BLOCK HF Study

Biventricular versus Right Ventricular Pacing in Patients with Left Ventricular Dysfunction and Atrioventricular Block – Preliminary Results

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Relationship of Ventricular Pacing to New/Worsened Heart Failure Outcome

Steinberg et al, JCE 2005
Relationship of Ventricular Pacing to ICD Therapy for VT/VF

Steinberg et al, JCE 2005
Summary of Deleterious Effects of RV Apical Pacing

- Intraventricular conduction delay
- LV mechanical and electrical dyssynchrony
- LV remodeling
- Abnormal myocardial histopathology
- LV systolic dysfunction
- Overt congestive heart failure
- Myocardial perfusion defects
- Mitral regurgitation
- Increased atrial fibrillation
- Left atrial dilation
- Promotion of ventricular arrhythmias
- Activation of sympathetic nervous system
No difference in:
- 6 min hall walk
- SF-36 QoL
- Heart failure hospitalizations

Yu et al, NEJM 2009
Study Purpose and Objectives

**Purpose:** Biventricular pacing is superior to RV apical pacing in patients with AV block and LVEF $\leq 50\%$ who require ventricular pacing

**Endpoints:**

**Primary:** Composite of:

- All-cause mortality,
- HF-related urgent care, defined as
  - HF hospitalization requiring IV therapy, or
  - Any unplanned visit requiring intravenous HF therapy, and
- Increase in left ventricular end systolic volume index (LVESVI) $\geq 15\%$

**Key Secondary:** All-cause mortality,

All-cause mortality/HF hospitalization,

HF hospitalization

BLOCK HF
**Study Design**

- **Implant (CRT-P/D)**
- **Establish OMT (30-60 days)**
- **Randomize 1:1**
  - **Control:** RV pacing
  - **Treatment:** BiV pacing
- **Double-Blind**
- **Follow-up Every 3 months**

**ELIGIBILITY CRITERIA**

- AV block necessitating pacing
- Left ventricular ejection fraction (LVEF) ≤ 50%
- NYHA functional class I, II or III
- Absence of a Class I indication for resynchronization therapy
- No previous pacemaker or implantable cardioverter defibrillator (ICD)
- Echocardiography performed at Randomization, 6, 12, 18 and 24 months

**OMT=** optimal medical therapy  
**CRT-P=** cardiac resynchronization therapy pacemaker  
**CRT-D=** CRT defibrillator
Study Flow Diagram

**Enrollment**
918 Assessed for eligibility

**Allocation**
691 Randomized 1:1

**Enrollment**
918 Assessed for eligibility

**Allocation**
691 Randomized 1:1

**Enrollment**
918 Assessed for eligibility

**Allocation**
691 Randomized 1:1

**349 Allocated to Biventricular Pacing**
- 346 Received allocated intervention
- 3 Did not receive allocated intervention

**342 Allocated to Right Ventricular Pacing**
- 342 Received allocated intervention

**Follow-up**
52 Exited/lost to follow-up
75 Deaths
13 Crossed over to Right Ventricular Pacing
- 3 Met primary endpoint prior to crossover

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**Analysis**
349 Analyzed
- 83 Censored for primary endpoint due to missing LVESVI data

**Analysis**
342 Analyzed
- 71 Censored for primary endpoint due to missing LVESVI data

227 Subjects not randomized:
- 95 Subjects for whom inclusion criteria not met (e.g., AV conduction testing criteria not met prior to implant)
- 14 Subject withdrawals prior to implant
- 51 Unsuccessful implants
- 67 Implanted subjects not randomized

**Follow-up**
52 Exited/lost to follow-up
75 Deaths
13 Crossed over to Right Ventricular Pacing
- 3 Met primary endpoint prior to crossover

**Follow-up**
50 Exited/lost to follow-up
90 Deaths
84 Crossed over to Biventricular Pacing
- 50 Met primary endpoint prior to crossover

**Analysis**
349 Analyzed
- 83 Censored for primary endpoint due to missing LVESVI data

**Analysis**
342 Analyzed
- 71 Censored for primary endpoint due to missing LVESVI data
### Baseline Demographics

<table>
<thead>
<tr>
<th></th>
<th>CRT-P (BiV N=243)</th>
<th>CRT-P (RV N=241)</th>
<th>CRT-D (BiV N=106)</th>
<th>CRT-D (RV N=101)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Male</td>
<td>75%</td>
<td>70%</td>
<td>82%</td>
<td>80%</td>
</tr>
<tr>
<td>Age, years</td>
<td>74 ± 10</td>
<td>74 ± 11</td>
<td>72 ± 9</td>
<td>71 ± 10</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>43 ± 7</td>
<td>43 ± 7</td>
<td>33 ± 8</td>
<td>33 ± 8</td>
</tr>
<tr>
<td>Heart Rate, beats/min</td>
<td>69 ± 23</td>
<td>69 ± 24</td>
<td>68 ± 17</td>
<td>69 ± 17</td>
</tr>
<tr>
<td>QRS Duration, ms</td>
<td>125 ± 33</td>
<td>125 ± 31</td>
<td>123 ± 30</td>
<td>119 ± 30</td>
</tr>
<tr>
<td>NYHA I</td>
<td>14%</td>
<td>20%</td>
<td>10%</td>
<td>16%</td>
</tr>
<tr>
<td>NYHA II</td>
<td>58%</td>
<td>52%</td>
<td>63%</td>
<td>57%</td>
</tr>
<tr>
<td>NYHA III</td>
<td>27%</td>
<td>28%</td>
<td>26%</td>
<td>27%</td>
</tr>
<tr>
<td>Left Bundle Branch Block</td>
<td>35%</td>
<td>31%</td>
<td>35%</td>
<td>27%</td>
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<tr>
<td>Ischemic Heart Disease</td>
<td>39%</td>
<td>38%</td>
<td>63%</td>
<td>58%</td>
</tr>
<tr>
<td>1\textsuperscript{st} Degree AV Block</td>
<td>17%</td>
<td>15%</td>
<td>27%</td>
<td>31%</td>
</tr>
<tr>
<td>2\textsuperscript{nd} Degree AV Block</td>
<td>33%</td>
<td>29%</td>
<td>33%</td>
<td>38%</td>
</tr>
<tr>
<td>3\textsuperscript{rd} Degree AV Block</td>
<td>49%</td>
<td>56%</td>
<td>40%</td>
<td>32%</td>
</tr>
<tr>
<td>ACE Inhibitor/ARB at Randomization</td>
<td>71%</td>
<td>74%</td>
<td>83%</td>
<td>88%</td>
</tr>
<tr>
<td>Beta Blocker at Randomization</td>
<td>75%</td>
<td>78%</td>
<td>92%</td>
<td>92%</td>
</tr>
<tr>
<td>Diuretics at Randomization</td>
<td>64%</td>
<td>66%</td>
<td>72%</td>
<td>70%</td>
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</table>
Primary Endpoint Results: Mortality/HF Urgent Care/LVESVI

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Estimated HR (95% CI)</th>
<th>Probability HR &lt; 1</th>
<th>Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Randomized Subjects</td>
<td>0.74 (0.60, 0.90)</td>
<td>0.9978</td>
<td>0.9775</td>
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<tr>
<td>CRT-P Only</td>
<td>0.73 (0.58, 0.91)</td>
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<tr>
<td>CRT-D Only</td>
<td>0.75 (0.57, 1.02)</td>
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<td></td>
</tr>
</tbody>
</table>
Clinical Components of Primary Endpoint: Mortality/HF Urgent Care Visits

- All Randomized Subjects: Estimated HR (95% CI) = 0.73 (0.57, 0.92), Probability HR < 1 = 0.997
- CRT-P Only: Estimated HR (95% CI) = 0.73 (0.56, 0.94)
- CRT-D Only: Estimated HR (95% CI) = 0.73 (0.53, 1.02)
Secondary Objective Results: HF Hospitalization and Mortality

<table>
<thead>
<tr>
<th>Cohort</th>
<th>HF Hospitalization</th>
<th>Mortality</th>
<th>Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimated HR (95% CI)</td>
<td>Probability HR &lt; 1</td>
<td>Estimated HR (95% CI)</td>
</tr>
<tr>
<td>All Randomized Subjects</td>
<td>0.70 (0.52, 0.93)</td>
<td>0.9922</td>
<td>0.83 (0.61, 1.14)</td>
</tr>
</tbody>
</table>

Event-Free Rate (%)

<table>
<thead>
<tr>
<th>Number of Months</th>
<th>BiV Arm</th>
<th>RV Arm</th>
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<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>12</td>
<td>90</td>
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<tr>
<td>24</td>
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<td>36</td>
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<td>48</td>
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<tr>
<td>60</td>
<td>50</td>
<td>50</td>
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<tr>
<td>72</td>
<td>40</td>
<td>40</td>
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</tbody>
</table>

Number at Risk

<table>
<thead>
<tr>
<th>Number of Months</th>
<th>BiV: 349</th>
<th>270</th>
<th>198</th>
<th>137</th>
<th>93</th>
<th>54</th>
<th>17</th>
<th>RV: 342</th>
<th>258</th>
<th>193</th>
</tr>
</thead>
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<tr>
<td>0</td>
<td>349</td>
<td>270</td>
<td>198</td>
<td>137</td>
<td>93</td>
<td>54</td>
<td>17</td>
<td>342</td>
<td>258</td>
<td>193</td>
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<tr>
<td>12</td>
<td>290</td>
<td>228</td>
<td>172</td>
<td>123</td>
<td>72</td>
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<td>24</td>
<td>222</td>
<td>168</td>
<td>111</td>
<td>72</td>
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<td>168</td>
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<td>152</td>
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**Strengths and Limitations**

**STRENGTHS:**
- Prospective, randomized, double-blind control design
- Largest, longest follow-up trial to date
- First to show difference in outcomes in AV block and LV systolic dysfunction patients with BiV vs. RV pacing

**LIMITATIONS:**
- Long enrollment duration
- Censoring due to missing LVESVI in primary objective
- Crossover imbalance between arms:
  - 24.6% crossed over from RV to BiV
  - 4.6% crossed over from BiV to RV
Conclusions

- In patients with AV block and LV systolic dysfunction (LVEF ≤ 50%), BiV pacing compared to RV pacing leads to a significant 26% reduction in the combined endpoint of mortality, heart-failure related urgent care, and increase in LVESVI.

- Furthermore, there is a 27% relative risk reduction in the composite endpoint of heart-failure urgent care and all-cause mortality.
Thank you!