New Treatments for Heart Failure

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Advanced Heart Failure & Transplant Fellowship
Assistant Professor of Clinical Medicine
The Ohio State University Wexner Medical Center

Disclosure

<table>
<thead>
<tr>
<th>Company</th>
<th>Nature of Affiliation</th>
<th>Unlabeled Product Usage</th>
</tr>
</thead>
<tbody>
<tr>
<td>St. Jude Medical</td>
<td>Consultant</td>
<td>None</td>
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</tbody>
</table>
Objectives

- Understand the mechanism of action and indications for sacubitril-valsartan
- Understand the mechanism of action and indications for ivabradine
- Understand how remote hemodynamic management of heart failure can be used to decrease heart failure hospitalizations

Heart Failure Definitions

- HFrEF (“systolic HF”): LVEF ≤ 40%
- HFpEF (“diastolic HF”): LVEF ≥ 40%
Heart Failure Treatment

• Medical therapy for HFrEF has been unchanged for years
  • ACE / ARB
  • B-blockers
  • Aldosterone antagonists
  • Hydralazine / Nitrates


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Heart Failure Treatment

<table>
<thead>
<tr>
<th>Medical Therapy for HFrEF: Magnitude of Benefit in RCTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>GDMT</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>ACEi or ARB</td>
</tr>
<tr>
<td>B-blocker</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
</tr>
<tr>
<td>Hydralazine / Nitrates</td>
</tr>
</tbody>
</table>

### Neprilysin

- **Enzyme that degrades several endogenous vasoactive compounds**
  - Natriuretic peptides
  - Bradykinin
  - Adrenomedullin
- **Inhibition of neprilysin increases levels of these substances**
  - Vasodilation
  - Natriuresis
  - Diuresis

### Neprilysin

- **Inhibiting neprilysin was a therapeutic target for several other compounds**
- **Combination neprilysin inhibitor and ACE inhibitor (Omapatrilat)**
  - Promising, but associated with severe angioedema
  - Angioedema d/t inhibition of 3 enzymes involved in bradykinin degradation
    - ACE
    - Neprilysin
    - Aminopeptidase P

Sacubitril-valsartan

- Combo of neprilysin inhibitor sacubitril and ARB valsartan
- Designed to minimize risk of angioedema by only blocking 1 bradykinin degrading enzyme


PARADIGM-HF

- 8442 patients
- LVEF ≤ 40%
- NYHA II-IV
- Randomized to sacubitril-valsartan (200 mg – equivalent to valsartan 160 mg BID) or enalapril 10 mg BID
- Primary outcome was composite CV death or first HF hospitalization
- Stopped early (median follow up 27 months) because of benefit seen in interim analysis

McMurray J, et al. NEJM 2014
PARADIGM-HF: Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>LCZ696 (n=4187)</th>
<th>Enalapril (n=4212)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63.8 ± 11.5</td>
<td>63.8 ± 11.3</td>
</tr>
<tr>
<td>Women (%)</td>
<td>21.0%</td>
<td>22.6%</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy (%)</td>
<td>59.9%</td>
<td>60.1%</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>29.6 ± 6.1</td>
<td>29.4 ± 6.3</td>
</tr>
<tr>
<td>NYHA functional class II / III (%)</td>
<td>71.6% / 23.1%</td>
<td>69.4% / 24.9%</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>N-terminal pro-BNP (pg/ml)</td>
<td>1631 (885-3154)</td>
<td>1594 (886-3305)</td>
</tr>
<tr>
<td>B-type natriuretic peptide (pg/ml)</td>
<td>255 (155-474)</td>
<td>251 (153-465)</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>35%</td>
<td>35%</td>
</tr>
<tr>
<td>Digitalis</td>
<td>29.3%</td>
<td>31.2%</td>
</tr>
<tr>
<td>Beta-adrenergic blockers</td>
<td>93.1%</td>
<td>92.9%</td>
</tr>
<tr>
<td>Mineralocorticoid antagonists</td>
<td>54.2%</td>
<td>57.0%</td>
</tr>
<tr>
<td>ICD and/or CRT</td>
<td>16.5%</td>
<td>16.3%</td>
</tr>
</tbody>
</table>

PARADIGM-HF: Results

- Sacubitril-valsartan reduced primary endpoint by 20%
  - NNT = 21
- Secondary endpoints
  - 20% reduction in CV death
  - 21% reduction in HF hospitalization
  - 16% reduction in all cause mortality
**Sacubitril-Valsartan**

- Approved by the FDA July 7, 2015
- “Entresto”
- NYHA Class II-IV
- EF ≤ 40%
- Used in place of ACE or ARB

**Sacubitril-Valsartan: Contraindications**

- Patients with history of angioedema due to ACE or ARB
- Pregnancy
- Do not use concurrently with ACE - hold for 36 hours after switching from ACE
- Avoid using with another ARB (i.e. avoid dual ARB therapy)
Ivabradine

• Selective inhibitor of sinoatrial pacemaker modulating “f-current” (If)
• Slows the sinus heart rate
• Mechanism of ivabradine in HFrEF likely due to heart rate reduction


SHIFT Trial

• 6558 patients
• LVEF ≤ 35%
• Sinus rhythm and resting HR ≥ 70 bpm
• Randomized to ivabradine or placebo
• Primary endpoint: composite CV death or HF hospitalization
• Median follow-up 23 months

### SHIFT Trial: Baseline Characteristic

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Ivabradine N=2052</th>
<th>Placebo N=2098</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Male, %</td>
<td>77</td>
<td>77</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>Mean HF duration, years</td>
<td>3.4</td>
<td>3.4</td>
</tr>
<tr>
<td>HF, ischemic cause, %</td>
<td>66</td>
<td>65</td>
</tr>
<tr>
<td>NYHA Class III, %</td>
<td>50</td>
<td>51</td>
</tr>
<tr>
<td>NYHA Class IV, %</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Mean LVEF, %</td>
<td>28.7</td>
<td>28.5</td>
</tr>
<tr>
<td>Mean HR, bpm</td>
<td>84.3</td>
<td>84.6</td>
</tr>
</tbody>
</table>

### SHIFT Trial: Baseline Characteristics

<table>
<thead>
<tr>
<th>GDMT</th>
<th>Ivabradine N=2052</th>
<th>Placebo N=2098</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-blocker, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least ½ target dose</td>
<td>55</td>
<td>56</td>
</tr>
<tr>
<td>At target dose</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td>ACEi / ARB, %</td>
<td>77</td>
<td>77</td>
</tr>
<tr>
<td>Diuretics, %</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>Aldosterone antagonists, %</td>
<td>3.4</td>
<td>3.4</td>
</tr>
</tbody>
</table>
SHIFT Trial: Results

• 24% reduction in primary end-point in ivabradine group

• Results largely d/t ↓ HF hospitalization (HR 0.74, 95% CI 0.66-0.83) and ↓ HF death (HR 0.74, 95% CI 0.58-0.94)

<table>
<thead>
<tr>
<th>SHIFT Trial: Results</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;65 years (n=4321)</td>
<td>407 (20.6%) 527 (25.6%) 0.74 (0.67-0.82) p&lt;0.001</td>
</tr>
<tr>
<td>≥65 years (n=2447)</td>
<td>388 (30.4%) 419 (33.9%)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male (n=4279)</td>
<td>634 (25.9%) 725 (32.9%) 0.74 (0.70-0.79) p&lt;0.001</td>
</tr>
<tr>
<td>Female (n=520)</td>
<td>305 (21.7%) 232 (18.4%) 0.74 (0.60-0.90) p=0.150</td>
</tr>
<tr>
<td><strong>β-blockers</strong></td>
<td></td>
</tr>
<tr>
<td>No β-blocker at randomisation (n=4885)</td>
<td>313 (29.4%) 374 (30.3%) 0.68 (0.62-0.76) p&lt;0.001</td>
</tr>
<tr>
<td>β-blocker at randomisation (n=552)</td>
<td>861 (23.4%) 180 (27.5%) 0.45 (0.30-0.64) p=0.101</td>
</tr>
<tr>
<td><strong>Cause of heart failure</strong></td>
<td></td>
</tr>
<tr>
<td>Non-ischaemic (n=2082)</td>
<td>218 (21.3%) 296 (27.9%)</td>
</tr>
<tr>
<td>Ischaemic (n=2483)</td>
<td>575 (26.4%) 643 (26.9%)</td>
</tr>
<tr>
<td><strong>NYHA class</strong></td>
<td></td>
</tr>
<tr>
<td>NYHA class II (n=3169)</td>
<td>301 (19.9%) 358 (22.5%)</td>
</tr>
<tr>
<td>NYHA class III/IV (n=3334)</td>
<td>493 (29.9%) 516 (34.5%)</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
</tr>
<tr>
<td>No history of diabetes (n=4336)</td>
<td>525 (23.7%) 613 (27.1%)</td>
</tr>
<tr>
<td>History of diabetes (n=479)</td>
<td>268 (27.4%) 234 (23.4%)</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
</tr>
<tr>
<td>No history of hypertension (n=4293)</td>
<td>274 (25.4%) 380 (29.7%)</td>
</tr>
<tr>
<td>History of hypertension (n=461)</td>
<td>510 (24.9%) 820 (38.2%)</td>
</tr>
<tr>
<td><strong>Baseline heart rate</strong></td>
<td></td>
</tr>
<tr>
<td>57 bpm (n=2164)</td>
<td>335 (24.2%) 355 (26.8%) 0.53 (0.40-0.71) p=0.003</td>
</tr>
<tr>
<td>57 bpm (n=3387)</td>
<td>454 (27.4%) 551 (34.2%) 0.75 (0.62-0.91) p&lt;0.001</td>
</tr>
</tbody>
</table>

• Significant benefit if resting HR ≥ 77 bpm, but not with lower HR
• Highlights importance of HR control in HF
Ivabradine

- Approved by the FDA on April 15, 2015
- “Corlanor”
- Stable HF with LVEF ≤ 35%
- Sinus rhythm with resting HR ≥ 70 bpm
- Either on max tolerated dose of β-blocker or have contraindication to β-blockers
- Not a full or partial substitute for β-blockade

Ivabradine: Contraindications

- Acute decompensated heart failure
- Hypotension (BP < 90/50)
- Sick sinus syndrome, sinoatrial block, or 3rd degree AV block
- Patients who are pacemaker dependent
- Severe hepatic impairment
- In combo with strong CYP34A inhibitors
Remote Hemodynamic Monitoring

<table>
<thead>
<tr>
<th>Pulmonary Artery Pressure Sensor</th>
<th>Patient Electronics System</th>
<th>CardioMEMS™ HF System Website</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Pulmonary Artery Pressure Sensor" /></td>
<td><img src="image2.png" alt="Patient Electronics System" /></td>
<td><img src="image3.png" alt="CardioMEMS™ HF System Website" /></td>
</tr>
</tbody>
</table>

CardioMEMS™ HF System

The pulmonary artery pressure sensor is implanted via a right heart catheterization procedure via femoral vein approach.

Target location for pulmonary artery pressure sensor

[Heart diagram](image4.png)
Patient Management Database

Trend Data
- Easy-to-read
- Physician alerts
- Home transmission
- Secure, encrypted web-based access

Discrete Data
Reading
Systolic: 24
Mean: 19
Diastolic: 16
Heart Rate: 81

CHAMPION: CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III HF Patients

Patients with NYHA III HF for at least 3 months, irrespective of LVEF and a HF hospitalization within past 12 months.

550 Pts with CardioMEMS™ HF System Implants
All Pts Take Daily readings

<table>
<thead>
<tr>
<th>Treatment</th>
<th>270 Pts Management Based on PA Pressure +Traditional Info</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Endpoint: Rate of HF Hospitalization</td>
<td></td>
</tr>
<tr>
<td>26 (9.6%) Exited &lt; 6 Months</td>
<td></td>
</tr>
<tr>
<td>15 (5.6%) Death</td>
<td></td>
</tr>
<tr>
<td>11 (4.0%) Other</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Control</th>
<th>280 Pts Management Based on Traditional Info</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary Endpoints:</td>
<td></td>
</tr>
<tr>
<td>- Change in PA Pressure at 6 months</td>
<td></td>
</tr>
<tr>
<td>- No. of patients admitted to hospital for HF</td>
<td></td>
</tr>
<tr>
<td>- Days alive outside of hospital</td>
<td></td>
</tr>
<tr>
<td>- QOL</td>
<td></td>
</tr>
<tr>
<td>26 (9.6%) Exited &lt; 6 Months</td>
<td></td>
</tr>
<tr>
<td>20 (7.1%) Death</td>
<td></td>
</tr>
<tr>
<td>6 (2.2%) Other</td>
<td></td>
</tr>
</tbody>
</table>

CHAMPION Clinical Trial: Managing to Target PA Pressures

550 Pts with CardioMEMS™ HF System Implants
All Pts Take Daily readings

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>270 Pts</td>
<td>280 Pts</td>
</tr>
<tr>
<td>Management Based on PA Pressure + Traditional Info</td>
<td>Management Based on Traditional Info</td>
</tr>
</tbody>
</table>

PA pressures were managed to target goal pressures by physicians with appropriate titration of HF medications.

Target Goal PA Pressures:
- PA Pressure Systolic 15 – 35 mmHg
- PA Pressure diastolic 8 – 20 mmHg
- PA Pressure mean 10 – 25 mmHg


CHAMPION Clinical Trial: PA Pressure-guided Therapy Reduces HF Hospitalizations

Patients managed with PA pressure data had significantly fewer HF hospitalizations as compared to the control group.


NNT = 4
HFpEF (diastolic HF) represents ~50% of all HF patients

- PAP-guided therapy significantly reduced hospitalizations in HFpEF patients in the treatment group by 46% at 6 months (p<0.0001) and by 50% at 18 months (p<0.0001)
- NNT = 2

Adamson PB, et al.. Circ Heart Fail. 2014.
## All Secondary Efficacy Endpoints Met

<table>
<thead>
<tr>
<th>Change from Baseline in Mean Pulmonary Artery Pressure at 6 Months Mean AUC</th>
<th>Treatment (n=270)</th>
<th>Control (n=280)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-156</td>
<td>33</td>
<td>0.008</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subjects Hospitalized for Heart Failure at 6 Months # (%)</th>
<th>Treatment (n=270)</th>
<th>Control (n=280)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>54 (20)</td>
<td>80 (29)</td>
<td>0.022</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Days Alive Outside Hospital at 6 Months Mean</th>
<th>Treatment (n=270)</th>
<th>Control (n=280)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>174.4</td>
<td>172.1</td>
<td>0.022</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Minnesota Living with Heart Failure Questionnaire at 6 Months Mean</th>
<th>Treatment (n=270)</th>
<th>Control (n=280)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>45</td>
<td>51</td>
<td>0.024</td>
</tr>
</tbody>
</table>


## CardioMEMS

- Approved by the FDA on May 28, 2014
- NYHA Class III patients
- HFrEF or HFpEF
- HF hospitalization within the past year
# CardioMEMS: Contraindications

- Active infection
- Recurrent PE or DVT
- Unable to tolerate right heart catheterization
- GFR < 25 ml/min
- Hypersensitivity or allergy to ASA and/or clopidogrel
- CRT within the past 3 months
- Chest circumference > 165 cm

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## What is New in Device Therapy for Heart Failure

Rami Kahwash, MD  
Assistant Professor of Internal Medicine  
Heart Failure and Cardiac Transplant Program  
Division of Cardiovascular Medicine  
The Ohio State University Wexner Medical Center
Learning Objectives

- Mode of death in heart failure and the impact of Sudden Cardiac Death (SCD)
- Implantable Cardioverter Defibrillator (ICDs) in primary prevention of SCD
- New defibrillation strategies (wearable ICD and subcutaneous ICD)
- Update in the indication of cardiac resynchronization therapy

Epidemiology of Symptomatic Heart Failure in the U.S.

- Major public health problem
- Final manifestation of many cardiac diseases
- \( \approx 5 \) million Americans with heart failure (increasing)
- 500,000 new cases diagnosed each year
- Most frequent cause of hospitalization in patients older than 65 years
- Causes or contributes to 250,000 deaths/year
- 1-Year mortality rate is about 10-15%
- 5-Year mortality rate approaches 50%
Mode of Death in Heart Failure

MERIT-HF Lancet 1999

NYHA Class 2

- CHF: 12%
- Other: 24%
- Sudden death: 64%

NYHA Class 3

- CHF: 26%
- Other: 15%
- Sudden death: 59%

NYHA Class 4

- Sudden death: 33%
- Other: 11%
- CHF: 56%

Beta Blockers’ Effects on total Mortality and Sudden Death in Patients with HF

US Carvedilol (n = 1014 patients)

- Total: 3.2% Carvedilol, 1.7% Placebo
- Sudden: 7.8% Carvedilol, 3.8% Placebo

CIBIS-2 (n = 2647 patients)

- Total: 11.8% Carvedilol, 3.6% Placebo
- Sudden: 17.3% Carvedilol, 6.3% Placebo

MERIT-HF (n = 3991 patients)

- Total: 7.2% Carvedilol, 3.9% Placebo
- Sudden: 10.8% Carvedilol, 6.6% Placebo

Heart 2001;85:97–103
### Incidence of SCD in Specific Populations and Annual SCD Numbers

<table>
<thead>
<tr>
<th>GROUP</th>
<th>Incidence of Sudden Death (% of group)</th>
<th>No. of Sudden Deaths Per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with high coronary-risk profile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with previous coronary event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with ejection fraction &lt; 35%, congestive heart failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with previous out-of-hospital cardiac arrest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with previous MI, low EF, and VT</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


### SCD Primary Prevention Trials (ICD Vs. Conventional Therapy)

- MADIT
- MADIT II
- SCD-HeFT
MADIT Survival Results

<table>
<thead>
<tr>
<th>Years</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defibrillator</td>
<td>101</td>
<td>80</td>
<td>53</td>
<td>31</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>Conventional Therapy</td>
<td>101</td>
<td>80</td>
<td>53</td>
<td>31</td>
<td>17</td>
<td>3</td>
</tr>
</tbody>
</table>

Probability of Survival %

Conventional Therapy

Defibrillator

RR = 0.46

p = 0.009

MADIT-II

Objective:

• Evaluate the effectiveness of ICD therapy (n = 742) compared to conventional therapy (n = 490) in high-risk post-MI patients

• Post-MI ≥ 4 weeks, and

• LVEF < 30%


MADIT-II Survival Results

Reduced overall mortality by 31% (p = 0.007)

Probability of Survival

Patients at Risk

<table>
<thead>
<tr>
<th>Years</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defibrillator</td>
<td>742</td>
<td>502 (0.91)</td>
<td>274 (0.94)</td>
<td>110 (0.78)</td>
<td>9</td>
</tr>
<tr>
<td>Conventional</td>
<td>490</td>
<td>329 (0.90)</td>
<td>170 (0.78)</td>
<td>65 (0.69)</td>
<td>3</td>
</tr>
</tbody>
</table>

SCD-HeFT Sudden Cardiac Death in Heart Failure Trial

- Determine if amiodarone or ICD will decrease the risk of death from any cause in patients with mild-to-moderate heart failure (Class II and III).
- Maximally treated CHF for ≥ 3 months with a LVEF of < .35

<table>
<thead>
<tr>
<th>Months of Follow-Up</th>
<th>Mortality Rate</th>
<th>Amiodarone vs. Placebo</th>
<th>ICD vs. Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.0</td>
<td>1.06 (0.86 - 1.30)</td>
<td>0.77 (0.62 - 0.96)</td>
</tr>
<tr>
<td>12</td>
<td>0.0</td>
<td>0.90 (0.75 - 1.08)</td>
<td>0.65 (0.50 - 0.84)</td>
</tr>
<tr>
<td>24</td>
<td>0.0</td>
<td>0.78 (0.63 - 0.96)</td>
<td>0.56 (0.41 - 0.76)</td>
</tr>
<tr>
<td>36</td>
<td>0.0</td>
<td>0.66 (0.51 - 0.86)</td>
<td>0.47 (0.32 - 0.69)</td>
</tr>
<tr>
<td>48</td>
<td>0.0</td>
<td>0.55 (0.40 - 0.75)</td>
<td>0.38 (0.24 - 0.59)</td>
</tr>
<tr>
<td>60</td>
<td>0.0</td>
<td>0.44 (0.30 - 0.64)</td>
<td>0.30 (0.18 - 0.51)</td>
</tr>
</tbody>
</table>

Hazard Ratio (97.5% CI) P-Value
- Amiodarone vs. Placebo: 1.06 (0.86 - 1.30) 0.53
- ICD vs. Placebo: 0.77 (0.62 - 0.96) 0.007

SCD-HeFT: Primary Conclusions

- In class II or III CHF patients with EF < 35% on good background drug therapy, the mortality rate for placebo-controlled patients is 7.2% per year over 5 years
- Simple, single lead, shock-only ICDs decrease mortality by 23%
- Amiodarone, when used as a primary preventative agent, does not improve survival

Who should get an ICD?

- All secondary prevention indications, e.g. sustained VT, cardiac arrest, syncope with induced VT, etc. (AVID, CASH, CIDS)
- CAD, Prior MI, LVEF <0.35, inducible VT (MADIT I)
- CAD, Prior MI, LVEF <0.30 (MADIT II)
- Ischemic and nonischemic dilated cardiomyopathy, NYHA class II/III CHF, LVEF < 35%. (SCD-HeFT)
Case 1

- 75 year old man with HTN, DM II and HLP admitted to the CCU with NSTEMI. Coronary angiography revealed 3 vessel CAD. He underwent successful 3V CABG. He was established on BB, ACE I, statin and ASA. LVEF at time of discharge was 25%. His functional class was c/w NYHA FC III. ECG: NSR, QRS: 100 ms, nonspecific ST changes

- ICD should be implanted before discharge
  A. True
  B. False

Primary Prevention ICDs with CABG Surgery
CABG-Patch

- CAD
- CABG
- LVEF < 0.35
- ++ SAECG
- ICD at the time of CABG

Prophylactic Use of ICDs After Acute Myocardial Infarction
DINAMIT
6-40 day post MI, LVEF< 35 %, evidence of autonomic dys

Death: Annual risks (6.9%) in the control group vs 62 (7.5%) in ICD patients (P = .66)

Do NOT implant an ICD if:

- CABG or PCI within the past 3 months (CABG-Patch).
- Acute MI within the past 40 days (DINAMIT).
- Concomitant disease with less than 1 year likelihood of survival.
Case 2

• 22 year old female college student presented to the ED with history of 1 week of progressive dyspnea on exertion. She reported flu like illness 3 weeks ago. Exam c/w sinus tachycardia 110, elevated JVP, + S3 gallop and rails in the lower lung fields. CXR c/w pulmonary edema. Echo showed severely decreased LVEF of 20% with global hypokinesis. ECG: sinus tachycardia, QRS: 88 ms, diffuse nonspecific ST changes. Cardiac biopsy reveals lymphocytic myocarditis. Symptoms improved to NYHA FC II with conventional heart failure therapy and she is ready for discharge.

• ICD is indicated before discharge
   A. True
   B. False

Wearable ICD System
**Wearable Defibrillator Indications**

- Post MI with low ejection fraction < 35 %
  - < 40 days after MI
  - < 90 days after PCI or CABG
- New onset nonischemic cardiomyopathy
  - < 3 months up to 9 months
- Pretransplant in NYHA FC IV
- ICD extraction due to infection, requires time for treatment with IV antibiotics.

**Case 3**

- 45 year old female patient with long standing history of type 1 DM, and Hx of ESRD s/p kidney-pancreas transplant on immunosuppressive therapy. She was also diagnosed with cardiomyopathy 3 years ago. Coronary angiography reveals small vessel disease not suitable for intervention. Despite 6 months of guideline directed medical therapy for heart failure, her LVEF remains 25%. She belongs to NYHA FC II. Her ECG shows NSR, normal intervals, QRS 90 ms, nonspecific Tw abnormalities.

- Intravenous ICD is favored over S-ICD.
  A. True
  B. False
Subcutaneous ICD

- 80 joules (delivered)
- 69cc, 145 grams
- Active can
- 5 year longevity
- Post-shock pacing
- Single lead connection
- Full featured episode storage
- No Brady pacing or ATP

S-ICD Sensing Features

- Three possible sensing vectors
- Optimal sense vector automatically selected by the device
# Subcutaneous ICD VS. Transvenous ICD

<table>
<thead>
<tr>
<th>Factors Favor S-ICD</th>
<th>Factors Favor TV- ICD</th>
</tr>
</thead>
</table>
| ➢ Young and active (less lead failure)  
➢ CHD that limits lead placement, valve surgery  
➢ Indwelling catheters  
➢ Immunocompromised  
➢ Inherited channelopathies (low VT risks).                                                                                                          | ➢ Recurrent monomorphic VT (role of ATP)  
➢ Bradycardia requiring pacing  
➢ Indication for CRT  
➢ High risk for VT (e.g. sarcoidosis, ARVD).  
➢ Preference for remote monitoring                                                                                                                  |

## Cardiac Resynchronization Therapy (CRT)
CRT Class I Indication

- There is strong evidence that CRT reduces mortality and hospitalization and improves cardiac function and structure in symptomatic chronic HF patients (Class III, IV) with optimal medical treatment, severely depressed LVEF (i.e. ≤35%) and complete LBBB (QRS> 120 ms).

CRT in NYHA Class I-II Heart Failure
MADIT-CRT:

n=1820
Ischemic: NYHA Class I & II
Non-ischemic: NYHA Class II
LVEF ≤30%
QRS ≥130 ms
ICD vs. CRT-D (2:3 randomization)

Primary endpoint of all-cause mortality or nonfatal HF events:
17.5% in CRT-D vs. 25.3% in ICD, HR 0.66 [0.52 to 0.84], p=0.001

CRT in NYHA Class I-II Heart Failure

MADIT-CRT:

41% reduction
HR 0.59 [0.47-0.74]

Magnitude of Benefit from CRT

2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy, Brignole et al. Europace (2013) 15, 1070–1118
## 2012 Focused Update Recommendations

### Class I

CRT is indicated for patients who have LVEF less than or equal to 35%, sinus rhythm, LBBB with a QRS duration greater than or equal to 150 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT. *(Level of Evidence: A for NYHA class III/IV; Level of Evidence: B for NYHA class II)*