Up to Date Management and Innovations for Heart Failure

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No Disclosures
Case Presentation

• 55 yo M with no past medical history, soccer referee, p/w increased fatigue and sob for three weeks.
• Vitals normal
  • Cr 1, Bun 17, Na 140, K 4.3
  • CXR shows cardiomegaly
• Echo: EF 20%, LV 8 cm
• Cardiac Cath: no obstructive CAD

• Patient is started on optimal medical therapy for HF – Carvedilol, Lisinopril, Spironolactone, Lasix
• After three months, NYHA II but no improvement in EF → ICD placed
• Patient was followed and did well for couple years
• Over the course of the next year, notices more fatigue with daily activities
• Patient is admitted twice to hospital for heart failure – diuretics increased
• Dose of carvedilol and lisinopril lowered due to low blood pressure
• Cr 1.5 (no proteinuria)
• Echo: EF 15%, 8.2 cm, RV dilated 5 cm, PASP 55 mmHg

• What next?
  – Continue current treatment plan and pretend you didn’t see the labs
  – Implant Cardiomems device
  – Refer to advanced heart failure clinic
• One day, patient experiences 4 ICD shocks → VT storm
• In hospital gets intubated for pulm edema
• Dobutamine and Dopamine started
• RHC: RA 15, PA 60/30, Wedge 28, Cardiac index 1.9

• What now?
  – Panic
  – Pray
  – Panic and Pray
  – Pursue advanced heart failure therapies (ie Heart transplant or MCS)
Who you gonna call?!
The Burden of Congestive Heart Failure

- Nearly 6.5 million Americans w/ HF (~ 8 million by 2030)
- male to female nearly 1:1
- > 1,000,000 new cases/yr
- #1 DRG -- $32 billion
- 50% readmitted within 6 mos
- 50% dead within 5 years

Class I
1.79 M
(35%)

Class II
1.79 M
(35%)

Class III
1.28 M
(25%)

Class IV
255 K
(5%)

“STAGE D”
100K

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Etiologies of Cardiomyopathies

- CAD
- Idiopathic
- Toxin (EtOH, Cocaine, ChemoTx)
- Infectious (Coxsackie, HIV, Chagas)
- CTD (SLE, RA)
- Endocrine (DM, T4, Vit B1 def)
- Iron Overload
- Tachy mediated
- Myocarditis (Giant cell)
- Familial (ARVD, Muscular dystrophies, Non-compaction)
- Hypereosinophilic (Loeffler’s)
- Takotsubo “stress induced”
- Peripartum
- Radiation
What can we do for our patients?
Cumulative % Reduction in Odds of Death At 24 Months With Each Sequentially Applied Guideline Recommended

**IMPROVE-HF**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>24-Month Mortality Reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blocker</td>
<td>-39% (-28% to -49%) P &lt; 0.0001</td>
</tr>
<tr>
<td>Beta-blocker + ACEI/ARB</td>
<td>-63% (-54% to -71%) P &lt; 0.0001</td>
</tr>
<tr>
<td>Beta-blocker + ACEI/ARB + ICD</td>
<td>-76% (-68% to -81%) P &lt; 0.0001</td>
</tr>
<tr>
<td>Beta-blocker + ACEI/ARB + ICD + HF education</td>
<td>-81% (-75% to -86%) P &lt; 0.0001</td>
</tr>
<tr>
<td>Beta-blocker + ACEI/ARB + ICD + HF education + anticoagulation for AF</td>
<td>-83% (-77% to -88%) P &lt; 0.0001</td>
</tr>
<tr>
<td>Beta-blocker + ACEI/ARB + ICD + HF education + anticoagulation for AF + CRT</td>
<td>-81% (-72% to -87%) P &lt; 0.0001</td>
</tr>
</tbody>
</table>

Fonarow G C et al. J Am Heart Assoc 2012;1:16-26
The Current Paradigm

- **NYHA I**
  - ACEI
  - ARB if ACEI-intolerant
  - Beta-blocker

- **NYHA II**
  - Spironolactone
  - CRT if LBBB, QRS > 150 msec, sinus rhythm
  - ICD if life-expectancy > 1 year

- **NYHA III**
  - Transplant/MCS evaluation
  - Isordil/hydralazine if Afr American
  - Ivabradine

- **NYHA IV**
  - Sacubitril/Valsartan
  - Spironolactone
  - CRT if LBBB, QRS > 150 msec, sinus rhythm
  - ICD if life-expectancy > 1 year

Transplant/MCS evaluation can be considered if life-expectancy > 1 year.
**NPS**

NP receptors \(\rightarrow\) Natriuretic Peptides

**Vasodilatation**
- \(\downarrow\) Blood pressure
- \(\downarrow\) Sympathetic Tone
- \(\downarrow\) Vasopressin
- \(\downarrow\) Aldosterone
- \(\downarrow\) Hypertrophy
- \(\downarrow\) Fibrosis
- \(\uparrow\) Natriuresis/Diuresis

**Vasoconstriction**
- \(\uparrow\) Heart rate
- \(\uparrow\) Contractility
- \(\uparrow\) RAAS activity
- \(\uparrow\) Vasopressin

**SNS** \(\times\) \(\beta\) blockers

Adrenaline, Noradrenaline \(\{\alpha_1, \beta_1, \beta_2\) receptors

**Vasoconstriction**

RAAS Inhibitors  ACEI, ARB, MRA

**ARNIs**

Blood pressure \(\uparrow\)
- Sympathetic Tone \(\uparrow\)
- Aldosterone \(\uparrow\)
- Hypertrophy \(\uparrow\)
- Fibrosis \(\uparrow\)
PARADIGM-HF study

• ~8400 patients
  – EF ≤ 35%
  – One HF hosp or ↑ BNP

• Outcomes
  – CV deaths: 17% → 13%
  – HF hosp: 16% → 13%

HR in HF … Cause or Effect?

• Higher HR is related to poor prognosis in HF, and many patients continue to have elevated HR despite maximally tolerated betablockers.

• Ivabradine inhibits the funny (I_f) channels in the SA node to reduce heart rate.

• Unlike beta-blockers or calcium channel blockers, ivabradine does NOT affect:
  – Myocardial contractility
  – Intra-cardiac conduction
  – Hemodynamics (e.g. blood pressure)
SHIFT study

• ~6500 pts
  – EF ≤ 35%
  – HR ≥ 70
  – One HF hosp
  – Max tolerated

• Outcomes
  – HF deaths 5% → 3%
  – HF hosp 21% → 16%
Development of Acute Decompensation

Filling pressures Increase

Autonomic Adaptation

Intrathoracic Impedance Changes

Weight Changes Symptoms

Decompensation

Hospitalization

Adamson PB *Current HF Reports* 2009;6:287-292
Intracardiac Pressures Rise Early Preceding HF Events

Depressed EF Heart Failure (N=122 events)
Preserved EF Heart Failure (N=41 events)

CardioMEMS™ HF System

PA Pressure Sensor on Catheter Delivery System

Patient Electronics Unit

Merlin.net PA Pressure Integrated Website
CHAMPION TRIAL: PA pressure monitoring to reduce heart failure admissions

Cardiomems

Champion trial SUB-analysis:

- HFpEF or diastolic HF patients represent ~50% of all HF patients.
- The effect in HFpEF patients demonstrates an estimated NNT = 2.

HF Hospitalization Reduction
(18 mo follow-up)

50% Reduction
p<0.0001 vs. control

PA pressure-guided therapy
SIGNIFICANTLY REDUCED HF HOSPITALIZATIONS
in HFpEF patients in the treatment group, demonstrating that the CardioMEMS™ HF System is the first effective treatment strategy to manage 50% of patients hospitalized with HF.

Device-Based Monitoring – Fluid Index Impedance

Changes in thoracic impedance are a more accurate predictor of worsening HF than weights.

PARTNERS HF Study

- P-Value = 0.003
- Hazard Ratio = 2.31
  (95% CI: 1.32, 4.05)

Optivol

Transcatheter Mitral-Valve Repair in Patients with Heart Failure

COAPT Trial

A Hospitalization for Heart Failure

- Control group
- Device group

Hazard ratio, 0.53 (95% CI, 0.40–0.70)
P<0.001

C Death from Any Cause

- Control group
- Device group

Hazard ratio, 0.62 (95% CI, 0.46–0.82)
P<0.001
WHEN ALL ELSE FAILS, EAT CHOCOLATE
When all else fails…Stage D Heart Failure

American College of Cardiology Foundation/American Heart Association

1. Repeated (≥2) hospitalizations or ED visits for HF in the past year
2. Progressive deterioration in renal function (eg, rise in BUN and creatinine)
3. Weight loss without other cause (eg, cardiac cachexia)
4. Intolerance of ACE inhibitors because of hypotension and/or worsening renal function
5. Intolerance of beta-blockers because of worsening HF or hypotension
6. Frequent systolic blood pressure <90 mm Hg
7. Persistent dyspnea with dressing or bathing requiring rest
8. Inability to walk 1 block on level ground because of dyspnea or fatigue
9. Recent need to escalate diuretics to maintain volume status, often reaching daily furosemide equivalent dose >160 mg and/or use of supplemental metolazone therapy
10. Progressive decline in serum sodium, usually to <133 mEq/L
11. Frequent ICD shocks
Who Needs a Heart Transplant?

Advanced heart disease with unacceptable quality of life or risk of sudden death despite maximal medical therapy

No other appropriate surgical options such as high risk CABG or valve replacement

No other medical illnesses (such as a metastatic malignancy) which would be expected to limit the patient’s 5 year survival

**Indications are similar for mechanical support though more options may be available as destination therapy – ie older patients, more recent malignancy
Durable Management Options for ESHD

370,000 Class IIIb/IV

~70,000 potential VAD candidates for DT

~100,000 Heart Tx candidates

~200,000 Non-Tx/VAD

2,300 Heart transplants/yr

~97,000 waiting medical Rx

~3-4,000 MCS* 2,800 LVADs 200 TAHs

Palliative Care
Heart Transplantation
Louis Washansky
South Africa - 1967
Smidt Heart Institute
Number of Heart Transplants per Year

# Tx


20 25 43 34 27 76 89 95 119 122 132 122 103

* *

** Ht Tx program moved from UCLA to CSMC

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Adult and Pediatric Heart Transplants
Kaplan-Meier Survival
(Transplants: January 1982 – June 2013)

Median survival = 11 years
Median survival conditional on surviving 1st year = 13 years

N = 112,521
N at risk at 30 years = 16
Not a walk in the park...
OHT Challenges...

• Early
  – Rejection
  – Infection

• Late
  – Cardiac allograft vasculopathy
  – Malignancy

• Common
  – HTN
  – Renal Insufficiency
  – Hyperlipidemia
  – Diabetes
“Heart in a Box”
But what if you can’t wait…
Mechanical Circulatory Support
Patient Selection for MCS
Strategies for MCS

Cardiogenic Shock

- Recovery
- Heart Transplant
- Destination

Short-term / temporary MCS

Decision or Long term Device

Temp MCS

BTR

BTT

DT

Long-term / durable MCS

Inotropes / IABP
Temporary MCS devices

• Left ventricular support
  – IABP
  – Impella

• Right ventricular support
  – RP Impella
  – Tandem Heart cannula
  – Centrimag

• Biventricular support
  – ECMO
  – “Tandella”
  – Centrimags (LV/RV)
The Impella Catheters

- Femoral / axillary artery cut-down – 21F
- Actively unloads the LV
- Provides up to 5.0 liters/min of flow
- Rapid insertion in cath lab or CVOR
ECMO
Short-term bridge to decision (BTD) or (BTB)
Durable MCS Devices

LVAD

TAH

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HeartMate II LVAD (axial flow)
A Fully Magnetically Levitated Circulatory Pump for Advanced Heart Failure

Mandeep R. Mehra, M.D., Yoshifumi Naka, M.D., Nir Uriel, M.D., Daniel J. Goldstein, M.D., Joseph C. Cleveland, Jr., M.D., Paolo C. Colombo, M.D., Mary N. Walsh, M.D., Carmelo A. Milano, M.D., Chetan B. Patel, M.D., Ulrich P. Jorde, M.D., Francis D. Pagani, M.D., Keith D. Aaronson, M.D., David A. Dean, M.D., Kelly McCants, M.D., Akinobu Itoh, M.D., Gregory A. Ewald, M.D., Douglas Horstmanshof, M.D., James W. Long, M.D., and Christopher Salerno, M.D., for the MOMENTUM 3 Investigators*
HeartMate III LVAD

- **Wide** blood-flow passages to reduce shear stress
- **Frictionless** with absence of mechanical bearings
- **Intrinsic Pulse** designed to reduce stasis and avert thrombosis
NYHA Functional Class Retreat: Impact of LVAD’s on Class IIIb/IV HF

For 1-year survivors on original therapy, significantly more LVAD patients improved to New York Heart Association (NYHA) functional class I or II compared with OMM patients. Patients with missing NYHA classifications were excluded (6 OMM, 3 LVAD). Abbreviations as in Figure 1.
Overall Survival of CF-VADs

Continuous Flow LVAD/BiVAD Implants: 2008 – 2014, n=12030

- Months: 1, 12, 24, 36, 48
- % Survival: 95%, 80%, 70%, 59%, 48%
- Deaths: 3188
- n at risk: 12030, 8264, 5705, 4033, 2770, 1944, 1314, 856, 511

Hazard

Months post implant

n=12030, Deaths=3188

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# Key Adverse Events:
## Pump Thrombosis, Neurological Events, Bleeding

<table>
<thead>
<tr>
<th>Event</th>
<th>HeartMate 3 (n=151)</th>
<th>HeartMate II (n=138)</th>
<th>RR</th>
<th>95% CI for RR</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Suspected or Confirmed Pump Thrombosis</strong></td>
<td>0 (0)</td>
<td>14 (10)</td>
<td>18</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>All Stroke</td>
<td>12 (7)</td>
<td>15 (10)</td>
<td>17</td>
<td>0.73</td>
<td>0.35-1.51</td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>4 (2)</td>
<td>8 (5)</td>
<td>8</td>
<td>0.46</td>
<td>0.14-1.48</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>8 (5)</td>
<td>9 (6)</td>
<td>9</td>
<td>0.81</td>
<td>0.32-2.05</td>
</tr>
<tr>
<td>Disabling Stroke</td>
<td>9(6)</td>
<td>5(3)</td>
<td>5</td>
<td>1.65</td>
<td>0.57-4.79</td>
</tr>
<tr>
<td>Other Neurologic Events*</td>
<td>9 (6)</td>
<td>8 (5)</td>
<td>8</td>
<td>1.03</td>
<td>0.41-2.59</td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td>50 (33)</td>
<td>54 (39)</td>
<td>98</td>
<td>0.85</td>
<td>0.62-1.15</td>
</tr>
<tr>
<td>Bleeding Requiring Surgery</td>
<td>15 (9)</td>
<td>19 (13)</td>
<td>21</td>
<td>0.72</td>
<td>0.38-1.36</td>
</tr>
<tr>
<td>Gastrointestinal Bleeding</td>
<td>24 (15)</td>
<td>21 (15)</td>
<td>36</td>
<td>1.04</td>
<td>0.61-1.79</td>
</tr>
</tbody>
</table>

**No Pump Thrombosis in the HeartMate 3 LVAS group**

**Similar Stroke and Bleeding rates in both groups**

RR, denotes Relative Risk and CI, confidence interval

*Includes transient ischemic attacks and neurologic events other than stroke

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HK: Destination Therapy Patient (7 yrs+)

Implant: 2/4/10

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M.L. (s/p HM II p-p CMY)
Candidates for Total Artificial Heart (TAH)

- Irreversible severe biventricular failure
- Hypertrophic, amyloid, giant cell CMY
- Heart tx w/ severe CAV or refractory reject
- Incessant VT/VF
Syncardia t-TAH

- **Indications:**
  - bridge to OHT (FDA approved)
  - severe irrev. bivent failure
  - Intractable VT/VF

- **79% successfully transplanted**
- **Nearly 1,600 implanted WW**
- **50 - 70 cc per each ventricle**
- **Freedom driver**

*Copeland J, Arabia F et al; NEJM 351: 859-867 2004*
Total Artificial Heart Patient at a Baseball Game

2 months post-implant w/ Yasiel Puig of LA Dodgers
Cardiac Transplantation

Climbing the Matterhorn

Kona Ironman Triathlon
• Multitude of trials for new medications including oral inotropes, amyloid CMY therapy, HCM

• Stem cell therapy

• Genetic markers for rejection

• Wireless (cordless) total artificial hearts or LVADS
Pearls

- Educate and update medical professionals and patients about optimal medical therapy for heart failure today (ie Entresto, Ivabradine)

- Consider structural interventions (ie mitraclip) or invasive monitoring (cardiomems)

- Know when to refer to an advanced heart failure clinic (its never too early!)

- Know that there are still great options when patients are beyond medical therapy (Heart Transplant and MCS)
“IN ADVANCED HEART FAILURE, IT IS ALWAYS BETTER TO REFER A PATIENT A YEAR TOO EARLY THAN A MINUTE TOO LATE!”
Heart Failure Management Requires Team Approach

TEAMWORK!
WORKING TOGETHER GETS THE GOODS!
Thank You! Questions?