Controversies in the management of heart failure - 2017

Clyde W. Yancy, MD, MSc
Professor of Medicine,
Professor, Medical Social Science
Chief, Cardiology
Associate Director, Bluhm CV Institute
&
Vice-Dean, Diversity & Inclusion
Northwestern University, FSM
&
Deputy Editor, JAMA Cardiology

No relevant disclosures
DISCLOSURES

• Consultant/speaker/honoraria: none

• Editor duties: JAMA Cardiology, Deputy Editor; Journal of the American College of Cardiology- senior associate editor (HF); American Journal of Cardiology, American Heart Journal, Circulation; Circulation-Heart Failure- editorial boards

• Guideline writing committees: Chair, ACC/AHA, chronic HF; member, atrial fibrillation; hypertrophic cardiomyopathy; syncope guideline committees. Chair, Performance Measures, Sudden Cardiac Death; Chair, ACC HF Consensus Pathways

• Federal appointments: FDA: Immediate Past Chair, Cardiovascular Device Panel; ad hoc consultant; NIH – Scientific Management and Review Board; AHRQ- adhoc consultant; NHLBI- consultant; PCORI- former methodology committee member; IOM- writing group member

• Volunteer Appointments: American Heart Association- President, American Heart Association, 2009-2010; American College of Cardiology, Founder-CREDO
Controversies in the Management of Heart Failure - 2017

• Incorporating new clinical practice guidelines
  – What’s new?
  – How will practice be changed?

• Identifying a new phenotype - heart failure with improved ejection fraction
  – What is this?
  – What’s the natural history?
  – Can it be manipulated?

• Device therapy in 2017
  – is the ICD still indicated?
  – Who gets a CRT device
### Stages, Phenotypes and Treatment of HF

#### STAGE A
At high risk for HF but without structural heart disease or symptoms of HF

- **Goals**
  - Control symptoms
  - Improve HRQOL
  - Prevent hospitalization
  - Prevent mortality

- **Strategies**
  - Identification of comorbidities

- **Treatment**
  - Diuresis to relieve symptoms of congestion
  - Follow guideline driven indications for comorbidities, e.g., HTN, AF, CAD, DM
  - Revascularization or valvular surgery as appropriate

- **Drugs**
  - ACEI or ARB as appropriate
  - Beta blockers as appropriate

- **In selected patients**
  - ICD
  - Revascularization or valvular surgery as appropriate

#### STAGE B
Structural heart disease but without signs or symptoms of HF

- **Goals**
  - Control symptoms
  - Improve HRQOL
  - Prevent hospitalization
  - Prevent mortality

- **Strategies**
  - Identification of comorbidities

- **Treatment**
  - Diuresis to relieve symptoms of congestion
  - Follow guideline driven indications for comorbidities, e.g., HTN, AF, CAD, DM
  - Revascularization or valvular surgery as appropriate

- **Drugs**
  - ACEI or ARB as appropriate
  - Beta blockers as appropriate

- **In selected patients**
  - ICD
  - Revascularization or valvular surgery as appropriate

#### STAGE C
Structural heart disease with prior or current symptoms of HF

- **Goals**
  - Control symptoms
  - Patient education
  - Prevent hospitalization
  - Prevent mortality

- **Drugs for routine use**
  - Diuretics for fluid retention
  - ACEI or ARB
  - Beta blockers
  - Aldosterone antagonists

- **Options**
  - Advanced care measures
  - Heart transplant
  - Chronic inotropes
  - Temporary or permanent MCS
  - Experimental surgery or drugs

- **In selected patients**
  - CRT
  - ICD
  - Revascularization or valvular surgery as appropriate

### Heart Failure

- **Goals**
  - Control symptoms
  - Patient education
  - Prevent hospitalization
  - Prevent mortality

- **Drugs for routine use**
  - Diuretics for fluid retention
  - ACEI or ARB
  - Beta blockers
  - Aldosterone antagonists

- **Options**
  - Advanced care measures
  - Heart transplant
  - Chronic inotropes
  - Temporary or permanent MCS
  - Experimental surgery or drugs

- **In selected patients**
  - CRT
  - ICD
  - Revascularization or valvular surgery as appropriate

---

Yancy C, et al. JACC, 2013
New Guidelines Have Emerged - 2016

2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America

Developed in Collaboration With the International Society for Heart and Lung Transplantation

WRITING COMMITTEE MEMBERS*

Clyde W. Yancy, MD, MSc, MACC, FAHA, FHFSA, Chair
Mariell Jessup, MD, FACC, FAHA, FESC, Vice Chair

Biykem Bozkurt, MD, PhD, FACC, FAHA†
Javed Butler, MD, MBA, MPH, FACC, FAHA‡
Donald E. Casey, Jr, MD, MPH, MBA, FACC§
Monica M. Colvin, MD, FAHA¶
Mark H. Drazner, MD, MSc, FACC, FAHA‡
Gerasimos Filippatos, MD, FESC
Gregg C. Fonarow, MD, FACC, FAHA, FHFSA‡
Michael M. Givertz, MD, FACC, FHFSA¶
### SUMMARY OF ACC/AHA/HFSA 2016 HF Guidelines; Focused Update

<table>
<thead>
<tr>
<th>Patient population</th>
<th>Treatment</th>
<th>Recommendation and LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2013 ACC/AHA guidelines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For all patients with HFrEF with volume overload, NYHA class II–IV</td>
<td>• Loop diuretics</td>
<td>Class I, LOE C</td>
</tr>
<tr>
<td></td>
<td>• In addition to ACE inhibitor or ARB and β-blocker</td>
<td></td>
</tr>
<tr>
<td>For persistently symptomatic African American patients, NYHA class III–IV, to</td>
<td>• Hydral-nitrates</td>
<td>Class I, LOE A</td>
</tr>
<tr>
<td>reduce morbidity and mortality</td>
<td>• In addition to ACE inhibitor, or ARB and β-blocker</td>
<td></td>
</tr>
<tr>
<td>For patients with NYHA class II–IV with eGFR &gt;30 ml/min/1.73 m² and K⁺ &lt;5.0 mEq/l</td>
<td>• Mineralocorticoid-receptor antagonists</td>
<td>Class I, LOE A</td>
</tr>
<tr>
<td>to reduce morbidity and mortality</td>
<td>• In addition to ACE inhibitor or ARB in conjunction with β-blocker</td>
<td></td>
</tr>
<tr>
<td><strong>2016 ACC/AHA/HFSA guideline update</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For patients with chronic HFrEF, to reduce morbidity and mortality</td>
<td>• ARNI in conjunction with β-blocker</td>
<td>Class I, LOE B–R</td>
</tr>
<tr>
<td>For patients with chronic symptomatic HFrEF, NYHA class II–III, who tolerate an</td>
<td>• ARNI to replace an ACE inhibitor or ARB</td>
<td>Class I, LOE B–R</td>
</tr>
<tr>
<td>ACE inhibitor or ARB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For patients with stable chronic HFrEF (LVEF ≤35%), NYHA class II–III, who are</td>
<td>• Ivabradine in addition to ACE inhibitor or ARB and β-blocker</td>
<td>Class IIa, LOE B–R</td>
</tr>
<tr>
<td>in sinus rhythm with a heart rate ≥70 bpm at rest, to reduce heart failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hospitalization</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Pharmacologic Treatment for Stage C HFrEF

**Strategies:**
- Cardiac Rehab
- Disease Management
- Process Improvement
- Patient Education
- Frailty Assessment
- Palliative Care
- Genetic Counseling

**Devices:**
- ICD
- CRT/D
- Remote PA monitoring

**HFrEF Stage C NYHA Class I – IV Treatment:**
- For NYHA class II-IV patients. Provided estimated creatinine >30 mL/min and K+ <5.0 mEq/dL.
- For persistently symptomatic African Americans, NYHA class III-IV.
- For NYHA class II-IV patients. Provided estimated creatinine >30 mL/min and K+ <5.0 mEq/dL.

**Class I, LOE A**
- ACEI or ARB AND Beta Blocker

**For all volume overload, NYHA class II-IV patients**
- Add Loop Diuretics

**For persistently symptomatic African Americans, NYHA class III-IV**
- Add Hydral-Nitrates

**For NYHA class II-IV patients. Provided estimated creatinine >30 mL/min and K+ <5.0 mEq/dL**
- Add Aldosterone Antagonist

**Valsartan/Sacubutril, COR I**

**Ivabradine. COR IIa**
Yancy et al
2017 ACC/AHA/HFSA Heart Failure Focused Update

2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America

Developed in Collaboration With the American Academy of Family Physicians, American College of Chest Physicians, and International Society for Heart and Lung Transplantation

WRITING GROUP MEMBERS*

Clyde W. Yancy, MD, MSc, MACC, FAHA, Chair
Mariell Jessup, MD, FACC, FAHA, Vice Chair

Biykem Bozkurt, MD, PhD, FACC, FAHA†
Javed Butler, MD, MBA, MPH, FACC, FAHA*†
Donald E. Casey, Jr, MD, MPH, MBA, FACC§
Monica M. Colvin, MD, FAHA
Mark H. Drazner, MD, MSc, FACC, FAHA, FHFS†
Gerasimos S. Filippatos, MD*
Gregg C. Fonarow, MD, FACC, FAHA, FHFS†
Michael M. Givertz, MD, FACC, FHFS*†

Steven M. Hollenberg, MD, FACC#
JoAnn Lindenfeld, MD, FACC, FAHA, FHFS*¶
Frederick A. Masoudi, MD, MSPH, FACC**
Patrick E. McBride, MD, MPH, FACC††
Pamela N. Peterson, MD, FACC, FAHA†
Lynne Warner Stevenson, MD, FACC*†
Cheryl Westlake, PhD, RN, ACNS-BC, FAHA, FHFS¶

Northwestern Medicine
2017 New Treatment Algorithm

Yancy et al
2017 ACC/AHA/HFSA Heart Failure Focused Update

Figure 2. Treatment of HFrEF Stage C and D

Step 1: Establish Dx of HFrEF; assess volume; initiate GDMT

Step 2: Consider the following patient scenario

Step 3: Implement indicated GDMT. Choices are not mutually exclusive, and no order is inferred

Step 4: Reassess symptoms

Step 5: Consider additional therapy

- Palliative care (COR I)
- Transplant (COR I)
- LVAD (COR IIa)
- Investigational studies

NYHA class II-IV, provided est. CrCl > 30 mL/min & K+ < 5.0 mEq/L

NYHA class II-III HF adequate BP on ACEI or ARB; No CI to ARB or sacubitril

NYHA class II-III HF

NYHA class III-IV, in black patients

NYHA class II-III, LVEF ≥ 35%; (caveat: < 1 y survival, > 40 d post MI)

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

NYHA class II-III, NSR, heart rate ≥ 70 bpm on maximally tolerated dose beta blocker

Adrenergic antagonist (COR I)

Discontinue ACEI or ARB; Initiate ARNI* (COR I)

Hydral-Nitrates† (COR I)

ICD (COR I)

CRT or CRT-D‡ (COR I)

Ivabradine (COR IIa)

Continue GDMT with serial reassessment & optimized dosing/adherence
ESC HFrEF Treatment Algorithm

**Patient with symptomatic** HFrEF**b**

- Therapy with ACE-I**a** and beta-blocker
  - (Up-titrate to maximum tolerated evidence-based doses)

  - Still symptomatic and LVEF ≤35%
    - No
    - Yes
      - Add MR antagonist**c**
        - (up-titrate to maximum tolerated evidence-based dose)
      - Still symptomatic and LVEF ≤35%
        - No
        - Yes
          - Diuretics to relieve symptoms and signs of congestion
          - If LVEF ≤35% despite OMT or a history of symptomatic VT/VF, implant ICD

          - Able to tolerate ACEI (or ARB)**d**
            - Sinus rhythm, QRS duration ≥130 msec
            - Sinus rhythm**, HR ≥70 bpm

            - ARNI to replace ACE-I
            - Evaluate need for CRT**e**
            - Ivabradine

          - These above treatments may be combined if indicated

          - Resistant symptoms
            - Yes
              - Consider digoxin or H-ISDN or LVAD, or heart transplantation
            - No
              - No further action required
              - Consider reducing diuretic dose
### 7.3.3. Pharmacological Treatment for Stage C HFpEF: Recommendations

<table>
<thead>
<tr>
<th>Recommendations for Stage C HFpEF</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COR</strong></td>
<td><strong>LOE</strong></td>
</tr>
<tr>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>IIb</td>
<td>B-R</td>
</tr>
</tbody>
</table>

See Online Data Supplement C.
Prevalence and prognostic significance of HF Stages

Survival (years)

Ammar et al. *Circulation* 2007; 115:1563
Lifetime risk for HF; indexed to blood pressure & sex

- Men:
  - BP <140/<90: 15.6%
  - BP 140-159/90-99: 27.4%
  - BP ≥160/≥100: 29.5%

- Women:
  - BP <140/<90: 12%
  - BP 140-159/90-99: 20.4%
# Primary and Secondary Outcomes and Renal Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients (%)</td>
<td>% per year</td>
<td>no. of patients (%)</td>
<td>% per year</td>
</tr>
<tr>
<td>All participants</td>
<td>(N = 4678)</td>
<td></td>
<td>(N = 4683)</td>
<td></td>
</tr>
<tr>
<td>Primary outcome†</td>
<td>243 (5.2)</td>
<td>1.65</td>
<td>319 (6.8)</td>
<td>2.19</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>97 (2.1)</td>
<td>0.65</td>
<td>116 (2.5)</td>
<td>0.78</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>40 (0.9)</td>
<td>0.27</td>
<td>40 (0.9)</td>
<td>0.27</td>
</tr>
<tr>
<td>Stroke</td>
<td>62 (1.3)</td>
<td>0.41</td>
<td>70 (1.5)</td>
<td>0.47</td>
</tr>
<tr>
<td>Heart failure</td>
<td>62 (1.3)</td>
<td>0.41</td>
<td>100 (2.1)</td>
<td>0.67</td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>37 (0.8)</td>
<td>0.25</td>
<td>65 (1.4)</td>
<td>0.43</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>155 (3.3)</td>
<td>1.03</td>
<td>210 (4.5)</td>
<td>1.40</td>
</tr>
<tr>
<td>Primary outcome or death</td>
<td>332 (7.1)</td>
<td>2.25</td>
<td>423 (9.0)</td>
<td>2.90</td>
</tr>
<tr>
<td>Participants with CKD at baseline</td>
<td>(N = 1330)</td>
<td></td>
<td>(N = 1316)</td>
<td></td>
</tr>
<tr>
<td>Composite renal outcome‡</td>
<td>14 (1.1)</td>
<td>0.33</td>
<td>15 (1.1)</td>
<td>0.36</td>
</tr>
<tr>
<td>≥50% reduction in estimated GFR§</td>
<td>10 (0.8)</td>
<td>0.23</td>
<td>11 (0.8)</td>
<td>0.26</td>
</tr>
<tr>
<td>Long-term dialysis</td>
<td>6 (0.5)</td>
<td>0.14</td>
<td>10 (0.8)</td>
<td>0.24</td>
</tr>
<tr>
<td>Kidney transplantation</td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Incident albuminuria¶</td>
<td>49/526 (9.3)</td>
<td>3.02</td>
<td>59/500 (11.8)</td>
<td>3.90</td>
</tr>
<tr>
<td>Participants without CKD at baseline‡</td>
<td>(N = 3332)</td>
<td></td>
<td>(N = 3345)</td>
<td></td>
</tr>
<tr>
<td>≥30% reduction in estimated GFR to &lt;60 ml/ min/1.73 m²§</td>
<td>127 (3.8)</td>
<td>1.21</td>
<td>37 (1.1)</td>
<td>0.35</td>
</tr>
<tr>
<td>Incident albuminuria¶</td>
<td>110/1769 (6.2)</td>
<td>2.00</td>
<td>135/1831 (7.4)</td>
<td>2.41</td>
</tr>
</tbody>
</table>

* CI denotes confidence interval, and CKD chronic kidney disease.
† The primary outcome was the first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.
‡ The composite renal outcome for participants with CKD at baseline was the first occurrence of a reduction in the estimated GFR of 50% or more, long-term dialysis, or kidney transplantation.
§ Reductions in the estimated GFR were confirmed by a second laboratory test at least 90 days later.
¶ Incident albuminuria was defined by a doubling of the ratio of urinary albumin (in milligrams) to creatinine (in grams) from less than 10 at baseline to greater than 10 during follow-up. The denominators for number of patients represent those without albuminuria at baseline.
|| No long-term dialysis or kidney transplantation was reported among participants without CKD at baseline.

### Treatment of Hypertension to Prevent HF:

#### Treatment effects of blood pressure lowering on heart failure outcomes in landmark hypertension trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of participants</th>
<th>Inclusion criteria</th>
<th>Intervention</th>
<th>Duration (yr)</th>
<th>Mean BP difference between groups (mmHg)</th>
<th>Absolute rates of heart failure</th>
<th>Relative reduction of heart failure (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHEP 1997</td>
<td>4,736</td>
<td>(\geq 60) yrs; SBP (\geq 160) mmHg</td>
<td>Chlorthalidone ± atenolol</td>
<td>4.5</td>
<td>-26.0 / -8.9</td>
<td>2.3% vs. 4.4%</td>
<td>RR 0.51 (0.37-0.71)</td>
</tr>
<tr>
<td>HYVET 2008</td>
<td>3,845</td>
<td>(\geq 80) yrs; SBP (\geq 160) mmHg</td>
<td>Indapamide ± perindopril</td>
<td>2.1</td>
<td>-15.0 / -6.1</td>
<td>5.3% vs. 14.8%</td>
<td>RR 0.36 (0.22-0.58)</td>
</tr>
<tr>
<td>ALLHAT 2002</td>
<td>33,357</td>
<td>(\geq 55) years; HTN + 1 CV risk factor</td>
<td>Chlorthalidone vs. Amlodipine; Chlorthalidone vs. Lisinopril</td>
<td>4.9</td>
<td>-0.8 / +0.8</td>
<td>7.7% vs. 10.2%</td>
<td>RR 0.62 (0.48-0.75)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ramipril</td>
<td>4.5</td>
<td>-3 / -2</td>
<td>9.0% vs. 11.5%</td>
<td>RR 0.77 (0.67-0.87)</td>
</tr>
<tr>
<td>SPRINT 2015</td>
<td>9,361</td>
<td>SBP (\geq 130) mmHg; increased CVD risk without DM</td>
<td>SBP target &lt;120 mmHg vs. SBP target &lt;140 mmHg</td>
<td>3.3</td>
<td>-18.2 / -9.4</td>
<td>1.3%/yr vs. 2.1%/yr</td>
<td>HR 0.62 (0.45-0.84)</td>
</tr>
</tbody>
</table>

For ALLHAT, mean blood pressure differences. Data for the chlorthalidone vs. doxazosin comparison is not presented since this arm was terminated early due to harm from doxazosin.
## The Prevention of Heart Failure

### 2017 Focused Update of the 2013 ACC/AHA HF Guidelines

<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 (189-193).</td>
<td>NEW: Recommendation reflects new RCT data.</td>
</tr>
</tbody>
</table>

A large RCT demonstrated that in those with increased cardiovascular risk (defined as age >75 years, established vascular disease, chronic renal disease, or a Framingham Risk Score >15%), control of blood pressure to a goal systolic pressure of <120 mm Hg, as determined by blood pressure assessment as per research protocol, was associated with a significant reduction in the incidence of HF (191) and an overall decrease in cardiovascular death. Blood pressure measurements as generally taken in the office setting are typically 5 to 10 mm Hg higher than research measurements; thus, the goal of <130/80 mm Hg is an approximation of the target blood pressure in conventional practice. **Targeting a significant reduction in systolic blood pressure in those at increased risk for cardiovascular disease is a novel strategy to prevent HF.**
New Guideline Takeaway messages:

• New effective medical therapies have now been fully incorporated in evidence based guideline directed treatment algorithms
• There is an increasing complexity in the treatment of HFrEF; this will require careful assessment of the clinical context/scenario
• The first therapy specifically for HFpEF has been endorsed
• Powerful new data should drive the PREVENTION of heart failure
• Avoiding entry into the “HF Club” is the best therapeutic approach
9. Important Comorbidities in HF

9.2. Anemia: Recommendations

<table>
<thead>
<tr>
<th>Recommendations for Anemia</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>COR</td>
<td>LOE</td>
</tr>
<tr>
<td>IIb</td>
<td>B-R</td>
</tr>
<tr>
<td>III: No Benefit</td>
<td>B-R</td>
</tr>
<tr>
<td>----------------</td>
<td>-----</td>
</tr>
<tr>
<td>See Online Data Supplement D.</td>
<td></td>
</tr>
</tbody>
</table>
### 9.5.2. Treating Hypertension in Stage C HFrEF: Recommendation

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>C-EO</td>
<td>Patients with HFrEF and hypertension should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg (191).</td>
<td>NEW: Recommendation has been adapted from recent clinical trial data but not specifically tested per se in a randomized trial of patients with HF.</td>
</tr>
</tbody>
</table>

See Online Data Supplements E and F.

Clinical trials evaluating goal blood pressure reduction and optimal blood pressure–lowering agents in the setting of HFrEF and concomitant hypertension have not been done. However, it is apparent that in those patients at higher risk, blood pressure lowering is associated with fewer adverse cardiovascular events. GDMT for HFrEF with agents known to lower blood pressure should consider a goal blood pressure reduction consistent with a threshold now associated with improved clinical outcomes but not yet proven by RCTs in a population with HF.
### 9.5.3. Treating Hypertension in Stage C HFrEF: Recommendation

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>C-LD</td>
<td>Patients with HFrEF and persistent hypertension after management of volume overload should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg (167, 169, 170, 194-199).</td>
</tr>
</tbody>
</table>

**Comment/Rationale**

NEW: New target goal blood pressure based on updated interpretation of recent clinical trial data.

The use of nitrates in the setting of HFrEF is associated with a signal of harm and, in most situations, should be avoided. For many common antihypertensive agents, including alpha blockers, beta blockers, and calcium channel blockers, there are limited data to guide the choice of antihypertensive therapy in the setting of HFrEF (172). Nevertheless, RAAS inhibition with ACE inhibitor, ARB (especially mineralocorticoid receptor antagonists), and possibly ARNI would represent the preferred choice. A shared decision-making discussion with the patient influenced by physician judgment should drive the ultimate choice of antihypertensive agents.
9.6. Sleep Disordered Breathing: Recommendations

(Moved from Section 7.3.1.4, Treatment of Sleep Disorders in the 2013 HF guideline.)

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>C-LD</td>
<td>In patients with NYHA class II–IV HF and suspicion of sleep disordered breathing or excessive daytime sleepiness, a formal sleep assessment is reasonable (200, 201).</td>
<td>NEW: Recommendation reflects clinical necessity to distinguish obstructive versus central sleep apnea.</td>
</tr>
</tbody>
</table>

Sleep disorders are common in patients with HF. A study of adults with chronic HF treated with evidence-based therapies found that 61% had either central or obstructive sleep apnea (202). It is clinically important to distinguish obstructive sleep apnea from central sleep apnea, given the different responses to treatment. Adaptive servo-ventilation for central sleep apnea is associated with harm (203). Continuous positive airway pressure (CPAP) for obstructive sleep apnea improves sleep quality, reduces the apnea-hypopnea index, and improves nocturnal oxygenation (200, 201).
Obstructive Sleep Apnea

In patients with cardiovascular disease and obstructive sleep apnea, CPAP may be reasonable to improve sleep quality and daytime sleepiness (204).

NEW: New data demonstrate the limited scope of benefit expected from CPAP for obstructive sleep apnea.

In patients with sleep apnea, a trial evaluated the impact of CPAP with usual therapy versus usual therapy alone on subsequent cardiovascular events, including HF (204). In this RCT of >2,700 patients, there was no evidence of benefit on cardiovascular events at a mean follow-up of 3.7 years for CPAP plus usual care compared with usual care alone. Improvements in sleep quality were noteworthy and represented the primary indication for initiating CPAP treatment (204). However, in patients with atrial fibrillation (AF) (a frequent comorbidity noted with HF), the use of CPAP for obstructive sleep apnea was helpful. In a trial of 10,132 patients with AF and obstructive sleep apnea, patients on CPAP treatment were less likely to progress to more permanent forms of AF than were patients without CPAP (205).
# Central Sleep Apnea

In patients with NYHA class II–IV HF<sub>r</sub>EF and central sleep apnea, adaptive servo-ventilation causes harm (203).

**NEW:** New data demonstrate a signal of harm when adaptive servo-ventilation is used for central sleep apnea.

<table>
<thead>
<tr>
<th>III: Harm</th>
<th>B-R</th>
</tr>
</thead>
<tbody>
<tr>
<td>See Online Data Supplement G.</td>
<td></td>
</tr>
</tbody>
</table>

Mortality rate (all cause and cardiovascular) was higher with adaptive servo-ventilation plus GDMT than with GDMT alone in a single RCT to test the addition of adaptive servo-ventilation (≥5 hours/night, 7 days/week) to GDMT in patients with HF<sub>r</sub>EF and central sleep apnea (203). A similar risk has been seen in another trial, and a third trial of adaptive servo-ventilation in central sleep apnea and HF was aborted because of ethical concerns.

The weight of evidence does not support the use of adaptive servo-ventilation for central sleep apnea in HF<sub>r</sub>EF.
Fig. 1. Associations between heart failure with preserved ejection fraction (HFP EF) and heart failure with reduced ejection fraction (HFrEF), with comorbidities. Pathways linking several common comorbidities to disease progression in both HFP EF and HFrEF are p...

**Targeting Comorbidities in Elderly Patients With Heart Failure: The OPTIMIZE-HFPEF Trial**

*Journal of Cardiac Failure, Volume 22, Issue 7, 2016, 545–547*  
Robert J. Mentz, Thomas M. Maddox  
http://dx.doi.org/10.1016/j.cardfail.2016.03.002
Systemic and myocardial signaling in HFPEF. Comorbidities induce systemic inflammation, evident from elevated plasma levels of inflammatory biomarkers such as soluble interleukin 1 receptor-like 1 (IL1RL1), C-reactive protein (CRP), and growth differentiation factor 15 (GDF15).

Phenotype-specific HFpEF treatment strategy using a matrix of predisposition phenotypes and clinical presentation phenotypes.

<table>
<thead>
<tr>
<th>HFpEF Predisposition Phenotypes</th>
<th>Lung Congestion</th>
<th>+Chronotropic Incompetence</th>
<th>+Pulmonary Hypertension (CpcPH)</th>
<th>+Skeletal muscle weakness</th>
<th>+Atrial Fibrillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overweight/obesity/metabolic syndrome/type 2 DM</td>
<td>+Diuretics (loop diuretic in DM) +Caloric restriction +Statins +Inorganic nitrite/nitrate +Sacubitril +Spirolonolactone</td>
<td>+Rate adaptive atrial pacing</td>
<td>+Pulmonary vasodilators (e.g. PDE5I)</td>
<td>+Exercise training program</td>
<td>+Cardioversion + Rate Control + Anticoagulation</td>
</tr>
<tr>
<td>+Arterial hypertension</td>
<td>+ACEI/ARB</td>
<td>+ACEI/ARB +Rate adaptive atrial pacing</td>
<td>+ACEI/ARB +Pulmonary vasodilators (e.g. PDE5I)</td>
<td>+ACEI/ARB +Exercise training program</td>
<td>+ACEI/ARB +Cardioversion + Rate Control + Anticoagulation</td>
</tr>
<tr>
<td>+Renal dysfunction</td>
<td>+Ultrafiltration if needed</td>
<td>+Ultrafiltration if needed +Rate adaptive atrial pacing</td>
<td>+Ultrafiltration if needed +Pulmonary vasodilators (e.g. PDE5I)</td>
<td>+Ultrafiltration if needed +Exercise training program</td>
<td>+Ultrafiltration if needed +Cardioversion + Rate Control + Anticoagulation</td>
</tr>
<tr>
<td>+CAD</td>
<td>+ACEI +Revascularization</td>
<td>+ACEI +Revascularization +Rate adaptive atrial pacing</td>
<td>+ACEI +Revascularization +Pulmonary vasodilators (e.g. PDE5I)</td>
<td>+ACEI +Revascularization +Exercise training program</td>
<td>+ACEI +Revascularization +Cardioversion + Rate Control + Anticoagulation</td>
</tr>
</tbody>
</table>

New Guideline Takeaways - Co-Morbidities

• Anemia
  – Fe deficiency; intravenous iron preferable to oral iron

• Sleep Apnea
  – Do NOT use servo control support for central sleep apnea
  – CPAP only for OSA
  – Sleep studies are indicated
  – No impact on HF outcomes but sleep quality is improved

• Hypertension
  – New target: < 130/80 mmHg in HF with HTN

• Bidirectional effect
  – Co0morbidities exaggerate adverse clinical outcomes and symptoms

• Causative inferences
  – especially with HFpEF
Controversies in the Management of Heart Failure - 2017

• Incorporating new clinical practice guidelines
  – What’s new?
  – How will practice be changed?
• Identifying a new phenotype - heart failure with improved ejection fraction
  – What is this?
  – What’s the natural history?
  – Can it be manipulated?
• Device therapy in 2017
  – is the ICD still indicated?
  – Who gets a CRT device
A new classification?

ESC HF GUIDELINES 2016

**Table 3.1**
Definition of heart failure with preserved (HFrEF), mid-range (HFmrEF) and reduced ejection fraction (HFpEF)

<table>
<thead>
<tr>
<th>Type of HF</th>
<th>HFrEF</th>
<th>HFmrEF</th>
<th>HFpEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Symptoms ± Signs(^a)</td>
<td>Symptoms ± Signs(^a)</td>
<td>Symptoms ± Signs(^a)</td>
</tr>
<tr>
<td>2</td>
<td>LVEF &lt;40%</td>
<td>LVEF 40–49%</td>
<td>LVEF ≥50%</td>
</tr>
<tr>
<td>3</td>
<td>1. Elevated levels of natriuretic peptides(^b); 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).</td>
<td></td>
<td>1. Elevated levels of natriuretic 2. At least one additional criter</td>
</tr>
</tbody>
</table>
2013 ACCF/AHA Guideline for the Management of Heart Failure

Developed in Collaboration With the American Academy of Family Physicians, American College of Chest Physicians, Heart Rhythm Society, and International Society for Heart and Lung Transplantation

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation

© American College of Cardiology Foundation and American Heart Association, Inc.
## Definition of Heart Failure

<table>
<thead>
<tr>
<th>Classification</th>
<th>Ejection Fraction</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I. Heart Failure with Reduced Ejection Fraction (HFrEF)</strong></td>
<td>≤40%</td>
<td>Also referred to as systolic HF. Randomized clinical 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><strong>II. Heart Failure with Preserved Ejection Fraction (HFpEF)</strong></td>
<td>≥50%</td>
<td>Also referred to as diastolic HF. Several different criteria have been used to further define HFpEF. The diagnosis of HFpEF 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. HFpEF, 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 HFpEF.</td>
</tr>
<tr>
<td>b. HFpEF, Improved</td>
<td>&gt;40%</td>
<td>It has been recognized that a subset of patients with HFpEF 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>
</table>
Characteristics and Outcomes of Adult Outpatients With Heart Failure and Improved or Recovered Ejection Fraction

Andreas P. Kalogeropoulos, MD, MPH, PhD; Gregg C. Fonarow, MD; Vasiliki Georgiopoulou, MD, MPH, PhD; Gregory Burkman, MD; Sarawut Siwamogsatham, MD; Akash Patel, MD; Song Li, MD; Lampros Papadimitriou, MD, PhD; Javed Butler, MD, MPH, MBA
Heart Failure with Improved EF?

Kalogeropoulos, A. et al. JAMA Cardiology 2016

• 2166 patients followed over 3 years
• 62% HFrEF
• 38% HFpEF
• 16.2% had HFpEF with previous evidence of LVEF < 0.40
• Mortality at 3 years: 16.3%; 13.2%; 4.8%
Kaplan-Meier Curves, Adjusted for Age and Sex, Across the 3 Heart Failure Groups

The stratified log-rank $\chi^2$ was 15.0 ($P < .001$) for difference in mortality between groups. HFpEF indicates heart failure with preserved ejection fraction; HFrecEF, heart failure with recovered ejection fraction; and HFrEF, heart failure with reduced ejection fraction.
A Death

Cumulative Mortality, %

Time, mo

HFrEF
HFpEF
HFrecEF

16.3%
13.2%
4.8%
D  Death or heart failure hospitalization

Cumulative Event Rate, %

Time, mo

40.1%
28.9%
11.8%
Figure 1. The MCS investigational setting is a unique transformative “research vehicle” that could help advance the science of cardiac recovery, HF reversal and MCS innovation. AVR: Aortic valve replacement/repair, CRT: Cardiac resynchronization, HF: Heart fai...
Heart Failure—A New Phenotype Emerges

Jane E. Wilcox, MD, MSc1; Clyde W. Yancy, MD, MSc1,2

[+] Author Affiliations

JAMA Cardiol. Published online July 06, 2016. doi:10.1001/jamacardio.2016.1356
**HFimprovedEF?**

*Wilcox J, Yancy CW. JAMA Cardiology 2016*

- Spontaneous Myocardial Recovery/Repair
  - Ischemia/revascularization
  - Arrhythmia management; AF/VT ablation
  - Neuregulin pathways
- Reverse Remodeling – super-responders
  - Restoration of beta receptor density
  - Active collagen turnover
  - Pharmacogenomics
- Reversible illnesses; e.g., myocarditis, metabolic cardiomyopathies, peripartum cardiomyopathy
- Myocardial Recovery LVAD supported
  - Restoration of calcium handling; restored mitochondrial function

**TREATMENT?**

- *Similar to HFrEF or HFpEF or both?*
Controversies in the Management of Heart Failure - 2017

• Incorporating new clinical practice guidelines
  – What’s new?
  – How will practice be changed?

• Identifying a new phenotype - heart failure with improved ejection fraction
  – What is this?
  – What’s the natural history?
  – Can it be manipulated?

• Device therapy in 2017
  – is the ICD still indicated?
  – Who gets a CRT device
The Effect of Cardiac Resynchronization on Morbidity and Mortality in Heart Failure

John G.F. Cleland, M.D., Jean-Claude Daubert, M.D., Erland Erdmann, M.D., Nick Freemantle, Ph.D., Daniel Gras, M.D., Lukas Kappenberger, M.D., and Luigi Tavazzi, M.D., for the Cardiac Resynchronization — Heart Failure (CARE-HF) Study Investigators

Kaplan–Meier Estimates of the Time to the Primary End Point (Panel A) and the Principal Secondary Outcome (Panel B).

Panel A:
- Percentage of Patients Free of Death from Any Cause or Unplanned Hospitalization for a Major Cardiovascular Event
- No. at Risk:
  - Cardiac resynchronization: 409, 323, 273, 166, 68, 7
  - Medical therapy: 404, 292, 232, 118, 48, 3

Panel B:
- Percentage of Patients Free of Death from Any Cause
- No. at Risk:
  - Cardiac resynchronization: 409, 376, 351, 213, 89, 8
  - Medical therapy: 404, 365, 321, 192, 71, 5

P < 0.001 for both panels.
Table 3. Hemodynamic, Echocardiographic, and Biochemical Assessments.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Difference in Means at 3 Mo (95% CI)</th>
<th>P Value</th>
<th>Difference in Means at 18 Mo (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>+1.1 (-1.2 to 3.4)</td>
<td>0.33</td>
<td>+1.0 (-1.5 to 3.6)</td>
<td>0.43</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>+5.8 (3.5 to 8.2)</td>
<td>&lt;0.001</td>
<td>+6.3 (3.6 to 8.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>+1.5 (0.1 to 2.9)</td>
<td>0.03</td>
<td>+1.3 (-1.8 to 4.4)</td>
<td>0.42</td>
</tr>
<tr>
<td>Interventricular mechanical delay (msec)</td>
<td>-21 (-25 to -18)</td>
<td>&lt;0.001</td>
<td>-21 (-25 to -17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>+3.7 (3.0 to 4.4)</td>
<td>&lt;0.001</td>
<td>+6.9 (5.6 to 8.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left ventricular end-systolic volume index (ml/m²)</td>
<td>-18.2 (-21.2 to -15.1)</td>
<td>&lt;0.001</td>
<td>-26.0 (-31.5 to -20.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mitral-regurgitation area†</td>
<td>-0.051 (-0.073 to -0.028)</td>
<td>&lt;0.001</td>
<td>-0.042 (-0.070 to -0.014)</td>
<td>0.003</td>
</tr>
<tr>
<td>N-terminal pro–brain natriuretic peptide (pg/ml)‡</td>
<td>-225 (-705 to 255)</td>
<td>0.36</td>
<td>-1122 (-1815 to -429)</td>
<td>&lt;0.002</td>
</tr>
</tbody>
</table>

* Differences were not adjusted for the higher mortality rate in the medical-therapy group. A plus sign indicates a greater value, and a minus sign a smaller value, in the cardiac-resynchronization group than in the medical-therapy group. CI denotes confidence interval.
† The area was calculated as the area of the color-flow Doppler regurgitant jet divided by the area of the left atrium in systole, both in square centimeters.
‡ To convert the values for N-terminal pro–brain natriuretic peptide to picomoles per liter, divide by 8.457.
Survival with Cardiac-Resynchronization Therapy in Mild Heart Failure

Ilan Goldenberg, M.D., Valentina Kutyifa, M.D., Ph.D., Helmut U. Klein, M.D.,
David S. Cannom, M.D., Mary W. Brown, M.S., Ariela Dan, Ph.D.,
James P. Daubert, M.D., N.A. Mark Estes III, M.D., Elyse Foster, M.D.,
Henry Greenberg, M.D., Josef Kautzner, M.D., Robert Klempfner, M.D.,
Malte Kuniss, M.D., Bela Merkely, M.D., Ph.D., Marc A. Pfeffer, M.D., Ph.D.,
Aurelio Quesada, M.D., Ph.D., Sami Viskin, M.D., Scott McNitt, M.S.,
Bronislava Polonsky, M.S., Ali Ghanem, M.D., Scott D. Solomon, M.D.,
David Wilber, M.D., Wojciech Zareba, M.D., Ph.D., and Arthur J. Moss, M.D.
MADIT-CRT (NEJM. 2009)

- 1820 ICM/NICM pts:
  - EF ≤ 30%
  - QRS ≥ 130 msec
  - NYHA I/II
- Randomization:
  - CRT-D vs. ICD-only
  - 3:2 ratio
- Mean Follow-up:
  - 2.4 yrs
- Outcome:
  - HR=0.66 (p=0.001)
LBBB: ALL-CAUSE MORTALITY

NNT = 9
**Indications for CRT Therapy**

- **Patient with cardiomyopathy on GDMT for >3 mo or on GDMT and >40 d after MI, or with implantation of pacing or defibrillation device for special indications**

- **LVEF ≤35%**
  - Evaluate general health status
  - Comorbidities and/or frailty limit survival with good functional capacity to <1 y
  - Continue GDMT without implanted device
  - Acceptable noncardiac health
  - Evaluate NYHA clinical status

**NYHA class I**
- LVEF ≤30%
- QRS ≥150 ms
- LBBB pattern
- Ischemic cardiomyopathy
- QRS ≤150 ms
- Non-LBBB pattern

**NYHA class II**
- LVEF ≤35%
- QRS ≥150 ms
- LBBB pattern
- Sinus rhythm
- LVEF ≤35%
- QRS 120-149 ms
- LBBB pattern
- Sinus rhythm
- LVEF ≤35%
- QRS 120-149 ms
- Non-LBBB pattern
- Sinus rhythm
- LVEF ≤35%
- QRS ≥150 ms
- Non-LBBB pattern
- Sinus rhythm
- QRS ≤150 ms
- Non-LBBB pattern

**NYHA class III & Ambulatory class IV**
- LVEF ≤35%
- QRS ≥150 ms
- LBBB pattern
- Sinus rhythm
- LVEF ≤35%
- QRS 120-149 ms
- LBBB pattern
- Sinus rhythm
- LVEF ≤35%
- QRS 120-149 ms
- Non-LBBB pattern
- Sinus rhythm
- LVEF ≤35%
- QRS ≥150 ms
- Non-LBBB pattern
- Sinus rhythm
- QRS ≥150 ms
- Non-LBBB pattern
- Sinus rhythm

**Special CRT Indications**
- Anticipated to require frequent ventricular pacing (>40%)
- Atrial fibrillation, if ventricular pacing is required and rate control will result in near 100% ventricular pacing with CRT

Colors correspond to the class of recommendations in the ACCF/AHA Table 1.

Benefit for NYHA class I and II patients has only been shown in CRT-D trials, and while patients may not experience immediate symptomatic benefit, late remodeling may be avoided along with long-term HF consequences. There are no trials that support CRT-pacing (without ICD) in NYHA class I and II patients. Thus, it is anticipated these patients would receive CRT-D unless clinical reasons or personal wishes make CRT-pacing more appropriate. In patients who are NYHA class III and ambulatory class IV, CRT-D may be chosen but clinical reasons and personal wishes may make CRT-pacing appropriate to improve symptoms and quality of life when an ICD is not expected to produce meaningful benefit in survival.
New Question?

CRT-P vs. CRT-D?
Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure


N Engl J Med
375(13):1221-1230
September 29, 2016
Study Overview

- In a randomized trial, more than 1100 patients with nonischemic heart failure (left ventricular ejection fraction ≤35%) were assigned either to receive or not to receive an ICD.

- At a median of 67.6 months, there was no significant difference in mortality between the two groups.
### Characteristics of the Patients at Baseline.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ICD Group (N = 556)</th>
<th>Control Group (N = 560)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (IQR) — yr</td>
<td>64 (56–72)</td>
<td>63 (56–70)</td>
</tr>
<tr>
<td>Female sex — no. (%)</td>
<td>151 (27)</td>
<td>156 (28)</td>
</tr>
<tr>
<td>Median blood pressure (IQR) — mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>123 (110–139)</td>
<td>124 (111–138)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>74 (65–81)</td>
<td>74 (66–82)</td>
</tr>
<tr>
<td>Median body-mass index (IQR)†</td>
<td>26.8 (23.9–30.5)</td>
<td>26.8 (23.8–30.1)</td>
</tr>
<tr>
<td>Median NT-proBNP level (IQR) — pg/ml</td>
<td>1244 (616–2321)</td>
<td>1110 (547–2166)</td>
</tr>
<tr>
<td>Median QRS duration (IQR) — msec</td>
<td>146 (114–156)</td>
<td>145 (110–164)</td>
</tr>
<tr>
<td>Median left ventricular ejection fraction (IQR) — %</td>
<td>25 (20–30)</td>
<td>25 (20–30)</td>
</tr>
<tr>
<td>Median estimated GFR (IQR) — ml/min/1.73 m²</td>
<td>74 (58–91)</td>
<td>73 (58–92)</td>
</tr>
<tr>
<td>NYHA class — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>297 (53)</td>
<td>300 (54)</td>
</tr>
<tr>
<td>III</td>
<td>252 (45)</td>
<td>253 (45)</td>
</tr>
<tr>
<td>IV</td>
<td>7 (1)</td>
<td>7 (1)</td>
</tr>
<tr>
<td>Median duration of heart failure (IQR) — mo</td>
<td>20 (8–72)</td>
<td>18 (8–60)</td>
</tr>
<tr>
<td>Coexisting conditions — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>181 (33)</td>
<td>167 (30)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>99 (18)</td>
<td>112 (20)</td>
</tr>
<tr>
<td>Permanent atrial fibrillation</td>
<td>135 (24)</td>
<td>113 (20)</td>
</tr>
<tr>
<td>Means of exclusion of ischemic cause of heart failure — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuclear study</td>
<td>5 (1)</td>
<td>8 (1)</td>
</tr>
<tr>
<td>CT angiogram</td>
<td>18 (3)</td>
<td>11 (2)</td>
</tr>
<tr>
<td>Catheterization</td>
<td>533 (96)</td>
<td>541 (97)</td>
</tr>
<tr>
<td>Cause of heart failure — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic</td>
<td>424 (76)</td>
<td>425 (76)</td>
</tr>
<tr>
<td>Valvular</td>
<td>20 (4)</td>
<td>21 (4)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>62 (11)</td>
<td>55 (10)</td>
</tr>
<tr>
<td>Other</td>
<td>50 (9)</td>
<td>59 (11)</td>
</tr>
<tr>
<td>Medications — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitor or ARB</td>
<td>533 (96)</td>
<td>544 (97)</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>509 (92)</td>
<td>517 (92)</td>
</tr>
<tr>
<td>Mineralocorticoid-receptor antagonist</td>
<td>326 (59)</td>
<td>320 (57)</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>34 (6)</td>
<td>32 (6)</td>
</tr>
<tr>
<td>CRT — no. (%)</td>
<td>322 (58)</td>
<td>323 (58)</td>
</tr>
<tr>
<td>Preexisting pacemaker or CRT pacemaker — no. (%)</td>
<td>56 (10)</td>
<td>46 (8)</td>
</tr>
</tbody>
</table>

* There were no significant differences (P<0.05) between the study groups. ACE denotes angiotensin-converting enzyme, ARB angiotensin-receptor blocker, CRT cardiac resynchronization therapy, CT computed tomography, GFR glomerular filtration rate, ICD implantable cardioverter-defibrillator, IQR interquartile range, NT-proBNP N-terminal pro-brain natriuretic peptide, and NYHA New York Heart Association.

† The body-mass index is the weight in kilograms divided by the square of the height in meters.
Time-to-Event Curves for Death from Any Cause, Cardiovascular Death, and Sudden Cardiac Death.

Adding Defibrillation Therapy to Cardiac Resynchronization on the Basis of the Myocardial Substrate

Sérgio Barra, MD, Serge Boveda, MD, Rui Providência, MD, PhD, Nicolas Sadoul, MD, PhD, Rudolf Duehmke, MD, PhD, Christian Reitan, MD, Rasmus Borgquist, MD, PhD.
Figure 1. Unadjusted Kaplan-Meier Survival Curves for the 4 Study Groups
CRT-D = cardiac resynchronization therapy defibrillator; CRT-P = cardiac resynchronization therapy pacemaker.

Sérgio Barra, Serge Boveda, Rui Providência, Nicolas Sadoul, Rudolf Duehmke, Christian Reitan, Rasmus Borgquist, Kumar Narayanan, Françoise Hidden-Lucet, Didier Klug, Pascal Defaye, Daniel Gras, Frédéric Anselme...

http://dx.doi.org/10.1016/j.jacc.2017.01.042
CENTRAL ILLUSTRATION: Cardiac Resynchronization Therapy With a Defibrillator Versus Cardiac Resynchronization Therapy With a Pacemaker in Ischemic and Nonischemic Dilated Cardiomyopathy


Sérgio Barra, Serge Boveda, Rui Providência, Nicolas Sadoul, Rudolf Duehmke, Christian Reitan, Rasmus Borgquist, Kumar Narayanan, Françoise Hidden-Lucet, Didier Klug, Pascal Defaye, Daniel Gras, Frédéric Anselme...

http://dx.doi.org/10.1016/j.jacc.2017.01.042
Improving CRT effectiveness?

Prognostic implications of left ventricular global longitudinal strain in heart failure patients with narrow QRS complex treated with cardiac resynchronization therapy: a subanalysis of the randomized EchoCRT trial

Jeroen J. Bax; Victoria Delgado; Peter Sogaard; Jagmeet P. Singh; William T. Abraham; Jeffrey S. Borer; Kenneth Dickstein; Daniel Gras; Josep Brugada; Michele Robertson

From: Prognostic implications of left ventricular global longitudinal strain in heart failure patients with narrow QRS complex treated with cardiac resynchronization therapy: a subanalysis of the randomized EchoCRT trial
Eur Heart J | Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2016. For Permissions, please email: journals.permissions@oup.com.
From: Prognostic implications of left ventricular global longitudinal strain in heart failure patients with narrow QRS complex treated with cardiac resynchronization therapy: a subanalysis of the randomized EchoCRT trial
Eur Heart J | Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2016. For Permissions, please email: journals.permissions@oup.com.
Implantable Cardioverter-Defibrillators With Versus Without Resynchronization Therapy in Patients With a QRS Duration >180 ms

Varun Sundaram, MD\textsuperscript{a,b}, Jayakumar Sahadevan, MD\textsuperscript{a,c}, Albert L. Waldo, MD, PhD, (Hon)\textsuperscript{a}, George J. Stukenborg, PhD\textsuperscript{d}, Yogesh N.V. Reddy, MD\textsuperscript{e}, Samuel J. Asirvatham, MD\textsuperscript{e}, Judith A. Mackall, MD\textsuperscript{a}

Journal of the American College of Cardiology, Volume 69, Issue 16, 2017, 2026–2036

http://dx.doi.org/10.1016/j.jacc.2017.02.042
Discussion

Contrary to our hypothesis, this large Medicare ICDR-based study demonstrated that a VWQRSD was associated with superior clinical outcomes after CRT-D compared with outcomes for a propensity-matched cohort receiving standard ICD, regardless of whether LBBB was present or absent.
A new platform emerges:

CRT-P vs. CRFT-D vs. CRT-H
Permanent His Bundle Pacing for Cardiac Resynchronization Therapy: Initial Feasibility Study in Lieu of Left Ventricular Lead

Olujimi A. Ajijola, MD PhD\textsuperscript{1,*}, Gaurav Upadhyay, MD\textsuperscript{2,*}, Carlos Macias, MD\textsuperscript{1}, Kalyanam Shivkumar, MD PhD FHRS\textsuperscript{1}, Roderick Tung, MD FHRS\textsuperscript{2}
Figure 4. Selective His bundle capture with QRS narrowing and an isoelectric segment (44 ms) between pacing stimulus and QRS which is shorter than the intrinsic HV interval (76 ms).

Olujimi A. Ajijola, Gaurav Upadhyay, Carlos Macias, Kalyanam Shivkumar, Roderick Tung

**Permanent His Bundle Pacing for Cardiac Resynchronization Therapy: Initial Feasibility Study in Lieu of Left Ventricular Lead**

Heart Rhythm, 2017, Available online 8 April 2017

http://dx.doi.org/10.1016/j.hrthm.2017.04.003
Figure 3. Example of nonselective His capture resulting in narrowing of QRS with left bundle branch block pattern from 200ms to 112 ms in a patient with ischemic cardiomyopathy. The prior q wave inferior myocardial infarction pattern is seen during His bundle...

Olujimi A. Ajijola, Gaurav Upadhyay, Carlos Macias, Kalyanam Shivkumar, Roderick Tung

**Permanent His Bundle Pacing for Cardiac Resynchronization Therapy: Initial Feasibility Study in Lieu of Left Ventricular Lead**

Heart Rhythm, 2017, Available online 8 April 2017

http://dx.doi.org/10.1016/j.hrthm.2017.04.003
Olujimi A. Ajijola, Gaurav Upadhyay, Carlos Macias, Kalyanam Shivkumar, Roderick Tung

**Permanent His Bundle Pacing for Cardiac Resynchronization Therapy: Initial Feasibility Study in Lieu of Left Ventricular Lead**

Heart Rhythm, 2017, Available online 8 April 2017

http://dx.doi.org/10.1016/j.hrthm.2017.04.003
Figure 7. Patient-level responses to permanent His bundle pacing demonstrating improvements in QRS duration and ejection fraction during follow-up.

Olujimi A. Ajijola, Gaurav Upadhyay, Carlos Macias, Kalyanam Shivkumar, Roderick Tung

**Permanent His Bundle Pacing for Cardiac Resynchronization Therapy: Initial Feasibility Study in Lieu of Left Ventricular Lead**

Heart Rhythm, 2017, Available online 8 April 2017

http://dx.doi.org/10.1016/j.hrthm.2017.04.003
Discussion

The major findings of the present study are:

1.) Electrical resynchronization via HBP was achieved in 76% of patients presenting with bundle branch block with an indication for CRT.

2.) Incorporation and programming of a HBP lead into the LV port in a standard CRT-D or CRT-P system is feasible.

3.) 15 out of 16 patients with QRS narrowing demonstrated non-selective His capture, with one case of selective His capture.

4.) Favorable echocardiographic indices with improvement in EF, reduction in LV size, and improvement in NYHA class were observed in this cohort of patients with nonselective His bundle pacing.
SUMMARY

• Cardiac Resynchronization Therapy is a class I recommendation in the treatment of HFrEF and is endorsed by all guideline writing bodies. COR I/LOE A is consistent

• CRT-D may be preferred in unselected cohorts and especially in those with ischemic etiologies

• CRT-P is beneficial in selected cohorts:
  – LBBB
  – Women
  – Non-ischemic etiologies

• The utility of CRT may be improved with better candidate selection:
  – Very wide QRS
  – Reduced global longitudinal strain with QRS < 130 msec & mechanical dyssynchrony may be harmed by CRT
  – HIS bundle pacing
Final Takeaways

• The treatment of heart failure continues to evolve with new therapies and emerging new devices
• New treatment algorithms addressing the increasing complexity of HF therapy
• Co-Morbidities matter; overzealous treatment may lead to harm
• Device based therapies require careful clinical assessments
• PREVENTION is a new reality
• “A mediocre physician treats advanced disease... A good physician treats disease ... A great physician prevents disease” – Chinese proverb

• We should all aim to be great physicians