Heart Failure in 2017

What's New, What Matters and What's Coming
I Have No Financial or Personal Disclosures…

…or do I?
1. Discuss the epidemiology and impact of heart failure nationwide

2. Discuss the current state of medical management for Heart Failure with Reduced Ejection Fraction (HFrEF)
   - Discuss the role of IVABRADINE and ENTRESTO

3. Discuss the current state of medical management for Heart Failure with Preserved Ejection Fraction (HFpEF)

4. Discuss ambulatory hemodynamic monitoring with the CardioMEMs system

5. Discuss the current state of advanced heart failure
Objectives

1. Be able to discuss current management of HFpEF and HFrEF
2. Understand current strategies to minimize rehospitalizations
3. Understand the future directions of heart failure management
4. Have a basic understanding of advanced heart failure therapies
   1. When to refer
   2. Who is a candidate
The Problem...

- As of 2014, **6.5 million** Americans had heart failure\(^{(2)}\) - this is estimated to rise to **>8 million by 2030**\(^{(3)}\).
- Each year, **960,000** new cases of heart failure are diagnosed\(^{(2)}\)
  - **>1 million** people are hospitalized with heart failure yearly\(^{(2)}\)
- By age **45 has a 1 in 5** lifetime risk of developing heart failure\(^{(3)}\)
- In **2013, 1 in 9** death certificates (284,388 deaths) in the United States mentioned heart failure as a contributing factor.\(^{(1)}\)
- Of incident hospitalized HF events, **53% had HF with reduced ejection fraction** and **47% had preserved ejection fraction**\(^{(3)}\)
  
  - For all comers, the **5 year mortality in regard to heart failure** is **50%**...
The Problem...

Survival at 5 years decreases in regard to ACC/AHA Stages of heart failure:
- 97% in stage A
- 96% in stage B
- 75% in stage C
- 20% in stage D
Cost of Heart Failure/Readmission

-Ten Conditions with highest all-cause, 30-day readmissions for Medicare Patients.
-Hospital Readmission Reduction Program
Cost of Heart Failure/Readmission

National Medicare Readmission Rates Started to Fall in 2012

- **Diagnosis for initial hospitalization:**
  - Heart Failure
  - Heart Attack
  - Pneumonia

*Performance (measurement) Time Period*

Notes: National readmission rates include unplanned hospitalizations for any cause within 30 days of discharge from an initial hospitalization for either heart failure, heart attack, or pneumonia. Readmission rates are risk-adjusted for certain patient characteristics, such as age and other medical conditions.

Source: Kaiser Family Foundation analysis of CMS Hospital Compare data files.
Cost of Heart Failure/Readmissions

- Up to 80% of direct costs are as a result of hospitalizations.

BY 2030, TOTAL OVERALL COSTS ARE EXPECTED TO MORE THAN DOUBLE TO NEARLY $70 BILLION IN THE UNITED STATES\(^1\)
Well established that with successive heart failure admissions, mortality increases.

Patient Centered Care

Cost Reduction
Management of Heart Failure

Yancy et al. JACC, April 2017.
Management of Heart Failure

1990: V-HeFT CONSENSUS
1995: SOLVD SAVE
2000: RALES CIBIS-2 MERIT-HF
2005: COPERNICUS Val-HeFT CHARM EPESUS COMPANION
2010: CARE-HF SCD-HeFT HeartMate II MADIT-CRT
2014: PARADIGM-HF SHIFT RAFT EMPHASIS

SHIFT
Management of Heart Failure: 2017 Guideline Update

2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America

Developed in Collaboration with the American Academy of Family Physicians, American College of Chest Physicians, and International Society for Heart and Lung Transplantation

Yancy et al. JACC, April 2017.
Management of Heart Failure

- Common medications in the treatment of heart failure with an emphasis on mean doses achieved in clinical trials

- 50% of patients on maximum doses of GDMT will improve their LVEF

Yancy et al. JACC, April 2017.
Management of Heart Failure

2013 ACCF/AHA Heart Failure Guidelines
Pharmacologic Treatment for Stage C HFrEF

Yancy et al. JACC, April 2017.
Management of Heart Failure:
Hydralazine and Long-Acting Nitrates

- **V-HEFT-I**[^5]
  - Digoxin + diuretic (no GDMT)
  - Reduction in Mortality and LVEF*

- **V-HEFT-II**[^6]
  - Combination Vasodilator versus Enalapril
  - Combination Vasodilator PLUS Enalapril yields superior mortality benefit

- **A-HEFT**[^7]
  - Compared combination vasodilator with ACEi in the African American Community
  - Reduction in Mortality, Hospitalization and improved QOL

- **Hy-C**[^8]
  - ACEi + Combination Vasodilator therapy reduces risk of SCD

[^5]: Reference: A
[^6]: Reference: B
[^7]: Reference: C
[^8]: Reference: D
Management of Heart Failure:

Digoxin

Class IIa

1. Digoxin can be beneficial in patients with HFrEF, unless contraindicated, to decrease hospitalizations for HF (483-490). *(Level of Evidence: B)*

-Recent Meta-analysis describes an INCREASE in all cause mortality in regards to concomitant use of digoxin in patients with atrial fibrillation, regardless of heart failure status(9).
-ARISTOTLE Trial-For every 0.5 ng/ml increase in the blood level of digoxin, the risk of death rose by 19 percent(10).
  -Risk of Mortality is HIGHEST when levels exceed 1.2 ng/ml
-Noted same trend in ROCKET-AF Trial and AFFIRM Trial
Management of Heart Failure: Valsartan/Sacubitril (Entresto®)

Natriuretic Peptides (CNP, ANP, BNP, BK)
- Vasodilation
- Natriuresis
- Diuresis
- Inhibition of pathologic growth/fibrosis

Angiotensin II
- Vasoconstriction
- Sodium/water retention
- Fibrosis/hypertrophy

LCZ696
- Neprilysin
  - Degradation products
- AT₁ Receptor
  - Vasoconstriction
  - Sodium/water retention
  - Fibrosis/hypertrophy

Valsartan

Nephrolysin Inhibition
- A membrane bound endopeptidase
- Found in many tissues but most frequently in the kidney
- Nephrolysin inhibition alone, increase in angiotensin II formation
- Omapatrilat Versus Enalapril Randomized Trial of Utility in Reducing Events (OVERTURE) trial with much more angioedema and HYPOtension
- Less bradykinin with ARB
Management of Heart Failure: Valsartan/Sacubitril (Entresto®)

PARADIGM- HF Trial\(^{(14)}\)

**Primary:**
- Cardiovascular death or heart failure hospitalization
- Cardiovascular death
- Heart failure hospitalization

**Secondary:**
- Death from any cause
- KCCQ (CSS - symptoms and physical limitations)
- New onset atrial fibrillation
- Decline in renal function
Management of Heart Failure: Valsartan/Sacubitril (Entresto®)

Single-blind run-in period

1. Enalapril 10 mg BID for 1-2 weeks
2. Enalapril 100 mg BID for 2-4 weeks
3. Enalapril 200 mg BID for 2-4 weeks

Double-blind period (1:1 randomization)

- LCZ696 200 mg BID
- Enalapril 10 mg BID
Management of Heart Failure: Valsartan/Sacubitril (Entresto®)

Trial stopped early after 27 month follow-up because the boundary for an overwhelming benefit had been crossed.

**LCZ696 was more effective than enalapril in . . .**
- Reducing the risk of CV death and HF hospitalization
- Reducing the risk of CV death by *incremental* 20%
- Reducing the risk of HF hospitalization by *incremental* 21%
- Reducing all-cause mortality by *incremental* 16%
- *Incrementally* improving symptoms and physical limitations

**LCZ696 was better tolerated than enalapril . . .**
- Less likely to cause cough, hyperkalemia or renal impairment
- Less likely to be discontinued due to an adverse event
- More hypotension, but no increase in discontinuations
- Not more likely to cause serious angioedema
Management of Heart Failure:
Valsartan/Sacubitril (Entresto®)

What is Being Compared?
• Why not equal dose valsartan + placebo versus Valsartan + sacubitril?

Why Fixed Dose Enalapril?
• The dose of valsartan is NOT equivalent to a fixed dose of 20mg of enalapril daily.

SOLVD Trial

Is the Run-in Phase Confounding?
• Are you simply masking side effects by eliminating those who do not tolerate the medication.

DEMENTIA
Case

62 Year old male presented to the ED with a mechanical fall and right scalp laceration. He has a history of CAD, HTN, Atrial Fibrillation and Type II DM. He has no complaints outside of a mild headache and embarrassment.

Medications: ASA, Metoprolol, Entresto, Spironolactone, Apixiban, Atorvastatin, Metformin.

The ER draws lab work which is below:
-Troponin: <0.04
-BNP: 651 (baseline 210)
-D-dimer: Elevated…so he got a chest CT...
Management of Heart Failure

<table>
<thead>
<tr>
<th>I</th>
<th>ARNI: B-R</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In patients with chronic symptomatic HFrEF NYHA class II or III who</td>
</tr>
<tr>
<td></td>
<td>tolerate an ACE inhibitor or ARB, replacement by an ARNI is</td>
</tr>
<tr>
<td></td>
<td>recommended to further reduce morbidity and mortality (19).</td>
</tr>
<tr>
<td>III:</td>
<td>Harm</td>
</tr>
<tr>
<td></td>
<td>B-R</td>
</tr>
<tr>
<td></td>
<td>ARNI should not be administered concomitantly with ACE inhibitors or</td>
</tr>
<tr>
<td></td>
<td>within 36 hours of the last dose of an ACE inhibitor (31, 32).</td>
</tr>
<tr>
<td>III:</td>
<td>Harm</td>
</tr>
<tr>
<td></td>
<td>C-EO</td>
</tr>
<tr>
<td></td>
<td>ARNI should not be administered to patients with a history of angioedema.</td>
</tr>
</tbody>
</table>

Management of Heart Failure: Ivabradine (Corlanor®)

**SHIFT Trial**\(^{(15)}\)

- Ivabradine selectively and specifically inhibits the cardiac pacemaker I\(_{f}\) "funny" current in the sinoatrial node and to a lesser degree, atrioventricular node, resulting in a dose-dependent reduction in heart rate.

- It has no effect on **myocardial contractility** and intra-cardiac conduction.

- It has no effect on **blood pressure**
Management of Heart Failure:
Ivabradine (Corlanor®)

Mechanism of Action-
-A Hyperpolarization-activated Cyclic Nucleotide-gated channel blocker (HCN channel blocker - mixed Na-K+)
-Reduces the activity of the SA node by selectively Inhibiting the $I_f$ Current resulting In HEART RATE REDUCTION
Management of Heart Failure: Ivabradine (Corlanor®)

SHIFT Trial-
Enrolled patients with stable, symptomatic chronic heart failure with LVEF <35% who were in SINUS RHYTHM with a resting HR of ≥ 70 AND:

- On MAXIMALLY tolerated beta-blockers OR
- Have a contraindication to beta-blocker use

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary composite endpoint</td>
<td>0.82</td>
<td>[0.75;0.90]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(CV death or hospital admission for worsening HF)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>0.90</td>
<td>[0.80;1.02]</td>
<td>0.092</td>
</tr>
<tr>
<td>Death from heart failure</td>
<td>0.74</td>
<td>[0.58;0.94]</td>
<td>0.014</td>
</tr>
<tr>
<td>All-cause hospital admission</td>
<td>0.89</td>
<td>[0.82;0.96]</td>
<td>0.003</td>
</tr>
<tr>
<td>Any CV hospital admission</td>
<td>0.85</td>
<td>[0.78;0.92]</td>
<td>0.0002</td>
</tr>
<tr>
<td>CV death/hospital admission for HF or non-fatal MI</td>
<td>0.82</td>
<td>[0.74;0.89]</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Management of Heart Failure: Ivabradine (Corlanor®)

- Ivabradine reduced CV mortality OR heart failure hospitalization by 18% ($p<0.0001$).
  - The absolute risk reduction was 4.2%.
- This beneficial effect was mainly driven by a favorable effect on hospital admission rather than mortality.
- FURTHERMORE a large portion of the patients whom showed benefit were NOT on optimal HR control with maximally tolerated beta-blocker.
- Overall, treatment with ivabradine was safe and well tolerated.
  - Bradycardia
  - Atrial Fibrillation
Management of Heart Failure:
Ivabradine (Corlanor®)

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HF rEF (LVEF ≤35%) who are receiving GDEM, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest (37-40).</td>
</tr>
</tbody>
</table>
Management of Heart Failure:
Heart Failure with Preserved Ejection Fraction (HFpEF)

**Systolic Heart Failure (HFrEF)**-
Heart failure as a result of a reduced ejection fraction $\leq 40\%$ \(^{(1)}\)

**Diastolic Heart Failure (HFpEF)**-
Individuals with clinical signs and symptoms of heart failure with:

a. Evidence of preserved or normal ejection fraction $\geq 50\%$

b. Evidence of abnormal left ventricular diastolic function confirmed by Doppler echocardiography or cardiac catheterization.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Ejection Fraction</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Heart Failure with Reduced Ejection Fraction (HFrEF)</td>
<td>$\leq 40%$</td>
<td>Also referred to as systolic HF. Randomized clinical trials have mainly enrolled patients with HFpEF and it is only in these patients that efficacious therapies have been demonstrated to date.</td>
</tr>
<tr>
<td>II. Heart Failure with Preserved Ejection Fraction (HFpEF)</td>
<td>$\geq 50%$</td>
<td>Also referred to as diastolic HF. Several different criteria have been used to further define HFpEF. The diagnosis of HFpEF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified.</td>
</tr>
<tr>
<td>a. HFpEF, Borderline</td>
<td>41% to 49%</td>
<td>These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patient with HFpEF.</td>
</tr>
<tr>
<td>b. HFpEF, Improved</td>
<td>$&gt;40%$</td>
<td>It has been recognized that a subset of patients with HFpEF previously had HFrEF. These patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. Further research is needed to better characterize these patients.</td>
</tr>
</tbody>
</table>
Management of Heart Failure:
Heart Failure with Preserved Ejection Fraction (HFpEF)

Signs and Symptoms of Heart Failure
- +/- Elevated CHF Peptide
- CXR with vascular congestion/pulmonary edema
- Shortness of Breath, Edema, JVD, etc

Echocardiogram
- Abnormal Diastology
- Elevated Filling Pressures
- Left Atrial Enlargement
- Left Ventricular Hypertrophy

Lack of ALTERNATIVE Diagnosis
Management of Heart Failure: Heart Failure with Preserved Ejection Fraction (HFpEF)

Ventricular stiffness
Arterial Stiffness
V-A coupling
Fibrosis
Chronotropic Incompetence
Pulmonary Venous Hypertension

Redfield, et al. NEJM 2016
Management of Heart Failure:
Heart Failure with Preserved Ejection Fraction (HFpEF)

- CHARM-Preserved
- DIG Trial
- PEP-CHF
- RELAX
- SENIORS
- TOPCAT*
- L-PRESERVE
Management of Heart Failure:
Heart Failure with Preserved Ejection Fraction (HFpEF)

<table>
<thead>
<tr>
<th>IIb</th>
<th>B-R</th>
<th>NEW: Current recommendation reflects new RCT data.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>In appropriately selected patients with HFpEF (with EF ≥45%, elevated BNP levels or HF admission within 1 year, estimated glomerular filtration rate &gt;30 mL/min, creatinine &lt;2.5 mg/dL, potassium &lt;5.0 mEq/L), aldosterone receptor antagonists might be considered to decrease hospitalizations (83,166,167). The use of ARBs might be considered to decrease hospitalizations for patients with HFpEF (169).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IIb</th>
<th>B</th>
<th>2013 recommendation remains current.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>The use of ARBs might be considered to decrease hospitalizations for patients with HFpEF (169).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>III: No Benefit</th>
<th>B-R</th>
<th>NEW: Current recommendation reflects new data from RCTs.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QoL in patients with HFpEF is ineffective (171,172).</td>
</tr>
</tbody>
</table>

See Online Data Supplement C.
Management of Heart Failure:
Heart Failure with Preserved Ejection Fraction (HFpEF)

TOPCAT (TOP: Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist; cardiac function HFpEF) trial - HFpEF patients were randomly assigned to receive either spironolactone or placebo. The incidence of the primary composite end point were not significantly lower: death from cardiovascular causes - hospitalization for heart failure - resuscitated cardiac arrest. However, the incidence of hospitalization for heart failure was significantly lower in the spironolactone group. Significant differences in the clinical profiles, event rates, and responses to spironolactone were identified between the patients who were enrolled in the Americas (United States, Canada, Brazil, and Argentina) and patients enrolled in Russia and Georgia.
Management of Heart Failure:
Heart Failure with Preserved Ejection Fraction (HFpEF)

TOPCAT
CV death, HF hospitalization or aborted cardiac arrest

US, Canada, Argentina, Brazil
HR=0.82 (0.69-0.98)
Placebo 31.8%

Spironolactone
Placebo 8.4%

Russia, Rep Georgia
HR=1.10 (0.79-1.51)

(N=119) (N=21)

P interaction=0.122
Management of Heart Failure:
Heart Failure with Preserved Ejection Fraction (HFpEF)
Management of Heart Failure: Future Directions

- Phase 2 clinical trial to assess the safety of ARNI in patients with HFpEF.

- 308 patients randomized (149 and 160 patients in a LCZ696 and Valsartan group respectively)

- Primary Objective: Reduction of NT-proBNP at 12 weeks
Management of Heart Failure:
Future Directions

**Inclusion**
- Age >40
- NYHA Class II-IV Symptoms
- LVEF >45%
- Plasma NT-proBNP >400 pg/ml
- On diuretics with SBP <140 mmHg or <160 mmHg if on triple therapy
- GFR >30
- K+ <5.2

**Exclusion**
- LVEF <45% at any time
- At 12 weeks, NT-proBNP was statistically lower in the LCZ696 group than in the valsartan ARM however, the statistical significance did NOT last past 36 weeks.
- LCZ696 resulted in:
  - Reduction in Left Atrial Size
  - Improvement in NYHA Class
Management of Heart Failure:
Heart Failure with Preserved Ejection Fraction (HFpEF)
## Management of Heart Failure: Comorbid Conditions

### HTN

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>RECOMMENDATIONS</th>
<th>COMMENT/RATIONALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>C-LD</td>
<td>In patients with NYHA class II–IV HF and suspicion of sleep-disordered breathing or excessive daytime sleepiness, a formal sleep assessment is reasonable (200,201).</td>
<td>NEW: Recommendation reflects clinical necessity to distinguish obstructive versus central sleep apnea.</td>
</tr>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>In patients with cardiovascular disease and obstructive sleep apnea, CPAP may be reasonable to improve sleep quality and daytime sleepiness (204).</td>
<td>NEW: New data demonstrate the limited scope of benefit expected from CPAP for obstructive sleep apnea.</td>
</tr>
<tr>
<td>III: Harm</td>
<td>B-R</td>
<td>In patients with NYHA class II–IV HFrEF and central sleep apnea, adaptive servo-ventilation causes harm (203).</td>
<td>NEW: New data demonstrate a signal of harm when adaptive servo-ventilation is used for central sleep apnea.</td>
</tr>
</tbody>
</table>

### Sleep Disordered Breathing

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>RECOMMENDATIONS</th>
<th>COMMENT/RATIONALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>III: No Benefit</td>
<td>B-R</td>
<td>In patients with HF and anemia, erythropoietin-stimulating agents should not be used to improve morbidity and mortality (176).</td>
<td>NEW: Current recommendation reflects new evidence demonstrating absence of therapeutic benefit.</td>
</tr>
</tbody>
</table>

### Anemia

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>RECOMMENDATIONS</th>
<th>COMMENT/RATIONALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>In patients with NYHA class II and III HF and iron deficiency (ferritin &lt;100 ng/mL or 100 to 300 ng/mL if transferrin saturation is &lt;20%), intravenous iron replacement might be reasonable to improve functional status and QoL (173,174).</td>
<td>NEW: New evidence consistent with therapeutic benefit.</td>
</tr>
</tbody>
</table>
Case

63 year old female with a history of Hypothyroidism, type II Diabetes Mellitus and rheumatoid arthritis. She developed acute heart failure, requiring hospitalization at outside hospital where she was discovered to have an LVEF of 10%. Angiography revealed a 40% mid-LAD lesion. She is here to seek a second opinion.

**Cardiac MRI with Adenosine Stress** - No evidence of ischemia. Mild LVH. No infiltrative disease.

**Medications** - Hydroxychloroquine for 25 years (Plaquenil), Synthroid, Metoprolol Succinate 25mg daily, Lisinopril 5mg and Spironolactone 25mg daily

**Vitals** - BP: 96/64  HR: 70  RR: 16  O2: 98%

**EKG** - Normal Sinus Rhythm, Rate 70, Normal Axis, **QRS 136 msec**
Case

Myelin Figures

Curvilinear Bodies
Rise of the Machines...

“...I mean with artificial intelligence we’re summoning the demon.”

Elon Musk
Management of Heart Failure: CardioMEMs

- Permanently implantable wireless system
- Provides ambulatory PA pressure measurements
  - Systolic
  - Diastolic
  - Mean PA
- PA pressure readings can guide medical therapy
- Components:
  - A battery-free sensor implanted in the pulmonary artery via right heart catheterization
  - A transvenous catheter to deploy the sensor
  - Electronics system to acquire, process, and transfer PA pressure measurements to a database

Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial

William T Abraham, Philip B Adamson, Robert C Bourge, Mark F Aaron, Maria Rosa Costanzo, Lynne W Stevenson, Warren Strickland, Suresh Neelagaru, Nirav Raval, Steven Krueger, Stanislav Weiner, David Shavelle, Bradley Jeffries, Jay S Yadav, for the CHAMPION Trial Study Group
Management of Heart Failure: 
CardioMEMs
Management of Heart Failure:
CardioMEMs

Progressive improvement in pulmonary pressures

Pressure waveform from CardioMEMs transmission
Management of Heart Failure: CardioMEMs

-Prospective, multicenter (n=64), single-blind, US

Previously hospitalized patients
- NYHA Class III symptoms (≥ 3 months)
- ≥ 18 years

Exclusion Criteria:
- History of recurrent pulmonary embolism or DVT
- Cardiac resynchronization with device implantation in the prior 3 months
- Stage IV or V CKD (GFR rate <25 mL/min per 1.73 m²)
- Excluded patients with ACC/AHA stage D HF
- Intolerance of clopidogrel and aspirin

No EF criteria for inclusion
- 1st device-based management strategy that improves outcomes in patients with HFpEF
Management of Heart Failure: 
CardioMEMs

- Over the entire randomized follow-up, the rate of HF-related hospitalizations was reduced by 37% in the treatment group
  - HFpEF > HFrEF

  - Greater reduction in pulmonary artery mean pressure, fewer patients admitted to hospital for heart failure, more days alive outside hospital, and better quality of life than the control group during 6 months of follow-up

  - LOS for HF-related hospitalizations was significantly shorter in the treatment group
Management of Heart Failure:
CardioMEMs
Management of Heart Failure:
Advanced Heart Failure

4,388 adult heart transplants

Kirklin et al. JHLT, 2017
...patients with truly refractory HF symptoms and is heralded by a tenuous clinical course of progressive debilitating symptoms with decreasing level of activity (NYHA III, IV), recurrent hospitalizations for volume overload, rhythm management and complications of HF and HF therapy (cardiorenal syndrome, medication side effects, pulmonary emboli, anticoagulation complications and others) and marked increases in the level of outpatient visits in efforts to avoid hospitalizations\(^4\).

-ADHERE-LMM was a multicenter, observational registry of 1433 patients with advanced HF defined as adults (≥18) with chronic HF and refractory symptoms on oral medical therapy that were required:

- NYHA functional class III or IV for ≥60 consecutive days
- hospitalized ≥2 times in the preceding year with
  a. primary diagnosis of HF
  b. secondary diagnosis of HF
- treated with ≥2 consecutive days of IV diuretic, vasoactive or inotropic medications, OR to have required either 2 complete IV infusions of a vasoactive or inotropic agent, each lasting ≥2 hrs OR 3 IV diuretic treatments, given either as a bolus or continuous drip, during the preceding 60 days\(^5\).
Management of Heart Failure:

Advanced Heart Failure

- Progressive symptoms
  - End-organ dysfunction
- Frequent Hospitalizations
  - ≥2 times in one year
- De-escalation of CHF Meds
- Functional Impairment
  - Cardiopulmonary Stress
  - 6 Minute Walk
Management of Heart Failure:
Advanced Heart Failure
Management of Heart Failure:
Advanced Heart Failure

Outflow Cannula

Inflow Cannula

Controller

Battery
Management of Heart Failure:
Advanced Heart Failure

Indications for Cardiac Transplantation and LVAD

<table>
<thead>
<tr>
<th>Indications</th>
<th>Absolute Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-stage heart disease refractory to medical or surgical therapy</td>
<td>Irreversible hepatic disease</td>
</tr>
<tr>
<td>Age below 60 years</td>
<td>Irreversible renal disease</td>
</tr>
<tr>
<td>New York Heart Association Class III-IV symptoms despite maximal therapy</td>
<td>Irreversible neurological disease</td>
</tr>
<tr>
<td>Prognosis for 1-year survival &lt; 75%</td>
<td>OMT</td>
</tr>
<tr>
<td>No other significant medical problems that might independently deter</td>
<td>Medical nonadherence</td>
</tr>
<tr>
<td>survival</td>
<td>Severe psychosocial limitations</td>
</tr>
<tr>
<td>Patient characteristics—mentally stable, motivated, compliant and with</td>
<td></td>
</tr>
<tr>
<td>supportive family</td>
<td></td>
</tr>
<tr>
<td>Contraindications</td>
<td></td>
</tr>
<tr>
<td>Age &gt; 65 yrs</td>
<td></td>
</tr>
<tr>
<td>Fixed pulmonary vascular resistance &gt; 6 Wood units</td>
<td></td>
</tr>
<tr>
<td>Brittle diabetes with end organ damage</td>
<td></td>
</tr>
<tr>
<td>Active infection</td>
<td></td>
</tr>
<tr>
<td>Major debilitating co-morbid disease</td>
<td></td>
</tr>
<tr>
<td>Active or recent malignancy ( &lt; 2 years)</td>
<td></td>
</tr>
<tr>
<td>LVF seroconversion</td>
<td></td>
</tr>
<tr>
<td>Morbid obesity (BMI &gt; 35)</td>
<td></td>
</tr>
<tr>
<td>History of severe mental illness or psychosocial instability</td>
<td></td>
</tr>
<tr>
<td>Evidence of active tobacco, alcohol or drug abuse</td>
<td></td>
</tr>
</tbody>
</table>
### Management of Heart Failure: Advanced Heart Failure

#### Table 5: Adverse Event Rates (Events/100 patient months) in the First 12 Months Post-implant by Era for CF LVADs/BiVADs ($n = 12,030$)

| Adverse event                          | Era 1 ($n = 4,744$): continuous 2008 to 2011 | Era 2 ($n = 7,286$): continuous 2012 to 2014 | Era 1 vs Era 2: 2008 to 2011 / 2012 to 2014 | p-value  
|----------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-------
| **Bleeding**                           | [Events, Rate]                               | [Events, Rate]                               | [Ratio]                                      |       
| Cardiac/vascular                       | [238, 0.57]                                  | [276, 0.49]                                  | [1.17]                                       | 0.07  
| Right heart failure                    | [29, 0.07]                                   | [34, 0.06]                                   | [1.16]                                       | 0.55  
| Myocardial infarction                  | [2,007, 4.80]                                | [2,303, 4.06]                                | [1.18]                                       | <0.0001
| Cardiac arrhythmia                     | [271, 0.65]                                  | [305, 0.54]                                  | [1.21]                                       | 0.02  
| Pericardial drainage                   | [182, 0.44]                                  | [115, 0.20]                                  | [2.15]                                       | <0.0001
| Hypertension                           | [70, 0.17]                                   | [94, 0.17]                                   | [1.01]                                       | 0.93  
| Arterial non-CNS thrombosis            | [304, 0.73]                                  | [286, 0.50]                                  | [1.44]                                       | <0.0001
| Venous thrombotic event                | [200, 0.48]                                  | [314, 0.55]                                  | [0.87]                                       | 0.11  
| Hemolysis                              | [3,435, 8.22]                                | [4,132, 7.28]                                | [1.13]                                       | <0.0001
| **Infection**                          | [487, 1.17]                                  | [916, 1.61]                                  | [0.72]                                       | <0.0001
| Stroke                                 | [601, 1.44]                                  | [876, 1.54]                                  | [0.93]                                       | 0.19  
| Renal dysfunction                      | [246, 0.59]                                  | [326, 0.57]                                  | [1.02]                                       | 0.76  
| Hepatic dysfunction                    | [1,104, 2.64]                                | [1,551, 2.73]                                | [0.97]                                       | 0.39  
| **Respiratory failure**                | [81, 0.19]                                   | [96, 0.17]                                   | [1.15]                                       | 0.36  
| Wound dehiscence                       | [486, 1.16]                                  | [525, 0.93]                                  | [1.26]                                       | 0.0003
| Psychiatric episode                    | [13,673, 32.72]                              | [16,569, 29.20]                              | [1.12]                                       | <0.0001

BIVAD, biventricular assist device; CF, continuous flow; CNS, central nervous system; LVAD, left ventricular assist device.
Management of Heart Failure:
Advanced Heart Failure

**HeartMate 3** - Recently approved

- RBCs, decrease risk of thrombosis/hemolysis
- Reduced RPM to create same cardiac output using less energy
Summary

1. Identify risk factors for heart failure (ACC/AHA Stage A) and treat accordingly.
2. Aggressively titrate guideline directed medical therapy (GDMT)
3. Close discharge follow-up to avoid medication compliance issues, medication side-effects, fluid retention before it becomes an issue.
4. Understand risk factors advanced heart failure and refer early
Works Cited

4. Weighted national estimates from a readmissions analysis file derived from the Agency for Healthcare Research and Quality (AHRQ), Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID), 2011