Acute and Chronic Heart Failure

Scott Kinkade, MD, MSPH, EdD

ACTIVITY DISCLAIMER

The material presented here is being made available by the American Academy of Family Physicians for educational purposes only. Please note that medical information is constantly changing; the information contained in this activity was accurate at the time of publication. This material is not intended to represent the only, nor necessarily best, methods or procedures appropriate for the medical situations discussed. Rather, it is intended to present an approach, view, statement, or opinion of the faculty, which may be helpful to others who face similar situations.

The AAFP disclaims any and all liability for injury or other damages resulting to any individual using this material and for all claims that might arise out of the use of the techniques demonstrated therein by such individuals, whether these claims shall be asserted by a physician or any other person. Physicians may care to check specific details such as drug doses and contraindications, etc., in standard sources prior to clinical application. This material might contain recommendations/guidelines developed by other organizations. Please note that although these guidelines might be included, this does not necessarily imply the endorsement by the AAFP.
DISCLOSURE

It is the policy of the AAFP that all individuals in a position to control content disclose any relationships with commercial interests upon nomination/invitation of participation. Disclosure documents are reviewed for potential conflict of interest (COI), and if identified, conflicts are resolved prior to confirmation of participation. Only those participants who had no conflict of interest or who agreed to an identified resolution process prior to their participation were involved in this CME activity.

All individuals in a position to control content for this session have indicated they have no relevant financial relationships to disclose.

The content of my material/presentation in this CME activity will not include discussion of unapproved or investigational uses of products or devices.

Scott Kinkade, MD, MSPH, EdD

Associate Professor, Department of Family and Community Medicine, University of Missouri School of Medicine, Columbia

Dr. Kinkade is the medical director for the family medicine inpatient service at University Hospital in Columbia, Missouri. He earned his medical degree from the University of Texas School of Medicine in Houston and completed a family medicine residency at Martin Army Community Hospital at Fort Benning, Georgia. Previously, he was director of undergraduate medical education in the military at Fort Hood, Texas, and at the University of Texas Southwestern Medical School in Dallas. He was a master educator fellow at the University of Missouri and earned a doctorate in education from the University of North Texas.
Learning Objectives

1. Use current ACC/AHA guidelines to evaluate and classify patients with suspected heart failure.
2. Use evidence-based criteria to identify appropriate diagnostic imaging and laboratory tests to identify causes or precipitating factors.
3. Establish guideline-directed medical therapy (GDMT), as indicated by the initial evaluation.
4. Develop collaborative care plans with patients that emphasize making healthy lifestyle changes and adherence to prescribed therapies.
5. Establish care coordination protocols aimed at reducing heart failure readmissions.

Associated Sessions

• (PBL) Acute and Chronic Heart Failure
HF Terminology

Heart Failure with Reduced EF
– HFrEF, systolic heart failure

EF < 40%

Heart Failure with Preserved EF
– HFpEF, diastolic heart failure

EF > 50%
HF Terminology

Heart Failure with Reduced EF  \(\text{EF} < 40\%\)  
  – HFrEF, systolic heart failure

Heart Failure with recovered EF  \(\text{EF} > 40\%\)

Heart Failure with midrange EF  \(\text{EF} 41-49\%\)

Heart Failure with Preserved EF  \(\text{EF} > 50\%\)  
  – HFpEF, diastolic heart failure

HF Classification - NYHA

I: No limitation of physical activity.

II: Slight limitation of physical activity.

III: Marked limitation of physical activity.

IV: Unable to carry out any physical activity w/o symptoms of heart failure, or symptoms of heart failure at rest.
HF Classification – AHA/ACC

A: High Risk for HF, no structural damage or signs/symptoms

B: Structural damage, no signs/symptoms

C: Structural damage with prior or current signs/symptoms

D: Refractory requiring specialized intervention
### ACC/AHA Stages vs. NYHA Functional Class

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>NYHA Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>High risk for HF</td>
<td>None</td>
</tr>
<tr>
<td>B</td>
<td>Asymptomatic</td>
<td>NYHA I</td>
</tr>
<tr>
<td>C</td>
<td>Symptomatic</td>
<td>NYHA I-IV</td>
</tr>
<tr>
<td>D</td>
<td>End-Stage</td>
<td>NYHA IV</td>
</tr>
</tbody>
</table>

### Stage A - HF prevention

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-R</td>
<td>In patients at increased risk, stage A HF, the optimal blood pressure in those with hypertension should be less than 130/80 mm Hg.</td>
<td><strong>NEW</strong>: Recommendation reflects new RCT data.</td>
</tr>
<tr>
<td>Ila</td>
<td>B-R</td>
<td>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.</td>
<td><strong>NEW</strong>: New data suggest that natriuretic peptide biomarker screening and early intervention may prevent HF.</td>
</tr>
</tbody>
</table>
STOP-HF

1,374 patients
• > 40 yo with CV risk factors
• Endpoint - Heart failure hospitalization
  - New systolic or diastolic dysfunction

Randomized

- Routine PCP care
- BNP screening and if > 50, Echo, cardiology eval

STOP-HF

New HF or new LV dysfunction

Overall

- 8.7% Control, 5.3% Intervention

- OR 0.55 (0.37-0.82) p=.003

BNP > 50

- 18.7% Control, 9.5% Intervention

- OR 0.44 (0.26-0.73) p=.002

JAMA. 2013;310:66-74
HF – Case 1

64 yo female c/o lower extremity edema. No shortness of breath, no angina. She can walk up 2 flights of stairs and do her shopping. No orthopnea/PND.

PMH: HTN, hyperlipidemia
Meds: amlodipine 10 mg, atorvastatin 20 mg
Exam: BP 138/70, P 68 BMI 24
  Neck: JVP < 6cm
  Lungs – Clear
  CV – RRR, no M/G
  Ext – 1+ BLE edema

Does this patient have heart failure?

Poll Question #1

Does this patient have heart failure?

A. No
B. Yes, at least Stage A HF
C. Yes, NYHA class 1 HF
D. Yes, NYHA class 2 HF
E. Not enough information to ascertain
HF – Case 1

64 yo female with
HTN and hyperlipidemia
NO SOB, orthopnea, PND
1+ BLE edema

“The cardinal manifestations of HF are dyspnea and fatigue, which may limit exercise tolerance, and fluid retention, which may lead to pulmonary and/or splanchnic congestion and/or peripheral edema.”

Circulation. 2013;128:e240-e327

---

Case 1

**BNP**

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>A</td>
<td>In patients presenting with dyspnea, measurement of natriuretic peptide biomarkers is useful to support a diagnosis or exclusion of HF.</td>
<td>MODIFIED: 2013 acute and chronic recommendations have been combined into a diagnosis section.</td>
</tr>
</tbody>
</table>

Circulation 2017; 136(6):e137-e161
Case 1

- BNP 855
- Echo EF 65% with grade 1 diastolic dysfunction

⇒ Stage B HFpEF, NYHA Class 1 HF

- Treatments?
Poll Question #2

Which treatment is best for HFpEF?

A. ACE inhibitor (lisinopril)
B. Beta-blocker (metoprolol succinate)
C. ARB (candesartan)
D. Calcium-channel blocker (amlodipine)
E. None of the above have been proven to help HFpEF

HFpEF

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B</td>
<td>Control systolic and diastolic BP</td>
</tr>
<tr>
<td>I</td>
<td>C</td>
<td>Diuretics should be used for relief of symptoms due to volume overload</td>
</tr>
<tr>
<td>IIA</td>
<td>C</td>
<td>Coronary revascularization is reasonable.</td>
</tr>
<tr>
<td>IIA</td>
<td>C</td>
<td>Management of AF</td>
</tr>
<tr>
<td>IIA</td>
<td>C</td>
<td>Use beta-blocking agents, ACE inhibitors, and ARBs for HTN.</td>
</tr>
<tr>
<td>IIB</td>
<td>B-R</td>
<td>In appropriately selected patients with HFpEF (with EF ≥45%, elevated BNP levels or HF admission within 1 year, estimated GFR&gt;30 mL/min, creatinine &lt;2.5 mg/dL, potassium &lt;5.0 mEq/L), aldosterone receptor antagonists might be considered to decrease hospitalizations.</td>
</tr>
<tr>
<td>IIB</td>
<td>B</td>
<td>The use of ARBs might be considered to decrease hospitalizations for patients with HFpEF.</td>
</tr>
</tbody>
</table>

Circulation 2017; 136(6):e137-e161
**HF Treatment - Diuretics**

<table>
<thead>
<tr>
<th><strong>Loop Diuretics</strong></th>
<th><strong>Thiazide Diuretics</strong></th>
<th><strong>Potassium-sparing Diuretics</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Furosemide</td>
<td>Hydrochlorothiazide</td>
<td>Spironolactone</td>
</tr>
<tr>
<td>20-40 mg</td>
<td>20-40 mg</td>
<td>12-25 mg</td>
</tr>
<tr>
<td>40-240 mg</td>
<td>40-240 mg</td>
<td>25 mg</td>
</tr>
<tr>
<td>Torsemide</td>
<td>Metolazone</td>
<td>Eplerenone</td>
</tr>
<tr>
<td>5-10 mg</td>
<td>5-10 mg</td>
<td>25 mg</td>
</tr>
<tr>
<td>10-20 mg</td>
<td>10-20 mg</td>
<td>50 mg</td>
</tr>
<tr>
<td>Bumetanide</td>
<td>Chlorthalidone</td>
<td></td>
</tr>
<tr>
<td>0.5 – 1 mg</td>
<td>12.5-25 mg</td>
<td></td>
</tr>
<tr>
<td>1-5 mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HFpEF - TOPCAT results**

- NEJM 2014; 370:1383-1392
HFpEF - TOPCAT

Circulation. 2015;131:34-42

HFpEF - TOPCAT

NEJM. 2017;376: 1690–1692
Case 2

Same patient 5 years later (65 yo F w/ HTN, HLD, HFpEF)

**CC:** increased swelling and shortness of breath with usual activity

**Meds:** amlodipine, atorvastatin, spironolactone 25 mg, furosemide 20 mg

**Exam:** BP 132/68, P 68. BMI 28

- Neck: JVP > 10cm
- CV – RRR, +S3
- Lungs – crackles lower 1/3
- Ext – 2+ BLE edema

**BNP:** 1,800

**Echo:** dilated LV, EF 35%

→ Now NYHA II, HF stage C

Poll Question #3

What medication change would you make?

A. start carvedilol
B. start digoxin
C. start lisinopril
D. stop spironolactone
E. change amlodipine to diltiazem
RRR in all-cause mortality from RCTs

![Graph showing RRR in all-cause mortality for different classes of medications.]

adapted from JAMA Cardiol. 2016;1:714–717

HFrEF – ACEI and ARB

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Daily Dose(s)</th>
<th>Target Doses(s)</th>
<th>Mean Doses Achieved in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACE Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Captopril</td>
<td>6.25 mg 3 times</td>
<td>50 mg 3 times</td>
<td>122.7 mg/d</td>
</tr>
<tr>
<td>Enalapril</td>
<td>2.5 mg twice</td>
<td>10 to 20 mg twice</td>
<td>16.6 mg/d</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>2.5 to 5 mg once</td>
<td>20 to 40 mg once</td>
<td>32.5 to 35.0 mg/d</td>
</tr>
<tr>
<td><strong>ARBs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candesartan</td>
<td>4 to 8 mg once</td>
<td>32 mg once</td>
<td>24 mg/d</td>
</tr>
<tr>
<td>Losartan</td>
<td>25 to 50 mg once</td>
<td>150 mg once</td>
<td>129 mg/d</td>
</tr>
<tr>
<td>Valsartan</td>
<td>20 to 40 mg twice</td>
<td>160 mg twice</td>
<td>254 mg/d</td>
</tr>
</tbody>
</table>

Circulation 2017; 136(6):e137-e161
HFrEF – ACEI or ARB

1. Decreases mortality
2. Creatinine and potassium limits:
   - Cr < 3.0 mg/dl
   - GFR > 30% drop
   - K+ > 5
3. No ACEI + ARB
4. If intolerant, try hydralazine/ISDN combination

HFrEF - Beta-blockers

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Daily Dose(s)</th>
<th>Target Doses(s)</th>
<th>Mean Doses Achieved in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta Blockers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>1.25 mg once</td>
<td>10 mg once</td>
<td>8.6 mg/d</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>3.125 mg twice</td>
<td>&lt;85 kg 25 mg twice &gt;85 kg 50 mg twice</td>
<td>37 mg/d</td>
</tr>
<tr>
<td>Metoprolol succinate</td>
<td>12.5 to 25 mg once</td>
<td>200 mg once</td>
<td>159 mg/d</td>
</tr>
</tbody>
</table>

Circulation 2017; 136(6):e137-e161
HFrEF - Beta-blockers

1. Decreases mortality
2. Start when stable, euvolemic
3. Stop or decrease if worsened HF symptoms
4. Titrate to target study dose

HF - MRA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Daily Dose(s)</th>
<th>Target Doses(s)</th>
<th>Mean Doses Achieved in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spironolactone</td>
<td>12.5 to 25 mg qd</td>
<td>25 mg qd</td>
<td>26 mg/d</td>
</tr>
<tr>
<td>Eplerenone</td>
<td>25 mg qd</td>
<td>50 mg qd</td>
<td>42.6 mg/d</td>
</tr>
</tbody>
</table>

Circulation 2017; 136(6):e137-e161
## HFrEF – MRA trials

<table>
<thead>
<tr>
<th></th>
<th>ACE/ARB</th>
<th>B-Blocker</th>
<th>Mortality Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>RALES (spironolactone)</td>
<td>94%</td>
<td>10%</td>
<td>35% vs. 46% RR 0.70 (95% CI 0.59-0.82)</td>
</tr>
<tr>
<td>Emphasis-HF (eplerenone)</td>
<td>94%</td>
<td>87%</td>
<td>12.5% vs. 15.5% HR 0.76 (95% CI 0.62 to 0.93)</td>
</tr>
<tr>
<td>Ephesus (eplerenone)</td>
<td>86%</td>
<td>75%</td>
<td>14.4% vs. 16.7% RR 0.85 (95% CI 0.75-0.96)</td>
</tr>
</tbody>
</table>

## HFrEF - MRA

1. Creatinine <2.5 mg/dL in men or <2.0 mg/dL in women (or estimated GFR > 30 mL/min) and potassium < 5.0
2. Caution: elderly (calculate GFR), higher dose ACEI or ARB, creatinine >1.5
3. Don’t use ACEI + ARB + MRA
4. Discontinue (or lower) K+ supplements
5. Monitor closely
## HFrEF – Hydralazine/Isosorbide

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Daily Dose(s)</th>
<th>Target Doses(s)</th>
<th>Mean Doses Achieved in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hydralazine &amp; Isosorbide Dinitrate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fixed dose combination</td>
<td>37.5 mg hydralazine/20 mg isosorbide dinitrate 3 times daily</td>
<td>75 mg hydralazine/40 mg isosorbide dinitrate 3 times daily</td>
<td>~175 mg hydralazine/90 mg isosorbide dinitrate daily</td>
</tr>
<tr>
<td>Hydralazine and isosorbide dinitrate</td>
<td>Hydralazine: 25 to 50 mg, 3 or 4 times daily</td>
<td>Hydralazine: 300 mg daily in divided doses and isosorbide dinitrate 120 mg daily in divided doses</td>
<td></td>
</tr>
</tbody>
</table>

Circulation 2017; 136(6):e137-e161

## HFrEF – Hydralazine/Isosorbide

1. Reduced mortality
2. Class 1 indication – “black patients” on optimal ACEI / ARB and B-blocker and NYHA III-IV
3. Class 2b indication – patients intolerant of ACEI / ARB
# HFrEF - ARNI

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/ Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.</td>
<td>NEW: New clinical trial data necessitated this recommendation.</td>
</tr>
</tbody>
</table>

**PARADIGM-HF - Sacubitril/Valsartan**

PARADIGM-HF (n=8,400)

- NYHA II-IV
- LVEF <35%
- BNP > 150 or recent HF hospitalization
- Tolerate equivalent of 10 mg enalapril daily
- Systolic BP ≥ 95 mm Hg, eGFR ≥ 30 ml/min/1.73 m² and serum K ≤ 5.4 mEq/L at randomization
- B-blocker (93%), MRA (54%)
**Sacubitril/Valsartan (Entresto)**

- Off ACEI for at least 36 hours
- Contraindicated in patients with history of angioedema
- Most common side effect is hypotension
- Monitor renal function and potassium
- Start at 24/26 mg → 49/51 mg → 97/103 mg BID
- Monitor NT-proBNP rather than BNP

---

**PARADIGM-HF: Cardiovascular Death or Heart Failure Hospitalization (Primary Endpoint)**

![Graph showing Kaplan-Meier Estimate of Cumulative Rates (%)](image)

- **Enalapril** (n=4212)
  - Days After Randomization: 0, 180, 360, 540, 720, 900, 1080, 1260
  - Kaplan-Meier Estimate: 0, 8, 16, 24, 32, 40
  - Kaplan-Meier Estimate at 1117 days: 914%

- **LCZ696** (n=4187)
  - Kaplan-Meier Estimate at 1117 days: 914%

**HR = 0.80 (0.73-0.87)**

**P = 0.0000002**

**Number needed to treat = 21**

Packer, M ESC Congress 2014 Barcelona
PARADIGM-HF: Cardiovascular Death

Enalapril (n=4212)
HR = 0.80 (0.71-0.89)
P = 0.00004
Number need to treat = 32

LCZ696 (n=4187)

Kaplan-Meier Estimate of Cumulative Rates (%)

Days After Randomization

PARADIGM-HF: All-Cause Mortality

Enalapril (n=4212)
HR = 0.84 (0.76-0.93)
P < 0.0001

LCZ696 (n=4187)

Kaplan-Meier Estimate of Cumulative Rates (%)

Days After Randomization

Packer, M ESC Congress 2014 Barcelona
HFrEF - Ivabradine

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HFrEF (LVEF ≤35%) who are receiving GDEM*, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest.</td>
<td>NEW: New clinical trial data.</td>
</tr>
</tbody>
</table>

NEW: New clinical trial data.

Circulation 2017; 136(6):e137-e161

---

HFrEF - Ivabradine

SHIFT (Systolic Heart failure treatment with the I$_{f}$ inhibitor ivabradine Trial)

- 6,500 pts
- LVEF <35% on standard background therapy
- Sinus rhythm > 70

CV death or hospital admission for worsening HF
- HR 0.82 (0.75-0.90) p<0.0001
- HR 0.90 (0.8-1.02) p=0.092

All-cause mortality
- HR 0.74 (0.58-0.94) p=0.014

Death from heart failure
- HR 0.89 (0.82-0.96) p < 0.003

All-cause hospital admission

Lancet. 2010;376:875-885
HFrEF Stage C

ACEI or ARB and B-Blocker

Still symptomatic with EF <40% ?

Add MR antagonist

Tolerating ACEI / ARB

African-American

SR w/ HR > 70

AR/ARNI

Hydral/ISDN

Ivabradine

NYHA class II-III, LVEF ≤ 35% (> 1yr survival, >40d post MI)

NYHA class II-IV, LVEF ≤ 35%, NSR & QRS > 150 ms with LBBB

Referral for ICD

Referral for CRT or CRT-D
HFrEF - Stage C

ACEI or ARB
+ B-blocker
+ Diuretic

NYHA II-IV, cr cl > 30, K < 5 → Aldosterone Antagonist
NYHA II-III, Adequate BP on ACEI or ARB, no CI to ARNI → Change ACEI or ARB to ARNI
NYHA III-IV in black patients → Hydralazine/ISDN
NYHA II-III, LVEF < 35%, (> 1 yr survival, 40d post MI) → ICD
NYHA II-IV, LVEF < 35%, NSR & QRS > 150 ms with LBB → CRT or CRT-D
NYHS class II-III, NSR, HR > 70, maximally tolerated beta blocker → Ivabradine

HF Pearls and Myths

• Diuretics
• Diabetes
• Salt intake
• Fluid restriction
Practice Recommendations

1. Echo to evaluate LV function
2. Diuresis
3. Start therapies that decrease mortality
4. Increase to maximally tolerated doses
5. Combine therapies

Contact Information

Scott Kinkade, MD, EdD
Kinkades@health.missouri.edu
Questions