CONTEMPORARY MANAGEMENT OF HEART FAILURE

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Primary Care Internal Medicine
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Disclosures: None
TOPICS TO BE ADDRESSED

- Therapy of Systolic Dysfunction
  - Current pharmacological treatment
  - Cardiorenal syndrome
  - Role of biomarker-guided treatment
  - Cardiac resynchronization therapy
  - Ambulatory device-based treatment

- Therapy of Diastolic Dysfunction
  - Changing physiologic paradigm
  - Treatment goals
  - Current pharmacological treatment
  - Ongoing clinical trials
AHA/ACC Class I Recommendations for Treatment of Patients with Symptomatic Left Ventricular Systolic Dysfunction (Stage C or D Disease)

- ACE inhibitor therapy is recommended for all patients with current or prior heart failure symptoms, unless contraindicated (Level of evidence: A)

- ARBs (specifically: candesartan, valsartan) are recommended for patients with current or prior symptoms of heart failure who are ACE intolerant or as first line therapy (Level of evidence: A)

- Beta-blockers (specifically: bisoprolol, carvedilol, or sustained release metoprolol succinate) are recommended for all patients with current or prior heart failure symptoms, unless contraindicated (Level of evidence: A)

- An aldosterone antagonist is recommended for all patients with NYHA class II-IV symptoms, creatinine > 30 ml/min and K⁺ < 5.0 mEq/L

CARDIO-RENAL SYNDROME

Definition: >25% increase in serum creatinine or rise ≥ 0.3 mg/dL that occurs during attempted diuresis and persists after diuresis has been accomplished

- 2-fold increase in mortality
- Associated with: older age, elevated baseline creatinine, lower BP, longer duration of heart failure symptoms, hyponatremia
- Not associated with “low output” hemodynamics
- Occurs with both systolic and diastolic heart failure

Potential therapies:
- adenosine antagonists [rolofylline]
- vasopressin antagonists [tolvaptan, conivaptan]
- ultrafiltration

OUTCOME FOR DEATH OR TRANSPLANTATION BY RENAL FUNCTION AND VOLUME STATUS

808 pts with ADHF randomized to receive:
- Continuous or IV bolus loop diuretic
- High dose IV (2.5 x oral) vs. low dose IV (1x oral) loop diuretic

EFFECT OF NESIRITIDE OR DOPAMINE ON RENAL FUNCTION IN ACUTE DECOMPENSATED HEART FAILURE

ROSE-HF TRIAL


- 360 patients admitted with ADHF and preexisting renal dysfunction were randomized to nesiritide (0.005 µg/kg/min) or dopamine (2 µg/kg/min).
- Baseline creatinine: 1.6 mg/dL
POTENTIAL BENEFITS AND CONCERNS ABOUT ULTRAFILTRATION

- More rapid removal of fluid
- Isotonic fluid removal & higher clearance of sodium load
- Lack of further activation of the SNS, renin-angiotensin-aldosterone system
- Renal tubules “resensitized” to diuretic/Na+ handling
- Efficacy versus equally aggressive weight loss on diuretics alone remains unknown
- Single positive trial, no data on mortality
- No clear benefit on renal function
- Greater cost
- Specialized nursing expertise required
- Catheter-related complications (infection, thrombosis)

ACC/AHA 2009 class IIa indication for refractory HF*


Patients had already sustained rise in creatinine > 0.3 mg/dl before randomization.

ULTRAFILTRATION IN ACUTE HEART FAILURE

THE CUORE TRIAL

Freedom from HF Rehospitalization

- 56 pts with ADHF randomized to IV diuretics or UF x 1 day + IV diuretics
- Baseline BUN/creatinine: 102/1.8 mg%
- Weight loss: 7.5 kg UF vs. 7.9 kg for diuretic alone
- Mean dose of diuretics was equal between groups

ongoing cardiorenal clinical trials

- **Ultrafiltration:** AVOID-HF trial
  - Ultrafiltration versus diuretics alone to achieve similar volume reductions during index hospitalization
  - Loop diuretic: 2.5 x oral dose; UF < 250 ml/hr
  - 90 day rehospitalization rate

- **Vasopressin Antagonist:** TACTICS trial
  - Adjunctive tolvaptan to diuretic therapy
  - Renal function and rehospitalization rate
IVABRADINE IN SYSTOLIC HEART FAILURE  
SHIFT TRIAL

- Ivrabadine inhibits $I_f$ channel and selective slows sinus node [no effect on AV node or contractility]
- SHIFT RCT in 6558 patients with LVEF $\leq$ 35%, HR $\geq$ 70 BPM, stable NYHA class II-III HF, 90% were receiving a beta blocker
- Key Findings:
  - Ivrabadine decreased HF hospitalizations (16% vs. 21%; $p < 0.001$)
  - Ivrabadine lowered HF deaths (3% vs. 5%, $p=0.14$)
  - NYHA class improved on active treatment

SHIFT TRIAL

PRIMARY ENDPOINT: DEATH OR HF HOSPITALIZATION

## ESC INDICATIONS FOR IVABRADINE

<table>
<thead>
<tr>
<th>Scenario</th>
<th>LVEF</th>
<th>Class</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA class II-IV symptoms on GBMT (ACE/ARB, β-blocker, Aldo antagonist)*</td>
<td>≤35%</td>
<td>IIA</td>
<td>B</td>
</tr>
<tr>
<td>NYHA class II-IV symptoms on GBMT and unable to tolerate blocker*</td>
<td>≤35%</td>
<td>IIB</td>
<td>C</td>
</tr>
<tr>
<td>NYHA class II-IV HF + angina + intolerant to β-blocker</td>
<td>IIA</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Symptomatic HF and active angina despite β-blocker</td>
<td>I</td>
<td>A</td>
<td></td>
</tr>
</tbody>
</table>

*HR ≥ 70/min

Neprilysin Inhibition Potentiates Actions of Endogenous Vasoactive Peptides to Balance Maladaptive Mechanisms in Heart Failure

Endogenous vasoactive peptides
(natriuretic peptides, adrenomedullin, bradykinin, substance P, calcitonin gene-related peptide)

- Neurohormonal activation
- Vascular tone
- Cardiac fibrosis, hypertrophy
- Sodium retention

Neprilysin inhibition

Inactive metabolites

Neprilysin
Sacubitril/valsartan (Entresto) is a novel, dual-acting agent which delivers concomitant neprilysin (NEP) inhibition and angiotensin (AT₁) receptor blockade. The drug results in increased levels of natriuretic peptides by inhibiting their breakdown and potent AT₁ receptor blockade.

PARADIGM HF TRIAL

CV Death or HF Hospitalization

- 8442 patients randomized to enalapril 20 mg bid or sacubitril/valsartan 200 mg bid
- Mean LVEF: 29% ± 6%
- NYHA class I: 5%
  - II: 70%
  - III: 24%
- Mean creatinine: 1.2 mg%
- Median NT-proBNP: 1600 pg/ml

McMurray JJ, et al. NEJM 2014;371:993-1004;
## PARADIGM-HF: Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>LCZ696 (n=4187)</th>
<th>Enalapril (n=4212)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prospectively identified adverse events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic hypotension</td>
<td>588</td>
<td>388</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Serum potassium &gt; 6.0 mmol/l</td>
<td>181</td>
<td>236</td>
<td>0.007</td>
</tr>
<tr>
<td>Serum creatinine ≥ 2.5 mg/dl</td>
<td>139</td>
<td>188</td>
<td>0.007</td>
</tr>
<tr>
<td>Cough</td>
<td>474</td>
<td>601</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Discontinuation for adverse event</strong></td>
<td>449</td>
<td>516</td>
<td>0.02</td>
</tr>
<tr>
<td>Discontinuation for hypotension</td>
<td>36</td>
<td>29</td>
<td>NS</td>
</tr>
<tr>
<td>Discontinuation for hyperkalemia</td>
<td>11</td>
<td>15</td>
<td>NS</td>
</tr>
<tr>
<td>Discontinuation for renal impairment</td>
<td>29</td>
<td>59</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Angioedema (adjudicated)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medications, no hospitalization</td>
<td>16</td>
<td>9</td>
<td>NS</td>
</tr>
<tr>
<td>Hospitalized; no airway compromise</td>
<td>3</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Airway compromise</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
BIOMARKER PROFILE IN HEART FAILURE

BNP-GUIDED THERAPY IN HEART FAILURE
THE STARS-BNP STUDY

Freedom from CHF Death or Hospitalization

- 220 NYHA class II or III patients receiving ACE and β-blockade were randomized to conventional or BNP-guided treatment at 3 month intervals

- CHF Deaths: 3 vs. 9
- CHF hospitalizations: 22 vs. 48 (p < 0.001)
- BNP < 100 pg/ml: 16%

# BNP-GUIDED HEART FAILURE THERAPY

## A META-ANALYSIS


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### All-Cause Mortality

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Weight</th>
<th>Hazard ratio (IV, Random, 95% CI)</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Christchurch pilot</td>
<td>0.9%</td>
<td>0.15 [0.02, 1.20]</td>
<td>2000</td>
</tr>
<tr>
<td>TIME-CHF</td>
<td>24.4%</td>
<td>0.67 [0.45, 1.00]</td>
<td>2009</td>
</tr>
<tr>
<td>Vienna</td>
<td>10.5%</td>
<td>1.00 [0.54, 1.85]</td>
<td>2010</td>
</tr>
<tr>
<td>PRIMA</td>
<td>26.1%</td>
<td>0.78 [0.53, 1.15]</td>
<td>2010</td>
</tr>
<tr>
<td>Signal-HF</td>
<td>3.4%</td>
<td>1.12 [0.38, 3.25]</td>
<td>2010</td>
</tr>
<tr>
<td>BATTLESCARRED</td>
<td>13.1%</td>
<td>0.94 [0.54, 1.63]</td>
<td>2010</td>
</tr>
<tr>
<td>STARBRITE</td>
<td>0.8%</td>
<td>0.33 [0.03, 3.18]</td>
<td>2011</td>
</tr>
<tr>
<td>UPSTEP</td>
<td>15.3%</td>
<td>1.03 [0.62, 1.71]</td>
<td>2011</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>94.4%</td>
<td><strong>0.82 [0.67, 1.01]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 0.00$, $\chi^2 = 5.95$, df = 7 ($P = 0.55$); $I^2 = 0\%$

Test for overall effect: $Z = 1.91$ ($P = 0.06$)

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### Aggregate data

<table>
<thead>
<tr>
<th>Study</th>
<th>Weight</th>
<th>Hazard ratio (IV, Random, 95% CI)</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>STARS_BNP</td>
<td>4.0%</td>
<td>0.61 [0.23, 1.64]</td>
<td>2007</td>
</tr>
<tr>
<td>Anguita et al.</td>
<td>1.6%</td>
<td>1.38 [0.28, 6.80]</td>
<td>2010</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>5.6%</td>
<td><strong>0.77 [0.33, 1.78]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 0.00$, $\chi^2 = 0.73$, df = 1 ($P = 0.39$); $I^2 = 0\%$

Test for overall effect: $Z = 0.62$ ($P = 0.54$)

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**Total (95% CI)**

<table>
<thead>
<tr>
<th>Weight</th>
<th>Hazard ratio (IV, Random, 95% CI)</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>100.0%</strong></td>
<td><strong>0.82 [0.67, 1.00]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 0.00$, $\chi^2 = 6.71$, df = 9 ($P = 0.67$); $I^2 = 0\%$

Test for overall effect: $Z = 2.00$ ($P = 0.05$)

Test for subgroup differences: $\chi^2 = 0.02$, df = 1 ($P = 0.88$), $I^2 = 0\%$
BNP-GUIDED HEART FAILURE THERAPY
A META-ANALYSIS

Heart Failure Hospitalization

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Weight</th>
<th>Hazard ratio</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IV, Random, 95% CI</td>
<td></td>
</tr>
<tr>
<td>1.4.1 Individual data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Christchurch pilot</td>
<td>2.7%</td>
<td>0.71 [0.23, 2.26]</td>
<td>2000</td>
</tr>
<tr>
<td>TIME-CHF</td>
<td>16.7%</td>
<td>0.70 [0.48, 1.01]</td>
<td>2009</td>
</tr>
<tr>
<td>Signal-HF</td>
<td>4.1%</td>
<td>0.53 [0.21, 1.32]</td>
<td>2010</td>
</tr>
<tr>
<td>PRIMA</td>
<td>15.7%</td>
<td>1.00 [0.68, 1.47]</td>
<td>2010</td>
</tr>
<tr>
<td>Vienna</td>
<td>11.1%</td>
<td>0.62 [0.38, 1.03]</td>
<td>2010</td>
</tr>
<tr>
<td>BATTLESCARRED</td>
<td>11.7%</td>
<td>0.78 [0.48, 1.27]</td>
<td>2010</td>
</tr>
<tr>
<td>PROTECT</td>
<td>5.2%</td>
<td>0.65 [0.29, 1.44]</td>
<td>2010</td>
</tr>
<tr>
<td>STARBRITE</td>
<td>4.8%</td>
<td>0.96 [0.42, 2.22]</td>
<td>2011</td>
</tr>
<tr>
<td>UPSTEP</td>
<td>16.7%</td>
<td>0.91 [0.63, 1.31]</td>
<td>2011</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>88.8%</td>
<td>0.79 [0.67, 0.94]</td>
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</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.00; \chi^2 = 4.52, df = 8 (P = 0.81); I^2 = 0$
Test for overall effect: $Z = 2.66 (P = 0.008)$

1.4.2 Aggregate data

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Weight</th>
<th>Hazard ratio</th>
<th>Year</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IV, Random, 95% CI</td>
<td></td>
</tr>
<tr>
<td>STARS_BNP</td>
<td>8.4%</td>
<td>0.32 [0.18, 0.59]</td>
<td>2007</td>
</tr>
<tr>
<td>Anguita et al.</td>
<td>2.8%</td>
<td>1.18 [0.38, 3.63]</td>
<td>2010</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>11.2%</td>
<td>0.56 [0.16, 1.98]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.63; \chi^2 = 3.96, df = 1 (P = 0.05); I^2 = 75$
Test for overall effect: $Z = 0.90 (P = 0.37)$

Total (95% CI)

<table>
<thead>
<tr>
<th>Weight</th>
<th>Hazard ratio</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IV, Random, 95% CI</td>
<td></td>
</tr>
<tr>
<td>100.0%</td>
<td>0.74 [0.60, 0.90]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.02; \chi^2 = 13.13, df = 10 (P = 0.22); I^2 = 24$
Test for overall effect: $Z = 3.07 (P = 0.002)$
Test for subgroup differences: $\chi^2 = 0.28, df = 1 (P = 0.60); I^2 = 0$

MGH PROTECT TRIAL
OUTCOME WITH NT-PRO-BNP GUIDED THERAPY

Days from study enrollment

Log rank p = 0.18
Age < 75 years

Log rank p = 0.01
Age ≥ 75 years

CARDIAC RESYNCHRONIZATION THERAPY

Hare JM. *NEJM* 2002;346:1903
Class I Indication (level of evidence: A)

- NYHA Class II, III or ambulatory class IV heart failure symptoms despite GDMT- diuretic, vasodilator and beta-blocker therapy
- Sinus rhythm
- LVEF ≤ 35
- QRS ≥150 msec
- LBBB

Class IIa Indication (level of evidence: B)

- NYHA Class II, III or ambulatory class IV heart failure symptoms despite GDMT- diuretic, vasodilator and beta-blocker therapy
- Sinus rhythm
- LVEF ≤35%
- QRS ≥ 120-149 msec
- LBBB (NYHA II) or non-LBBB (NYHA class III/IV)

BILDETT BRANCH BLOCK MOPHOLSABY AND OUTCOME FOLLOWING CARDIAC RESYNCHRONIZATION THERAPY MEDICARE REGISTRY

MADIT-CRT TRIAL
SURVIVAL IN MILD HEART FAILURE

- 854 patients in post-trial registry from original 1818 patients
- NYHA class I (ischemic only): 15%
- NYHA class II: 85%
- LVEF < 25%: 63%
- LBBB: 74%
- ACE/ARB: 97%
- Beta-blocker: 95%

Goldenberger I, et al. NEJM 2014;370:1694-701
MADIT-CRT LONG-TERM STUDY
TAKE HOME MESSAGE

• Early intervention with CRT-D was associated with a significant long-term survival [> 7 year] benefit in patients with NYHA class I/II symptoms, LBBB, and QRS > 150 msec

• No benefits were not observed among mild HF patients with RBBB or IVCD

• Beneficial response on survival or LV remodeling cannot be extrapolated to patients with LBBB and QRS 120-149 msec
Class IIb Indication

- Patients with LVEF $\leq 35\%$, NYHA functional class I or II symptoms on optimal medical treatment, who are undergoing permanent pacer or ICD implantation with frequent anticipated ventricular pacing (level of evidence: C)

PACING STRATEGIES FOR HEART BLOCK WITH SYSTOLIC DYSFUNCTION

- 691 patients with 2nd or 3rd degree AV block
- LVEF for pacer only cohort: 42%
- LVEF for pacer + ICD cohort: 32%

Freedom from primary outcome event: any cause death, urgent HF visit, LVEDVI > 15%

HR: 0.74

DETECTION OF IMPENDING DECOMPENSATION

Insight from Continuous Physiologic Monitoring

- Filling pressures increase
- Intrathoracic Impedance Changes
- Symptoms Weight Change

Time Preceding Hospitalization


**INTRATHORACIC IMPEDANCE MONITORING AND OUTCOME**

**THE DOT-HF TRIAL**

- 335 patients with ICD (20%) or CRT/ICD and OptiVol hemodynamic monitoring and alarms
- NYHA class: II (62%), III (35%)
- Mean LVEF: 25% ± 7%
- Primary Endpoint: death of HF hospitalization

Hazard ratio, 1.52 (CI, 0.97-2.37)  
\( P = 0.063 \)

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Access Arm</th>
<th>Control Arm</th>
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</thead>
<tbody>
<tr>
<td>168</td>
<td>156</td>
<td>144</td>
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<tr>
<td>156</td>
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<td>151</td>
<td>136</td>
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<tr>
<td>113</td>
<td>67</td>
<td>66</td>
</tr>
<tr>
<td>47</td>
<td>46</td>
<td>47</td>
</tr>
</tbody>
</table>
CHAMPION TRIAL OF DIRECT PULMONARY ARTERY PRESSURE MONITORING

Catheter-based delivery system

Pressure sensor

Home electronics

CHAMPION TRIAL

Cumulative Heart Failure Hospitalizations

Target range (mmHg):
- PA systolic: 15-35
- PA diastolic: 8-20
- PA mean: 10-25

- 30%↓ in HF hospitalizations at 6 months
- 35%↓ in annualized heart failure hospitalization rate
- ↑Quality of life score with treatment group

CONVENTIONAL AND EMERGING THERAPIES FOR ADVANCED SYSTOLIC HEART FAILURE

Thinking “Outside of the Box”

- Diuretics
- Spironolactone
- Digoxin
- ACEIs
- Beta-blockers
- ARBs
- HYD/ISDN
- Lifestyle Δs

- ICD
- Bi-V pacing
- NEP Inhibitors
- Serelaxin?
- Ivabradine
- Htx
- VAD
- Ultrafiltration
- Cell Tx
- Gene Therapy
- Iron deficiency
- OSA
- CSA

Adapted from Young JL
DIASTOLIC HEART FAILURE
OLD PARADIGM: PRESSURE-VOLUME RELATION

Approximately 40% of heart failure cases occur in patients with normal or near normal (LVEF >45%) ventricular systolic function.

Diastolic dysfunction

Longitudinal systolic dysfunction

Chronotropic incompetence

Extra-cardiac causes of volume overload

Arterial stiffness

Abnormal ventricular-arterial coupling

Pulmonary hypertension / RV failure

Endothelial dysfunction

Autonomic dysfunction

HFpEF

GOALS OF THERAPY IN HEART FAILURE WITH PRESERVED EJECTION FRACTION

- Decrease diastolic filling pressures
  - Diuretics, nitrates
- Control blood pressure and heart rate
  - Rest and exercise
- Prevent or regress left ventricular hypertrophy
  - RAS inhibitors, SNS antagonists, ? autonomic modulation
- Manage medical co-morbidities
  - Diabetes, obesity, ischemia, arrhythmias, sleep apnea
- Promote exercise and decrease deconditioning
EXERCISE TRAINING IN HF-PEF
THE EX-DHF PILOT STUDY

- 64 patients with HF-PEF were randomized to 3 months (32 sessions) of supervised endurance/resistance training versus usual care.
- Sessions 2X per week for first month increasing to 3x per week.
- Mean age: 65 years.
- Mean LVEF: 67% ± 8%.
- NYHA class II: 84%; III: 16%.

TREATMENT EFFECT ON MORTALITY IN RANDOMIZED CONTROLLED TRIALS OF HEART FAILURE WITH PRESERVED EJECTION FRACTION

- ACE-I
- ARBs
- Vasodilators
  - hydralazine
  - nitrates
  - prazosin
- β-blockers

TREATMENT EFFECT ON EXERCISE CAPACITY IN RANDOMIZED CONTROLLED TRIALS IN HEART FAILURE WITH PRESERVED EJECTION FRACTION


- ACE-I
- ARBs
- Verapamil
- Spironolactone
- ß-blockers
TOPCAT TRIAL
CV Death, HF Hosp, or Resuscitated Cardiac Arrest

HR = 0.89 (0.77 – 1.04)
p=0.138

351/1723 (20.4%)
320/1722 (18.6%)

Placebo
Spironolactone

HR = 0.89 (0.77 – 1.04)
p=0.138

Number at risk
Spiro 1722 1502 1168 870 614 330 53
Placebo 1723 1462 1145 834 581 331 53
# ACC/AHA Treatment Recommendations for Heart Failure with Preserved Ejection Fraction

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic and diastolic blood pressure should be controlled according to published clinical practice guidelines</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Diuretics should be used for relief of symptoms due to volume overload</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Coronary revascularization for patients with CAD in whom angina or demonstrable myocardial ischemia is present despite GDMT</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Management of AF according to published clinical practice guidelines for HFpEF to improve symptomatic HF</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Use of beta-blocking agents, ACE inhibitors and ARBs for hypertension in HFpEF</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>ARBs might be considered to decrease hospitalizations in HFpEF</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Nutritional supplementation is not recommended in HFpEF</td>
<td>III: No Benefit</td>
<td>C</td>
</tr>
</tbody>
</table>

EFFECT OF IVABRADINE ON EXERCISE PERFORMANCE IN HEF-PEF

- 61 patients with HeF-PEF were randomized to placebo or ivabradine 5 mg twice daily
- Background therapy: ACE: 97%; beta blocker: 54%; calcium blocker: 38%; diuretic: 79%
- Heart rate reduction in treatment group: 72 to 62/min
- MET increase 4.1 to 6.0
- VO2: 12.8 to 16.1

RENAL NERVE ANATOMY PERMITS A CATHETER-BASED APPROACH

• Standard interventional technique
• 4-6 two-minute treatments per artery

Courtesy of: Ardian
ONGOING CLINICAL TRIALS OF RENAL DENERVATION FOR HE-PEF

• **DIASTOLE**  Change in E/E’ at 12 months

• **RESPECT-HF**  Change in LAVi and/or LVMi by cMRI at 6 months

• **RDT-PEF**  Change in symptoms, exercise tolerance, biomarkers, LV filling and remodeling at 12 months
THE EPHEMERAL NATURE OF ↑PCWP IN HF-PEF

Borlaug et al. Circ Heart Fail 2010 & unpublished
BEETROOT JUICE (NO DONOR) IN HF-PEF

Zamani et al. Circulation 2015
HEART FAILURE WITH PRESERVED EJECTION FRACTION

“TAKE HOME MESSAGES”

• Current therapy should be aimed at improving symptoms and increasing functional capacity
  – Preload reduction (diuretics and nitrates)
  – Tight control of hypertension
• No agent has been shown to improve mortality which is actually similar to heart failure with systolic dysfunction
• Adequate rate control and ? rhythm control in atrial fibrillation can improve symptoms
• Regression of LVH (when present) is a therapeutic goal
• New agents are urgently needed