Recent Advances in Heart Failure

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Disclosures

• Amgen – research support
• Takeda Oncology – consultant
• Astrazeneca – consultant
Distribution of EF in Pts. Hospitalized with HF

40,239 Medicare pts enrolled in GWTG-HF from 2005-11

HF-PEF vs. HFrEF
• Older
• Female
• HTN
• CKD
• A Fib
• ↓ CAD

HFbEF like HFpEF
• ↑ CAD

Outcomes after HF Hospitalization, by EF

HFrEF vs. HFbEF vs. HFpEF
• Mortality:
  – 30d: 9.5% vs. 8.2% vs. 8.5%
  – 1 yr: 37.5% vs. 35.1% vs. 35.6%

• All-cause Readmission:
  – 30d: 19.7% vs. 20.9% vs. 20.5%
  – 1 yr: 59.6% vs. 63.2% vs. 62.5%

Stages of Heart Failure

ACC/AHA Classification

A. At risk patients without structural heart disease
B. Structural heart disease without symptoms
C. Structural heart disease with prior or current symptoms
D. Refractory heart failure

NYHA Classification

I. Cardiac disease without functional limitation
II. Slight limitation of physical activity
III. Marked limitation of physical activity
IV. Inability to carry on physical activity without discomfort

- Limited Randomized Trial Data to Guide Management of ADHF
- Guidelines driven primarily by expert consensus
Guideline-Directed Medical Therapy for HFrEF: 2013

### Relief of Congestive Symptoms

- **Diuretics**
  - Loop (thiazide)
  - ACEi/ARB
  - Beta-Blocker

### EF ≤ 40%

- **NYHA I-IV**
  - Lisinopril, etc.
  - Carvedilol
  - Metoprolol bisoprolol

### EF ≤ 40%

- **NYHA II-IV**
  - Spironolactone
  - Eplerenone
  - MRA

### Still Symptomatic?

- Hydral/Isordil
- Digoxin

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Heart Failure Case

- **53 y.o. man presents for f/u after 2nd admission for ADHF**
- **Non-ischemic CMP (EF 25%, LVEDD 7.5 cm)**
- **PAF/VT w/ ICD therapies**
- **Metoprolol succinate 200 mg daily, losartan 50 mg daily, spironolactone 25 mg daily, digoxin 0.125 mg daily, furosemide 80 mg bid, and apixaban 5 mg bid**

- **BP 100/50, HR 85**
- **JVP 10 cm water, min. HJR**
- **Clear lungs**
- **RRR. NI s1, s2. + Soft MR m**
- **No HSM**
- **No edema**

- **Na 130, K 4.6, BUN 26, Cr 1.6**
- **Hb 10, Fe 25, TIBC 150, ferritin 300**
Question

*What would be the next best step to lower his risk of HF hospitalization?

A. Change metoprolol to carvedilol
B. Change losartan to sacubitril-valsartan
C. Add ivabradine
D. Give IV iron infusions

Sacubitril/Valsartan: Mechanism of Action

Vardeny O et al. JACC: Heart Failure 2014;2:663-70.
PARADIGM-HF

• N=8,442
• RCT:
  – Enalapril 10mg bid vs. LCZ696 200mg bid
• Inclusion Criteria:
  – EF ≤ 40% → 35%
  – NYHA II-IV
  – BNP ≥ 150, NT-BNP ≥ 600
  – BNP ≥ 100 if hosp w/in 12 mths
  – On optimal Rx
  – SBP ≥ 95
  – eGFR > 30 ml/min
  – K < 5.4


• Increased hypotension, less renal dysfunction.
• No increase in hyperkalemia, angioedema, or cough.

Guideline Update

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-R</td>
<td>ACEi OR ARB OR ARNI in conjunction with beta-blockers + MRA (where appropriate) is recommended for patients with chronic HFrEF to reduce morbidity and mortality.</td>
</tr>
<tr>
<td>I</td>
<td>B-R</td>
<td>In patients with chronic, symptomatic HFrEF NYHA class II or III who tolerate and ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality</td>
</tr>
<tr>
<td>III</td>
<td>B-R</td>
<td>ARNI should NOT be administered concomitantly with ACEi or within 36 hours of last ACEi dose</td>
</tr>
<tr>
<td>III</td>
<td>C=EO</td>
<td>ARNI should NOT be administered to patients with a history of angioedema</td>
</tr>
</tbody>
</table>

Population | Initial Dose |
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Enalapril &gt; 10 mg/d or Valsartan &gt; 160 mg/d</td>
<td>49/51 mg twice daily</td>
</tr>
<tr>
<td>Low dose ACE-I/ARB</td>
<td></td>
</tr>
<tr>
<td>ACE-I/ARB naïve</td>
<td></td>
</tr>
<tr>
<td>eGFR&lt;30 mL/min/m²</td>
<td>24/26 mg twice daily</td>
</tr>
<tr>
<td>Moderate Hepatic Impairment (Child-Pugh Class B)</td>
<td></td>
</tr>
<tr>
<td>Elderly</td>
<td></td>
</tr>
</tbody>
</table>

- Ensure 36 hrs off ACEi
- Adequate BP
- eGFR ≥ 30 ml/min/1.73 m²
- Assess tolerability
- Up-titrate in step-wise fashion to 97/103 mg bid
- Re-assess BP, K and Cr after each dose increase

Ivabradine: A Selective $I_f$ Inhibitor

$I_f$ inhibition reduces the diastolic depolarization slope, thereby lowering heart rate.

No effect on myocardial contractility or relaxation.

Use-dependent block = low risk of bradycardia.


SHIFT: Ivabradine ($I_f$ inhibitor in SA node)

- N=6,558
- EF ≤ 35%, NYHA II-IV
- Resting HR ≥ 70 bpm on max tolerated BB
- Ivabradine: 5 bid → 7.5 bid
- Average HR: 64 vs. 75 bpm @1 yr
- Greater benefit w/ greater reduction in HR
- Side effects
  - Symptomatic bradycardia: 5 vs 1%
  - Phosphenes: 3 vs 1%

**Guideline Update**

<table>
<thead>
<tr>
<th>COR</th>
<th>LOR</th>
<th>B-R</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>Moderate</td>
<td></td>
</tr>
</tbody>
</table>

Ivabradine may be beneficial to reduce HF hospitalization for patients with symptomatic stable chronic HFrEF who are receiving GDMT, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of ≥ 70 bpm at rest.

- Ensure that b-blockers maximized
- Assess eligibility for ivabradine

**Iron Repletion in HF**

- 50% HF patients have iron deficiency, with or without anemia
- Iron deficiency in HF is associated with ↑ mortality, independent of anemia
- No improvement in all-cause mortality and HF hospitalization with darbopoietin
- No improvement in functional capacity or QOL with oral iron


**Guideline Update**

**Recommendations for Anemia**

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>In patients with NYHA class II and III HF and iron deficiency (ferritin &lt;100 ng/mL or 100 to 300 ng/mL if transferrin saturation is &lt;20%), intravenous iron replacement might be reasonable to improve functional status and QoL. (173, 174).</td>
</tr>
<tr>
<td>III: No Benefit</td>
<td>B-R</td>
<td>In patients with HF and anemia, erythropoietin-stimulating agents should not be used to improve morbidity and mortality (176).</td>
</tr>
</tbody>
</table>

See Online Data Supplement D.

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**SGLT-2i Reduce HF Hospitalizations in Type II DM**

- 34,322 pts w/ established CVD or at high-risk for CVD + Type II DM
- Meta-analysis of 3 RCTs of SGLT-2i vs. placebo

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**SGLT-2i in HFrEF**

**DAPA-HF:**
- N=4744, EF≤40% ± DM II, NYHA II-IV
- CV Death/HF hospitalization/ED visit

**EMPEROR-REDUCED:**
- N=3730, EF≤40% ± DM II, NYHA II-IV
- CV Death/HF hospitalization

Dapagliflozin 10 mg daily
Placebo
Empagliflozin 10 mg daily

Also lower rate of decline of eGFR; Side Effects: Hypovolemia, UTI (Fungal), Balanitis, DKA


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**Vericiguat: Soluble Guanylate Cyclase Stimulator/Sensitizer (VICTORIA)**

- Hazard ratio, 0.90 (95% CI, 0.82–0.98)
- P=0.02

Placebo
Vericiguat 10 mg daily

Absolute risk reduction: 4.2 events/100 pt-yrs
NNT = 24

Major Side Effects:
- Hypotension
- Syncope
- Anemia

**Question**

- *What would be the next best step in his management?*

A. Change metoprolol to carvedilol  
B. Add dapagliflozin  
C. Add ivabradine  
D. Give IV iron infusions

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**Heart Failure Case**

- He presents 3 mths later w/ dyspnea w/ minimal exertion and 10 lb weight gain despite doubling of diuretic dose  
- Metoprolol succinate 200 mg daily, valsartan-sacubitril 24/26 bid, spironolactone 25 mg daily, dapagliflozin 10 mg daily, digoxin 0.125 mg daily, furosemide 160 mg bid, and apixaban 5 mg bid  
- BP 90/70, HR 90  
- JVD to angle of jaw  
- Clear lungs  
- RRR. Nl s1, s2. + s3, MR, TR  
- Liver edge 2 cm below costal margin  
- Trace edema, lukewarm to touch, 2+ distal pulses  
- Na 128, K 4.6, BUN 30, Cr 1.8
Symptomatic HF is a Clinical Diagnosis

Accuracy of Physical Findings for Elevated LV Filling Pressure

<table>
<thead>
<tr>
<th>Finding</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopnea (≥2 pillows)</td>
<td>85%</td>
<td>24%</td>
</tr>
<tr>
<td>Rales (≥1/3 lungs fields)</td>
<td>15%</td>
<td>89%</td>
</tr>
<tr>
<td>S3</td>
<td>63%</td>
<td>34%</td>
</tr>
<tr>
<td>Edema (&gt;1+)</td>
<td>41%</td>
<td>67%</td>
</tr>
<tr>
<td>Elevated JVP (&gt;10 cm)</td>
<td>67%</td>
<td>72%</td>
</tr>
</tbody>
</table>

Sensitivity and specificity for predicting PCWP > 22 mm Hg

Drazner M et al. Circ Heart Fail 2008;1:170
BNP to Assist Diagnosis of HF

BNP to Assist Diagnosis of HF

Diagnostic Limitations of Natriuretic Peptides

- Imperfect surrogate for filling pressures
  - Levels increase with age, female gender, pressure overload, renal failure
  - Levels decrease with obesity, medical treatment
- Levels are lower in HF-PEF
- Levels may be elevated even in compensated chronic HF
- Levels can be elevated in diseases other than HF
- Only NT-proBNP predictive w/ Valsartan-Sacubitril
Diagnostic Limitations of Natriuretic Peptides

- Imperfect surrogate for filling pressures
  - Levels increase with age, female gender, pressure overload, renal failure
  
  Measurement of NPs is most useful when there is diagnostic uncertainty or for prognostic indications

- Levels are lower in HF-PEF
- Levels may be elevated even in compensated chronic HF
- Levels can be elevated in diseases other than HF
- Only NT-proBNP predictive w/ Valsartan-Sacubitril


Treatment Goals in ADHF

- Address precipitating factors
- Optimize volume status and perfusion
- Optimize oral heart failure regimen
- Manage Related Risks (e.g. SCD, VTE)
- Patient Education
- Initiate Longitudinal Disease Management
Precipitating Factors

- Acute coronary syndromes/coronary ischemia
- Severe hypertension
- Atrial or ventricular arrhythmias
- Infection
- Pulmonary emboli
- Renal failure
- Medications (e.g. NSAIDs, steroids, TZDs, L-type CCBs)
- Nonadherence (e.g. sodium and fluid restriction, medications)
- Other cardiac dz (acute endocarditis, acute dissection, acute myopericarditis)

Treatment of Acute Decompensated Heart Failure

Vasodilators
- Nitroprusside
- Nitroglycerin
- Nesiritide

Inotropic Drugs
- Dopamine
- Dobutamine
- Milrinone
Diuresis in ADHF

- Loop diuretics: IV bolus or continuous infusion
  - Furosemide, torsemide, bumetanide
    - 80 mg po furosemide = 40 mg IV furosemide = 20 mg po/IV torsemide = 1 mg po/IV bumetanide
  - Initiate rapidly at dose ≥ oral regimen
    - i.e. if home dose 80 mg p.o. furosemide, give 80 mg l.V. furosemide
  - Give at frequent intervals
    - At least b.i.d. or t.i.d.
  - Give higher doses in pts with elevated BUN
    - *Aldosterone antagonists are weak diuretics and used mostly for K-sparing and neurohormonal effects

- Lower filling pressures lead to improved outcomes
- Aim for JVP < 10 cm H₂O or PCWP < 20 mm Hg
- In RV failure, may have to settle for a slightly higher JVP

Hospital Course

- Day 1:
  - 200 mg IV furosemide b.i.d. → BUN/Cr 30/1.8 → 40/2.2
  - Net urine output 500 ml
- Day 2:
  - 200 mg IV furosemide b.i.d. + metolazone 5 mg
  - Cr 45/2.5, K 3.2
  - Net urine output 700 ml
Diuretic Resistance

- Reduced natriuretic response to a given dose of diuretic, necessitating the use of higher doses and combinations of loop and non-loop diuretics in order to achieve net sodium and fluid loss, often at the expense of worsening renal function.

Strategies to Overcome “Diuretic Resistance”

- Increase diuretic dose
  - Increase the previous dose to max. furosemide 200 mg IV t.i.d.

- Continuous vs. bolus diuretic infusion
  - 2.5 to 20 mg/hr furosemide drip

- Addition of thiazide diuretics
  - Metolazone 1.25 to 5 mg p.o. b.i.d. or diuril 250 to 500 mg IV t.i.d.

- Inotropic support
DOSE Trial

- N=308 pts with ADHF, < 24 hrs admission

**HIGH vs. LOW DOSE Diuretics**
- ↑ improvement in dyspnea @ 72 hrs
- ↑ net diuresis and weight loss @ 72 hrs
- ↑ proportion w/ WRF (↑Cr > 0.3 mg/dL)
- No diff in death, re-hospitalization, or ED visits @ 60d

**BOLUS vs. CONTINUOUS Diuretic Infusion**
- No difference in any outcomes

Felker et al. NEJM 2011;364:797-805.

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CARESS: UF vs. IV Diuretics

- N=188
- HFrEF or HFpEF
- ≥ 2 signs of ADHF
- ↑Scr ≥ 0.3, 12 wk prior to or 10 d after admit
- No IV vasoactive meds
- Scr < 3.5 mg/dL
- 1º End-pt: Δ in weight and Cr @ 96 hr

Bart et al. NEJM 2012;367:2269-304
ROSE-AHF

- 360 pts admitted with ≥ 1 symptom and sign of ADHF (HFrEF or HFpEF)
- eGFR 15-60 ml/min
- Randomized to nesiritide, dopamine, or placebo within 24 hrs
- Primary end-points: urine volume and change in cystatin C at 72 hrs

Table 2. Coprimary End Points. Effect of Low-Dose Dopamine vs Placebo or Low-Dose Nesiritide vs Placebo on Cumulative Urine Volume During 72 Hours and Change in Cystatin C Level From Baseline to 72 Hours

<table>
<thead>
<tr>
<th></th>
<th>Mean (95% CI)</th>
<th>Treatment Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (n = 119)</td>
<td>Dopamine (n = 122)</td>
<td></td>
</tr>
<tr>
<td>Cumulative urine volume from randomization to 72 h, ml</td>
<td>8296 (7762 to 8830)</td>
<td>8524 (7917 to 9131)</td>
<td>229 (-714 to 1171)</td>
</tr>
<tr>
<td>Change in cystatin C level from randomization to 72 h, mg/l</td>
<td>0.11 (0.06 to 0.16)</td>
<td>0.12 (0.06 to 0.18)</td>
<td>0.01 (-0.08 to 0.10)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 119)</th>
<th>Nesiritide (n = 119)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative urine volume from randomization to 72 h, ml</td>
<td>8296 (7762 to 8830)</td>
<td>8574 (8014 to 9114)</td>
<td>379 (-618 to 1176)</td>
</tr>
<tr>
<td>Change in cystatin C level from randomization to 72 h, mg/l</td>
<td>0.11 (0.06 to 0.16)</td>
<td>0.07 (0.01 to 0.13)</td>
<td>~0.04 (~0.13 to 0.05)</td>
</tr>
</tbody>
</table>

JAMA. 2013;310(23):2533-2543

Hospital Course

- Day 3:
  - IV furosemide drip @ 20 mg/h → BUN 50, Cr 3.1
  - Net urine output 1000 ml
  - Transient drop

- Day 4:
  - Weaned off metoprolol w/out improvement

- Day 5:
  - Stopped valsartan-sacubitril w/out improvement

What do you do next?
When to consider PA Catheter?

ESCAPE Trial

- Severe clinical decompensation with uncertain hemodynamic profile by bedside evaluation
- Hypotension or worsening renal function with empiric therapy
- Presumed cardiogenic shock
- Apparent inotrope dependence or refractory symptoms
- Evaluation for VAD or transplant candidacy
- Evaluation of pulmonary arterial hypertension


Hospital Course

- PA catheter: RA 16, PCW 34, CI 1.5, SVR 1800
- Did not tolerate IV nitroprusside due to hypotension
- Started on IV milrinone with improved urine output and renal function
- Attempts to wean milrinone unsuccessful
Hospital Course

- PA catheter: RA 16, PCW 34, CI 1.5, SVR 1800
- Did not tolerate IV nitroprusside due to hypotension
- Started on IV milrinone with improved urine output and renal function
- Attempts to wean milrinone unsuccessful

What do you do next?

Inotropes Increase Mortality in ADHF: ESCAPE

When to consider advanced therapies: MCS/Transplant

- Escalating diuretic requirements
- Progressive renal dysfunction
- Increasing frequency of HF hospitalization
- Increasing burden of ventricular arrhythmias
- Withdrawal of previously tolerated ACEi or BB
- Refractory HF symptoms
- Need for inotropic support
- > 5% non-fluid related weight loss (cachexia)

Hospital Discharge

- Ensure adequate decongestion (JVP < 10 cm H₂O)
- Institute evidence-supported therapies prior to d/c
- Careful discharge planning, including written instructions for
  - Discharge medications
  - Diet (2 gm Na and 2 L fluid restriction)
  - Weight monitoring
  - What to do if symptoms worsen
  - Follow-up appointment with 1 week of discharge
- Disease Management Program
PCWP, not CI, Predicts Outcomes After HF Hospitalization: ESCAPE Trial


Utilization and Adherence to GDMT

Utilization and Adherence to GDMT

- Starting GDMT during admission increases likelihood of being on it after discharge
- GDMT improves long-term outcomes

Post-Discharge Survival By Beta-Blocker Therapy (OPTIMIZE-HF Registry)

Post-Discharge Survival By Beta-Blocker Therapy (OPTIMIZE-HF Registry)

Continuation of beta-blockers associated with lower risk
Withdrawal of beta-blockers associated with higher risk

Impact of Various Transitional Care Interventions on HF Outcomes

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcome at 3-6 Months</th>
<th>N Studies</th>
<th>N Subjects</th>
<th>Finding</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Home-visiting programs</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>All-cause readmission</td>
<td>9</td>
<td>1563</td>
<td></td>
<td>✓</td>
<td>0.75 (0.63 to 0.86)</td>
</tr>
<tr>
<td>HF-specific readmission</td>
<td>1</td>
<td>282</td>
<td></td>
<td>✓</td>
<td>0.51 (0.31 to 0.82)</td>
</tr>
<tr>
<td>Composite endpoint*</td>
<td>4</td>
<td>624</td>
<td></td>
<td>✓</td>
<td>0.78 (0.63 to 0.94)</td>
</tr>
<tr>
<td>Mortality</td>
<td>8</td>
<td>1693</td>
<td></td>
<td>✓</td>
<td>0.77 (0.60 to 0.97)</td>
</tr>
<tr>
<td>Number of hospital days at readmission</td>
<td>3</td>
<td>483</td>
<td></td>
<td>✓</td>
<td>WMD: -1.17 (2.44 to 0.09)</td>
</tr>
<tr>
<td><strong>Structured telephone support</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>All-cause readmission</td>
<td>8</td>
<td>2180</td>
<td></td>
<td>✓</td>
<td>0.92 (0.77 to 1.10)</td>
</tr>
<tr>
<td>HF-specific readmission</td>
<td>7</td>
<td>1790</td>
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<td>✓</td>
<td>0.74 (0.61 to 0.90)</td>
</tr>
<tr>
<td>Composite endpoint*</td>
<td>3</td>
<td>977</td>
<td></td>
<td>✓</td>
<td>0.81 (0.58 to 1.12)</td>
</tr>
<tr>
<td>Mortality</td>
<td>7</td>
<td>2011</td>
<td></td>
<td>✓</td>
<td>0.74 (0.56 to 0.97)</td>
</tr>
<tr>
<td>Number of hospital days at readmission</td>
<td>5</td>
<td>1189</td>
<td></td>
<td>✓</td>
<td>WMD: -0.95 (2.43 to 0.53)</td>
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<tr>
<td><strong>Telemonitoring</strong></td>
<td></td>
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<tr>
<td>All-cause readmission</td>
<td>3</td>
<td>434</td>
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<td>✓</td>
<td>1.11 (0.87 to 1.42)</td>
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<tr>
<td>HF-specific readmission</td>
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<td>182</td>
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<td>✓</td>
<td>1.70 (0.92 to 3.51)</td>
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<tr>
<td>Composite endpoint*</td>
<td>2</td>
<td>306</td>
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<td>✓</td>
<td>0.80 (0.43 to 1.51)</td>
</tr>
<tr>
<td>Mortality</td>
<td>3</td>
<td>536</td>
<td></td>
<td>✓</td>
<td>0.93 (0.75 to 1.18)</td>
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<tr>
<td><strong>Multidisciplinary HF-clinic</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause readmission</td>
<td>2</td>
<td>336</td>
<td></td>
<td>✓</td>
<td>0.70 (0.55 to 0.90)</td>
</tr>
<tr>
<td>HF-specific readmission</td>
<td>1</td>
<td>106</td>
<td></td>
<td>✓</td>
<td>0.70 (0.29 to 1.70)</td>
</tr>
<tr>
<td>Composite endpoint*</td>
<td>2</td>
<td>306</td>
<td></td>
<td>✓</td>
<td>0.80 (0.43 to 1.51)</td>
</tr>
<tr>
<td>Mortality</td>
<td>3</td>
<td>536</td>
<td></td>
<td>✓</td>
<td>0.56 (0.34 to 0.92)</td>
</tr>
<tr>
<td><strong>Nurse-led HF-clinic</strong></td>
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</tr>
<tr>
<td>All-cause readmission</td>
<td>2</td>
<td>264</td>
<td></td>
<td>✓</td>
<td>0.88 (0.57 to 1.37)</td>
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<tr>
<td>HF-specific readmission</td>
<td>1</td>
<td>138</td>
<td></td>
<td>✓</td>
<td>0.95 (0.69 to 1.32)</td>
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<tr>
<td>Composite endpoint*</td>
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<td>106</td>
<td></td>
<td>✓</td>
<td>0.66 (0.43 to 1.01)</td>
</tr>
<tr>
<td>Mortality</td>
<td>2</td>
<td>264</td>
<td></td>
<td>✓</td>
<td>0.70 (0.42 to 1.13)</td>
</tr>
<tr>
<td><strong>Primarily educational interventions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause readmission</td>
<td>1</td>
<td>200</td>
<td></td>
<td>✓</td>
<td>1.14 (0.84 to 1.54)</td>
</tr>
<tr>
<td>HF-specific readmission</td>
<td>1</td>
<td>223</td>
<td></td>
<td>✓</td>
<td>0.53 (0.31 to 0.90)</td>
</tr>
<tr>
<td>Composite endpoint*</td>
<td>2</td>
<td>423</td>
<td></td>
<td>✓</td>
<td>0.92 (0.58 to 1.47)</td>
</tr>
<tr>
<td>Mortality</td>
<td>2</td>
<td>473</td>
<td></td>
<td>✓</td>
<td>1.10 (0.52 to 2.36)</td>
</tr>
</tbody>
</table>

**CHAMPION**

Heart Failure Management Guided by Implantable PA pressure Sensor vs. Usual Care (N=550)

<table>
<thead>
<tr>
<th>Days</th>
<th>Treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>210</td>
<td>280</td>
</tr>
<tr>
<td>30</td>
<td>216</td>
<td>267</td>
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<tr>
<td>60</td>
<td>219</td>
<td>252</td>
</tr>
<tr>
<td>90</td>
<td>220</td>
<td>215</td>
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<td>198</td>
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<tr>
<td>180</td>
<td>168</td>
<td>213</td>
</tr>
<tr>
<td>210</td>
<td>163</td>
<td>170</td>
</tr>
<tr>
<td>240</td>
<td>130</td>
<td>138</td>
</tr>
<tr>
<td>270</td>
<td>107</td>
<td>105</td>
</tr>
<tr>
<td>300</td>
<td>81</td>
<td>67</td>
</tr>
<tr>
<td>330</td>
<td>28</td>
<td>25</td>
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<td>360</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>390</td>
<td>1</td>
<td>0</td>
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</table>

RRR=30%
P<0.001


---

**HF w/ Preserved EF: Guidelines**

<table>
<thead>
<tr>
<th>Recommendations for Stage C HFrEF</th>
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<tbody>
<tr>
<td>COR</td>
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<tr>
<td>-----</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>IIA</td>
</tr>
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<td>IIA</td>
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<tr>
<td>IIA</td>
</tr>
</tbody>
</table>

Yancy et al. *Circulation* 2017;136:e137-161
HF w/ Preserved EF: Guidelines

TOPCAT: Spironolactone decreased HF hosp. vs. placebo (12 vs. 14.2%, p = 0.04)

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<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 glomerular filtration rate &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. 1,10,11,12</td>
</tr>
</tbody>
</table>

CHARM-Preserved: Candesartan decreased HF hosp. vs. placebo (15.9 vs. 18.3%, p=0.072)

| IIb | B | The use of ARBs might be considered to decrease hospitalizations for patients with HfPEF. 10 |

NEAT-HFpEF and RELAX trials showed no benefit on exercise capacity

| III: No Benefit | B-R | Routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QoL in patients with HfPEF is ineffective. 13,14 |

Yancy et al. Circulation 2017;136:e137-161

PARAGON-HF

- N=4,822 pts, age ≥ 55 yrs, EF ≥ 45%, NYHA II-IV, LAA or LVH on echo, HF hosp. w/in 9 mths or elevated NT-proBNP

HF Hospitalizations + CV Death

- HR 0.87, p=0.06
- 160 mg bid Valsartan
- Sacubitril–valsartan 97-103 mg bid

Solomon et al. DOI: 10.1056/NEJMoa1908655
Summary

- Optimize GDMT to improve outcomes, including consideration of ARNI
- ADHF is a clinical diagnosis, but BNP can be useful when there is diagnostic uncertainty
- Treatment of HF should be targeted at optimization of volume status with maintenance of adequate end-organ perfusion
- Patients should be diuresed to JVP < 10 cm H₂O when possible and routine use of inotropes should be avoided
- Initiate lifesaving therapies prior to hospital discharge and coordinate longitudinal follow-up
- Consider ivabradine, IV iron, and SGLT-2i to reduce HF hospitalization
- Patients with refractory/recurrent symptoms that are resistant to standard therapy should be referred for consideration of advanced therapies
- Therapy for HFpEF remains limited