Modern Day Therapy of Heart Failure: A Long Way From Dig and Diuretics!

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Heart Failure Is a Common Illness

• 5 million patients in US
• Disease of elderly: #1 Medicare DRG
• US Cost: ~ $40 billion per year

Outline

• Chronic systolic HF
• Advanced Heart Failure
  - Identification (simple clinical clues)
  - Treatment (LVAD/Heart Transplantation)
Outline
- Chronic systolic HF
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Importance of Knowing LVEF in CHF

LVEF

- Low
  - Well-studied
  - Proven therapies

- Normal
  - Poorly studied
  - Generalizations

# of Class I Recommendations

- 12
- 2
  - Control BP
  - Diuretics as needed

ACC/AHA HF Guidelines, 2013

Treatment of Systolic Heart Failure in 2015

Control Volume
- Diuretics
- Sodium restriction

Reduce Mortality
- ACEI (ARB)
- β-Blocker
- Aldosterone Antagonist
- CRT ± an ICD^*
- Hyd/ISDN^*

*For indicated patients
- CRT if QRS > 120-140 msec, esp. LBBB
- ICD if LVEF ≤ 35%
- Hyd/ISDN if patient is black

Treat Residual Symptoms
- Digoxin

^*For indicated patients
**Cumulative Impact of Heart Failure Therapies**

<table>
<thead>
<tr>
<th>Relative-Risk</th>
<th>2 Year Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>- -</td>
</tr>
<tr>
<td>ACE Inhibitor</td>
<td>23%</td>
</tr>
<tr>
<td>Aldosterone Ant</td>
<td>30%</td>
</tr>
<tr>
<td>Beta-Blocker</td>
<td>35%</td>
</tr>
<tr>
<td>CRT +/- ICD</td>
<td>36%</td>
</tr>
</tbody>
</table>

Cumulative risk reduction if all four therapies are used: 77%
Absolute risk reduction: 27%, NNT = 4


**Outline**

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**Defining Advanced HF**

- Lack of standard definition
- Various names
  - Advanced HF
  - End-stage HF
  - Refractory HF
  - Stage D HF
### INTERMACS Profiles

<table>
<thead>
<tr>
<th>Level</th>
<th>Key feature of level</th>
<th>Descriptive label</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Critical cardiogenic shock</td>
<td>&quot;Crash and burn&quot;</td>
</tr>
<tr>
<td>2</td>
<td>Progressive decline</td>
<td>Inotropes, sliding</td>
</tr>
<tr>
<td>3</td>
<td>Stable but inotropic dependent</td>
<td>Inotropes, stable</td>
</tr>
<tr>
<td>4</td>
<td>Resting symptoms</td>
<td>Rest symptoms</td>
</tr>
<tr>
<td>5</td>
<td>Exertion intolerant</td>
<td>Housebound</td>
</tr>
<tr>
<td>6</td>
<td>Exertion limited (fatigue within minutes)</td>
<td>&quot;Walking wounded&quot;</td>
</tr>
<tr>
<td>7</td>
<td>Advanced NYHA III</td>
<td></td>
</tr>
</tbody>
</table>

Stevenson, J Heart Lung Transplant, 2009

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### How to Identify a Patient with Advanced Heart Failure

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### Chronic Parenteral Inotrope Use Is Associated with Very Poor Outcome

- N=36
  - Oregon Health and Science University
  - Hershberger, J Cardiac Failure, 2003

- Propensity matched
  - N=112; Cleveland Clinic
  - Gorodeski, Circ HF, 2009
Simple Clinical Clues to Identify Advanced Heart Failure

- Rehospitalization for CHF
- High doses of diuretic
- Unable to tolerate ACE-I or BBL
- Bad news from EP
- Labile renal function
- Unintentional weight loss

Heart Failure Rehospitalizations

- 20-25% at 30 days
- ~50% at 6 months

1-Year Mortality After Index HF Hospitalization

<table>
<thead>
<tr>
<th></th>
<th>VA</th>
<th>EFFECT-HF</th>
<th>ADHERE-LM</th>
<th>Medicare</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Year Mortality (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Number of CHF Hospitalizations is An Adverse Prognostic Factor

Mortality vs. Years

1st Hospitalization

4th Hospitalization

n = 3,358

n = 14,374

Setoguchi, 2007

20%
40%
60%
80%
100%
Simple Clinical Clues to Identify Advanced Heart Failure

- Rehospitalization for CHF
- High doses of diuretic
- Unable to tolerate ACE-I or BBL
- Bad news from EP
- Labile renal function
- Unintentional weight loss

Furosemide Dose and Mortality

Eshaghian, 2006

ACE-Inhibitor Intolerance is Adverse Prognostic Sign

Kittleson, JACC, 2003
ACE-Inhibitor Intolerance is Adverse Prognostic Sign

Kittleson, JACC, 2003

Simple Clinical Clues to Identify Advanced Heart Failure
- Rehospitalization for CHF
- High doses of diuretic
- Unable to tolerate ACE-I or BBL
- Bad news from EP
  - ICD shocks
  - Nonresponder to BiV pacing
- Labile renal function
- Unintentional weight loss

Outline
- Chronic systolic HF
- Advanced Heart Failure
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  - Treatment (LVAD/Heart Transplantation)
Advanced Therapies for Advanced Heart Failure

- Chronic Inotropes/Palliative care
- Ventricular Assist Device
- Transplantation

Primary Roles of VAD

- Bridge to transplant
- Destination therapy (non-transplant candidate)
REMATCH

HeartMate II
2nd Generation VAD with Continuous Flow

Axial flow

HeartMate II: Destination Outcomes

- Approved
  - HeartMate II: Bridge to Transplant
  - HeartMate II: Destination Therapy
  - HeartWare: Bridge to Transplant
- Investigational
  - HeartWare: Destination Trial

HeartWare

Which VAD for Which of Your Patients?
How to Improve LVAD Outcomes

- Better technology
- Better patient selection

INTERMACS Profile and Post-VAD 6-Month Outcome

INTERMACS 3-4
INTERMACS 1-2

Toronto Aiba, J Heart Lung Transplant, 2009

Finding the “Sweet Spot”

Operative Risk

- Futile Implants
- Successful Implants

Optimal "window" for LVAD implant

Too Early Too Late

Worsening of nutritional state, end-organ and right ventricular function with progressive heart failure

Lietz, 2008
Complications with Continuous Flow LVADs

- Right heart failure
- Infections (driveline)
- Aortic valve insufficiency
- GI bleeding
  - Often from AVMs
  - Similarity to that seen with Aortic stenosis
  - Shearing of von Willebrand factor by VAD
- LVAD thrombosis
Complications with Continuous Flow LVADs

- Right heart failure
- Infections (Driveline)
- Aortic valve insufficiency
- GI bleeding – often from AVMs
- LVAD thrombosis
- Strokes
  - HeartMate II requires coumadin + aspirin
  - 13% per patient year in Destination Trial

High Stroke Rate Post-Continuous LVAD

5th INTERMACS Report

Kirklin, J Heart Lung Transplant, 2013
HeartMate II vs. XVE vs. Medical Therapy

Fang, NEJM, 2009
Kirklin, JHLTx, 2013

5th INTERMACS Survival:
80% 1 year; 70% 2 years

Fang, NEJM, 2009
Kirklin, JHLTx, 2013

Rapid Increase in Destination LVADs:
6th INTERMACS Report

Kirklin, J Heart Lung Transplant, 2014
Spike in Google Searches in Month (July, 2010) When VP Cheney had LVAD implant

Future Ventricular Assist Device Technology to Reintroduce Pulsatility

Generating a Pulse with Continuous Flow BIVAD HeartMate III’s
Advanced Therapies for Advanced Heart Failure

- Chronic Inotropes/Palliative care
- Ventricular Assist Device
- Transplantation

Donor Hearts Are Scarce

- Supply of donor hearts is limited
  - N = 2,000 US donor hearts
  - 40,000+ could potentially benefit from heart transplant
- Donor hearts are a precious resource

Criteria for Transplant

- Identify patients who are:
  - Sick enough to need a transplant
  - Well enough to benefit from it
Poor CHF prognosis + Absence of comorbidities

Trading Baggage

CHF
- Dyspnea
- Fatigue
- Anorexia
- Sudden death

Transplant
- Infection
- Cancer
- Steroids
- Rejection

Adult Heart Transplants
Kaplan-Meier Survival by Era
(Transplants: January 1982 – June 2012)
Conclusions

- Powerful benefits of evidence-based therapies for systolic HF

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Treat Residual Symptoms
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Conclusions
- Powerful benefits of evidence-based therapies for systolic HF
- Advanced HF represents spectrum of illness
  - INTERMACS
- Dependence on inotropes is ominous
- For those not on inotropes, simple clinical clues
  - Rehospitalization
  - Intolerance to ACEi / BBL; need for high-dose diuretic
  - Worsening renal function
  - ICD shock/nonresponder to BiV-pacemaker
  - Cachexia

Conclusions (continued)
- VADs are rapidly emerging
  - Survival better than medical therapy
  - Complications including GI bleeding, Aortic insufficiency, LVAD thrombosis, Stroke
  - Improved LVAD technologies and patient selection
  - ? Tipping point
- Transplantation provides excellent option but limited number of donors