The Who, How and When of Advanced Heart Failure Therapies

9th Annual Dartmouth Conference on Advances in Heart Failure Therapies
Dartmouth-Hitchcock Medical Center
Lebanon, NH
May 20, 2013

Joseph G. Rogers, M.D.
Associate Professor of Medicine
Senior Vice Chief for Clinical Affairs, Division of Cardiology
Medical Director, Cardiac Transplant and Mechanical Circulatory Support Program
Duke University

Disclosures

- Consultant: Thoratec Corporation
- Principal Investigator, HeartWare ENDURANCE trial

What is Advanced Heart Failure?

European Society of Cardiology Committee on Heart Failure

- NYHA class III-IV symptoms
- Clinical signs of fluid retention and/or peripheral hypoperfusion
- Objective evidence of severe LV dysfunction
  - LVEF ≤ 0.30
  - Pseudonormal or restrictive mitral inflow pattern by Doppler
  - High left and/or right-sided filling pressures
  - Elevated b-type natriuretic peptide
- Severe reduction in exercise capacity
  - 6 minute walk distance < 300 meters
  - Peak VO2 < 12-14 ml/kg/min
- > 1 hospitalization in the past 6 months
- Presence of above despite optimal medical management

Eur J Heart Failure 2007; 9:684-94
Heart Failure Risk Stratification

Defining the patient who is “in trouble”

- Signs, symptoms, and clinical course
- Ventricular structure and function
- Medication use and intolerance
- End-organ dysfunction
- Functional limitations
- Biomarkers
- Right heart function

Prognostic Importance of Symptoms

![Graph showing cumulative survival over time for different NYHA classes.](image)

NYHA Functional Class is Insensitive to Mortality
Sub-stratification using Seattle HF Score

![Bar chart showing survival rates for different Seattle HF scores.](image)
**Freedom From Congestion Predicts Survival Despite Previous Class IV Symptoms of HF**

- 146 patients hospitalized with class IV heart failure
- Assessed 4 to 6 weeks after hospitalization for congestion

*Am Heart J.* 2000;140:840–847

**The Impact of Heart Failure Hospitalization on Mortality Risk**

- A retrospective analysis of the CHARM Trial

*Circulation* 2007; 116: 1482-7

**Heart Failure Risk Stratification: Cardiac Structure and Function**

- Mortality vs EF in CHARM
- Subgroup Analysis from SAVE
Importance of RV Function on VAD Outcomes

Post-VAD RV failure contributes to:
- Hepatic congestion
- Renal failure
- Bleeding
- Prolonged mechanical ventilation
- MSOF
- Prolonged LOS

Predictors of RV failure during LVAD support

Evaluating Right Heart Function

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Desirable Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVSWI [(mPA-mCVP) x SV/BSA]</td>
<td>&gt; 300 mmHg x mL/m²</td>
</tr>
<tr>
<td>CVP</td>
<td>&lt;15 mmHg</td>
</tr>
<tr>
<td>Presence of tricuspid regurgitation</td>
<td>Minimal to moderate</td>
</tr>
<tr>
<td>PVR and TPG</td>
<td>PVR &lt;4 Woods Units and TPG &lt;15 mmHg</td>
</tr>
<tr>
<td>RV size</td>
<td>RVESV &lt;200 mL and RVEDV &lt;177 mL</td>
</tr>
<tr>
<td>Need for preoperative ventilator support</td>
<td>None</td>
</tr>
</tbody>
</table>
Heart Failure Risk Stratification
Circulatory-Renal Limitations to Therapy


Prognosis on Chronic Dobutamine or Milrinone Infusions

The Prognostic Value of Functional Limitations

\[ \text{VO}_2\text{max} = (\text{AO}_2 - \text{VO}_2) \times \text{CO} \]

[Graph showing cumulative survival and VO2 max values]
Is Physician Gestalt Important?

- ESCAPE Registry included 439 patients not randomized in trial but received a PAC
- No difference in hemodynamics except higher SVO2 and CI in Trial patients

<table>
<thead>
<tr>
<th></th>
<th>Trial (n=433)</th>
<th>Registry (n=439)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOS, days</td>
<td>6 (3-8)</td>
<td>13 (7-26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6-Month Mortality (%)</td>
<td>19.7</td>
<td>33.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LOS given as median (interquartile range). ESCAPE: Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness; LOS, length of stay for index hospitalization; PAC, pulmonary artery catheter.

What Is a Biomarker?

"A characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or the response to a therapeutic intervention."

Atkinson et al, Clin Pharmacol Ther 2001

*If it costs less than 10 bucks it’s a lab test. If it costs more, it’s a biomarker.

Alan Maisel

Common Biomarkers Useful in Risk Stratification

- Natriuretic peptides
- Serum sodium
- BUN
- Creatinine
- Hemoglobin
- RDW
- Albumin
Physiology of BNP

Hemodynamic (balanced vasodilation)
- veins
- arteries
- coronary arteries

Neurohumoral
- aldosterone
- endothelin
- norepinephrine

Renal
- diuresis
- natriuresis
- GFR

Cardiac
-lusitropic
-antifibrotic
- anti-remodeling

Heart Failure Risk Stratification: Biomarkers

Anemia in Heart Failure
Diagnostic Value of Glomerular Filtration Rate in Patients With Heart Failure

Heart Failure Risk Stratification: Multivariable Models
Seattle Heart Failure Model

Who Should Be Referred for Advanced Heart Failure Therapies?

- Heart failure hospitalization and hypotension
- Failing standard medical and electrical therapies
- Resistant to diuretics
- Inability to walk > 1 block
- Severe LV dysfunction
- Kidney dysfunction (particularly BUN)