Structural and Functional Adaptations to Heart Failure

Session 16
INTRODUCTION
Heart Failure is a Syndrome

Heart-related factors:
- Atrial fibrillation
- Heart muscle dysfunction (cardiomyopathy)
- Other cardiac disorders (e.g., cardiac tamponade)
- Poor blood supply (myocardial ischaemia)
- Failure to take heart failure medications
- Starting certain medications (e.g., that affect cardiac function or salt retention)
- Diet (excessive salt/fluid intake)
- Excessive physical activity
- Alcohol or drug misuse
- Infections

Lung-related factors:
- High blood pressure
- Poor blood supply (pulmonary embolism)
- Lung disease (asthma, COPD)
- Pulmonary hypertension
- Anaemia
- Renal dysfunction

Other medical conditions:
- Other medical conditions
- Diabetes
- Thyroid disorders

Treatment and lifestyle factors:
- Heart Failure
Heart Failure is a Syndrome

- HF results from disorders of the pericardium, myocardium, endocardium, heart valves, or great vessels, or metabolic abnormalities
- Symptoms from impaired LV myocardial function
- Key term is the ejection fraction, the percentage of blood ejected from the left ventricle
- HF classified as either heart failure with preserved ejection fraction (HFpEF) or heart failure with reduced ejection fraction (HFrEF)

[Yancy Circulation 2013 /p11 A]
## Heart Failure Categorization

<table>
<thead>
<tr>
<th>Classification</th>
<th>EF (%)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Heart failure with reduced ejection fraction (HFrEF)</td>
<td>≤40</td>
<td>Also referred to as systolic HF. Randomized controlled trials have mainly enrolled patients with HFrEF, and it is only in these patients that efficacious therapies have been demonstrated to date.</td>
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<tr>
<td>II. Heart failure with preserved ejection fraction (HFpEF)</td>
<td>≥50</td>
<td>Also referred to as diastolic HF. Several different criteria have been used to further define HFpEF. The diagnosis of HFpEF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified.</td>
</tr>
<tr>
<td>a. HFpEF, borderline</td>
<td>41 to 49</td>
<td>These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patients with HFpEF.</td>
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<tr>
<td>b. HFpEF, improved</td>
<td>&gt;40</td>
<td>It has been recognized that a subset of patients with HFpEF previously had HFrEF. These patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. Further research is needed to better characterize these patients.</td>
</tr>
</tbody>
</table>
THE REMODELING HYPOTHESIS
Cardiac Remodeling

- Many physiological functions designed for homeostasis
- When a system is compromised, a compensatory mechanism is triggered

Myocardial Infarction injury

Cardiac output decreases

LV volume increases

LV hypertrophy

[Cohn JACC 2000; Konstam J Am Coll Cardiol 2011; D’Elia J Am Coll Cardiol 2015; Burchfield Circulation 2013]
Cardiac Remodeling

- Myocardial infarction
- Pressure overload
- Inflammatory heart muscle disease
- Idiopathic dilated cardiomyopathy
- Volume overload

Pathophysiological Stimuli:
- Cardiomyocyte Loss
- Cardiomyocyte Hypertrophy
- Fibrosis
- Insulin Resistance
- Electrophysiological Changes

Phenotypes:
- Ischemic Phenotype
- Hypertrophic Phenotype

Heart Failure

References:
[Cohn JACC 2000; Konstam J Am Coll Cardiol 2011; D’Elia J Am Coll Cardiol 2015; Burchfield Circulation 2013]
ARS Question

Which of the following would be a cause of cardiac remodeling from pressure overload?

A. Valvular regurgitation  
B. Aortic stenosis  
C. Dilated cardiomyopathy  
D. Coronary artery disease
Which of the following would be a cause of cardiac remodeling from pressure overload?

A. Valvular regurgitation

B. **Aortic stenosis**

C. Dilated cardiomyopathy

D. Coronary artery disease

(Continue to next slide for supporting information)
Cardiac Remodeling: Pressure Overload

- Radiologist read this as a non-diagnostic study
- Recent ejection fraction by echocardiogram was 53%
- Patient presents with exercise intolerance and resting heart rate of 95/minute
- The LV was thick and non-compliant
- Further investigation revealed aortic stenosis

Patient with aortic stenosis
ARS Question

How quickly does cardiac remodeling occur after myocardial infarction?

A. Immediately
B. Minutes
C. Hours
D. Days
How quickly does cardiac remodeling occur after myocardial infarction?

A. Immediately
B. Minutes
C. Hours
D. Days

(Continue to next slide for supporting information)
Cardiac Remodeling: Myocardial Infarction

• Radiologist read this as pulmonary edema
• Patient developed shortness of breath and chest pain due to an acute anterior MI
• LV volume initially increased to compensate for decreased cardiac output
• One year later, cardiac output was higher because hypertrophy of the LV wall had developed
Cardiac Remodeling

The process of cardiac remodeling involves several steps:

1. **Myocytes stretch**
2. **Neurohumoral activation occurs***
3. **Myocyte hypertrophy stimulated**
4. **Cardiac performance further deteriorates**

*Local norepinephrine activity and angiotensin and endothelin release are increased

[References: Cohn JACC 2000; Konstam J Am Coll Cardiol 2011; D’Elia J Am Coll Cardiol 2015; Burchfield Circulation 2013]
Gross Changes During Remodeling After MI

- As the heart remolds, the geometry changes
- The heart is less elliptical and more spherical to optimize the relationship between LV volume and cardiac output
- Over time, changes in ventricular mass, composition and volume develop
ARS Question

Which of the following has higher circulating blood levels as part of the cardiac remodeling process?

A. Angiotensin II
B. Epinephrine
C. Corticosteroids
D. Dopamine
ARS Question

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(Continue to next slide for supporting information)
Changes in Hemodynamic Load

Normal  Early LV dilation  Global ventricular hypertrophy  Limited adaptation  Progressive dilation

TIME

[Cohn JACC 2000 /pS71 B]
Reverse Cardiac Modeling

Remodeled Left Ventricle

After Partial Reversal

Less hypertrophy

Improved function

Thickening of the myocardium of the left ventricle

Right ventricle

Left ventricle

[Koitabashi Nature Reviews Cardiology 2012 /p148 C]
MYOCARDIAL HYPERTROPHY
What is Myocardial Hypertrophy?

- Adaptive response to:
  - ↑ pressure in the circulation
  - ↑ pressure inside the LV
  - ↑ cardiac work

- Heart’s version of pumping iron

- Hypertrophy occurs in:
  - Ischemic heart disease (resulting from CAD and not from increased pressure in the heart or circulation)
  - Hypertension
  - Heart failure from any cause
  - Valvular heart disease

- Associated with ↑ risk of heart failure and life-threatening cardiac arrhythmias

[Burchfield Circulation 2013 /p390 A]
What Happens to Cardiac Tissues During Hypertrophy?

- Changing loading conditions appear to be the primary driving force behind myocardial hypertrophy in HF
- Other factors act as modulators or facilitators of the process
- Hyperplasia, or an increase in new myocardial cells, can occur to some extent under conditions of excessive loading or myocyte loss
- Primary response to altered load is the assembly of new working units or sarcomeres per myocardial cell

[Burchfield Circulation 2013 /p390 A]
Response to Altered Cardiac Load: Clinical Characteristics

Primary response to altered load is the creation of new contracting units (sarcomeres)

- **Pressure overload** results in new contracting units working in the same direction
- **Volume overload** leads to new contracting units that work in different directions
- **Biochemical changes** alter how the contracting units work
Response to Altered Cardiac Load – Clinical Characteristics

- Dyspnea on exertion
- Dyspnea at rest in more extreme cases
- Decreased exercise tolerance
- Increased heart rate
- Cardiac arrhythmias
5 minutes

VASCULAR REMODELING
Mechanisms and Pathophysiology

Capillary sprouting

Mature network

[Burchfield Circulation 2013 /p393 A]
Mechanisms and Pathophysiology

- Growth and proliferation
- Inflammation
- Apoptosis
- Vascular fibrosis
LV Hypertrophy or Heart Failure?
LV Hypertrophy or Heart Failure?

[Kusumoto Chapter 10 Pathophysiology of Disease 2013]
Questions?