MANAGING PATIENTS WITH HEART FAILURE: FOCUS ON REDUCED EJECTION FRACTION

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DISCLOSURES

I have no disclosures relevant to this presentation.

OBJECTIVES

• Discuss implications of recent clinical practice guidelines of pharmacologic treatment of heart failure (HF) with reduced ejection fraction.
• Determine how to titrate optimal therapy using the most appropriate pharmacologic agents for treating adults with reduced ejection fraction.
• Review what circumstances would trigger a referral to a HF specialist.
• Apply knowledge to case scenario of patient with HF with reduced ejection fraction.

DEFINITION: HEART FAILURE WITH REDUCED EJECTION FRACTION

Clinical diagnosis of heart failure and a left ventricular ejection fraction of 40% or less
Abbreviated as HFrEF

ESTABLISHED THERAPIES FOR CHRONIC HF

• Angiotensin Converting Enzyme inhibitors (ACE-i)
• Angiotensin receptor blockers (ARBs)
• Beta-blockers (only the ones approved)
• Loop diuretics
• Aldosterone antagonists
• Hydralazine/isosorbide dinitrate (HYD/ISDN)

All (except loop diuretics) have been shown to improve symptoms, reduce hospitalization, and/or help patients live longer.

NEW TREATMENT GUIDELINES FOR HEART FAILURE WITH REDUCED EJECTION FRACTION

• Updated recommendations on biomarkers
• Two new medications for patients with HFrEF
  • Angiotensin receptor neprilysin inhibitor (ARNI) (sacubitril/valsartan)
  • Sinoatrial node modulator (ivabradine)
• Info on heart failure with preserved ejection fraction (HFpEF)
• Info on comorbidities including sleep apnea, anemia and hypertension
• Insights regarding HF prevention

We will focus on these for this presentation (about HF with reduced EF)

UPDATED RECOMMENDATIONS ON BIOMARKERS:

7 PREVENTION

- For patients at risk of developing HF, natriuretic peptide biomarker-based screening followed by team-based care (including a cardiovascular specialist optimizing GDMT) can be useful to prevent the development of left ventricular dysfunction (systolic or diastolic) or new-onset HF.

8 DIAGNOSIS

- In patients presenting with dyspnea, measurement of natriuretic peptide biomarkers is useful to support a diagnosis or exclusion of HF.

9 PROGNOSIS

- Measurement of BNP or NT-proBNP is useful for establishing prognosis or disease severity in chronic HF (unchanged from 2013).
- Measurement of baseline levels of natriuretic peptide biomarkers and/or cardiac troponin on admission to the hospital is useful to establish a prognosis in acutely decompensated HF (modified).
- During a HF hospitalization, a predischarge natriuretic peptide level can be useful to establish a post-discharge prognosis (new).
- In patients with chronic HF, measurement of other clinically available tests, such as biomarkers of myocardial injury or fibrosis, may be considered for additive risk stratification (modified).

Excerpted from: Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure with Reduced Ejection Fraction

December 2017
DOI: 10.1016/j.jacc.2017.11.025
### BETA BLOCKERS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Target Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisoprolol</td>
<td>1.25 mg q day</td>
<td>10 mg q day</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>3.125 mg bid</td>
<td>25 mg bid (if wt &lt; 85 kg), otherwise 50 mg bid</td>
</tr>
<tr>
<td>Metoprolol succinate</td>
<td>12.5-25 mg q day</td>
<td>200 mgqd</td>
</tr>
</tbody>
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Target Dose: 10 mg q day

### ACE-I (SOME EXAMPLES)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Target Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>6.25 mg tid</td>
<td>50 mg tid</td>
</tr>
<tr>
<td>Enalapril</td>
<td>2.5 mg bid</td>
<td>10-20 mg bid</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>2.5-5 mg bid</td>
<td>20-40 mg bid</td>
</tr>
<tr>
<td>Ramipril</td>
<td>1.25 mg q day</td>
<td>10 mg q day</td>
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### ARBS (SOME EXAMPLES)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Target Dose</th>
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<tbody>
<tr>
<td>Candesartan</td>
<td>4 – 8 mg q day</td>
<td>32 mg daily</td>
</tr>
<tr>
<td>Losartan</td>
<td>25 – 50 mg q day</td>
<td>150 mg daily</td>
</tr>
<tr>
<td>Valsartan</td>
<td>40 mg bid</td>
<td>160 mg twice daily</td>
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### ALDOSTERONE ANTAGONISTS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Target Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eplerenone</td>
<td>25 mg q day</td>
<td>50 mg q day</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>12.5 - 25 mg q day</td>
<td>25 – 50 mg q day</td>
</tr>
</tbody>
</table>

New recommendation: Aldosterone antagonists may reduce hospitalizations in some patients with HFpEF.

Important: Monitor kidney function and potassium within 2-3 days, again at 7 days.

### VASODILATORS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Target Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydralazine</td>
<td>25 mg tid</td>
<td>75 mg tid</td>
</tr>
<tr>
<td>Isosorbide DN</td>
<td>20 mg tid</td>
<td>40 mg tid</td>
</tr>
<tr>
<td>Fixed dose combo</td>
<td>20 mg/3.75 mg (one tab) tid</td>
<td>2 tabs tid</td>
</tr>
</tbody>
</table>

### SACUBITRIL/VALSARTAN (ARNI)

- **Indications**
  - HFrEF (EF ≤ 40%)
  - NYHA Class II or III
- **Contraindications**
- **Cautions**
  - Renal impairment
  - Angioedema (9.3% vs. 1.0%)
  - Hypotension
  - QRS prolongation
  - New or worsening atrial fibrillation
  - New or worsening pulmonary edema
  - Increased creatinine
  - Hypotension
  - Pulmonary edema
19 SACUBITRIL/VALSARTAN (ARNI)

- **Starting dose:** 24/26 mg – 49/51 mg twice daily
- **When to start with lower dose**
- **When to start with higher dose**
- **Target dose:** 97/103 mg twice daily


20 CONVERSION OF ACE-I TO ARNI (*SACUBITRIL/VALSARTAN*)

- **Need 36 hour washout period of ACE-I to avoid angioedema**
- **Would not need to do this if on an ARB**
- **eGFR <30 mL/min/1.73 m2**
- **Starting dose**
  - If taking < 10 mg enalapril (or equivalent) start with 24/26 mg twice daily
  - If taking > 10 mg enalapril (or equivalent) start with 49/51 mg twice daily
- **Reassess in 2-4 weeks**
- **If tolerance, up-titrate to 97/103 mg twice daily**
- **Ongoing monitoring (BP, electrolytes, renal function after initiation and each up titration)**


21 IVABRADINE

- **Indications:**
  - HFrEF (EF ≤ 35%)
  - On maximum tolerated doses of beta-blocker
  - Sinus rhythm with resting HR of ≥ 70 bpm
  - NYHA Class II or III HF
- **Contraindications**
- **Cautions**


22 IVABRADINE

- **Starting dose:** 2.5 – 5 mg twice daily
- **Lower dose if of conduction defects or Age ≥ 75**
- **Target dose:** titrate to heart rate 50-60 beats/minute.
- **Maximum dose:** 7.5 mg twice daily


23 PEARLS FOR STARTING THERAPY

- **Pearls for starting new patients on meds**
  - Starting ACE-I or ARBS = often better tolerated if started when a little “wet”
  - Starting beta-blockers = often better tolerated if started when a little “dry” (as long as heart rate is adequate)
  - Could start both (low doses)


24 Evaluation of the patient with heart failure

- Revised in October 2017 (new guidelines for adults)
- Symptom-limited exercise testing (SL ET)
- New York Heart Association (NYHA) class
- 6-minute walk test
- Quality of life
- 24-hour Holter monitor
- Echocardiography
- Cardiac biomarkers

TRIGGERS FOR HF PATIENT REFERRAL TO HF PROGRAM (OR SPECIALIST)

• New onset HF
• Chronic HF with high risk features
• To assist with managing guideline directed medical therapy (GDMT)
• Persistently reduced LVEF (< 35%) despite GDMT for ≥ 3 months
• Need 2nd opinion
• Annual review for established HF patients with advanced disease
• Participation in a clinical trial

CASE STUDY

• 55 year old male with HFrEF who has been seen in your HF clinic for past 6 months.
• PMH: Hx of 2 vessel coronary heart disease
• Last LVEF: 30% (after being on a stable dose of meds for ~4 months)
• Functional heart class: NYHA Class III
• Weight: 75 kg (euvolemic)

• Blood pressure 110/70 (lying & standing)
• HR 66 beats per min
• Labs: K+ 4.0, BUN 10, Creat 1.4

Is he on guideline directed medical therapy (GMDT)?
Are each of the meds at target dose?
What other treatment could be added (since he remains symptomatic)?
Switch ACE-I to ARNI?
Add Hydralazine/isosorbide dinitrate?

HF WITH PRESERVED EJECTION FRACTION

In appropriately selected patients with HFpEF (with EF ≥45%, elevated BNP levels or HF admission within 1 year, estimated glomerular filtration rate >30 mL/min, creatinine clearance < 2.5 mg/dL, potassium < 5.0mEq/L), aldosterone receptor antagonists might be considered to decrease hospitalization.

Translated Into Clinical Apps

Access this Decision Pathway and Others Through the Link Below

http://www.acc.org/decisionpathways