Pathophysiology: Heart Failure
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Irving Assistant Professor of Medicine

Outline
• Definitions and Classifications
• Epidemiology
• Muscle and Chamber Function
• Pathophysiology

Heart Failure: Definitions
• An inability of the heart to pump blood at a sufficient rate to meet the metabolic demands of the body (e.g. oxygen and cell nutrients) at rest and during effort or to do so only if the cardiac filling pressures are abnormally high.
• A complex clinical syndrome characterized by abnormalities in cardiac function and neurohormonal regulation, which are accompanied by effort intolerance, fluid retention and a reduced longevity
• A complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood.

Heart Failure
• Not a disease
• A syndrome
– From "syn" meaning "together" and "dromos" meaning "a running".
– A group of signs and symptoms that occur together and characterize a particular abnormality.
• Diverse etiologies
• Several mechanisms

Etiologies

Etiologies

Ischemia
Hypertrophy
Arterial Stiffness
Atrial Fibrillation
Diabetes
Hypertension
CAD
Valvular Disease
Infiltrative Disease
Pericardial Disease

Ischemic cardiomyopathy
Valvular cardiomyopathy
Hypertensive cardiomyopathy
Inflammatory cardiomyopathy
Metabolic cardiomyopathy
General system disease
Muscular dystrophies.
Neuromuscular disorders.
Sensitivity and toxic reactions.
Peripartal cardiomyopathy

Circulation. 1996;93:841-842
Heart Failure: Classifications

- Right vs. Left Sided
- Cardiac vs. Non-cardiac
- Dilated vs. Hypertrophic vs. Restrictive
- Acute vs. Chronic
- Forward vs. Backward
- Systolic vs. Diastolic
- Compensated vs. Decompensated
- High vs. Low Output

Heart Failure Paradigms

- Cardiovascular model
- Hemodynamic model
- Neurohormonal model
- Genetic model

Heart Failure Paradigms

- Cardiorenal model
- Hemodynamic model
- Neurohormonal model
- Genetic model

Epidemiology Heart Failure: The Problem

- 3.5 million in 1991, 4.7 million in 2000, estimated 10 million in 2037
- Incidence: 550,000 new cases/year
- Prevalence: 1% ages 50–59, >10% over age 80
- More deaths from HF than from all forms of cancer combined
- Most common cause for hospitalization in age >65

Cardiac Muscle Function

Preload

- The length of a cardiac muscle fiber prior to the onset of contraction.
- Frank Starling

Afterload

- The against which a cardiac muscle fiber must shorten.
- Isotonic Contraction

Contractility

- The force of contraction independent of preload and afterload.
- Inotropic State

From Muscle to Chamber

The Pressure Volume Loop

- LV Pressure vs. LV Volume
- Diastolic Systolic
The Pressure Volume Loop

Volume vs. Pressure

Compliance/Stiffness vs Capacitance

Cardiac Chamber Function

Preload
- EDV
- EDP
- Wall stress at end diastole

Afterload
- Aortic Pressure
- Total peripheral resistance
- Arterial impedance
- Wall stress

Contractility
- Pressure generated at given volume.
- Inotropic State

Frank Starling Curves

Pathophysiology - PV Loop

Pathophysiology of myocardial remodeling:
Transition from compensated hypertrophy to heart failure

Insult / Remodeling Stimuli
- Wall Stress
- Cytokines
- Neurohormones
- Oxidative stress

Increased Wall Stress

Mycocyte Hypertrophy
- Altered interstitial matrix
- Fetal Gene Expression
- Altered calcium handling proteins
- Myocyte Death

Ventricular Enlargement
Diastolic Dysfunction
Systolic Dysfunction
Ventricular Remodeling

Where \( P \) = ventricular pressure, \( r \) = ventricular chamber radius and \( h \) = ventricular wall thickness

Neurohormonal Activation in Heart Failure

Myocardial injury to the heart (CAD, HTN, CMP, valvular disease)

Initial fall in LV performance, ↑ wall stress

Remodeling and progressive worsening of LV function

Fibrosis, apoptosis, hypertrophy, cellular/molecular alterations, myotoxicity

Peripheral vasoconstriction

Sodium retention

Hemodynamic alterations

Heart failure symptoms

Fatigue
Activity altered
Chest congestion
Edema
Shortness of breath

RAS, renin-angiotensin system; SNS, sympathetic nervous system.

Neurohormones in Heart Failure

Myocardial injury

Fall in LV Performance

Activation of RAAS and SNS (endothelin, ANP, cytokines)

Myocardial Toxicity

Change in Gene Expression

Remodeling and Progressive Worsening of LV Function

Morbidity and Mortality

HF Symptoms


Neurohormonal Activation

Angiotensin II

Norepinephrine

Hypertrophy, apoptosis, ischemia, arrhythmias, remodeling, fibrosis

Morbidity and Mortality

Adrenergic Pathway in Heart Failure Progression

↑ CNS sympathetic outflow

↑ Cardiac sympathetic activity

↑ Vascular sympathetic activity

↑ Renal sympathetic activity

Myocyte hypertrophy

Myocyte injury

Increased arrhythmias

Vasoconstriction

Renal sodium retention

Disease progression
Pathophysiology of Heart Failure

Four Basic Mechanisms
1. Increased Blood Volume (Excessive Preload)
2. Increased Resistant to Blood Flow (Excessive Afterload)
3. Decreased contractility
4. Decreased Filling

Increased Blood Volume

- Aortic Regurgitation
- AI + Remodeling
- AI + HF

Etiologies
- Mitral Regurgitation
- Aortic Regurgitation
- Volume Overload
- Left to Right Shunts
- Chronic Kidney Disease

Increased Afterload

- Hypertension
- HTN + DD
- HTN + DD + HF

Etiologies
- Aortic Stenosis
- Aortic Coarctation
- Hypertension

Decreased Contractility

- MI
- MI + Remodeling
- MI + Heart Failure

Etiologies
- Ischemic Cardiomyopathy
- Myocardial Infarction
- Myocarditis
- Toxins
  - Anthracycline
  - Alcohol
  - Cocaine

Decreased Filling

- Normal
- HCM
- HCM + HF

Etiologies
- Mitral Stenosis
- Constriction
- Restrictive Cardiomyopathy
- Cardiac Tamponade
- Hypertrophic Cardiomyopathy
- Infiltrative Cardiomyopathy

Heart Failure: Classifications
**Types of Heart Failure**

<table>
<thead>
<tr>
<th>SHF</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Coronary Artery Disease</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>Hypertension</td>
</tr>
<tr>
<td>&gt; 60 years</td>
<td>All ages</td>
</tr>
<tr>
<td>Impaired Contraction</td>
<td>Impaired filling</td>
</tr>
</tbody>
</table>

**Pathophysiology**

**Demographics**

**1st Cause**

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**Systolic Versus Diastolic Failure**

- **Systolic Dysfunction**
  - Pressure
  - Volume

- **Diastolic Dysfunction**
  - Pressure
  - Volume

**Diastolic** vs. **Systolic** Failure

**Volume** vs. **Pressure**

**Diastolic Dysfunction**

**Normal**

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**Heart Failure: Classifications**

- **Heart Failure**
  - Systolic vs. Diastolic
  - High vs. Low Output
  - Right vs. Left Sided
  - Cardiac vs. Non-cardiac
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  - Compensated vs. Decompensated

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**Decompensated Heart Failure**

**Heart Failure: Classifications**

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High vs. Low Output Failure

- Causes:
  - Anemia
  - Systemic arteriovenous fistulas
  - Hyperthyroidism
  - Beriberi heart disease
  - Paget disease of bone
  - Glomerulonephritis
  - Polycythemia vera
  - Carcinoid syndrome
  - Obesity

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Dilated vs. Hypertrophic vs. Restrictive

<table>
<thead>
<tr>
<th>Type</th>
<th>Definition</th>
<th>Sample Etiologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilated</td>
<td>Dilated left/both ventricle(s) with impaired contraction</td>
<td>Ischemic, idiopathic, familial, viral, alcoholic, toxic, valvular</td>
</tr>
<tr>
<td>Hypertrophic</td>
<td>Left and/or right ventricular hypertrophy</td>
<td>Familial with autosomal dominant inheritance</td>
</tr>
<tr>
<td>Restrictive</td>
<td>Restrictive filling and reduced diastolic filling of one/both ventricles, Normal/near normal systolic function</td>
<td>Idiopathic, amyloidosis, endomyocardial fibrosis</td>
</tr>
</tbody>
</table>

Clinical Manifestations

- Symptoms
  - Reduced exercise tolerance
  - Shortness of breath
  - Congestion
  - Fluid retention
  - Difficulty in sleeping
  - Weight loss

Diagnosis of heart failure

- Physical examination
- Chest X ray
- EKG
- Echocardiogram
- Blood tests: Na, BUN, Creatinine, BNP
- Exercise test
- MRI
- Cardiac catheterization
**NYHA Classification**

<table>
<thead>
<tr>
<th>Class</th>
<th>Patient Symptoms</th>
</tr>
</thead>
</table>
| I     | Mild | • No limitation of physical activity  
• No undue fatigue, palpitation, or dyspnea |
| II    | Mild | • Slight limitation of physical activity  
• Comfortable at rest  
• Less than ordinary activity results in fatigue, palpitation, or dyspnea |
| III   | Moderate | • Marked limitation of physical activity  
• Comfortable at rest  
• Less than ordinary activity results in fatigue, palpitation, or dyspnea |
| IV    | Severe | • Unable to carry out any physical activity without discomfort  
• Symptoms of cardiac insufficiency at rest  
• Physical activity causes increased discomfort |

**ACC/AHA Staging System**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Patient Description</th>
</tr>
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</table>
| A     | High risk for developing heart failure  
• Hypertension  
• Coronary artery disease  
• Diabetes mellitus  
• Family history of cardiomyopathy |
| B     | Asymptomatic heart failure  
• Previous myocardial infarction  
• Left ventricular systolic dysfunction  
• Asymptomatic valvular disease |
| C     | Symptomatic heart failure  
• Known structural heart disease  
• Shortness of breath and fatigue  
• Reduced exercise tolerance |
| D     | Refractory end-stage heart failure  
• Marked symptoms at rest despite maximal medical therapy (e.g., those who are recurrently hospitalized or cannot be safely discharged from the hospital without specialized interventions) |

**Goals of Treatment**

1. Identification and correction of underlying condition causing heart failure.  
2. Elimination of acute precipitating cause of symptoms.  
4. Improve long term survival.

**Treatment**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Patient Treatment</th>
</tr>
</thead>
</table>
| A     | High risk for developing heart failure  
• Optimal pharmacologic therapy (OPT)  
• Aspirin, ACE inhibitors, statins, b-blockers, a-b-blockers (carvedilol/diabetic therapy) |
| B     | Asymptomatic heart failure  
• OPT  
• ICD if left ventricular (LV) dysfunction (systolic) present |
| C     | Symptomatic heart failure  
• OPT  
• ICD if LV dysfunction (systolic) present  
• CRT if QRs wide, LVEF<35% |
| D     | Refractory end-stage heart failure  
• OPT  
• Intermittent IV inotropes  
• ICD as a bridge to transplantation  
• CRT  
• Other devices (LVAD, pericardial restraint) |

**Targets of Treatment**

**Standard Pharmacological Therapy**

- ACE inhibitors  
- Angiotensin Receptor Blockers  
- Beta Blockers  
- Diuretics  
- Aldosterone Antagonists  
- Statins  
- Vasodilators  
- Inotropes
ACC/AHA Staging System

Treatment

Summary

• Complex Clinical Syndrome
• Multiple Etiologies and Classification Systems
• Physiologic Understanding Essential

http://www.columbia.edu/itc/hs/medical/heartsim/