WHAT’S NEW IN HEART FAILURE
Drugs, Devices and Diagnostics

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DISCLOSURES

• Medtronic
• Saint Jude Medical
• NHLBI
• HeartWare
• Thoratec
• INTERMACS
WHAT’S NEW IN HEART FAILURE

• Epidemiology
• Drugs
  – Heart failure with reduced ejection fraction
  – Heart failure with preserved ejection fraction
• Heart Transplantation
• Devices
  – Mechanical circulatory support
• Diagnostics
  – Sensors for heart failure
HF PREVALENCE

Heidenreich, Circ Heart Failure 2013; 6:606-619
# HFrEF RESULTS OF STANDARD THERAPY

<table>
<thead>
<tr>
<th>GDMT</th>
<th>RR Reduction in Mortality (%)</th>
<th>NNT for Mortality Reduction (Standardized to 36 mo)</th>
<th>RR Reduction in HF Hospitalizations (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor or ARB</td>
<td>17</td>
<td>26</td>
<td>31</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>34</td>
<td>9</td>
<td>41</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>30</td>
<td>6</td>
<td>35</td>
</tr>
<tr>
<td>Hydralazine/nitrate</td>
<td>43</td>
<td>7</td>
<td>33</td>
</tr>
</tbody>
</table>

*Circulation. 2013;128:1810-1852*
HFrEF TARGETS FOR INTERVENTION

- Renin-angiotensin-aldosterone system
  - ACEi
  - ARB
  - Aldosterone antagonists
- Sympathetic activation – beta blockers
- Sudden death - ICD
- Dyssynchrony - CRT
- Naturetic peptides
NEPRILYSIN LEVELS AND SURVIVAL

A

CV death or HF hospitalization

B

CV death

Bayes-Genis J Am Coll Cardiol 2015; 65:658-665

Cumulative Event-free Survival

Cumulative Survival

Years of Follow-up

Years of Follow-up

p=0.003

p<0.001

Nepriysin < median

Nepriysin ≥ median
LCZ696 vs ENALAPRIL
CV DEATH OR HOSPITALIZATION

A Primary End Point

Hazard ratio, 0.80 (95% CI, 0.73–0.87)
P<0.001

No. at Risk
LCZ696  4187  3922  3663  3018  2257  1544  896  249
Enalapril  4212  3883  3579  2922  2123  1488  853  236

LCZ696
ALL CAUSE MORTALITY

D  Death from Any Cause

Hazard ratio, 0.84 (95% CI, 0.76–0.93)
P<0.001

Cumulative Probability

Days since Randomization

No. at Risk
LCZ696  4187  4056  3891  3282  2478  1716  1005  280
Enalapril  4212  4051  3860  3231  2410  1726  994  279

LCZ696 vs ENALAPRIL
HOSPITALIZATIONS PER 100 PTS

Rate ratio 0.77 (0.67-0.89)
P < 0.001

Packer M Circulation. 2015;131:54-61
HFpEF

- 50% of heart failure
- Mortality similar to HFrEF
- Disease of aging
- Hypertension
- LV stiffness – both systolic and diastolic
- Fibrosis
- Vascular stiffness
- BNPs not as high as HFrEF (lower wall stress)
- Poor response to exercise
HFpEF
BETA BLOCKERS
HF DEATH OR HF HOSPITALIZATION

van Veldhuisen J Am Coll Cardiol 2009; 53:2150-2158
HFpEF
RAAS INHIBITORS

Favors RAS inhibition

Favors placebo

Cochran Q = 0.05,
Overall P = 0.62

0.5  1  2
Odds ratio (95% confidence interval)

All-cause mortality

Favors RAS inhibition

Favors placebo

Cochran Q = 1.01,
Overall P = 0.60

0.5  1  2
Odds ratio (95% confidence interval)

Heart failure hospitalization

Shah, J Cardiac Failure 2010; 16:260-267
ALDOSTERONE AND FIBROSIS

Aldosterone/Salt

Aldosterone/Salt + Eplerenone

HFpEF
SPIRONOLACTONE

Pitt, NEJM 2014; 370:1383-1392
# HFpEF: Exercise Program

## Study ID

<table>
<thead>
<tr>
<th>Study</th>
<th>Group Difference - MLWHF units (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gary 2007</td>
<td>-19.00 (-32.09, -5.91)</td>
</tr>
<tr>
<td>Smart 2007</td>
<td>-5.70 (-13.91, 2.51)</td>
</tr>
<tr>
<td>Edelmann 2011</td>
<td>-5.00 (-11.00, 1.00)</td>
</tr>
<tr>
<td>Kitzman 2011</td>
<td>-9.00 (-18.05, 0.05)</td>
</tr>
<tr>
<td>Overall</td>
<td>-7.32 (-11.38, -3.26)</td>
</tr>
</tbody>
</table>

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*Taylor, Int J Cardiol 2012; 162:6-13*
HFpEF
EXERCISE PROGRAM

Study	ID
---
Smart 2007	-
Korzeniowska-Kubacka 2010	-
Edelmann 2011	-
Kitzman 2011	-
Overall	-

Between Group Difference - ml/kg/min (95% CI)

- Smart 2007: 3.80 (2.58, 5.02)
- Korzeniowska-Kubacka 2010: 2.06 (0.86, 3.26)
- Edelmann 2011: 3.20 (2.10, 4.30)
- Kitzman 2011: 2.70 (1.41, 3.99)
- Overall: 2.96 (2.36, 3.56)

Taylor, Int J Cardiol 2012; 162:6-13
HFpEF TREATMENT

• Avoid harmful drugs (NSAIDS)
• Control volume overload
• Control BP
  – Beta blockers
  – RAAS antagonists
• Appropriate management of atrial fibrillation
• Appropriate management of ischemia
• Exercise program

Circulation 2013;128:1810-1852
HEART TRANSPLANTATION
THE 3% SOLUTION

320 million

8 million

4 million

150,000 Class IV

75,000 < 75 years old

2500 TRANSPLANT

LONG-TERM MECHANICAL CIRCULATORY SUPPORT
HeartMate II

- Axial flow pump
- Percutaneous driveline
- Electrically powered
- Fixed speed operating mode
- Most commonly used VAD
VAD vs MEDICAL THERAPY

Observed Survival (%)

Years

HVAD Advance
SHFM Medical Therapy
HVAD – CAP*
BTT - Europe

* Data as of 09/05/12
CONTINUOUS FLOW VAD SURVIVAL
SENTARA NORFOLK GENERAL HOSPITAL

Post Implant Survival - Primary LVADs - CONTINUOUS FLOW
Primary Prospective Implants: June 23, 2006 to September 30, 2014

% Percent Survival
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%

% Percent Survival

At Risk: 133
10929
5179
2484
1131
404
103

0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51 54 57 60

Months After Device Implant

Shaded areas indicate 70% confidence limits
p (log-rank) = 0.0150
Event: Death (censored at transplant or recovery)

Percent Survival

<table>
<thead>
<tr>
<th>Months after Device Implant</th>
<th>INTERMACS</th>
<th>VANG-0146</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>95%</td>
<td>98%</td>
</tr>
<tr>
<td>3</td>
<td>91%</td>
<td>97%</td>
</tr>
<tr>
<td>6</td>
<td>87%</td>
<td>94%</td>
</tr>
<tr>
<td>12</td>
<td>81%</td>
<td>85%</td>
</tr>
<tr>
<td>24</td>
<td>70%</td>
<td>81%</td>
</tr>
<tr>
<td>36</td>
<td>60%</td>
<td>74%</td>
</tr>
<tr>
<td>48</td>
<td>48%</td>
<td>68%</td>
</tr>
<tr>
<td>60</td>
<td>42%</td>
<td></td>
</tr>
</tbody>
</table>
HEARTMATE II RISK SCORE
Age, albumin, creatinine, INR

BTT & DT Patients (N=1101)

- Low Risk (HMRS < 1.58)
- Medium Risk (HMRS: 1.58-2.48)
- High Risk (HMRS > 2.48)

P (Log-Rank) < 0.001

At Risk:
- 0 months: 455, 322, 223, 162, 121
- 6 months: 422, 275, 205, 136, 97
- 12 months: 224, 129, 91, 61, 48
- 18 months: 224, 129, 91, 61, 48
- 24 months: 224, 129, 91, 61, 48

Cowger, J Am Coll Cardiol, 2013; 61:313-321
# INTERMACS

<table>
<thead>
<tr>
<th>INTERMACS SCORE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Critical cardiogenic shock</td>
</tr>
<tr>
<td>2</td>
<td>Progressive decline</td>
</tr>
<tr>
<td>3</td>
<td>Stable on inotropes</td>
</tr>
<tr>
<td>4</td>
<td>Resting symptoms</td>
</tr>
<tr>
<td>5</td>
<td>Exertion intolerant</td>
</tr>
<tr>
<td>6</td>
<td>Exertion limited</td>
</tr>
<tr>
<td>7</td>
<td>Class III Heart Failure</td>
</tr>
</tbody>
</table>
SURVIVAL TO DISCHARGE

Boyle, J Heart Lung Transplant 2011;30:402–407
HeartWare HVAD
WHEN TO REFER FOR MCS

- Early Class IV heart failure (some symptoms at rest)
- Late Class III heart failure despite optimal medical management
- One or more heart failure hospitalizations within 6 months
- Inability to tolerate optimal medical management
- Predicted poor outcome using SHFM or MVO2 < 50% predicted
- Chronic diuretic dose > equivalent 1.5 mg/kg furosemide
DON’T WAIT FOR

- Inotrope or pressor dependence
- Progressive end organ dysfunction
- Cardiac cachexia
- Frequent hospitalizations
- Late Class IV Heart Failure (bedridden)
- Pulmonary Hypertension
HEART FAILURE PROGRESSION

Adapted from Adamson. Curr Heart Fail Reports, 2009
TELE HF

- Provide a scale
- Daily toll-free call
- Questions
  - HF
  - Weight
  - General health
  - Depression
- Center notified of variances
- Center calls patient for intervention

Chaudhry. J Cardiac Failure 2007; 13:709-714
TELE-HF

Chaudhry, N Engl J Med 2010; 2301-2309
IMPEDEANCE MONITORING

Worsening HF → ↑ Fluid Retention → ↓ Impedance

↑ LA Filling (Wedge) Pressure

Wang, Am J Cardiol 2007; 99(suppl):3G-10G
van Veldhuisen, Circulation 2011;124:1719-1726
LA PRESSURE SENSOR
PULMONARY ARTERY SENSOR

Diagram showing a pulmonary artery sensor with dimensions: 45 mm, 15 mm, 3.4 mm, and thickness = 2 mm.
CHAMPION TRIAL

Abraham, Lancet, 2011; 377:658-666
CHAMPION TRIAL

Number of medication changes during Primary Endpoint Period

- Total: Treatment 2517, Control 1061
- Based on signs & symptoms: Treatment 1113, Control 1061
- Based on knowledge of PA pressures: Treatment 1404

Treatment | Control
SUMMARY

• Prevalence of heart failure is increasing
• Naturetic peptide system offer new line of attack on HFrEF
• Manage comorbid factors for HFpEF
• Transplantation is limited by donors
• Results of mechanical circulatory support are improving
• New diagnostic tools may improve HF care