Heart I.
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What is the purpose of the cardiovascular system?

- Supply oxygen and nutrients to the tissues and organs, and to remove waste products
- To defend the supply of nutrients to organs by
  - maintaining cardiac output
    - sympathetic, RAAS, endothelin, nitric oxide, fluid retention
    - maintaining organ perfusion pressure

1. Function of a cardiomyocyte

Cardiomyocytes consist of three linked systems:

- excitation system: participates in spread of the action potential into adjacent cells and initiates further intracellular events
- excitation-contraction coupling system: converts the electrical signal to a chemical signal
- contractile system: a molecular motor driven by ATP
Depolarization and/or a β-adrenergic influence → opening of dihydropyridin receptors (DHP) → Ca2+ from the T-tubules → opening of the ryanodin receptors → outflow of Ca2+ from the SR into the myoplasm → triggering of the contraction

Na/Ca antiport extrudes the excessive Ca2+ by the end of a diastole – important role in relaxation

Contractility can be separated from the preceding two terms only with difficulty, the separation has only clinical application

2. Systolic myocardial function
Magnitude of the afterload determines the developed active tension and influences the velocity and extent of shortening

Isometric = isovolumic maxima curve represents a limit (envelope) at the same time on which both isotonic contraction curves and afterloaded contraction curves end. The definitive length of a muscle at the end of the contraction is proportionally dependent on the afterload, but it is independent on the length of a muscle before the contraction, i.e., on a preload

The preload of a ventricle could be defined as an end-diastolic tension in a wall and the afterload as its maximum systolic tension
Laplace’s law for a sphere:

\[ P \times r = \frac{\sigma}{2h} \]

The preload of a myocardium is defined as its end-diastolic tension in its wall and the afterload as its maximum systolic tension.

Working diagramm of the myocardium is situated between the myocardium compliance curve and the end-systolic-pressure-volume-curve (ESPVL, approaching considerably the isovolumic maxima curve).

Sum of the external and internal work represents the total mechanical work of contraction and this is directly proportional to oxygen consumption of the myocardium. Pressure work of the heart consumes more oxygen than volume work, so that the effectivity of the former is lower than that of the latter.

Compensatory mechanisms for decreased cardiac output

- Increased SNS activity
  - Increase HR and SVR which increases BP
- Frank-Starling mechanism:
  - \( \uparrow \text{LVEDP} = \uparrow \text{SV} \)
- Activation of Renin-angiotensinaldosterone system (RAAS)
- Myocardial Remodeling
  - Concentric hypertrophy
  - Eccentric hypertrophy
Volume overload → eccentric hypertrophy
Prolongation of myocytes by serial apposition of sarcomeres → ↑ velocity and extent of shortening with an unchanged tension
Less internal work expended than in pressure overload
Pressure overload → concentric hypertrophy
Thickening of myocytes by parallel apposition of sarcomeres → ↑ tension with an unchanged extent of shortening

Hypertrophy generally:
↓ ratio capillaries/cardiomyocytes → ischemization → ↓ contractility → temporary maintaining od CO → later cardiac failure
→ fibrotization → ↓ compliance
→ ↓ active relaxation
thickening → ↓ compliance = diastolic dysfunction
3. Diastolic myocardial function

Active: ability to exhaust Ca\(^{2+}\) out of sarcoplasm (against affinity of contractile proteins to Ca)

↓

Passive: isovolemic drop of blood tension (pressure)

"Absolute" – thickness of a ventricle

"Relative" – rigidity of the myocardial tissue itself

Myocardial turgor

Amount of connective myocardial tissue

Pericardium

Diastolic ventricle interaction

Normal Cardiac Function

- Cardiac Output = Heart rate x Stroke volume
- Heart rate – controled by SNS and PNS
- Stroke – dependent on preload, afterload and contractility
- Preload = LVEDP and is measured as PCWP
- Afterload = SVR
- Contractility: ability of contractile elements to interact and shorten against a load (+ inotropy - inotropy)

Cardiac Innervation

- **Parasympathetic System**
  - Slow heart rate
  - Reduce cardiac output
- **Sympathetic System**
  - Increase heart rate
  - Increase force of contraction
  - Increase cardiac output

Heart Failure

- A condition that exists when the heart is unable to pump sufficient blood to meet the metabolic needs of the body

Forms of Heart Failure

- **Systolic & Diastolic**
- **High Output Failure**
  - Pregnancy, anemia, thyrotoxisis, A/V fistula, Beriberi, Pagets disease
- **Low Output Failure**
- **Acute**
  - large MI, aortic valve dysfunction---
- **Chronic**

Left vs. Right Heart Failure

**Left Heart Failure**
- pulmonary congestion
- peripheral edema
- sacral edema
- elevated JVP
- ascites
- hepatomegaly
- splenomegaly
- pleural effusion

**Right Heart Failure**
-
Systolic dysfunction

- Impairment of the contraction of the left ventricle such that stroke volume (SV) is reduced for any given end-diastolic volume (EDV)
- Ejection fraction (EF) is reduced (below 40-45%)
- EF=SV/EDV

Diastolic Dysfunction

- Ventricular filling rate and the extent of filling are reduced or a normal extent of filling is associated with an inappropriate rise in ventricular diastolic pressure. Normal EF is maintained.

Systolic vs. Diastolic Dysfunction

Presentation
- Pulmonary edema
- PCWP
- LVEDV

Mechanism
- PCWP
- LVEDV
- EF
- Dilated LV

Diagnosis
- Pulmonary edema
- PCWP
- Normal EF
- Small LV diameter
- LVH (hypertension)

Compensatory Mechanisms in Heart Failure

- increased preload
- increased sympathetic tone
- increased circulating catecholamines
- increased Renin-angiotensin-aldosterone
- increased vasopressin
- increased atrial natriuretic factor
Physiologic Response to Heart Failure

- Renal-Adrenal
- Renin-Angiotensin
- Aldosterone
- Sodium and fluid retention
- Carotid and LA Baroreceptors
- Sympathetic Output
- Tachycardia
- Vasconstriction

Neurohormonal Mechanismus of CHF

- Direct toxic effects of Norepinephrine (NE) and Angiotensin II (AII)
  (Arrhythmias, Apoptosis)
- Impaired diastolic filling
- Increased myocardial energy demand
- Increased pre- and after-load
- Platelet aggregation
- Desensitization to catecholamines

Neurohormonal Mechanism of CHF

- Components
  - Endothelin
  - Vasopressin (ADH)
  - Natriuretic Peptides
  - Endothelium-Derived Relaxing Factor
  - RAAS
  - SNS
  - Cytokines

NYHA Functional Classification

- **Class I:** patients with cardiac disease but no limitation of physical activity
- **Class II:** ordinary activity causes fatigue, palpitations, dyspnea or anginal pain
- **Class III:** less than ordinary activity causes fatigue, palpitations, dyspnea or angina
- **Class IV:** symptoms even at rest

Stages of Heart Failure

- **Stage A:**
  - High risk for development of heart failure
- **Stage B:**
  - Structural heart disease
  - No symptoms of heart failure
- **Stage C:**
  - Symptomatic heart failure
- **Stage D:**
  - End-stage heart failure
Precipitating Causes of Heart Failure

1. ischemia
2. change in diet, drugs or both
3. increased emotional or physical stress
4. cardiac arrhythmias (eg. atrial fib)
5. infection
6. concurrent illness
7. uncontrolled hypertension
8. New high output state (anemia, thyroid)
9. pulmonary embolism
10. Mechanical disruption (sudden MR, VSD, AR)

Heart Failure
Clinical Manifestations

Symptoms
- dyspnea
- fatigue
- exertional limitation
- weight gain
- poor appetite
- cough

Signs
- palpitations, tachypnea
- edema
- jugular venous distension
- pulmonary rales
- pleural effusion
- hepato/ splenomegaly
- ascites
- cardiomegaly
- S3 gallop

Organic consequences of the heart failure
„Forward” and „backward” failure

Cardiogenic Pulmonary Edema

Cardiomyopathies
Classification

- Dilated (congestive)
- Hypertrophic
- Restrictive

Systolic Dysfunction

- Dilated Cardiomyopathy
  - Ischemic disease
    myocardial ischemia
    myocardial infarction
  - Non-ischemic disease
    Primary myocardium muscle dysfunction
    valvular abnormalities
    hypertension
    alcohol and drug-induced
    idiopathic
Cardiomyopathies
Dilated (congestive)
Ejection fraction-- <40%
• Mechanism of failure--
  – Impairment of contractility (systolic dysfunction)
• Causes--
  – Idiopathic, alcohol, peripartum, genetic, myocarditis, hemochromatosis, chronic anemia, doxorubicin, sarcoidosis
• Indirect causes (not considered cardiomyopathies)--
  – Ischemic heart disease, valvular disease, HTN, congenital heart disease

Diastolic Dysfunction

• Hypertrophic Cardiomyopathy
  - Hypertension
  - Myocardial ischemia and infarction
  - Restrictive Cardiomyopathy
    - Amyloidosis
    - Sarcoidosis

Cardiomyopathies
Hypertrophic
• Ejection fraction-- 50-80%
• Mechanism of failure-- impairment of compliance (diastolic dysfunction)
• Causes-- Idiopathic, genetic, Friedreich ataxia, storage dz, DM mother
• Indirect causes-- HTN heart dz, aortic stenosis

Etiology
Familial in ~ 55% of cases with autosomal dominant transmission
Mutations in one of 4 genes encoding proteins of cardiac sarcomere account for majority of familial cases
Remainder are spontaneous mutations

A gross example of IHSS (left) with prominent asymmetric hypertrophy with a prominent septum. The anterior leaflet of the mitral valve is held in the clamp; you can imagine how the high pressure flow through the outflow tract might pull this leaflet down (Venturi effect) further compromising the LV outflow. The micro photo on the right shows the myocyte disarray and large amounts of interstitial collagenous fibrosis (blue material) typical of IHSS (trichrome stain).
Cardiomyopathies

Restrictive

- Ejection fraction-- 45-90%
- Mechanisms of failure-- Impairment of compliance (diastolic dysfunction)
- Causes-- Idiopathic, amyloidosis, radiation-induced fibrosis
- Indirect causes-- pericardial constriction

Restrictive (infiltrative) Cardiomyopathy Etiology

- Infiltration of the myocardium with something other than muscle
- Stiff heart that cannot fill or pump well
  (Filling appears to be the main problem)

Etiologies

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<thead>
<tr>
<th>Etiologies</th>
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<tbody>
<tr>
<td>Pericarditis</td>
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<tr>
<td>Pericardial Blood</td>
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<tr>
<td>Hypertrophic</td>
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<td>Hypotrophic</td>
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<tr>
<td>Myocarditis</td>
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<tr>
<td>Myocardial injury</td>
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<tr>
<td>Troponin</td>
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<tr>
<td>Microvascular (endothelial or smooth muscle)</td>
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<tr>
<td>Myoglobin</td>
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<tr>
<td>Free radicals</td>
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<td>Nutritional</td>
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The vicious circle in cardiogenic shock