Heart Failure October 8, 2011

HFpEF

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Goals of Presentation
- Touch on pathophysiology of chronic systolic heart failure
- Review assessment and outpatient pharmacologic management of HFpEF
- Highlight non-pharmacologic therapy for chronic systolic heart failure and when to refer
- Cardiac Rehab for HFpEF

Stages of Heart Failure

At Risk:
- STAGE A: High risk for developing HF

Symptomatic:
- STAGE B: Asymptomatic LV dysfunction
- STAGE C: Past or current symptoms of HF
- STAGE D: End-stage HF
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It is recommended that the following common potential precipitating factors for acute HF be identified as recognition of these comorbidities, is critical to guide therapy:

- acute coronary syndromes/coronary ischemia
- severe hypertension
- atrial and ventricular arrhythmias
- infections
- pulmonary emboli
- renal failure
- medical or dietary noncompliance

**Hospitalized Patient**

Precipitating Factors for Acute HF

**Volume Status**

**Initial Clinical Assessment of Heart Failure**

Identifying and Evaluating Noncardiac Disorders or Behaviors
Initial assessment should be made of the patient’s ability to perform activities of daily living.

**Estimated Energy Requirements of Selected Activities (METs)**

- Walking (2 mph) 2.5
- Mowing lawn (power mower) 3.0
- Walking (3 mph) 3.3
- Cycling (leisurely) 3.5
- Gardening (no lifting) 4.4
- Chopping wood 4.9
- Cycling (moderate) 5.7
Initial laboratory evaluation CBC, urinalysis, serum electrolytes (including calcium and magnesium), BUN, serum creatinine, fasting blood glucose (glycohemoglobin), lipid profile, liver function tests, and TSH.

Screening for hemochromatosis, sleep-disturbed breathing, or HIV is reasonable in selected patients who present with HF.

- Diagnostic tests for rheumatologic diseases, amyloidosis, or pheochromocytoma are reasonable in patients presenting with HF in whom there is a clinical suspicion of these diseases.

Measurement of natriuretic peptides (BNP) can be useful in the evaluation of patients presenting in the urgent care setting in whom the clinical diagnosis of HF is uncertain. Measurement of natriuretic peptides can be helpful in risk stratification.
Initial Clinical Assessment of Heart Failure

Twelve-lead EKG, chest radiograph (posterior-anterior and lateral) should be performed.

Initial Clinical Assessment of Heart Failure

Echocardiography with Doppler should be performed to assess (LVEF), left ventricle size, wall thickness, and valve function. Radionuclide ventriculography can be performed to assess LVEF and volumes.

Noninvasive imaging to detect myocardial ischemia is reasonable in patients presenting with HF who have known coronary artery disease and no angina.
Coronary arteriography is reasonable for patients presenting with HF who have chest pain that may or may not be of cardiac origin who have not had evaluation of their coronary anatomy.

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Diuretics and salt restriction are indicated in patients with current or prior symptoms of HF and reduced LVEF who have evidence of fluid retention.

### Oral Diuretics Recommended for Use in the Treatment of Fluid Retention in Chronic Heart Failure

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Daily Dose(s)</th>
<th>Maximum Total Daily Dose</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loop diuretics</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Furosemide</td>
<td>5 to 10 mg once or twice</td>
<td>40 mg</td>
<td>4 to 6 hours</td>
</tr>
<tr>
<td>Torsemide</td>
<td>10 to 20 mg once or twice</td>
<td>240 mg</td>
<td>8 to 12 hours</td>
</tr>
<tr>
<td>Thiazide diuretics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorothiazide</td>
<td>50 to 200 mg once or twice</td>
<td>1000 mg</td>
<td>12 to 48 hours</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>50 mg once or twice</td>
<td>240 mg</td>
<td>12 to 48 hours</td>
</tr>
<tr>
<td>Indapamide</td>
<td>0.5 to 5 mg once or twice</td>
<td>5 mg</td>
<td>24 hours</td>
</tr>
<tr>
<td>Metolazone</td>
<td>2.5 mg once or twice</td>
<td>20 mg</td>
<td>12 to 24 hours</td>
</tr>
<tr>
<td>Potassium-sparing diuretics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiloride</td>
<td>5 mg once or twice</td>
<td>40 mg</td>
<td>24 hours</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>12.5 to 25 mg once or twice</td>
<td>50 mg</td>
<td>2 to 3 days</td>
</tr>
<tr>
<td>Triamterene</td>
<td>100 to 200 mg twice</td>
<td>200 mg</td>
<td>7 to 10 days</td>
</tr>
</tbody>
</table>

**Sequential nephron blockade:**
- **Methylprednisolone:** 2.5 to 10 mg once or twice plus loop diuretic
- **Hydrochlorothiazide:** 50 to 150 mg once or twice plus loop diuretic
- **Chlorthalidone (V):** 50 to 100 mg once or twice plus loop diuretic

*mg indicates milligrams; IV, intravenous; *Higher dose may occasionally be used with close monitoring. (Expression, although
in parenthesis, is not to be selected for initiation of the drug or increase in other dose.

Angiotensin-converting enzyme (ACE) inhibitors are recommended for all patients with current or prior symptoms of HF and reduced LVEF.
Reduced Left Ventricular Ejection Fraction

bisoprolol, carvedilol, and sustained release metoprolol succinate is recommended for all stable patients with current or prior symptoms of HF and reduced LVEF.

Beta Blockers

Inhibitors of the Renin-Angiotensin-Aldosterone System and Beta-Blockers Commonly Used for the Treatment of Patients With Heart Failure With Low Ejection Fraction (Slide 2 of 2)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Daily Dose(s)</th>
<th>Maximum Dose(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta Blockers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>1.25 mg once</td>
<td>10 mg once</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>3.125 mg twice</td>
<td>25 mg twice</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>10 to 25 mg once</td>
<td>200 mg once</td>
</tr>
</tbody>
</table>

ACE indicates angiotensin-converting enzyme; mg, milligrams; and kg, kilograms.
Reduced Left Ventricular Ejection Fraction

Angiotensin II Receptor Blockers

Angiotensin II receptor blockers are recommended inpatient with current or prior symptoms of HF and reduced LVEF who are ACE-inhibitor intolerant.

Avoid nonsteroidal anti-inflammatory drugs, most antiarrhythmic drugs, and most calcium channel blocking drugs.

Angiotensin Receptor Blockers

Inhibitors of the Renin-Angiotensin-Aldosterone System and Beta-Blockers Commonly Used for the Treatment of Patients With Heart Failure With Low Ejection Fraction (Slide 1 of 2)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Angiotensin Receptor Blockers</th>
<th>Initial Daily Dose(s)</th>
<th>Maximum Dose(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candesartan</td>
<td>Candesartan</td>
<td>4 to 8 mg once</td>
<td>32 mg once</td>
</tr>
<tr>
<td>Enalapril</td>
<td>Enalapril</td>
<td>20 to 40 mg once</td>
<td>80 mg once</td>
</tr>
</tbody>
</table>

The Risks of Aldosterone Antagonists

Addition of an aldosterone antagonist is recommended in selected patients with moderately severe to severe symptoms of HF and reduced LVEF who can be carefully monitored for preserved renal function and normal potassium concentration. Under circumstances where monitoring for hyperkalemia or renal dysfunction is not anticipated to be feasible, the risks may outweigh the benefits of aldosterone antagonists.
**Spironolactone/Aldactone**

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<tr>
<td>Aldosterone Antagonists</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spironolactone</td>
<td>12.5 to 25 mg once</td>
<td>25 mg once or twice</td>
</tr>
<tr>
<td>Eplerenone</td>
<td>25 mg once</td>
<td>50 mg once</td>
</tr>
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</table>

**Reduced Left Ventricular Ejection Fraction**

__Recommendations for Hydralazine and Nitrates__

1. The combination of hydralazine and nitrates is recommended to improve outcomes for patients self-described as African-Americans, with moderate-severe symptoms on optimal therapy with ACE inhibitors, beta blockers, and diuretics.

2. The addition of a combination of hydralazine and a nitrate is reasonable for patients with reduced LVEF who are already taking an ACE inhibitor and beta blocker for symptomatic HF and who have persistent symptoms.

__Reduced Left Ventricular Ejection Fraction__

A combination of hydralazine and a nitrate might be reasonable in patients with current or prior symptoms of HF and reduced LVEF who cannot be given an ACE inhibitor or ARB because of drug intolerance, hypotension, or renal insufficiency.
Digitalis can be beneficial in patients with current or prior symptoms of HF and reduced LVEF to decrease hospitalizations for HF.

Sacubitril/Valsartan

Nephrilysin inhibitor, sacubitril, (neutral endopeptidase; NEP) via LBQ657, the active metabolite of the prodrug sacubitril increased levels of peptides that are degraded by nephrilysin, such as natriuretic peptides.

Angiotensin angiotensin II type-1 (AT1) receptor blocker valsartan.

All-cause Mortality PARADIGM-HF
Number randomized: Ernento = 4,187  Enalapril = 4,212
All-cause mortality 711 (17.0%) versus 835 (19.8%)
Risk ratio 0.80 (0.76, 0.93) p= 0.0009
16% reduction
Sacubitril/Valsartan

ADVERSE REACTIONS:
Angioedema, Hypotension, Impaired Renal Function, Hyperkalemia
Sacubitril/Valsartan is contraindicated with concomitant use of an
angiotensin-converting enzyme (ACE) inhibitor.
If switching from an ACE inhibitor to ENTRESTO allow a washout
period of 36 hours between administration of the two drugs.
The recommended starting dose of ENTRESTO is 49/51 mg twice-
daily. Double the dose of ENTRESTO after 2 to 4 weeks to the
target maintenance dose of 97/103 mg twice daily, as tolerated.

Ivabradine

Corlanor (ivabradine) is a hyperpolarization-activated cyclic
nucleotide-gated channel blocker indicated to reduce the risk of
hospitalization for worsening heart failure in patients with stable,
symptomatic chronic heart failure with left ventricular ejection
fraction ≤ 35%, who are in sinus rhythm with resting heart rate ≥ 70
beats per minute and either are on maximally tolerated dose

Ivabradine

Contraindications: Acute decompensated heart failure, Blood
pressure less than 90/50 mmHg, Sick sinus syndrome, sinoatrial
block or 3rd degree AV block, unless a functioning demand
pacemaker is present, Resting heart rate less than 60 bpm prior to
treatment, Severe hepatic impairment, Pacemaker dependence
(heart rate maintained exclusively by the pacemaker) (4) In
combination with strong cytochrome CYP3A4 inhibitors.
**Ivabradine**

Dose Adjustment Heart Rate Dose Adjustment:
- > 60 bpm: Increase dose by 2.5 mg (given twice daily) up to a maximum dose of 7.5 mg twice daily
- 50-60 bpm: Maintain dose
- < 50 bpm or signs and symptoms of bradycardia: Decrease dose by 2.5 mg (given twice daily); if current dose is 2.5 mg twice daily, discontinue therapy

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Patients With Reduced Left Ventricular Ejection Fraction

Secondary Prevention: ICD
Implantable Cardioverter-Defibrillator

A cardioverter-defibrillator (ICD) is recommended as secondary prevention to prolong survival in patients with a history of cardiac arrest, ventricular fibrillation, or hemodynamically destabilizing ventricular tachycardia.

Reduced Left Ventricular Ejection Fraction

Primary Prevention: ICD

ICD therapy is recommended for primary prevention of sudden cardiac death to reduce total mortality in patients with nonischemic dilated cardiomyopathy or ischemic heart disease at least 40 days post-myocardial infarction, have an LVEF less than or equal to 35%, with NYHA functional class II or III symptoms while receiving chronic optimal medical therapy, and who have expectation of survival for more than 1 year.
Patients with LVEF less than or equal to 35%, sinus rhythm, and NYHA functional class III or ambulatory class IV symptoms despite recommended, optimal medical therapy and who have cardiac dyssynchrony, which is currently defined as a QRS duration greater than or equal to 0.12 seconds, should receive cardiac resynchronization therapy, with or without an ICD.

The Centers for Medicare & Medicaid Services (CMS) has determined that the evidence is sufficient to expand coverage for cardiac rehabilitation services under 42 C.F.R. § 410.49(b)(1)(vii) to beneficiaries with stable, chronic heart failure defined as patients with left ventricular ejection fraction of 35% or less and New York Heart Association (NYHA) class II to IV symptoms despite being on optimal heart failure therapy for at least six weeks. Stable patients are defined as patients who have not had recent (≤6 weeks) or planned (≤6 months) major cardiovascular hospitalizations or procedures.
A major trial of exercise and HF randomly assigned 2331 patients (mean EF, 25%; ischemic etiology, 52%) to either exercise training for 3 months or usual care. In unadjusted analyses, there was no significant difference.
When adjusted for coronary heart disease risk factors, there was an 11% reduction in all-cause mortality, cardiovascular disease mortality, or hospitalizations (P<0.03) in the exercise training group.
Cardiac Rehabilitation for Systolic Heart Failure

The ExTraMATCH study, a meta-analysis, demonstrated improved peak oxygen consumption and decreased all-cause mortality with exercise.

Cardiac rehabilitation can be useful in clinically stable patients with HF to improve functional capacity, exercise duration, HRQOL, and mortality.

Cardiac Rehabilitation for Heart Failure


Exercise training (or regular physical activity) is recommended as safe and effective for patients with HF who are able to participate to improve functional status.


