Chronic Heart Failure
Pathophysiology & Pharmacotherapy

Robert J. Straka, Pharm.D. FCCP
Associate Professor
University of Minnesota
College of Pharmacy

Objectives

- Describe basic pathophysiology of CHF
- Explain terminology related to CHF
- Describe signs & symptoms of CHF
- Outline therapeutic goals of treating CHF
- Describe the general approach to treatment of CHF

The Heart as a Target Organ

HEART FAILURE

Coronary Artery Disease
Arrhythmia
Valvular Heart Disease
Cardiomyopathy

HYPERTENSION

Sympathetic Activation in Heart Failure

\[ \text{CNS sympathetic outflow} \]
\[ \text{Cardiac sympathetic activity} \]
\[ \text{Sympathetic activity to kidneys} \]
\[ \text{Activation of RAS} \]

\[ \beta_1 \text{ receptors} \]
\[ \beta_2 \text{ receptors} \]
\[ \alpha_1 \text{ receptors} \]

Myocyte death
Increased arrhythmias
Vasoconstriction
Sodium retention
Disease progression

Stages of Heart Failure

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>High risk of developing HF because of presence of conditions associated with development of HF. No structural or functional abnormalities of heart and has never shown s/s HF</td>
<td>HTN, CAD, diabetes mellitus, history of rheumatic fever, family history of cardiomyopathy, history of cardiotoxic drug therapy or alcohol abuse</td>
</tr>
<tr>
<td>B</td>
<td>Patients who have developed structural heart disease that is strongly associated with development of HF, but have never shown s/s HF</td>
<td>Left ventricular hypertrophy or fibrosis, asymptomatic valvular heart disease, previous MI, left ventricular dilatation or hypokinesia</td>
</tr>
<tr>
<td>NYHA I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Patients who have current or prior symptoms of HF associated with underlying structural heart disease</td>
<td>Dyspnea or fatigue due to LV systolic dysfunction; asymptomatic patients who are undergoing treatment for prior symptoms of HF</td>
</tr>
<tr>
<td>NYHA II-III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>Patients with advanced structural heart disease marked symptoms of HF at rest despite maximal medical therapy and who require specialized interventions</td>
<td>Frequent hospitalizations for HF, on transplant list, hospice setting for management of HF, continuous intravenous support</td>
</tr>
<tr>
<td>NYHA IV</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Management of Heart Failure

Correct Underlying Causes: Hypertension, Ischemic Heart Disease, arrhythmias etc.

Restrict Fluid Intake: 1.5-2 liters is advised
Mod. alcohol intake is permitted

Restrict Sodium Intake: Intake should be limited to 2 grams/day (1 tsp table salt)

Drug Therapy:
- Diuretics
- Vasodilators(ACE-Inh, ARBs)
- Beta-blockers
- Digoxin
- Spironolactone
### Stages for Systolic HF

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Risk factor reduction, ACE Inhibitors and Beta-blockers in selected patients, Cardiac resynchronization if LBB, Aldosterone antagonist, Sodium restriction, diuretics, digoxin</td>
</tr>
<tr>
<td>B</td>
<td>ACE Inhibitors and Beta-blockers, Sodium restriction, diuretics, digoxin</td>
</tr>
<tr>
<td>C</td>
<td>ACE Inhibitors and Beta-blockers, Sodium restriction, diuretics, digoxin</td>
</tr>
<tr>
<td>D</td>
<td>ACE Inhibitors and Beta-blockers, Sodium restriction, diuretics, digoxin</td>
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</table>

### Key Evidence-Based HF Trials

- **ACEI**: SOLVD (Prev. vs. Treatment)
- **β-blockers**: MERIT-HF, COPERNICUS, COMET
- **Diuretics**: RALES, EPHESUS (Post-MI)
- **Digoxin**: DIG
- **ARBs**: CHARM, Val-HeFT

- Vasodilators: V-HeFT I
- CCB: PRAISE

### Diuretics

- Consider for all patients predisposed to fluid retention
- Loops are considered the drug of choice
- Metolazone may be used in addition to a loop in cases of severe volume overload
- Monitor: daily weight, potassium, renal function

### Diuretics in Heart Failure

- Have the potential to alter the efficacy and toxicity of agents used to treat heart failure
  - **Underdosing** may lead to fluid retention and ↑ the response to ACE inhibitors and ↓ risk of treating with beta-blockers
  - **Overdosing** may lead to volume depletion and increase the risk of renal insufficiency with ACE inhibitors & ARBs (also additional metabolic side effects)

### Diuretics for CHF

<table>
<thead>
<tr>
<th>Medication</th>
<th>Relative Potency</th>
<th>Half-life (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furosemide</td>
<td>1</td>
<td>0.3-3.4</td>
</tr>
<tr>
<td>Burmetanide</td>
<td>40</td>
<td>0.3-1.5</td>
</tr>
<tr>
<td>Ethacrynic Acid</td>
<td>0.7</td>
<td>0.5-1</td>
</tr>
<tr>
<td>Torsemide</td>
<td>3</td>
<td>0.8-6</td>
</tr>
<tr>
<td>Chlorothiazide</td>
<td>0.1</td>
<td>1.5</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>Indapamide</td>
<td>20</td>
<td>10-22</td>
</tr>
<tr>
<td>Metolazone</td>
<td>10</td>
<td>4-5</td>
</tr>
</tbody>
</table>

### ACE Inhibitors in Heart Failure

- Start low and wait at least two weeks before increasing dose
- Dose titration is based on **target dose** rather than symptomatic improvement (Atlas Trial)
  - Consider dividing the dose if necessary
- Monitor: BP, renal function, potassium
Beta-blockers in Heart Failure

- Patient should be on background ACE inhibition
- Start at a low dose
- Wait at least two weeks before increasing dose
- Monitor BR, HR, clinical status (congestion, mental status)
- Use caution when starting in an unstable NYHA III or IV patient
- Avoid in patients with reactive airway disease, symptomatic bradycardia, or advanced heart block

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### Beta-blockers for CHF

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand Name</th>
<th>Initiating Dose</th>
<th>Maintenance Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carvedilol</td>
<td>Coreg</td>
<td>3.125mg BID</td>
<td>25mg BID 50mg BID if pt &gt;85kg</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>Lopressor</td>
<td>6.125mg BID</td>
<td>75mg BID</td>
</tr>
<tr>
<td>Metoprolol XL</td>
<td>Toprol XL</td>
<td>12.5-25mg QD</td>
<td>200mg QD</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>Zebeta</td>
<td>1.25mg QD</td>
<td>20mg QD</td>
</tr>
</tbody>
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Digoxin in Heart Failure

- Use in patients who remain symptomatic despite use of an ACE inhibitor & β-blocker
- No need to load for chronic heart failure
- Use low dose (0.125mg QD or QOD) if patient is >70 y.o. or has impaired renal fxn
- Little evidence to support monitoring levels in chronic heart failure
- Monitor: HR, GI, Neuro
- Withdrawal of digoxin is NOT recommended

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Spironolactone in Heart Failure

- Consider using in patients who remain symptomatic (NYHA III) despite the use of an ACE inhibitor, β-blocker, digoxin and diuretics
- Monitor potassium

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ARBs in Heart Failure

- Clearly beneficial when ACE inhibitors cannot (sign. Cough/angioedema) be used (CHARM-Alternative, ValHeFT)
- Appear to be beneficial when added to optimal HF therapy (CHARM-Added) IIb
- Not to be used before a beta-blocker
- Monitor: BP, renal function, potassium

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Summary

- Diuretics
- ACE inhibitors
- Beta-Blockers
- Digoxin
- Aldosterone Antagonists
- ARBs