Management of Chronic Congestive Heart failure

(changing paradigms)

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2009 Focused Update: ACCF/AHA Guidelines for the Diagnosis and Management of Heart Failure in Adults: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: Developed in Collaboration With the International Society for Heart and Lung Transplantation

2009 WRITING GROUP TO REVIEW NEW EVIDENCE AND UPDATE THE 2005 GUIDELINE FOR THE MANAGEMENT OF PATIENTS WITH CHRONIC HEART FAILURE WRITING ON BEHALF OF THE 2005 HEART FAILURE WRITING COMMITTEE

- Defined pre-clinical disease / treatment
- Standardized Optimal Pharmacologic Therapy in HFrEF
2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

- Addresses: Surgical Interventional and Device-based therapies
- Briefly addresses HFpEF
- Does not address CHF in Children, Adult Congenital Heart Disease, or emerging therapies
NHYA Class

• NHYA I  Cardiac disease but no sx or limitation.
• NYHA II  Mild sx and slight limitation.
• NYHA III  Marked limitation, Comfortable only at rest.
• NYHA IV  Severe limitation, sx even at rest.
Stages in the Development of Heart Failure / Recommended Therapy by Stage
Recovered Heart Failure (HF-Recovered)

- Stage E?
- EF > 50% with history of prior HF
  - Abnormal Biomarkers (troponin, BNP)
  - Increased risk of HF hospitalization

“Once HF, Always HF”

-Basuray, Fang et.al. Circulation May 2014
HF $r$ EF: Starling Relationships

(Stage C-D, Class II-IV)
Acute Management: Optimize Pt’s Curve (improve class)
General Measures

- Self care *(class I)* Reduces hospital utilization
- Exercise training *(class I)* Improves functional status
- Cardiac rehab *(class IIa)* Improves mortality
- Sodium restriction *(class IIa)* Probably helps, but may worsen neurohumoral status
Volume Reduction

– DOSE trial
– Vasopressin antagonists (IIb in hypervolemic hyponatremic on GDMT w/wo MS changes)
– Mechanical volume reduction (UF IIb)
– Natrecor ASCEND -HF (IIb in normotensive acute CHF)
Chronic Management: Normalize Patient’s Curve (improve stage)
So how do we get there?
So how do we get there?

• Ionotropy?
So how do we get there?

• Ionotropy?
  Dobutamine ($B_1$ agonist)
  Milranone (PDE III inhibitor) OPTIME-CHF PROMISE
  Flosequinon (quinolone vasodilator) PROFILE
  Digoxin (cardiac glycoside) DIG RADIANCE

improve hemodynamics structure cardiac output and symptoms but increase mortality
So how do we get there?

• Ionotropy
• Ischemia?
So how do we get there?

• Ionotropy

• Ischemia?
  – 60% of HFrEF is ischemic, and we’ve gotten really good at treating it: 1742 CABG / 3827 PCI per million in US
  – CASS: retrospective subgroup analysis (possible benefit in: LMCA, 3VD, 2VD c prox LAD)
  – STITCH: Improved CV mortality, but no overall mortality benefit
So how do we get there?

- Ionotropy
- Ischemia
- Impedance? (afterload reduction)
So how do we get there?

• Ionotropy
• Ischemia
• Impedance? (afterload reduction)
  – Dinitrate / Hydralazine vs Prazosin vs Placebo
So how do we get there?

- Ionotropy
- Ischemia
- Impedance?

V-HeFT I: Isosorbide Dinitrate / Hydralazine vs Prazosin vs Placebo

V- HeFT II: Isosorbide Dinitrate / Hydralazine -vs- Enalapril vs Historic control
So how do we get there?

- Ionotropy
- Ischemia
- Impedance
- Endocrinology?!??!!
So how do we get there?

- Ionotropy
- Ischemia
- Impedance
- Endocrinology?!??!! Yup, it’s Endocrinology.
Why Endocrinology?

• The RAAS is involved in:
  – Peripheral vasoconstriction
  – Na and H\textsubscript{2}O retention

• Which leads to:
  – Myocyte hypertrophy
  – Myocardial fibrosis
  – Apoptosis

• A process called negative remodeling
So how do we get there?

Neurohumoral Paradigm

‘Modification of maladaptive neurohormones which lead to sodium retention, sympathetic activation and ultimately negative remodeling improves outcome in HF r EF ’

(Cohen, Packer et al circa 1991)
What else happened in 1991?

- Baseball officially bans Pete Rose
- Desert Storm begins
- Iceland recognizes Lithuanian independence
- Roger is finishing his Cardiology Fellowship
- I was applying for a Cardiology Fellowship
- Bittenbender starts 5th grade
- Bill starts talking about “slowing down”
So how do we get there?
{ Neurohumoral Modification Therapy }

• V-HeFT CONSENSUS SOLVD SAVED trials
  -Established the Neurohumoral Paradigm

• USCHFSG COPERNICUS COMET MERIT-HF CIBIS trials
  -Established the role of the Sympathetic Nervous System

• RALES EMPHASIS-HF
  -Established the role of Specific Aldosterone Antagonism

• VAL-HeFT CHARM
  -Confirmed Non-inferiority of ARB’s
Medical Therapy for Stage C (HF r EF) Magnitude of Benefit in Randomized Controlled Trials


<table>
<thead>
<tr>
<th>Therapy</th>
<th>Risk Reduction for Mortality</th>
<th>Number Needed to treat/ 36 months</th>
<th>Risk Reduction for CHF admissions %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-I/ARB</td>
<td>17</td>
<td>26</td>
<td>31</td>
</tr>
<tr>
<td>Beta- Blockers</td>
<td>34</td>
<td>9</td>
<td>41</td>
</tr>
<tr>
<td>Adlosterone-antagonist</td>
<td>30</td>
<td>6</td>
<td>35</td>
</tr>
<tr>
<td>Hydralazine/Nitrate</td>
<td>43</td>
<td>7</td>
<td>33</td>
</tr>
</tbody>
</table>
Neurohumoral Modification Guidelines

- **Class I:**

  - ACE-I or ARB (if ACE-I intolerant) Beta-blocker (Carvedilol, Bisoprolol, Metoprolol Succinate), Aldosterone inhibitor for mortality reduction

  - Use of Isosorbide dinitrate and Hydralazine in self-described African American pts with class III-IV HFrEF on optimal therapy with ACE-I and Beta-blockers for mortality benefit.
Neurohumoral Modification Guidelines

- **Class Ila**

- ARB may be first line Rx if the pt is already on an ARB for other indications

- Isosorbide dinitrate and Hydralazine can be used as an alternative for mortality reduction in patients who are ACE and ARB intolerant
Neurohumoral Modification Guidelines

• Class IIb

• Addition of ARB to ACE-I and Beta-blocker in symptomatic patients who are aldosterone antagonist intolerant
Neurohumoral Modification Guidelines

- **Class III**
- Routine combined use of ACE-I ARB, and Aldosterone antagonist
- Use of Aldosterone antagonist with Cr >2.5mg/dL
Paradigm-HF

- Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure
- John J.V. McMurray, M.D., Milton Packer, M.D., et al. for the PARADIGM-HF Investigators
- NEJM 9/11/14
- ‘Potentiation of Adaptive Neurohormones will improve outcome in HF r EF’
Design

- 8442 pts Class II-IV HF r EF (<35%) on GDMT
- Double-Blind Prospective Randomized
- Enalapril (10 mg bid) vs LCZ696 (200 mg bid)
  ARB / Neprilysin inhibitor (Valsartan 160 mg bid + Sacubitril 40 mg bid)
- Death from cardiovascular causes, HF admission, Overall mortality, over 27 months
Why ARB-Neprilysin Inhibition?

• Neprilysin degrades Natriuretic peptides, (Bradykinins Endothelin and AT-I)

• Inhibition of Neprilysin **augments** Natriuretic peptides (ANP BNP Urodilatin) which:
  – Potentiates natureosis, diuresis
  – Inhibits RAAS
  – Reduces sympathetic drive
  – Has antiproliferative and antihypertrophic effects
Why ARB-Neprilysin Inhibition?

- Neprilysin degrades Natriuretic peptides, (Bradykinins, Endothelin, and AT-I)
- Inhibition of Neprilysin **augments** Bradykinin, Endothelin, and AT-I which:
  - Activates RAAS
  - Increases vascular tone
  - Causes angioedema
Why ARB-Neprilysin Inhibition?

• Neprilysin inhibition augments adaptive Natriuretic peptides
• Neprilysin inhibition augments maladaptive Bradykinins Endothelin and AT-I
Why ARB-Neprilysin Inhibition?

- Neprilysin inhibition augments adaptive natriuretic peptides
- Neprilysin inhibition augments maladaptive bradykinins, endothelin, and AT-I blocked by ARB
Why Neprilysin Inhibition?
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>LCZ696 (N = 1197)</th>
<th>Enalapril (N = 1212)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age — yr</td>
<td>63.8±11.3</td>
<td>63.8±11.3</td>
</tr>
<tr>
<td>Female sex — no. (%)</td>
<td>879 (21.0)</td>
<td>953 (22.6)</td>
</tr>
<tr>
<td>Race or ethnic group — no. (%)†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>2763 (66.0)</td>
<td>2781 (66.0)</td>
</tr>
<tr>
<td>Black</td>
<td>213 (5.1)</td>
<td>215 (5.1)</td>
</tr>
<tr>
<td>Asian</td>
<td>759 (18.1)</td>
<td>750 (17.8)</td>
</tr>
<tr>
<td>Other</td>
<td>452 (10.8)</td>
<td>466 (11.1)</td>
</tr>
<tr>
<td>Region — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td>310 (7.4)</td>
<td>292 (6.9)</td>
</tr>
<tr>
<td>Latin America</td>
<td>713 (17.0)</td>
<td>720 (17.1)</td>
</tr>
<tr>
<td>Western Europe and other‡</td>
<td>1026 (24.5)</td>
<td>1025 (24.3)</td>
</tr>
<tr>
<td>Central Europe</td>
<td>1393 (33.3)</td>
<td>1433 (34.0)</td>
</tr>
<tr>
<td>Asia–Pacific</td>
<td>745 (17.8)</td>
<td>742 (17.6)</td>
</tr>
<tr>
<td>Systolic blood pressure — mm Hg</td>
<td>122±15</td>
<td>121±15</td>
</tr>
<tr>
<td>Heart rate — beats/min</td>
<td>72±12</td>
<td>73±12</td>
</tr>
<tr>
<td>Body-mass index§</td>
<td>28.1±5.5</td>
<td>28.2±5.5</td>
</tr>
<tr>
<td>Serum creatinine — mg/dl</td>
<td>1.13±0.3</td>
<td>1.12±0.3</td>
</tr>
<tr>
<td>Clinical features of heart failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic cardiomyopathy — no. (%)</td>
<td>2506 (59.9)</td>
<td>2530 (60.1)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction — %</td>
<td>29.6±6.1</td>
<td>29.4±6.3</td>
</tr>
<tr>
<td>Median B-type natriuretic peptide (IQR) — pg/ml</td>
<td>255 (155–474)</td>
<td>251 (153–465)</td>
</tr>
<tr>
<td>Median N-terminal pro–B-type natriuretic peptide (IQR) — pg/ml</td>
<td>1631 (885–3154)</td>
<td>1594 (886–3305)</td>
</tr>
<tr>
<td>NYHA functional class — no. (%)§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>180 (4.3)</td>
<td>209 (5.0)</td>
</tr>
<tr>
<td>II</td>
<td>2998 (71.6)</td>
<td>2921 (69.3)</td>
</tr>
<tr>
<td>III</td>
<td>969 (23.1)</td>
<td>1049 (24.9)</td>
</tr>
<tr>
<td>IV</td>
<td>33 (0.8)</td>
<td>27 (0.6)</td>
</tr>
<tr>
<td>Missing data</td>
<td>7 (0.2)</td>
<td>6 (0.1)</td>
</tr>
<tr>
<td>Medical history — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>2969 (70.9)</td>
<td>2971 (70.5)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1451 (34.7)</td>
<td>1456 (34.6)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1517 (36.2)</td>
<td>1574 (37.4)</td>
</tr>
<tr>
<td>Hospitalization for heart failure</td>
<td>2607 (62.3)</td>
<td>2667 (63.3)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1818 (43.4)</td>
<td>1816 (43.1)</td>
</tr>
<tr>
<td>Stroke</td>
<td>355 (8.5)</td>
<td>370 (8.8)</td>
</tr>
<tr>
<td>Pretrial use of ACE inhibitor‡</td>
<td>3266 (78.0)</td>
<td>3266 (77.5)</td>
</tr>
<tr>
<td>Pretrial use of ARB‡</td>
<td>929 (22.2)</td>
<td>963 (22.9)</td>
</tr>
<tr>
<td>Treatments at randomization — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretic</td>
<td>3363 (80.3)</td>
<td>3375 (80.1)</td>
</tr>
<tr>
<td>Digitalis</td>
<td>1223 (29.2)</td>
<td>1316 (31.2)</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>3899 (93.1)</td>
<td>3912 (92.9)</td>
</tr>
<tr>
<td>Mineralocorticoid antagonist</td>
<td>2271 (54.2)</td>
<td>2400 (57.0)</td>
</tr>
<tr>
<td>Implantable cardioverter–defibrillator</td>
<td>623 (14.9)</td>
<td>620 (14.7)</td>
</tr>
<tr>
<td>Cardiac resynchronization therapy</td>
<td>292 (7.0)</td>
<td>282 (6.7)</td>
</tr>
</tbody>
</table>

* Plus–minus values are means ±SD. There were no significant differences between the two groups except for the use of digitalis (P=0.04) and mineralocorticoid-receptor antagonists (P=0.01), with values not adjusted for multiple testing. Percentages may not total 100 because of rounding. More details about the baseline characteristics are provided in Section 3 in the Supplementary Appendix. To convert the values for creatinine to micromoles per liter, multiply by 88.4. IQR denotes interquartile range.
† Race or ethnic group was reported by the investigators.
‡ This category includes South Africa and Israel.
§ The body-mass index is the weight in kilograms divided by the square of the height in meters.
¶ The data for New York Heart Association (NYHA) class reflect the status of patients at the time of randomization. Patients were required to have at least NYHA class II symptoms at screening. At the screening visit, 20 patients were not receiving the protocol-required treatment with an angiotensin-converting–enzyme (ACE) inhibitor or an angiotensin-receptor blocker (ARB), and 45 patients were taking both drugs. Doses of pretrial ACE inhibitors and ARBs are provided in the Supplementary Appendix.

You couldn’t read that slide

- Basically it said that pts were well matched
- Patients were treated with guideline determined background medical and device therapy
- But that’s what you would expect from an original article in the New England freakin’ Journal of Medicine isn’t it?
Table 2. Primary and Secondary Outcomes.*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>LCZ696 (N = 4187)</th>
<th>Enalapril (N = 4212)</th>
<th>Hazard Ratio or Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary composite outcome — no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death from cardiovascular causes or first hospitalization for worsening heart failure</td>
<td>914 (21.8)</td>
<td>1117 (26.5)</td>
<td>0.80 (0.73–0.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>558 (13.3)</td>
<td>693 (16.5)</td>
<td>0.80 (0.71–0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>First hospitalization for worsening heart failure</td>
<td>537 (12.8)</td>
<td>658 (15.6)</td>
<td>0.79 (0.71–0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Secondary outcomes — no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death from any cause</td>
<td>711 (17.0)</td>
<td>835 (19.8)</td>
<td>0.84 (0.76–0.93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Change in KCCQ clinical summary score at 8 mo†</td>
<td>−2.99±0.36</td>
<td>−4.63±0.36</td>
<td>1.64 (0.63–2.65)</td>
<td>0.001</td>
</tr>
<tr>
<td>New-onset atrial fibrillation‡</td>
<td>84 (3.1)</td>
<td>83 (3.1)</td>
<td>0.97 (0.72–1.31)</td>
<td>0.83</td>
</tr>
<tr>
<td>Decline in renal function§</td>
<td>94 (2.2)</td>
<td>108 (2.6)</td>
<td>0.86 (0.65–1.13)</td>
<td>0.28</td>
</tr>
</tbody>
</table>

* Hazard ratios were calculated with the use of stratified Cox proportional-hazard models. P values are two-sided and were calculated by means of a stratified log-rank test without adjustment for multiple comparisons.
† Scores on the Kansas City Cardiomyopathy Questionnaire (KCCQ) range from 0 to 100, with higher scores indicating fewer symptoms and physical limitations associated with heart failure. The treatment effect is shown as the least-squares mean (±SE) of the between-group difference.
‡ A total of 2670 patients in the LCZ696 group and 2638 patients in the enalapril group who did not have atrial fibrillation at the randomization visit were evaluated for new-onset atrial fibrillation during the study.
§ A decline in renal function was defined as end-stage renal disease or a decrease of 50% or more in the estimated glomerular filtration rate (eGFR) from the value at randomization or a decrease in the eGFR of more than 30 ml per minute per 1.73 m², to less than 60 ml per minute per 1.73 m².
Kaplan–Meier Curves for Key Study Outcomes, According to Study Group.

### Table 3. Adverse Events during Randomized Treatment.*

<table>
<thead>
<tr>
<th>Event</th>
<th>LCZ696 (N=4187)</th>
<th>Enalapril (N=4212)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>588 (14.0)</td>
<td>388 (9.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Symptomatic with systolic blood pressure &lt; 90 mm Hg</td>
<td>112 (2.7)</td>
<td>59 (1.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Elevated serum creatinine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 2.5 mg/dl</td>
<td>139 (3.3)</td>
<td>188 (4.5)</td>
<td>0.007</td>
</tr>
<tr>
<td>≥ 3.0 mg/dl</td>
<td>63 (1.5)</td>
<td>83 (2.0)</td>
<td>0.10</td>
</tr>
<tr>
<td>Elevated serum potassium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 5.5 mmol/liter</td>
<td>674 (16.1)</td>
<td>727 (17.3)</td>
<td>0.15</td>
</tr>
<tr>
<td>&gt; 6.0 mmol/liter</td>
<td>181 (4.3)</td>
<td>236 (5.6)</td>
<td>0.007</td>
</tr>
<tr>
<td>Cough</td>
<td>474 (11.3)</td>
<td>601 (14.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Angioedema†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No treatment or use of antihistamines only</td>
<td>10 (0.2)</td>
<td>5 (0.1)</td>
<td>0.19</td>
</tr>
<tr>
<td>Use of catecholamines or glucocorticoids without hospitalization</td>
<td>6 (0.1)</td>
<td>4 (0.1)</td>
<td>0.52</td>
</tr>
<tr>
<td>Hospitalization without airway compromise</td>
<td>3 (0.1)</td>
<td>1 (&lt;0.1)</td>
<td>0.31</td>
</tr>
<tr>
<td>Airway compromise</td>
<td>0</td>
<td>0</td>
<td>—</td>
</tr>
</tbody>
</table>

* Shown are results of the analyses of prespecified safety events at any time after randomization. The numbers of patients who permanently discontinued a study drug were as follows: for hypotension, 36 (0.9%) in the LCZ696 group and 29 (0.7%) in the enalapril group (P=0.38); for renal impairment, 29 (0.7%) and 59 (1.4%), respectively (P=0.002); and for hyperkalemia, 11 (0.3%) and 15 (0.4%), respectively (P=0.56).

† Angioedema was adjudicated in a blinded fashion by an expert committee.
Caution re: “Irrational Exuberance”

-A. Greenspan

- **Novartis AG (ADR)**
- NYSE: NVS - Sep 10 10:06 AM ET
- 93.610.22 (0.23%)
- 1 day 5 day 1 month 3 month 1 year 5 year max

![Graph showing stock performance](image)

5 YEAR CHANGE 96.83%
Caution re: “Irrational Exuberance”

-A. Greenspan

- Apples and Oranges
- Plaques and Tangles
- Samuel Clemens
The trail doesn’t end here...
...So how do we get there?

- Neurohumoral modification therapy
- Electrical remodeling CRT-P/D (Companion MADIT-CRT)
- Structural remodeling TAVR MITRA Parachute
- Advance heart failure therapies LVAD OHT
- Regenerative therapies (REPAIR- MI C-CURE)
- Unraveling HF $p$ EF the “Gordian Knot”
TAVR

A catheter is used to thread a balloon device, with the new valve attached, to the diseased valve.

The interventional cardiologist or surgeon places the artificial valve in the diseased valve and inflates the balloon.

Once in place, the replacement valve starts to work as a normal valve would.
MITRA
Parachute
...So how do we get there?

• Neurohumoral modification therapy
• Electrical remodeling CRT-P/D (Companion MADIT-CRT)
• Structural remodeling TAVR MITRA Parachute
• Advance heart failure therapies LVAD OHT
• Regenerative therapies (REPAIR- MI C-CURE)
• Unraveling HF $p$ EF the “Gordian Knot”
Thank you for your attention
...So how do we get there?

{ Sudden death prevention and remodeling }

- AVID MADIT SCD-HeFT trials
  - Established the role of device Rx over Drug for secondary and primary sudden death prevention in ischemic and non-ischemic LVSD
...So how do we get there?
{ Sudden death prevention and remodeling }

• AVID MADIT SCD-HeFT trials
  – Established the role of device Rx over Drug for secondary and primary sudden death prevention in ischemic and non-ischemic LVSD

• CARE-HF COMPANION MIRACLE and MADIT-CRT (Class II-IV EF≤35% QRSd 120-140 LBBB)
  – establish the role of resynchronization in reducing mortality symptoms and hospitalization
Kaplan–Meier Estimates of the Time to the Primary End Point of Death from or Hospitalization for Any Cause (Panel A), the Time to the Secondary End Point of Death from Any Cause (Panel B), the Time to Death from or Hospitalization for Cardiovascular Causes (Panel C), and the Time to Death from or Hospitalization for Heart Failure (Panel D).
...So how do we get there?
{ Arrhythmia Management }

• Atrial Fibrillation
  – 5% (Class I) 40% (Class IV)
  – No clear benefit to Rhythm vs Rate Control
  – Beta-blockers are preferred for rate control
  – PVI may improve LV EF and HFQOL scores
  – Individualized anticoagulation strategy for cardioembolic protection
...So how do we get there?
{ Sudden death prevention and remodeling }

• **AVID MADIT SCD-HeFT** trials
  – Established the role of device Rx over Drug for secondary and primary sudden death prevention in ischemic and non-ischemic LVSD

• **CARE-HF COMPANION MIRACLE** and **MADIT-CRT** (Class II-IV EF≤35% QRSd 120-140 LBBB)
  – establish the role of resynchronization in reducing mortality symptoms and hospitalization

• **CERTIFY**
  – Mortality benefit of CRT-D/ AVNA over CRT-D/ rate control in AF
Device Rx Guidelines

- **Class I**

- ICD for primary prevention in Non-ischemic or Ischemic (>40d p MI) EF≤35% NYHA II-III on GDMT w expected survival> 1 year

- ICD for primary prevention EF≤ 30% > 40d p MI NYHA I on GDMT with survival>1 year

- CRT-D for EF≤35% NSR LBBB (>150ms) NYHA II, III, or ambulatory IV on GDMT
Device Rx Guidelines

• **Class IIa**
  • CRT “can be useful” EF<35% NSR non-LBBB QRSd>150ms NYHA III-IV ambulatory on GDMT
  • CRT “can be useful” EF<35% NSR LBBB QRSd 120-149ms NYHA II, III, IV ambulatory on GDMT
  • CRT “can be useful” AF EF<35% on GDMT if pacing is needed d/t AVNÅ or Med Rx
  • CRT “can be useful” EF<35% on GDMT undergoing new or replacement device if anticipated need for pacing is >40%
Device Rx Guidelines

- **Class IIb**
  - Usefulness is uncertain in pts with high risk of nonsudden death: frequent hospitalization, frailty, comorbidities, systemic malignancy, or renal dysfunction
  - CRT “may be considered” EF<35% NSR Non-LBBB QRSd 120-149ms NYHA class III-IV ambulatory on GDMT
  - CRT “may be considered” EF<35% NSR Non-LBBB QRSd >150 ms NYHA class II on GDMT
  - CRT “may be considered” ischemic EF<30% NSR Non-LBBB QRSd >150 ms NYHA class I on GDMT
Device Rx Guidelines

- Class III
- CRT is not recommended NYHA I-II non-LBBB QRSd<150ms
- CRT is not indicated for patients whose comorbidities limit survival with good functional capacity to less than 1 year
...So how do we get there?
Treatment of Structural and Ischemic disease

- Guideline Recommendations:
  - CABG or PCI for HF on GDMT w LMCA/ LM equivalent (class I)
  - CABG for survival in EF 35-50% w 3VD or prox LAD and viable myocardium (class IIa)
  - CABG or GDMT for M&M in EF<35% and significant CAD (class IIa)
...So how do we get there?
Treatment of Structural and Ischemic disease

• Guideline Recommendations:
  – AVR for Critical AS and OR Mortality<10% (class IIa)
  – TAVR for Critical AS who are inoperable (class IIa)
  – CABG for survival in EF<35% w operable anatomy whether or not viability is present (class IIb)
  – MVR or transcatheter repair for functional MR in HF on GDMT is of uncertain benefit (class IIb)
  – Surgical aneurysmectomy for intractable HF and ventricular arrhythmias is of uncertain benefit (class IIb)
...So how do we get there?
Advanced Heart Failure Therapies (Stage D)
Defined as the following (on GDMT, CRT as indicated)

- NYHA III-IV
- Recurrent Congestive or Low Output HF at rest
- One of: EF<30%  Stage III-IV diastolic dysfunction
  PCWP> 16 RAP>12  Elevated BNP/ NT-BNP
- One of: 6 min walk <300m  Inability to exercise
  VO$_2$<14
- $\geq$ 1 HF adm in 6 mo
...So how do we get there?

Advanced Heart Failure Therapies (Stage D)

• Short term Ionotrope support in cardiogenic shock (class I) or bridge to MCS or OHT (class IIa)
• MCS bridge to Decision Recovery or Transplant or Destination therapy in selected patients (class IIa)
• OHT evaluation indicated for stage D on GDMT device and surgical management (class I)
...So how do we get there?

Adjuvant care

- **CPAP**
  - Improves EF and functional capacity
- **Omega-3**
  - Adjuvant Rx in Class II-IV HFrEF/HFpEF for mortality reduction and decreased hospitalization (class IIa)
- **Depression (63% opts)**
  - Lower QOL Increased Utilization Poorer Outcome. Effective intervention strategy is unknown
- **Anemia**
  - Mixed results with erythropoietin analogs or iron infusion. No formal recommendation.
- **Palliative care**
  - Long term ionotropes (the former paradigm!)
...So how do we get there?

Regenerative Therapies

- Activation of endogenous or introduction of exogenous progenitor cells have been shown to decrease infarct size and improve EF and functional status (Repair AMI and C-CURE trials)

https://www.youtube.com/watch?v=j9XzN0-TQZc