CARDIOMYOPATHIES

Cardiac pathology Lecture 8

By

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CARDIOMYOPATHIES

- Are group of diseases that are caused by intrinsic myocardial dysfunction (heart muscle disease).
- They include:
  - Inflammatory disorders (*myocarditis*)
  - Immunologic diseases (e.g., sarcoidosis)
  - Systemic metabolic disorders (e.g., hemochromatosis).
  - Muscular dystrophies.
  - Genetic disorders of cardiac muscle cells.

- **They are divided into two major groups:**

1. ***Primary*** includes those entities in which the disease is solely or predominantly confined to the heart muscle
2. ***Secondary*** in which heart is involved as a part of a generalized multi-organ disorder.

➢ Within each of these two groups, some diseases are genetic, others are acquired, and many are idiopathic.

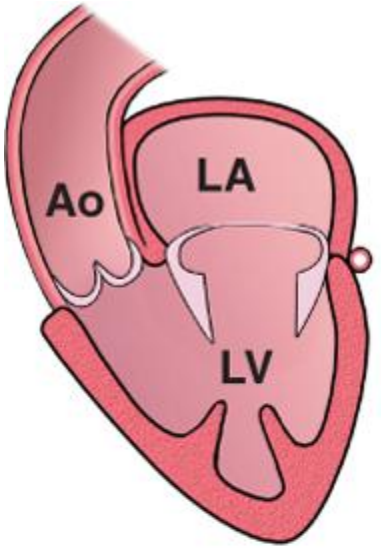
- A more clinical and functional classification divides cardiomyopathies into three groups

1. **Dilated cardiomyopathy**
2. **Hypertrophic cardiomyopathy**
3. **Restrictive cardiomyopathy**

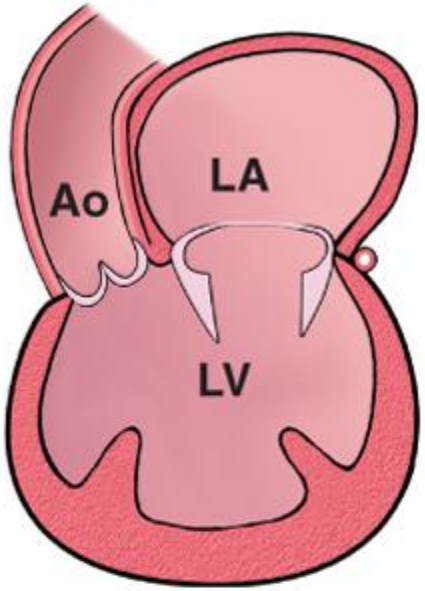
Cardiomyopathy and Indirect Myocardial Dysfunction: Functional Patterns and Causes

Functional Pattern	Left Ventricular Ejection Fraction*	Mechanisms of Heart Failure	Causes	Indirect Myocardial Dysfunction (Not Cardiomyopathy)
Dilated	<40%	Impairment of contractility (systolic dysfunction)	Idiopathic; alcohol; peripartum; genetic; myocarditis; chronic anemia; doxorubicin (Adriamycin)	Ischemic heart disease; valvular heart disease; hypertensive heart disease; congenital heart disease
Hypertrophic	50% to 80%	Impairment of compliance (diastolic dysfunction)	Genetic; Friedreich ataxia; storage diseases; infants of diabetic mothers	Hypertensive heart disease; aortic stenosis
Restrictive	45% to 90%	Impairment of compliance (diastolic dysfunction)	Idiopathic; amyloidosis; hemochromatosis; sarcoidosis; radiation-induced fibrosis	Pericardial constriction

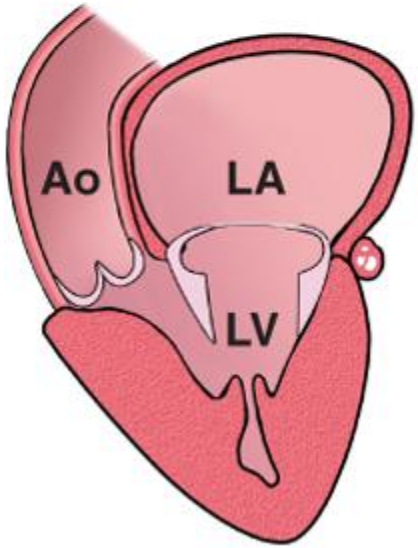
- **Dilated cardiomyopathy** It is most common (90% of cases), and **restrictive cardiomyopathy** is the least frequent.



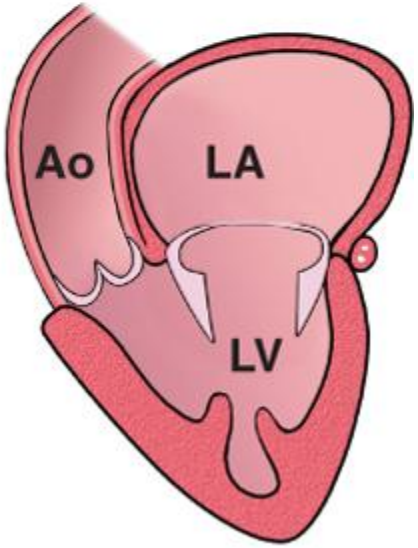
Normal



Dilated cardiomyopathy



Hypertrophic cardiomyopathy



Restrictive cardiomyopathy

- **Dilated Cardiomyopathy**
- It is characterized by progressive cardiac **dilation** and *contractile (**systolic**) dysfunction,* usually with concurrent **hypertrophy**.
- It is sometimes called **congestive cardiomyopathy**.

❑Approximately 25% to 35% of DCM cases have a familial (genetic) basis.

- Others result from a variety of acquired myocardial insults including
  - **Toxic exposures (e.g., chronic alcoholism), myocarditis, and**
  - **Pregnancy-associated changes.**
- In some patients, the cause of DCM is unknown. Such cases are appropriately called ***idiopathic dilated cardiomyopathy.***
- Regardless of the cause, all share a similar **clinicopathologic picture**.

- **<u>Pathogenesis</u>**
- The causes of DCM can be grouped into four broad categories:

1. *Viral.* coxsackievirus B
2. *Alcohol or other toxic exposure.* include certain chemotherapeutic agents, particularly doxorubicin (Adriamycin), and cobalt.

3. *Genetic influences.*

- Familial forms of DCM account for 25% to 35% of cases; autosomal dominant inheritance is the predominant pattern; X-linked, autosomal recessive, and mitochondrial inheritances are less common.

4. *Peripartum cardiomyopathy* occurs late in gestation or several weeks to months postpartum.

- The etiology is multifactorial, including pregnancy-associated **hypertension**, **volume overload**, **nutritional deficiency**, **metabolic derangement, immunologic response** (e.g., abnormal cytokine production).
- Approximately half of these patients spontaneously recover normal function.

- **Clinical Features**
- DCM can occur at any age
- it most commonly occurs between ages 20 and 50 years.
- It typically presents with slowly progressing CHF (e.g., shortness of breath and poor exertional capacity).

Hypertrophic Cardiomyopathy

- Hypertrophic cardiomyopathy (HCM) (also known as idiopathic hypertrophic subaortic stenosis) is characterized by *myocardial hypertrophy,* ***abnormal diastolic filling,*** and-in a third of **cases-*ventricular outflow obstruction***.
- **The heart is thick-walled, heavy, and hypercontracting, in striking contrast to the flabby, poorly contractile heart in DCM.**

- Systolic function is usually preserved in HCM, but the myocardium does not relax and therefore shows primary diastolic dysfunction.

- The characteristic histologic features in HCM are **severe myocyte hypertrophy, myocyte (and myofiber) disarray,** and interstitial **fibrosis**.

- **Pathogenesis**
- Almost all cases of HCM are caused by missense point mutations in one of several genes encoding the sarcomeric proteins that form the contractile apparatus of striated muscle.
- In most cases, the pattern of transmission is **autosomal dominant**.

- **Clinical Features**
- *HCM is characterized by a massively hypertrophied left ventricle that paradoxically provides a markedly reduced stroke volume.*
- This pathophysiologic effect is a direct consequence of *impaired diastolic filling* and overall smaller chamber size.
- In addition, roughly 25% of patients have dynamic obstruction to the left ventricular outflow by the anterior leaflet of the mitral valve.

- Reduced cardiac output and a secondary increase in pulmonary venous pressure cause **exertional dyspnea**, and there is a ***harsh systolic ejection murmur***.
- A combination of massive hypertrophy, high left ventricular pressures, and compromised intramural coronary arteries frequently leads to **myocardial ischemia** (with **angina**), even in the absence of concomitant coronary artery disease.
- Major clinical problems include **atrial fibrillation** with mural thrombus formation, **IE** of the mitral valve, **CHF**, **arrhythmias**, and **sudden death**.

Restrictive Cardiomyopathy

- It is characterized by a *primary decrease in ventricular compliance, resulting in impaired ventricular filling during diastole*.
- The contractile (**systolic) function** of the left ventricle is usually unaffected.
- Thus, the functional state can be confused with that of constrictive pericarditis or hypertrophic cardiomyopathy.

- Restrictive cardiomyopathy can be **idiopathic** or associated with systemic diseases that also happen to affect the myocardium-for example:
- **Radiation fibrosis**,
- **Amyloidosis**,
- **Hemochromatosis**, **sarcoidosis**,
- **Inborn errors of metabolism**.

- Morphology
- In idiopathic restrictive cardiomyopathy the ventricles are of approximately normal size or slightly enlarged, the cavities are not dilated, and the **myocardium is firm**.
- Biatrial dilation is commonly observed.
- Microscopically there is **interstitial fibrosis**, varying from **minimal** and patchy to **extensive and diffuse**.

- **Myocarditis**
- In myocarditis there is inflammation of the myocardium with resulting injury.
- *The inflammatory process is the cause of- rather than a response to-myocardial injury.*
- Microscopically, active myocarditis shows an interstitial inflammatory infiltrate, with focal necrosis of myocytes adjacent to the inflammatory cells.

Pathogenesis

- viral infections are the most common cause of myocarditis. Coxsackieviruses A and B and other enteroviruses probably account for most of the cases.
- The protozoan *Trypanosoma cruzi* is the agent of Chagas disease.
- *Toxoplasma gondii*
- *Trichinosis* is the most common helminthic disease with associated cardiac involvement.
- Myocarditis occurs in approximately 5% of patients with Lyme disease
- *Noninfectious causes of myocarditis* include systemic diseases of immune origin, such as lupus erythematosus and polymyositis.
- Drug hypersensitivity reactions *(hypersensitivity myocarditis)*.

- **Clinical Features**
- The clinical spectrum of myocarditis is broad. At one end, the disease is **asymptomatic** and patients recover without sequelae, and at the other end is the precipitous onset of **heart failure** or **arrhythmias**, occasionally with **sudden death**.