Advances in the Monitoring & Treatment of Heart Failure

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Disclosures

No disclosures
Advances in Heart Failure

• Defining Heart Failure

• Monitoring Heart Failure
  • Standard invasive techniques
  • Novel invasive techniques

• Pharmacologic Treatment of Heart Failure
  • Standard therapy
  • Novel therapy
Defining Heart Failure

Table 3. Definitions of HFrEF and HFrEF

<table>
<thead>
<tr>
<th>Classification</th>
<th>EF (%)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Heart failure with reduced ejection fraction</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>
</tr>
<tr>
<td>II. Heart failure with preserved ejection fraction</td>
<td>≥50</td>
<td>Also referred to as diastolic HF. Several different criteria have been used to further define HFrEF. The diagnosis of HFrEF 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. HFrEF, 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 HFrEF.</td>
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<tr>
<td>b. HFrEF, improved</td>
<td>&gt;40</td>
<td>It has been recognized that a subset of patients with HFrEF 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>
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EF indicates ejection fraction; HF, heart failure; HFrEF, heart failure with preserved ejection fraction; and HFrEF, heart failure with reduced ejection fraction.

- Estimated annual cost of $30 billion
- Mean cost of a heart failure related hospitalization = $23,077

Yancy et al: 2013 ACC/AHA Heart Failure Guidelines
## Defining Heart Failure

### Table 4. Comparison of ACCF/AHA Stages of HF and NYHA Functional Classifications

<table>
<thead>
<tr>
<th>ACCF/AHA Stages of HF</th>
<th>NYHA Functional Classification</th>
</tr>
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<tbody>
<tr>
<td>A At high risk for HF but without structural heart disease or symptoms of HF</td>
<td>None</td>
</tr>
<tr>
<td>B Structural heart disease but without signs or symptoms of HF</td>
<td>I No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.</td>
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<tr>
<td>C Structural heart disease with prior or current symptoms of HF</td>
<td>II Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.</td>
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<tr>
<td></td>
<td>III Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.</td>
</tr>
<tr>
<td>D Refractory HF requiring specialized interventions</td>
<td>IV Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest.</td>
</tr>
</tbody>
</table>

ACCF indicates American College of Cardiology Foundation; AHA, American Heart Association; HF, heart failure; and NYHA, New York Heart Association.

Yancy et al: 2013 ACC/AHA Heart Failure Guidelines
Monitoring Heart Failure

- **Invasive Hemodynamic Monitoring** with a pulmonary artery catheter should be performed to guide therapy in patients who have respiratory distress or clinical evidence of impaired perfusion in whom the adequacy or excess of intracardiac filling pressures cannot be determined by clinical assessment.
  - Fluid status, perfusion, or pulmonary of systemic vascular resistance is uncertain
  - Systolic pressure remains low, or is associated with symptoms despite initial therapy
  - Renal function is worsening with therapy
  - Require parenteral vasoactive agents
  - Patients who may need consideration for mechanical support device or transplantation

Yancy et al: 2013 ACC/AHA Heart Failure Guidelines
Monitoring Heart Failure

- Invasive Hemodynamic Monitoring
  - CardioMEMS
Monitoring Heart Failure

- Invasive Hemodynamic Monitoring
  - CardioMEMS HF System
    - Sensor
    - Patient electronics system
    - CardioMEMS HF System website
- The patient electronics system performs the following:
  - Powers the sensor with radiofrequency energy
  - Receives and converts information into pressure readings
Monitoring Heart Failure

• Invasive Hemodynamic Monitoring

The CHAMPION Clinical Trial Achieved Primary Safety and Efficacy Endpoints Over Study Duration

Safety endpoints based on 575 patients:
- 550 randomized + 25 consented not-randomized, not implanted
  - Objective performance criteria (OPC) based upon complication and failure rates for other HF monitoring devices and similar to OPCs accepted by the FDA

1. Freedom from Device/System Related Complications (DSRC) 567/575 (98.6%, lower 95.2% CI=97.3%)
   - Compared to Pre-specified OPC of 80%, p<0.0001
2. Freedom from Pressure Sensor Failure 550/550 100%, lower 95.2% CI=99.3%
   - Compared to Pre-specified OPC of 90%, p<0.0001
Treating Heart Failure

- Angiotensin Converting Enzyme Inhibitors
- Aldosterone Receptor Antagonists
- Angiotensin Receptor Blockers
- Beta Blockers
- Digoxin
- Diuretics
- Hydralazine & Isosorbide Dinitrate
Treating Heart Failure

- The Importance of Heart Rate
  - An elevated heart rate
    - has been found to be an independent risk factor for cardiovascular disease
    - is an independent predictor or cardiovascular morbidity and mortality
    - is associated with an increased incidence of sudden cardiac death
    - may be a marker of sympathetic nervous system activation
    - is associated with greater atherosclerosis and plaque disruption
  - A lower heart rate
    - decreases myocardial oxygen demand through the reduction in overall cardiac work
    - increases the length of diastole and diastolic filling time
    - increases intracoronary and subendothelial blood flow
Treating Heart Failure

• Intrinsic Cardiac Pacemaker
  • Heart rate is determined by slow, spontaneous depolarization of specialized pacemaker cells within the sino-atrial node.
  • When the cell’s membrane potential rises to the threshold level, an action potential is activated.
  • This slow pacemaker current is dependant on multiple ionic currents, mainly involving calcium channels.
  • Initiation of the slow depolarization phase appears to depend on a slow sodium and potassium inward current.
  • This inward current is unusual as it is activated by hyperpolarization and it was therefore named I_f or 'funny' channel.[24]
  • The channel is modulated by cAMP binding, such that adrenergic stimuli, by increasing cAMP, increase the likelihood of opening and thereby increase heart rate.[25] Cholinergic stimuli conversely decrease cAMP levels and reverse this process.[26]

• The I_f channel was discovered in 1979. Researchers sought to develop an agent capable of pure heart rate reduction.
Treating Heart Failure

• Ivabridine (Corlanor)
  • Mechanism
    • Specific inhibitor of the $I_f$ current in the sinoatrial node
    • It has no action on other channels in the heart or vascular system
    • Unlike beta blockers, it does not modify myocardial contractility and intracardiac conduction
  • Indicated to reduce the risk of hospitalization for worsening heart failure in patients with:
    • Stable symptomatic chronic heart failure
    • Left ventricular ejection fraction $\leq 35\%$
    • Sinus rhythm with heart rate $\geq 70$ AND
    • Either are on maximally tolerated dose of beta blockers OR
    • Are intolerant to beta blockers
Figure 2: Mean heart rate during the study in the total study population, by allocation groups

Lancet 2010; 376: 875-885
Treating Heart Failure

Placebo (937 events)
Ivabradine (793 events)

HR 0.82 (95% CI 0.75–0.90), p < 0.0001

Number at risk
Placebo group 3264 2868 2489 2061 1089 439
Ivabradine group 3241 2928 2600 2173 1191 447

Lancet 2010; 376: 875-885
Treating Heart Failure

- The role of neprilysin and B-type natriuretic peptide
  - Neprilysin is a neutral endopeptidase that degrades natriuretic peptides, bradykinin and adrenomedullin.
  - Inhibition of neprilysin will increase the levels of these substances thereby countering the neurohormonal overactivation that contributes to:
    - Vasoconstriction
    - Sodium retention
    - Maladaptive remodeling
Treating Heart Failure

• PARADIGM-HF
  • compared the angiotensin receptor–neprilysin inhibitor LCZ696 with enalapril in patients who had heart failure with a reduced ejection fraction.
  • randomly assigned 8442 patients with class II, III, or IV heart failure and an ejection fraction of 40% or less to receive either LCZ696 or enalapril, in addition to recommended therapy.
  • trial was stopped early after a median follow-up of 27 months because the boundary for an overwhelming benefit with LCZ696 had been crossed
Figure 2. Kaplan–Meier Curves for Key Study Outcomes, According to Study Group.
Shown are estimates of the probability of the primary composite end point (death from cardiovascular causes or first hospitalization for heart failure) (Panel A), death from cardiovascular causes (Panel B), first hospitalization for heart failure (Panel C), and death from any cause (Panel D).
References


• Heidland UE, Strauer BE. Left ventricular muscle mass and elevated heart rate are associated with coronary plaque disruption. Circulation, 2001; 104: 1477-82.


Thank You!