Heart failure is the pathological process in which the systolic or/and diastolic function of the heart is impaired, and as a result, cardiac output decreases and is unable to meet the metabolic demands of the body.
Prevalence

- 5 million Americans have heart failure.
- 500,000 new cases diagnosed each year in US
- HF is the reason for at least 20% of all hospital admissions among persons older than 65.
Prevalence

- The prevalence of heart failure rises from below 1% in individuals below 60 years to nearly 10% in those over age 80 years.

- Symptomatic HF has a worse prognosis than the majority of cancers, with one-year mortality of approximately 45%.
Pathophysiology

Systolic functions of the heart is governed by four major determinants:

- The contractile state of the myocardium
- The preload of the ventricle
- The afterload applied to the ventricle
- The heart rate
Etiological causes

Dysfunction of myocardium

- Myocardial damage:
  - myocardial infarction;
  - Cardiomyopathy;
  - Myocarditis

- Metabolic disturbance
  - ischemia and hypoxia;
  - beriberi
Etiological causes

Overload for myocardium

- Pressure overload (afterload)
  - Hypertension, aortic stenosis;
  - Pulmonary hypertension
- Volume overload (preload)
  - Mitral regurgitation
- Restriction of cardiac dilation
  - Pericardial effusion
The precipitating causes

- Infection
  especially, lung infection
- Arrhythmia
  Tachycardia: atrial fibrillation
  Bradycardia
The precipitating causes

- Excessive physical activity
- Pregnancy and delivery
- Anemia
The precipitating causes

- Administration of inappropriate drug
- Medication noncompliance
- Excess fluid intake
- Thyrotoxicosis
Pathophysiological Mechanisms

Cardiac abnormalities

Structural abnormalities
- Myocardium or myocyte
  - Abnormal excitation-contraction coupling
  - β-Adrenergic desensitization
- Hypertrophy
- Necrosis
- Fibrosis
- Apoptosis
- Left ventricular chamber
  - Remodeling
    - Dilatation
    - Increased sphericity
    - Aneurysmal dilatation or wall thinning
- Coronary arteries
  - Obstruction
  - Inflammation

Functional abnormalities
- Mitral regurgitation
- Intermittent ischemia or hibernating myocardium
- Induced atrial and ventricular arrhythmias
- Altered ventricular interaction
Pathophysiological Mechanisms

- Biologically active tissue and circulating substances
- Renin–angiotensin–aldosterone system
- Sympathetic nervous system (norepinephrine)
- Vasodilators (bradykinin, nitric oxide, and prostaglandins)
- Natriuretic peptides
- Cytokines (endothelin, tumor necrosis factor, and interleukins)
- Vasopressin
- Matrix metalloproteinases
Pathophysiological Mechanisms

Other factors
Genetic background, including effects of sex
Age
Environmental factors, including use of alcohol, tobacco, and toxic drugs

Coexisting conditions
Diabetes mellitus
Hypertension
Renal disease
Coronary artery disease
Anemia
Obesity
Sleep apnea
Depression
<table>
<thead>
<tr>
<th>Response</th>
<th>Short-Term Effects</th>
<th>Long-Term Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salt and Water Retention</td>
<td>Augments Preload</td>
<td>Pulmonary Congestion, Anasarca</td>
</tr>
<tr>
<td>Vasoconstriction</td>
<td>Maintains BP for perfusion of vital organs</td>
<td>Exacerbates pump dysfunction (excessive afterload), increases cardiac energy expenditure</td>
</tr>
<tr>
<td>Sympathetic Stimulation</td>
<td>Increases HR and ejection</td>
<td>Increases energy expenditure &amp; risk of dysrhythmia &amp; sudden death</td>
</tr>
</tbody>
</table>
Ventricular Remodeling

- Ventricular remodeling is the process by which mechanical, neurohormonal, and possibly genetic factors alter ventricular size, shape, and function.

- Remodeling occurs in several clinical conditions, including myocardial infarction, hypertension and cardiomyopathy.

- Its hallmarks include hypertrophy, loss of myocytes, and increased interstitial fibrosis.
Mitral regurgitation

- A potential deleterious outcome of remodeling

- As the LV dilates and the heart assumes a more globular shape, the geometric relation between the papillary muscles and the mitral leaflets changes, causing MR.

- The presence of MR results in an increasing volume overload on the overburdened LV that further contributes to remodeling, the progression of disease, and symptoms.
**Ventricular remodeling after acute infarction**

Initial infarct → Expansion of infarct (hours to days) → Global remodeling (days to months)

**Ventricular remodeling in diastolic and systolic heart failure**

Normal heart → Hypertrophied heart (diastolic heart failure) → Dilated heart (systolic heart failure)
Clinical classification

According to the course of disease
  Acute HF
  Chronic HF

According to the cardiac output (CO)
  Low-output HF
  High-output HF

According to the location of heart failure
  Left-side heart failure (LHF)
  Right-side heart failure (RHF)
  Biventricular failure (whole heart failure)

According to the function impaired
  Systolic failure
  Diastolic failure
Chronic Heart Failure
Left ventricular failure

Pulmonary congestion +
low cardiac output
LV failure -- Symptom

Dyspnea
- Exhausted dyspnea
- Orthopnea
- Paroxysmal nocturnal dyspnea
- Acute pulmonary edema
LV failure--Symptom

- Cough
- Fatigue
- Symptom of urinary system
LV failure--Sign

Cardiac sign
- Enlargement of LV
- Gallop rhythm
- Systolic murmur in apex

Pulmonary sign
- Dry rales
- Moist rales
Right ventricular failure

- Symptom of gastrointestinal
- Symptom of Renal
- Pain in hepatic area
- Dyspnea
RV failure--Sign

- Hepatojugular reflux
- Hepatomegaly
- Edema
- Pleural fluid and ascites
Biventricular Failure

LV failure + RV failure
What Are The Symptoms of Heart Failure?

Think FACES...

- Fatigue
- Activities limited
- Chest congestion
- Edema or ankle swelling
- Shortness of breath
What Are The Symptoms of Heart Failure?

- Shortness of breath
- Swelling of feet & legs
- Chronic lack of energy
- Difficulty sleeping at night due to breathing problems
- Swollen or tender abdomen with loss of appetite
- Cough with frothy sputum
- Increased urination at night
- Confusion and/or impaired memory
What Are The Symptoms of Heart Failure?

- Coughing
- Tiredness
- Shortness of breath
- Pulmonary edema (excess fluid in lungs)
- Pumping action of the heart grows weaker
- Pleural effusion (excess fluid around lungs)
- Swelling in abdomen (ascites)
- Swelling in ankles and legs
JVP = jugular venous pressure
Edema
Ascites
HF—lab test

Brain natriuretic peptide (BNP)

>100 pg/ml   Heart failure
Pulmonary edema

Butterfly sign
Swan-Ganz catheter
NYHA Classification of heart failure

- Class I: No limitation of physical activity
- Class II: Slight limitation of physical activity
- Class III: Marked limitation of physical activity
- Class IV: Unable to carry out physical activity without discomfort
6 minutes walk test (6MWT)

- 6MWT < 150 m  Serious cardiac dysfunction
- 6MWT 150~425 m  Moderate cardiac dysfunction
- 6MWT 426~550 m  Mild cardiac dysfunction
Four stages of heart failure

- Stage A: Asymptomatic with no heart damage but have risk factors for heart failure
- Stage B: Asymptomatic but have signs of structural heart damage
- Stage C: Have symptoms and heart damage
- Stage D: Endstage disease

ACC/AHA guidelines, 2001
Figure 1. Stages in the Evolution of Heart Failure/Recommended Therapy by Stage

**Stage A**
At high risk for heart failure but without structural heart disease or symptoms of HF
- e.g., Patients with:
  - hypertension
  - coronary artery disease
  - diabetes mellitus
  - Patients using cardiotoxins with FHx CM
- Therapy
  - Treat hypertension
  - Encourage smoking cessation
  - Treat lipid disorders
  - Encourage regular exercise
  - Discourage alcohol intake, illicit drug use
  - ACE inhibition in appropriate patients (see text)

**Stage B**
Structural heart disease but without symptoms of HF
- e.g., Patients with:
  - previous MI
  - LV systolic dysfunction
  - asymptomatic valvular disease
- Symptoms of HF develop
- Therapy
  - All measures under stage A
  - ACE inhibitors in appropriate patients (see text)
  - Beta-blockers in appropriate patients (see text)

**Stage C**
Structural heart disease with prior or current symptoms of HF
- e.g., Patients with:
  - known structural heart disease
  - shortness of breath and fatigue, reduced exercise tolerance
- Therapy
  - All measures under stage A
  - Drugs for routine use: Diuretics
  - ACE inhibitors
  - Beta-blockers
  - Digitalis
  - Dietary salt restriction

**Stage D**
Refractory HF requiring specialized interventions
- e.g., Patients who have 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)
- Therapy
  - All measures under stages A, B, and C
  - Mechanical assist devices
  - Heart transplantation
  - Continuous (not intermittent) IV inotropic infusions for palliation
  - Hospice care
Figure 3. Stages of Heart Failure and Treatment Options for Systolic Heart Failure.
Treatment Strategies of HF
Treatment Strategies of HF

etiology therapy

- Treatment of etiology causes
- Treatment of precipitating causes
- Improve life-style
Treatment Strategies of HF

Lessen cardiac load

- Rest
- Limitation of salt intake
- Water intake
- Diuretics
Diuretics

- Indicated in patients with symptoms of heart failure who have evidence of fluid retention
- Enhance response to other drugs in heart failure such as beta-blockers and ACE inhibitors
- Therapy initiated with low doses followed by increments in dosage until urine output increases and weight decreases by 0.5-1kg daily
Diuretics in HF

Benefits:
- Improves symptoms of congestion
- Can improve cardiac output
- Improved neurohormonal milieu
- No inherit nephrotoxicity

Limitations
- Excessive volume depletion
- Electrolyte disturbance
- Unknown effects on mortality
- Ototoxicity
positive inotropic agents

- Digitalis
- Dopamine and Dobutamine
- Milrinone
Digitalis

- Enhances LV function, normalizes baroreceptor-mediated reflexes and increases cardiac output at rest and during exercise
- Recommended to improve clinical status of patients with heart failure due to LV dysfunction and should be used in conjunction with diuretics, ACE inhibitors and beta-blockers
- Also recommended in patients with heart failure who have atrial fibrillation
- Adverse effects include cardiac arrhythmias, GI symptoms and neurological complaints (eg. visual disturbances, confusion)
Digitalis

Use with caution:

- Hypertrophic cardiomyopathy
- Mitral stenosis with sinus rhythm
- Constrictive pericarditis
- High degree AVB
- AMI within 24 hours
ACE Inhibitors: clinical benefits

- Increases exercise capacity improves functional class
- Attenuation of LV remodeling post MI
- Decrease in the progression of chronic HF
- Decreased hospitalization
- Enhanced quality of life
- Improved survival
ACE Inhibitor

- All patients with symptomatic heart failure and those in functional class I with significantly reduced left ventricular function should be treated with an ACE inhibitor, unless contraindicated or not tolerated.
- ACE inhibitors should be continued indefinitely.
- It is important to titrate to the dosage regimen used in the clinical trials ... in the absence of symptoms or adverse effects on end-organ perfusion.
Effects of SNS Activation in Heart Failure

- Dysfunction/death of cardiac myocytes
- Provokes myocardial ischemia
- Provokes arrhythmias
- Impairs cardiac performance
Beta-adrenergic receptor bloker

- Dry weight
- Initiate with low dosage
- Titration to target dosage
- Metoprolol
- Bisoprolol
- Carvedilol
Treatment Strategies of HF

- Aldosterone antagonist:
  - RALES, serious HF

- Angiotensin receptor blocker:
  - substitute, not replace
# Summary of drug treatment for CHF

<table>
<thead>
<tr>
<th>Asymptomatic LV dysfunction</th>
<th>Mild to moderate CHF</th>
<th>Moderate to severe CHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor</td>
<td>Digoxin</td>
<td>Digoxin</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>Diuretics</td>
<td>Diuretics</td>
</tr>
<tr>
<td></td>
<td>ACE inhibitor</td>
<td>ACE inhibitor</td>
</tr>
<tr>
<td></td>
<td>Beta blocker</td>
<td>Beta blocker</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Spironolactone</td>
</tr>
<tr>
<td>Drug</td>
<td>Initial Dose</td>
<td>Maximum Dose</td>
</tr>
<tr>
<td>-----------------------</td>
<td>----------------------------------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Loop diuretics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bumetanide</td>
<td>0.5 to 1.0 mg once or twice daily</td>
<td>Titrate to achieve dry weight (up to 10 mg daily)</td>
</tr>
<tr>
<td>Furosemide</td>
<td>20 to 40 mg once or twice daily</td>
<td>Titrate to achieve dry weight (up to 400 mg daily)</td>
</tr>
<tr>
<td>Torsemide</td>
<td>10 to 20 mg once or twice daily</td>
<td>Titrate to achieve dry weight (up to 200 mg daily)</td>
</tr>
<tr>
<td><strong>ACE inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Captopril</td>
<td>6.25 mg three times daily</td>
<td>50 mg 3 times daily</td>
</tr>
<tr>
<td>Enalapril</td>
<td>2.5 mg twice daily</td>
<td>10 to 20 mg twice daily</td>
</tr>
<tr>
<td>Fosinopril</td>
<td>5 to 10 mg once daily</td>
<td>40 mg once daily</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>2.5 to 5.0 mg once daily</td>
<td>20 to 40 mg once daily</td>
</tr>
<tr>
<td>Quinapril</td>
<td>10 mg twice daily</td>
<td>40 mg twice daily</td>
</tr>
<tr>
<td>Ramipril</td>
<td>1.25 to 2.5 mg once daily</td>
<td>10 mg once daily</td>
</tr>
<tr>
<td><strong>Beta-receptor blockers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>1.25 mg once daily</td>
<td>10 mg once daily</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>3.125 mg twice daily</td>
<td>25 mg twice daily; 50 mg twice daily for patients greater than 85 kg</td>
</tr>
<tr>
<td>Metoprolol tartrate</td>
<td>6.25 mg twice daily</td>
<td>75 mg twice daily</td>
</tr>
<tr>
<td>Metoprolol succinate extended release+</td>
<td>12.5 to 25 mg daily</td>
<td>200 mg once daily</td>
</tr>
<tr>
<td><strong>Digitalis glycosides</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td>0.125 to 0.25 mg once daily</td>
<td>0.125 to 0.25 mg once daily</td>
</tr>
</tbody>
</table>

ACE indicates angiotensin converting enzyme.

*Thiazide diuretics are not listed in this table but may be appropriate for patients with mild heart failure or associated hypertension or as a second diuretic in patients refractory to loop diuretics alone.*

*Referred to in some publications as metoprolol CR/XL.
Cardiac resynchronization therapy (CRT)

CRT device:

- Patients with NYHA Class III/IV
- Symptomatic despite optimal medical therapy
- QRS ≥ 130 msec
- LVEF ≤ 35%

CRT plus ICD:

- Same as above with ICD indication
The Donkey Analogy

Ventricular dysfunction limits a patient’s ability to perform the routine activities of daily living...
Diuretics, ACE inhibitors

Reduce the number of sacks on the wagon
Beta-blockers

Limit donkey’s speed, thus saving energy
digitalis

Like the carrot placed in front of the donkey
CRT/CRT-D

Increase the donkey’s (heart) efficiency
Heart failure: More than just drugs.

- Dietary counseling
- Patient education
- Physical activity
- Medication compliance
- Aggressive follow-up
- Sudden death assessment
Take home message

- Heart failure is clinical diagnosis
- ACEI should be titrated to highest dose tolerable
- Beta-blockers should be used universally but must titrated slowly
- Spironolactone should be used in NYHA III/IV patients
- Digoxin can be used to reduce morbidity
- Role of ARB remains to be determined in patient intolerating ACEI
- Preventive therapy or patient education is the key to reduction of burden
Questions to determine therapeutic strategy in patients presenting with HF

- Is heart failure present?
- What caused the problem?
- What precipitated deterioration?
- How severe is the heart failure?
- What is the prognosis?
- What is the best acute therapeutic strategy?
- What is the best chronic therapeutic strategy?
- Can the initiating/precipitating problem be cured, and can the state of HF be attenuated?
CHF with preserved systolic function (Diastolic HF)

Differential Diagnosis

- Wrong Dx
- Inaccurate measurement of LVEF
- Primary valvular disease
- Restrictive (infiltrative) cardiomyopathies
- Pericardial constriction
- Episodic/reversible LV systolic dysfunction
- High output failure (AVF, Thyroid, anemia)
- Pulmonary disease
- Atrial myxoma
- Diastolic dysfunction
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Diastolic Heart Failure</th>
<th>Systolic Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Frequently elderly</td>
<td>All ages, typically 50–70 yr</td>
</tr>
<tr>
<td>Sex</td>
<td>Frequently female</td>
<td>More often male</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td>Preserved or normal, approximately 40% or higher</td>
<td>Depressed, approximately 40% or lower</td>
</tr>
<tr>
<td>Left ventricular cavity size</td>
<td>Usually normal, often with concentric left ventricular hypertrophy</td>
<td>Usually dilated</td>
</tr>
<tr>
<td>Left ventricular hypertrophy on electrocardiography</td>
<td>Usually present</td>
<td>Sometimes present</td>
</tr>
<tr>
<td>Chest radiography</td>
<td>Congestion with or without cardiomegaly</td>
<td>Congestion and cardiomegaly</td>
</tr>
<tr>
<td>Gallop rhythm present</td>
<td>Fourth heart sound</td>
<td>Third heart sound</td>
</tr>
</tbody>
</table>
## Diastolic HF vs Systolic HF

<table>
<thead>
<tr>
<th>Coexisting conditions</th>
<th>Diastolic HF</th>
<th>Systolic HF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Obesity</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Long-term dialysis</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>+ (usually paroxysmal)</td>
<td>+ (usually persistent)</td>
</tr>
</tbody>
</table>
CHF with preserved systolic function (Diastolic HF)

- Treatment of etiology causes
- Relaxation of myocardium
- Reverse LV hypertrophy: ACEI, beta-blocker
- Lower preload: Diuretics, Nitrates
- Maintainance sinus rhythm
Acute Heart Failure

Typical causes of acute HF

- Acute myocardial infarction or severe ischemia
- Exacerbation of chronic HF
- Acute volume overload of left ventricle (valvular regurgitation)
- Mitral stenosis
Acute Heart Failure

Clinical findings:

- Severe dyspnea
- Pink and frothy sputum
- Cyanosis
- Orthopnea
- Moist Rales, wheezing
Acute Heart Failure

- Body position: a sitting position with legs dangling over the side of the bed
- Oxygen
  - Oxygen delivered by mask
  - Noninvasive pressure support ventilation
  - Mechanical ventilation
- Morphine
  - Increasing venous capacitance
  - Lowering left atrial pressure
  - Relieving anxiety
Acute Heart Failure

- **Diuretics**: venodilation prior to the onset of diuresis
- **Vasodilator**: Nitroprusside, Nitroglycerin
  - Reducing blood pressure
  - Reducing LV filling pressure
- **Digitalis**
- **aminophylline**