilated cardiomyopathy has been termed idiopathic
- 50 to 60% of such patients have familial disease, and disease-causing mutations currently can be identified in 10 to 20% of such families.
- A trigger with immune-mediated pathogenesis in genetically predisposed individuals
- One third of probands and family members develop low-titer, organ-specific autoantibodies to cardiac α-myosin
- Viral persistence has also been implicated as an ongoing trigger of immune-mediated damage

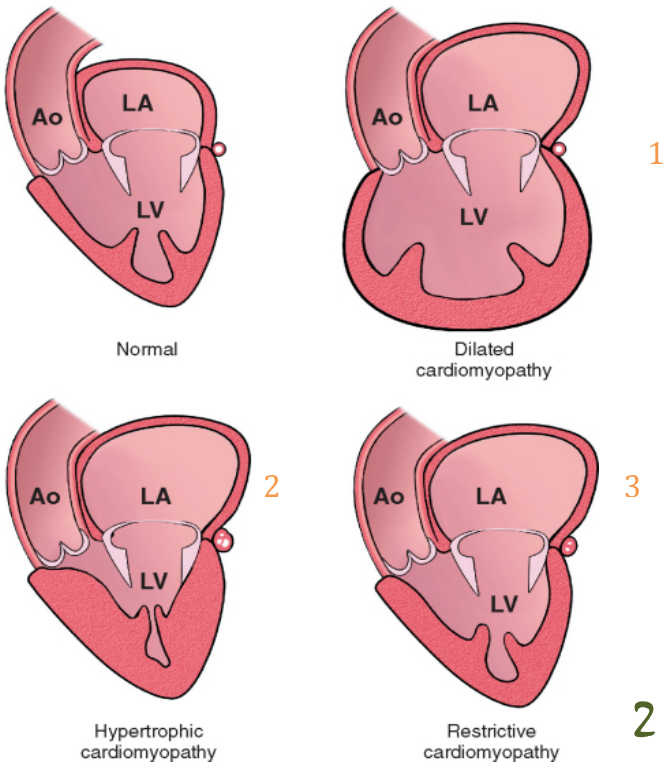
Clinical Manifestations of DCM:

- Gradual decrease in exercise capacity may be appreciated only in retrospect.
- The initial presentation is often with acute decompensation triggered by an unrelated problem, such as anemia, thyrotoxicosis, or infection

✗ Restrictive cardiomyopathy usually shows up on echo as a "mickey mouse" appearance.

[1] Atrium is dilated because of pressure of not being able to pump the blood. Dysfunction of systole

[2, 3] Atria are dilated because of back pressure of ventricles. Dysfunction of diastole



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Alcoholic Cardiomyopathy:

- Alcohol and its metabolite, acetaldehyde, are cardiotoxins acutely and chronically.
- Myocardial depression is initially reversible but, if sustained, can lead to irreversible vacuolization, mitochondrial abnormalities, and fibrosis
- The amount of alcohol necessary to produce symptomatic cardiomyopathy in susceptible individuals is not known
- Abstinence (restraining from consuming alcohol) leads to improvement in at least 50% of patients with severe symptoms, some of whom normalize their left ventricular ejection fractions

Chemotherapy:

- Doxorubicin (Adriamycin) cardiotoxicity causes characteristic histologic changes on endomyocardial biopsy, with overt heart failure in 5 to 10% of patients who receive doses greater than or equal to 450 mg/m2 of body surface area
- Cyclophosphamide and ifosfamide can cause acute severe heart failure and malignant ventricular arrhythmias
- 5-Fluorouracil can cause coronary artery spasm and depressed left ventricular contractility.
- Trastuzumab has been associated with an increased incidence of heart failure

Metabolic Causes:

- Excess catecholamines, as in pheochromocytoma increase sympathetic
- Cocaine increases synaptic concentrations of catecholamines by inhibiting reuptake at nerve terminals; the result may be an acute coronary syndrome or chronic cardiomyopathy.
- Thiamine (vit B1) deficiency can cause beriberi heart disease, with vasodilation and high cardiac output followed by low output.
- Calcium deficiency resulting from hypoparathyroidism, gastrointestinal abnormalities, or chelation directly compromises myocardial contractility.
- Hypophosphatemia which may occur in alcoholism, during recovery from malnutrition, and in hyperalimentation, also reduces myocardial contractility.
- Patients with magnesium depletion owing to impaired absorption or increased renal excretion also may present with left ventricular dysfunction.

Skeletal Myopathies

- Duchenne's muscular dystrophy and Becker's X-linked skeletal muscle dystrophy typically include cardiac dysfunction
- Maternally transmitted mitochondrial myopathies such as Kearns-Sayre syndrome frequently cause cardiac myopathic changes

Peripartum Cardiomyopathy:

- Peripartum cardiomyopathy appears in the last month of pregnancy or in the first 5 months after delivery in the **absence of preexisting cardiac disease**
- Lymphocytic myocarditis, found in 30 to 50% of biopsy specimens, suggests an immune component
- The prognosis is improvement to normal or near-normal ejection fraction during the next 6 months in more than 50% of patients.

✗ The most specific signs of HF are: Paroxysmal nocturnal dyspnea, orthopnea and elevated JVP.

✗ How to measure JVP
https://www.youtube.com/watch?v=8m86ElKLkDM
Common misconception in measuring JVP: the column of blood is measured from the sternal angle, **not from the clavicle.**

Modified Framingham clinical criteria for the diagnosis of heart failure

Major
Paroxysmal nocturnal dyspnea
Orthopnea
Elevated jugular venous pressure
Pulmonary rales
Third heart sound
Cardiomegaly on chest x-ray
Pulmonary edema on chest x-ray
Weight loss ≥4.5 kg in five days in response to treatment of presumed heart failure
Minor
Bilateral leg edema
Nocturnal cough
Dyspnea on ordinary exertion
Hepatomegaly
Pleural effusion
Tachycardia (heart rate ≥120 beats/min)
Weight loss ≥4.5 kg in five days
Diagnosis
The diagnosis of heart failure requires that **2 major or 1 major and 2 minor criteria** cannot be attributed to another medical condition.

From Senni, M, Tribouilloy, CM, Rodeheffer, RJ, et al, Circulation 1998; 98:2282; adapted from McKee, PA, Castelli, WP, McNamara, PM, Kannel, WB. N Engl J Med 1971; 85:1441.

UpToDate

B: Hypertrophic Cardiomyopathy:

- Genetically determined myocardial disease
- Defined clinically by the presence of unexplained left ventricular hypertrophy
- Pathologically by the presence of myocyte disarray surrounding increased areas of loose connective tissue
- Usually familial, with **autosomal dominant inheritance**. Screen family of the patient.
- Abnormalities in sarcomeric contractile protein genes account for approximately 50 to 60% of cases

Pathology of HCM:

- Typically, heart weight is increased and the interventricular septum is hypertrophic
- Any pattern of thickening may occur
- Histologically, the hallmark of hypertrophic cardiomyopathy is myocyte disarray.
- Clinical expression of left ventricular hypertrophy usually occurs during periods of **rapid somatic growth**,
- May be during the first year of life or childhood but more typically during adolescence and, occasionally, in the early 20s
- Most patients are asymptomatic or have only mild or intermittent symptoms.
- Symptomatic progression is usually slow, age related, and associated with a gradual deterioration in left ventricular function over decades
- Symptoms may develop at any age, even many years after the appearance of LVH
- Occasionally, sudden death may be the initial presentation.

Diagnosis of HCM:

- The initial diagnostic evaluation includes a family history focusing on premature cardiac disease or death
- Differentials: Causes of left ventricular hypertrophy:
  - Long-standing systemic hypertension
  - Aortic stenosis
  - Highly trained athletes

Gene	Protein	Frequency
MYH7	β-Myosin heavy chain	25–35%
MYBPC3	Cardiac myosin binding protein C	20–30%
TNNT2	Cardiac troponin T	3–5%
TNNI3	Cardiac troponin I	<5%
TPM1	α-Tropomyosin	<5%
MYL2	Regulatory myosin light chain	<5%
MYL3	Essential myosin light chain	Rare
ACTC	α-Cardiac actin	Rare
TTN	Titin	Rare
TNNC1	Cardiac troponin C	Rare
MYH6	α-Myosin heavy chain	Single study
CRP3	Muscle LIM protein	Rare

< Most common gene mutation of HCM

C: Restrictive Cardiomyopathy:

- Characterized by impaired filling and reduced diastolic volume of the left and/or right ventricle despite normal or near-normal systolic function and wall thickness
- Primary forms are uncommon,
- Secondary forms, the heart is affected as part of a multisystem disorder,
- Usually present at the advanced stage of an infiltrative disease (e.g., **amyloidosis** or sarcoidosis) or a systemic storage disease (e.g., hemochromatosis).
- Restrictive cardiomyopathy may be familial
- Part of the genetic and phenotypic expression of hypertrophic cardiomyopathy caused by sarcomeric contractile protein gene abnormalities
- Secondary forms: amyloidosis, hemochromatosis, several of the glycogen storage diseases, and Fabry's disease
- Reported in association with skeletal myopathy and conduction system disease as part of the phenotypic spectrum caused by mutations in lamin A or C.

Causes of RCM:

- **INFILTRATIVE DISORDERS:** Amyloidosis - Sarcoidosis
- **STORAGE DISORDERS:** Hemochromatosis - Fabry's disease - Glycogen storage diseases
- **FIBROTIC DISORDERS:** Radiation – Scleroderma - Drugs (e.g., doxorubicin, serotonin, ergotamine)
- **METABOLIC DISORDERS:** Carnitine deficiency - Defects in fatty acid metabolism
- **ENDOMYOCARDIAL DISORDERS:** Endomyocardial fibrosis - Hypereosinophilic syndrome (Lofler's endocarditis)
- **MISCELLANEOUS CAUSES:** Carcinoid syndrome

Pathophysiology of RCM:

- Increased stiffness of the endocardium or myocardium, induces ventricular pressures to rise disproportionately to small changes in volume until a maximum is reached.

Summary:

- Heart failure is a constellation of signs and symptoms in the clinical presentation of the patient.
- Two main features characterize heart failure: congestion and low perfusion
- Coronary artery disease is the most common cause of HF
- Dilated cardiomyopathy is known to be idiopathic but theories suggest autoimmunity.
- Hypertrophic cardiomyopathy has the most familial connection among cardiomyopathies and is easily diagnosed pathologically by detecting myocyte disarrays
- HCM usually occurs during periods of rapid somatic growth
- Restrictive cardiomyopathy usually comes secondary to an advanced stage of an infiltrative disease (amyloidosis)

Questions:

1. Heart failure with preserved systolic function is characteristic of
   A. Hypertensive heart disease
   B. Ischemic heart disease
   C. Hypertrophic cardiomyopathy
   D. Restrictive cardiomyopathy
   E. Dilated cardiomyopathy

2. Dilated cardiomyopathy is
   A. Usually idiopathic
   B. Associated with pathognomonic ECG changes
   C. A recognized complication of HIV infection
   D. Associated with chronic alcohol misuse
   E. Caused by Coxsackie A infection

3. Regarding restrictive cardiomyopathies:
   A. Amyloidosis mainly affects the right heart
   B. Diastolic function is usually normal
   C. Never appears in the elderly
   D. In cardiac amyloidosis the ECG usually shows ventricular hypertrophy
   E. Can be associated with high eosinophilic count

4. The following are classified as high-output states: (true-false)
   A. Hypertension
   B. Sepsis
   C. Hypothyroidism
   D. Pregnancy
   E. Arteriovenous malformations

Answer Key:
1- B E
2- A C D E
3- E
4- B D E