When Drugs and Devices are Not Enough: Referral for Advanced Heart Failure Therapies

Gregory P. Macaluso MD
Associate Director Advanced Heart Failure and Transplant Cardiology Fellowship
Advocate Christ Medical Center
Clinical Assistant Professor of Medicine The University of Illinois at Chicago
May 7, 2016
Objectives

• Discuss classification schemes for advanced heart failure (HF)

• Identify clinical clues of advanced HF

• Review prognostic markers of advanced HF

• Discuss various clinical risk models to help determine patient prognosis

• Determine when to refer patients for advanced therapies and why?
New York Heart Association Class

- **Class I**: no symptoms with ordinary activity
- **Class II**: symptoms with moderate activity
- **Class III**: symptoms with ADLs, very limited
- **Class IV**: symptoms at rest
Natural History of Chronic and Acute Heart Failure

Initial phase

Normal heart

Chronic heart failure
5 million in the US
10 million in Europe

Death

Heart Viability

Initial myocardial injury

First ADHF episode:
Pulmonary edema
ER admission

Later ADHF episodes:
Rescue therapy
ICU admission

>60% mortality within 5 years after diagnosis

Gheorghiade M. Am J Cardiol. 2005;96(suppl 6A):1-4G.
ACC/AHA Guidelines
Heart Failure Diagnosis and Management

**Stage A**
At high risk for HF but without structural heart disease or symptoms of HF
- Hypertension
- CAD
- Diabetes mellitus or Patients
- Using cardiotoics
- With FHx CM

**Stage B**
Structural heart disease but without symptoms of HF
- Previous MI
- LV systolic dysfunction
- Asymptomatic valvular disease

**Stage C**
Structural heart disease with prior or current symptoms of HF
- Known structural heart disease
- Shortness of breath and fatigue, reduced exercise tolerance

**Stage D**
Refractory HF requiring specialized interventions
- Patients who have symptoms at rest despite maximal medical therapy (e.g., those who are recurrently hospitalized or cannot be safely discharged from hospital without specialized interventions)

**Therapy**
- Treat hypertension
- Encourage smoking cessation
- Treat lipid disorders
- Encourage regular exercise
- Discourage alcohol intake, illicit drug use
- ACE inhibition in appropriate patients

**Therapy**
- All measures under stage A
- ACE inhibitors in appropriate patients
- Beta-blockers in appropriate patients

**Therapy**
- All measures under stage A
- Drugs for routine use:
  - Diuretics
  - ACE inhibitors
  - Beta-blockers
  - Digitalis
  - Dietary salt restriction

**Therapy**
- All measures under stages A, B, and C
- Mechanical assist devices
- Heart transplantation continuous (not intermittent) IV inotropic infusions for palliation
- Hospice care
LV dysfunction – Natural History

5-7 Million patients with CHF

Risk Factors          Asymptomatic    Mild          Moderate    Severe

Mechanism of death
40%  SCD
40%  ↑ CHF
20%  Other

AHA Classification

AHA Stage A  AHA Stage B  AHA Stage C  AHA Stage D

% Survival

Annual Mortality

<5%  10%  20-30%  30-80%
Further Characterization of Advanced Heart Failure

To identify patients for medical, pacing, transplantation or circulatory support:

INTERMACS PROFILES 1-7
<table>
<thead>
<tr>
<th>PROFILE-LEVEL</th>
<th>PRIMARY LVADs 12-09</th>
<th>Official Shorthand (after Lynne Stevenson)</th>
<th>NYHA CLASS</th>
<th>Modifier option</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERMACS LEVEL 1</td>
<td>633</td>
<td>“Crash and burn”</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>INTERMACS LEVEL 2</td>
<td>841</td>
<td>“Sliding fast” on ino</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>INTERMACS LEVEL 3</td>
<td>284</td>
<td>Stable but Ino-Dependent. Can be hosp or home</td>
<td>IV ish</td>
<td></td>
</tr>
<tr>
<td>INTERMACS LEVEL 4</td>
<td>185</td>
<td>Resting symptoms on oral therapy at home.</td>
<td>ambul IV</td>
<td>+FF frequent flyer A for arrhythmia</td>
</tr>
<tr>
<td>INTERMACS LEVEL 5</td>
<td></td>
<td>“Housebound”, Comfortable at rest, symptoms with minimum activity ADL</td>
<td>ambul IV</td>
<td>+ FF A</td>
</tr>
<tr>
<td>INTERMACS LEVEL 6</td>
<td></td>
<td>“Walking wounded”-ADL possible but meaningful activity limited</td>
<td>IIIB</td>
<td>+FF A</td>
</tr>
<tr>
<td>INTERMACS LEVEL 7</td>
<td>(5,6,7 = 119)</td>
<td>Advanced Class III</td>
<td>IIIB</td>
<td>A only</td>
</tr>
</tbody>
</table>

**CURRENT VAD INDICATIONS**

**ROADMAP TRIAL**
INTERMACS Levels - Outcome

The figure illustrates seven INTERMACS levels of clinical severity of end-stage heart failure with the corresponding survival. The time frame for consideration of mechanical circulatory support and evidence from clinical trials of 1-year survival benefit with LVAD implantation is shown in the table.

<table>
<thead>
<tr>
<th>Intermacs level</th>
<th>Survival</th>
<th>VAD benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–7</td>
<td>Months to years</td>
<td>Not established</td>
</tr>
<tr>
<td>3–4</td>
<td>Weeks to months</td>
<td>Yes</td>
</tr>
<tr>
<td>1–2</td>
<td>Hours to weeks</td>
<td>Yes</td>
</tr>
<tr>
<td>MOF</td>
<td>Hours to days</td>
<td>Bridge to decision in selected cases</td>
</tr>
</tbody>
</table>
Objectives

• Discuss classification schemes for advanced heart failure (HF)

• Identify clinical clues of advanced HF

• Review prognostic markers of advanced HF

• Discuss various clinical risk models to help determine patient prognosis

• Determine when to refer patients for advanced therapies and why?
Clinical Clues

• Dyspnea and fatigue

• Weight
  – Rapid and recurrent gains
  – Eventually weight loss (cachexia)

• Signs of hypoperfusion
  – Narrow Pulse Pressure

Example:
BP 90/70...PP is 20
25% of 90 is 23 mmHg
20 < 23 and therefore correlates with CI <2.2

91% sensitivity and 83% specificity

a pulse pressure of <25% of the systolic pressure is associated with a cardiac index of <2.2 L/min/m².
Clinical Clues

• Dyspnea and fatigue

• Weight loss

• Signs of hypoperfusion
  – Narrow Pulse Pressure
  – Sleepy/obtunded
  – Cool extremeties
  – Renal dysfunction
Rapid Assessment of Hemodynamic Status

Congestion at Rest

<table>
<thead>
<tr>
<th>Low Perfusion</th>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Warm &amp; Dry</td>
<td></td>
<td>Warm &amp; Wet</td>
</tr>
<tr>
<td>(Low Profile)</td>
<td>L</td>
<td>(Complex)</td>
</tr>
<tr>
<td>Cold &amp; Dry</td>
<td></td>
<td>Cold &amp; Wet</td>
</tr>
</tbody>
</table>

Signs/Symptoms of Congestion:
- Orthopnea / PND
- JV Distension
- Hepatomegaly
- Edema
- Rales (rare in chronic heart failure)
- Elevated est. PA systolic

Possible Evidence of Low Perfusion:
- Narrow pulse pressure
- Cool extremities
- Sleepy / obtundened
- Hypotension with ACE inhibitor
- Low serum sodium
- Renal Dysfunction (one cause)

R. Bourge, UAB (adpt from L. Stevenson) Stevenson LW. *Eur J Heart Failure* 1999
End Organ Dysfunction

- Pulmonary hypertension
  - Pulmonary venous congestion
  - PAH: Arterial remodeling $\rightarrow$ elevated TPG (MPA-PCWP)

- RV enlargement/dysfunction

- Hepatic or bowel congestion
  - Early satiety, nausea
  - Diuretic resistance
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Prognostic Markers

- **General**
  - Age, diabetes, sex, weight (BMI), etiology of HF, comorbidities (COPD, cirrhosis)

- **Laboratory markers**
  - Na, creatinine (and eGFR), urea, BUN,
  - Hgb, % lymphocytes,
  - Uric acid
  - Low HDL
  - Insulin resistance

- **Urine**
  - Abluminuria
  - NGAL - neutrophil gelatinase associated lipocalin

- **Biomarkers**
  - BNP, NT pro BNP, troponin, CRP, cystatin C, GDF-15 (growth differentiation factor), serum cortisol, TNF, ET, NE, midregional-pro-adrenomedullin (MR-proADM), pro-apoptotic protein apoptosis-stimulating fragment (FAS)

- **Medication**
  - Intolerance to ACEI, diuretic dose

- **FC IV**
  - Especially if sustained > 90 days
  - 6 minute walk

- **Cardiopulmonary markers**
  - Peak VO2, % predicted, VE/VCO2, AT, workload, systolic BP < 130, HR recovery

- **Clinical Exam markers**
  - BP (admission and discharge), heart rate, JVP, +S3, cachexia
  - Depression
  - Obstructive sleep apnea

- **Echo parameters**
  - EF, chamber size (LV, LA, RA), sphericity, DT

- **RNA**
  - RVEF, LVEF

- **Recurrent hospitalizations**

- **ECG**
  - IVCD

- **Hemodynamic markers**
  - PA pressures, CO, CI, MVO2

- **Endomyocardial biopsies**
  - Microarrays transcriptomic biomarkers

- **Marital status**
Hemodynamic Status and Prognosis

Congestion at Rest

Adequate Perfusion

<table>
<thead>
<tr>
<th>CONGESTION</th>
<th>Event-Free Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ A dry-warm (N=123)</td>
<td>1.0</td>
</tr>
<tr>
<td>+ B wet-warm (N=222)</td>
<td>0.8</td>
</tr>
<tr>
<td>- C dry-cold (N=16)</td>
<td>0.6</td>
</tr>
<tr>
<td>- L wet-cold (N=91)</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Signs/Symptoms of Congestion:
- Orthopnea / PND
- JV Distension
- Hepatomegaly
- Edema
- Rales (rare in chronic heart failure)

Possible Evidence of Low Perfusion:
- Narrow pulse pressure
- Cool extremities
- Sleepy / obtunded
- Hypotension with ACE inhibitor
- Low serum sodium
- Renal Dysfunction (one cause)

Adapted From Starling. 2009 CCBR
In-Hospital Mortality Rates by Admission Systolic Blood Pressure Deciles (n = 48,567)


Copyright restrictions may apply.
Kaplan-Meier survival curves to 60 days by admission serum sodium quartiles (unadjusted analysis) – OPTIME CHF

Prognosis - NYHA FC

SOLVD - Treatment

SOLVD NEJM 1991
Prognosis - EF

Annual Mortality (%) vs Ejection Fraction

V-HeFT I
V-HeFT II

Adapted from Cohn et al Circ 1993
LV Chamber Size

2 Year Survival (%)

LV index
>4  <4

LVEDD
>7.5  <7.5

Lee et al, AJC 1993
Left Ventricular Filling Pattern

Meta-analysis Research Group in Echocardiography (MeRGE) Heart Failure

3540 patients

Hazard ratio 2.42 (CI 2.06, 2.83)

Irrespective of LVEF

Both in ischemic and non-ischemic patients

Log rank $\chi^2 = 126$, p-value < 0.0001

Eur J Heart Fail 2008;10:786-792
Hemodynamic Data is Vital

Miller, et al JACC HF 2013
Kaplan-Meier plots by RVEF categories for
A → All-cause mortality (A)
B → HF hospitalization (B)

**Conclusions**—Baseline RVEF 20% is a significant independent predictor of mortality and HF hospitalization in systolic HF.
Relationship Between BNP and Mortality in Patients with Advanced HF

BNP > 485 pg/ml

BNP < 485 pg/ml

RR 3.7, 95% CI 2.0-6.9

p<0.0001

N=238
Referred for HTx

BNP cut point by ROC

ADHERE – troponin/hospital days
N=67,924

Odds ratio for death
(+) troponin 2.55

Oxidative Stress: Uric Acid

- UA < 565 mmol/L
- UA > 565 mmol/L

P < 0.0001

Anker et al, Circ 2003
Sudden Cardiac Death in Heart Failure

QRS Complex and Mortality

- VEST study analysis
- NYHA II-IV
- 3,654 ECGs
- QRS duration was found to be an independent predictor of mortality

Adapted from V Gottipaty, MD.

Renal Dysfunction and HF outcomes

Death or unplanned admission
By quintile of eGFR
N=2680

CHARM study

ANCHOR study – Hemoglobin and death

N=59,772
Northern California community
Mean age 72
46% women

Mortality Rates based on Hgb

Go et al, Circ 2006;113:2713
Prognosis - VO2

Annual Mortality (%) vs. Peak Oxygen Consumption (ml/kg/min)

Adapted from Cohn et al Circ 1993
6MWT and Prognosis SOLVD

% Risk of death 242 days

<300 m highest risk of hospitalization 41% vs 20%

Bitner JAMA 1993
6-Min Walk Test Provides Prognostic Utility Comparable to Cardiopulmonary Exercise Testing in Ambulatory Outpatients With Systolic Heart Failure

Daniel E. Forman, MD,*† Jerome L. Fleg, MD,‡ Dalane W. Kitzman, MD,§ Clinton A. Brawner, MS,‖ Ann M. Swank, PhD,¶ Robert S. McKelvie, MD, PhD,# Robert M. Clare, MS,** Stephen J. Ellis, PhD,** Mark E. Dunlap, MD,†† Vera Bittner, MD, MSPH‡‡

Boston, Massachusetts; Bethesda, Maryland; Winston-Salem and Durham North Carolina; Detroit, Michigan; Louisville, Kentucky; Hamilton, Ontario, Canada; Cleveland, Ohio; and Birmingham, Alabama

Table 5 Prognostic Utility of 6MWD Versus CPX Indices in Predicting All-Cause Mortality

<table>
<thead>
<tr>
<th>Model</th>
<th>Parameter</th>
<th>Chi-Square Statistic</th>
<th>p Value</th>
<th>Hazard Ratio* (95% Confidence Interval)</th>
<th>C-Index (95% Confidence Interval)</th>
<th>IDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted univariate predictors</td>
<td>6MWD</td>
<td>94</td>
<td>&lt;0.0001</td>
<td>0.61 (0.55–0.67)</td>
<td>0.65 (0.62–0.68)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Peak VO₂</td>
<td>123</td>
<td>&lt;0.0001</td>
<td>0.48 (0.42–0.55)</td>
<td>0.68 (0.65–0.71)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VE/VCO₂ slope</td>
<td>130</td>
<td>&lt;0.0001</td>
<td>1.58 (1.46–1.71)</td>
<td>0.65 (0.61–0.68)</td>
<td></td>
</tr>
<tr>
<td>Adjusted†</td>
<td>6MWD</td>
<td>55</td>
<td>&lt;0.0001</td>
<td>0.65 (0.57–0.73)</td>
<td>0.72 (0.69–0.75)</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Peak VO₂</td>
<td>77</td>
<td>&lt;0.0001</td>
<td>0.51 (0.44–0.59)</td>
<td>0.73 (0.71–0.76)</td>
<td>0.010</td>
</tr>
<tr>
<td></td>
<td>VE/VCO₂ slope</td>
<td>45</td>
<td>&lt;0.0001</td>
<td>1.37 (1.25–1.51)</td>
<td>0.71 (0.68–0.74)</td>
<td>0.004</td>
</tr>
</tbody>
</table>
Objectives

• Discuss classification schemes for advanced heart failure (HF)

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• Discuss various clinical risk models to help determine patient prognosis

• Determine when to refer patients for advanced therapies

• What is advanced therapy and why do it?
Prognostic Models

• Inpatient
  – ADHERE
  – EFFECT
  – ESCAPE

• Ambulatory
  – HFSS
  – SHFS
  – MUSIC risk score
Predictors of In-Hospital Mortality
ADHERE

Predictors of In-Hospital Mortality OPTIMIZE-HF

Figure 2  In-Hospital Mortality by SCr and SBP

The relationship between serum creatinine (SCr) and systolic blood pressure (SBP) as measured at hospital admission and in-hospital mortality.

Abraham et al, JACC 2008;52:347-56
Prognostic Models

• Inpatient
  – ADHERE
  – EFFECT
  – ESCAPE

• Ambulatory
  – HFSS
  – SHFS
  – MUSIC risk score
In the United States, 5 million individuals have heart failure. Each year, 550,000 new cases are diagnosed, and there are 1 million hospitalizations. The direct and indirect costs of heart failure are estimated at $29 billion per year. Although heart failure presents enormous healthcare burdens, outcomes in heart failure are highly variable, with annual mortality varying from 5% to 75%. Physicians need to counsel patients about prognosis to enable informed decisions about medications, devices, transplantation, and end-of-life care.

Previous heart failure (HF) risk models stratify patients into three risk groups using peak oxygen consumption (VO2). An individualized estimate of survival in HF has not been reported. The Seattle Heart Failure Model was derived by retrospectively investigating predictors of survival among 1,125 HF patients in PRAISE-1 (NYHA 3B-4, EF<30%, ACEI, diuretics, 403 deaths). A stepwise Cox proportional hazard model was used to develop a multivariate risk model, which identified age, gender, ischemic etiology, NYHA, ejection fraction, systolic blood pressure, K-sparing diuretic use, statin use, allopurinol use, hemoglobin, % lymphocyte count, uric acid, sodium, cholesterol, and diuretic dose/kg as significant predictors of survival. The model was prospectively validated in 5 additional cohorts totaling 9,942 heart failure patients and 17,307 person-years of follow-up. The Seattle Heart Failure Model provides an accurate estimate of 1-, 2-, and 3-year survival with the use of easily obtained clinical, pharmacological, device, and laboratory characteristics.

The Java applet to calculate the score was designed by Drs. Linker and Levy and programmed by Dr. David T. Linker.
# First Visit

## Baseline Characteristics

### Clinical

<table>
<thead>
<tr>
<th>Age</th>
<th>65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
</tr>
<tr>
<td>NYHA Class</td>
<td>4</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80</td>
</tr>
<tr>
<td>EF</td>
<td>20</td>
</tr>
<tr>
<td>Syst BP</td>
<td>120</td>
</tr>
</tbody>
</table>

- **Ischemic**: Yes

### Medications

- ACE-I
- Beta-blocker
- ARB
- Statin
- Allopurinol
- Aldosterone blocker

### Diuretics

- Furosemide: 40
- Bumetanide: 0
- Torsemide: 0
- Metolozane: 0
- HCTZ: 0

### Lab Data

- Hgb: 13.6
- Lymphocyte %: 24
- Uric Acid: 9
- Total Chol: 190
- Sodium: 137

- **QRS >120 msec**: Yes

### Devices

- **None**
- BiV Pacer
- ICD
- BiV ICD

---

**Note:** Some devices may be disabled if CMS clinical criteria are not met. See below.
Added BB and Statin

### Baseline Characteristics

**Clinical**
- Age: 65
- Gender: Male
- NYHA Class: 4
- Weight (kg): 80
- EF: 20
- Syst BP: 120

**Medications**
- ACE-I
- Beta-blocker
- Statin

**Diuretics**
- Furosemide: 40
- Bumetanide: 0
- Torsemide: 0
- Metolazone: 0
- HCTZ: 0

**Lab Data**
- Hgb: 13.6
- Lymphocyte%: 24
- Uric Acid: 9
- Total Chol: 190
- Sodium: 137
- QRS >120 msec

**Devices**
- None
- BiV Pacer
- ICD
- BiV ICD

**Interventions**
- ACE-I
- Beta-blocker
- Statin
- Aldosterone Blocker

**Note:** Some devices may be disabled if CMS clinical criteria are not met. See below.
Benefit of Aldosterone

Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
</tr>
<tr>
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<td>80</td>
</tr>
<tr>
<td>EF</td>
<td>20</td>
</tr>
<tr>
<td>Syst BP</td>
<td>120</td>
</tr>
</tbody>
</table>

Medications

- ACE-I
- Beta-blocker
- Statin
- Aldosterone blocker

Diuretics

- Furosemide
- Bumetanide
- Torsemide
- Metolazone
- HCTZ

Lab Data

- Hgb: 13.6
- Lymphocyte%: 24
- Uric Acid: 9
- Total Chol: 190
- Sodium: 137
- QRS > 120 msec

Interventions

- ACE-I
- Beta-blocker
- Statin
- Aldosterone Blocker

Devices

- None
- BiV Pacer
- ICD
- BiV ICD

Note: Some devices may be disabled if CMS clinical criteria are not met. See below.
Benefit of BiV ICD

Survival:
- Baseline 1 year: 91%
- Baseline 2 year: 83%
- Baseline 5 year: 63%
- Post-intervention 1 year: 94%
- Post-intervention 2 year: 89%
- Post-intervention 5 year: 74%

Mortality:
- Baseline 1 year: 9%
- Baseline 2 year: 17%
- Baseline 5 year: 37%
- Post-intervention 1 year: 6%
- Post-intervention 2 year: 11%
- Post-intervention 5 year: 26%

Mean life expectancy:
- Baseline: 7.4 years
- Post-intervention: 9.6 years

Baseline Characteristics:
- Clinical:
  - Age: 65
  - Gender: Male
  - NYHA Class: 4
  - Weight (kg): 80
  - EF: 20
  - Syst BP: 120
  - Ischemic: Yes

- Medications:
  - ACE-I
  - Beta-blocker
  - Statin
  - Aldosterone blocker

- Diuretics:
  - Furosemide: 40
  - Bumetanide: 0
  - Torsemide: 0
  - Metolazone: 0
  - HCTZ: 0

- Lab Data:
  - Hgb: 13.6
  - Lymphocyte%: 24
  - Uric Acid: 9
  - Total Chol: 190
  - Sodium: 137
  - QRS >120 msec

- Devices:
  - None
  - BiV Pacer
  - ICD
  - BiV ICD

Interventions:
- ACE-I
- Beta-blocker
- Statin
- Aldosterone Blocker

Devices:
- None
- BiV Pacer
- BiV ICD
- ICD
- LVAD

Note: Some devices may be disabled if CMS clinical criteria are not met. See below.
# Risk Prediction in Heart Failure

<table>
<thead>
<tr>
<th>Predictors:</th>
<th>Age</th>
<th>Renal function</th>
<th>Blood pressure</th>
<th>Sodium</th>
<th>Ejection fraction</th>
<th>Gender</th>
<th>BNP (or NT-pro BNP)</th>
<th>NYHA class</th>
<th>Diabetes</th>
<th>Weight / BMI</th>
<th>Exercise tolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total occurrences as candidate variable</td>
<td>41</td>
<td>36</td>
<td>30</td>
<td>28</td>
<td>26</td>
<td>36</td>
<td>10</td>
<td>13</td>
<td>25</td>
<td>21</td>
<td>8</td>
</tr>
<tr>
<td>Total occurrences as final variable</td>
<td>33</td>
<td>27</td>
<td>21</td>
<td>18</td>
<td>15</td>
<td>14</td>
<td>8</td>
<td>11</td>
<td>10</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Weighted Score</td>
<td>230</td>
<td>199</td>
<td>138</td>
<td>87</td>
<td>104</td>
<td>73</td>
<td>71</td>
<td>72</td>
<td>55</td>
<td>53</td>
<td>52</td>
</tr>
<tr>
<td>Final Inclusion Ratio (occurrences as final variable / occurrences as candidate variable)</td>
<td><strong>80%</strong></td>
<td><strong>75%</strong></td>
<td><strong>70%</strong></td>
<td><strong>64%</strong></td>
<td><strong>58%</strong></td>
<td><strong>39%</strong></td>
<td><strong>80%</strong></td>
<td><strong>85%</strong></td>
<td><strong>40%</strong></td>
<td><strong>48%</strong></td>
<td><strong>88%</strong></td>
</tr>
</tbody>
</table>

![Graph showing risk prediction in heart failure](image)

**Legend:**
- Red diamond: Variable included as candidate
- Blue circle: Variable included in final model

**References:**
- Adlam D (2005) (w11)
- Feiker GM (2004) (w10)
- Lee DS (2003) (w8)
- Hisch EM (2011) (w30)
- Krumholz H (2006) (w14)
- Pocock SJ (2008) (w16)
- AU AG (2012) (w38)
- O'Connor CM (2010) (w28)
- Manzano L (2011) (w32)
- Tabak YP (2007) (w17)
- Foranrow GC (2005) (w12)
- Bartera S (2013) (w46)
- Senri M (2013) (w48)
- O'Connor CM (2008) (w21)
- Abraham WT (2008) (w19)
- Vazquez R (2008) (w22)
- O'Connor CM (2012) (w42)
- Van Spall HGJC (2011) (w36)
- Lee DS (2012) (w41)
- Lee DS (2010) (w27)
- Bilchick (2012) (w49)
- Peterson PN (2010) (w29)
- Bayes-Genis A (2012) (w39)
- Amaraisingham R (2010) (w24)
- Wang L (2012) (w45)
- Yamokoski LM (2007) (w18)
- Wedel H (2009) (w23)
- Postmus D (2012) (w44)
- Komajda M (2011) (w21)
- Bouvy ML (2003) (w5)
- Zheng J (2011) (w37)
- Pocock SJ (2012) (w43)
- Levy WC (2006) (w15)

**Note:**
- Variable by cohort
- Variable by trial
- Graphically

Rahimi, K. JACC HF Oct 2014
Prognostic Models

- Inpatient
  - ADHERE
  - EFFECT
  - ESCAPE

- Ambulatory
  - HFSS
  - SHFS
  - MUSIC risk score
Objectives

• Discuss classification schemes for advanced heart failure (HF)

• Identify clinical clues of advanced HF

• Review prognostic markers of advanced HF

• Discuss various clinical risk models to help determine patient prognosis

• Determine when to refer patients for advanced therapies and why?
Patients With Refractory End-Stage Heart Failure (Stage D)

Referral of Patients with Refractory End-Stage HF

Referral for cardiac transplantation in potentially eligible patients is recommended for patients with refractory end-stage HF.

Referral of patients with refractory end-stage HF to an HF program with expertise in the management of refractory HF is useful.

ACC/AHA Guidelines Heart Failure. 2009.
Patients with refractory end-stage HF and implantable defibrillators should receive information about the option to inactivate defibrillation.

Severe Symptoms in Patients With Refractory End-Stage HF HF

Options for end-of-life care should be discussed with the patient and family when severe symptoms in patients with refractory end-stage HF persist despite application of all recommended therapies.

Consideration of a left ventricular assist device as permanent or “destination” therapy is reasonable in highly selected patients with refractory end-stage HF and an estimated 1-year mortality over 50% with medical therapy.

ACC/AHA Guidelines Heart Failure. 2009.
Indications for Advanced HF Therapy

- NYHA Class IIIb/IV
- Worsening renal function
- Intolerance to ACE I and Beta blockers due to hypotension and CKD
- 1 hospitalization in last 6 months
- 2 or more hospitalizations 1 yr
- Inability to walk one block without dyspnea
- Diuretic dose > 1.5 mg/kg/day
- Refractory ventricular arrhythmias
- LVEF < 25%
- Severe refractory angina
- Severe restrictive cardiomyopathy
- CRT nonresponder
- Measured peak VO2 < 14 ml/kg/min or < 50% age-gender predicted on treadmill
- 6MWT < 300 meters

Peura, et al. Circulation Nov 2012;126:00-00
Russell SD, Miller LW, Pagani FD. Congest Heart Fail. 2008;14:316-321
Patient Selection – Pearls

• Don’t wait for progressive renal dysfunction and recurrent ascites

• Don’t wait till multiple pressors are required

• Don’t wait for cardiac cachexia

• ICD shocks as persistent elevation of LVEDP – not just scar mediated VT/VF
Patient Selection – Pearls

• Patients who require inotrope therapy to reverse/manage renal dysfunction or pulmonary hypertension are VERY high risk patients despite symptoms (inotrope dependence)

• Patients with significant secondary pulmonary hypertension
  – Pre-operative pulmonary hypertension contraindication to OHT
  – a good sign RV can pump effectively (protective with VAD)
  – Worry about the dilated RV, low PA pressures and high CVP

• Hospital admission – 34% risk of death at 1 year
Establish Risk and Schedule Referral

**Advanced CHF Risk Tool**

- 2 admits in the last year for CHF
- LVEF < 25%
- BNP > 485
- Serum Na < 134 mmol/L
- BUN > 50
- Serum Cr > 2 mg/dL or GFR < 40
- Use of any intravenous inotrope:
  - milrinone, dobutamine, dopamine
Clinical Course is Variable:

Refer Early

Peura, et al. Circulation Nov 2012;126:00-00
The Advanced Heart Failure Team: Therapeutic Decision Tree

- Ongoing Medical Therapy
- Other surgery
- VAD
- Transplant
- Palliative Care Hospice
Transplant Survival is the Gold Standard

Candidacy is tricky...

Half-life = 9.9 years
Conditional Half-life = 13 years

N=69,536
N followed at longest time point: 28,463

J Heart Lung Transplant 2006;25:869-79
Transplants Are Limited

- 5-7 million patients with CHF (50% HFpEF)
- 200,000 CHF patients Stage D (5%)
- Approximately 4,000 transplants worldwide each year
  - Numbers have plateaued
- Many Stage D patients are not transplant candidates
Orthotopic Heart Transplantation

• Dying mostly of heart failure
  – Absence of other non-cardiac conditions that would limit life expectancy

• Multidisciplinary evaluation

• Acceptable characteristics on continuous intravenous high dose inotropes with inability to wean

• Recovery of end organs and pulmonary vascular resistance/reversible pulmonary HTN
Destination Therapy survival improvement over time

Importance of Quality of Life

Most patients weighted quality of life as having similar importance as survival post implantation and many noted that quality of life was even more important than survival.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>90 Days</th>
<th>180 Days</th>
<th>365 Days</th>
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<tbody>
<tr>
<td><strong>NYHA Class</strong></td>
<td>3.7</td>
<td>1.4*</td>
<td>1.2*</td>
<td>1.2*</td>
</tr>
<tr>
<td><strong>6 Minute Walk</strong></td>
<td>122.7</td>
<td>414.3*</td>
<td>487.4*</td>
<td>478.4*</td>
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<tr>
<td><strong>MLHF total score</strong></td>
<td>76.5</td>
<td>32.0*</td>
<td>26.4*</td>
<td>28.2*</td>
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<tr>
<td><strong>MLHF Physical Score</strong></td>
<td>34.7</td>
<td>13.4*</td>
<td>11.3*</td>
<td>10.6*</td>
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<tr>
<td><strong>MLHF Emotional Score</strong></td>
<td>15.0</td>
<td>5.9*</td>
<td>5.2*</td>
<td>6.1*</td>
</tr>
</tbody>
</table>

*p < 0.0001

Courtesy of Coyle, L. ACMC. ISHLT 2009.
“Unlearn” Advanced Heart Failure

• There are patients in our community with subtle clues of a very sick heart

• Patients are at greater risk of treatment failure, complications, or absolute contraindications for advanced therapies when they are critically ill

• Patients should be evaluated by multidisciplinary advanced heart failure team early in the course of the disease to determine optimal timing of advanced therapies

• MCS or Transplantation is superior to medical therapy in patients with advanced heart failure and can provide excellent improvements in both quantity and quality of life