The Left Ventricular-Based Cardiac Stimulation Post AV Nodal Ablation Evaluation Study

Rahul N. Doshi, MD, FACC
Sunrise Hospital and Medical Center
Las Vegas, NV
For the PAVE Study Group
Disclosures

The PAVE trial was sponsored by
St. Jude Medical
The PAVE Investigators

Rahul Doshi, MD - Las Vegas, NV
Emile Daoud, MD - Columbus, OH
Christopher Fellows, MD – Seattle, WA
Kyong Turk, MD – Lincoln, NE
Aurelio Duran, MD – Orlando, FL
Mohamed Hamdan, MD – Dallas, TX
David Delurgio, MD – Atlanta, GA
Ray Kawasaki, MD – Elmhurst, IL
Jay Franklin, MD – Dallas, TX
Stuart Winston, DO – Ann Arbor, MI
Luis Pires, MD – Detroit, MI
Jonathan Steinberg, MD – New York, NY
Ann Curtis, MD – Gainesville, FL
Jay Patterson, MD – Jacksonville, FL
Charles Hafajee, MD – Boston, MA
W. Ben Johnson, MD – Des Moines, IA
Steven Zukerman, MD – Neptune, NJ
Stephen Keim, MD – Lakeland, FL
Wesley Haisty, MD – Winston-Salem, NC
Andrew Kaplan, MD – Mesa, AZ
Larry Chintitz, MD – New York, NY
David Broudy, MD – Seattle, WA
Jeffrey Rottman, MD – Nashville, TN
J. Rod Gimbel, MD – Knoxville, TN
Allan Greenspan, MD – Newark, DE

Robert Rea, MD – Rochester, MN
Judith Mackall, MD – Cleveland, OH
G. Stephen Greer, MD – Little Rock, AR
Timothy Malinowski, MD – Greenville, SC
Gery Tomassoni, MD – Lexington, KY
Raymond Miller, MD – Newark, DE
Donald Chilson, MD – Spokane, WA
Seth Worley, MD – Lancaster, WA
Samir Saba, MD – Pittsburgh, PA
Mark Myers, MD – Pasadena, CA
Bruce Lerman, MD – New York, NY
Larry Price, MD – Temple, TX
Erick Burton, MD – Fort Myers, FL
Kreigh Moulton, MD – Springfield, IL
Leslie Saxon, MD – Los Angeles, CA
Westby Fisher, MD – Evanston, IL
Mark Kremers, MD – Charlotte, NC
Bendt Herweg, MD – Tampa, FL
Pramod Deshmukh, MD – Sayre, PA
Bernard Thibault, MD – Montreal, Quebec
Anthony Tang, MD – Ottawa, Ontario
David Newman, MD – Toronto, Ontario
Sajad Gulamhusein, MD – Edmonton, Alberta
Mark Burns, MD – Hamilton, Ontario
Background

• **Biventricular (BV) Pacing**
  – Provides correction of mechanical dysynchrony in patients with heart failure and intrinsic conduction system disease

• **Right Ventricular (RV) Pacing**
  – Alters the natural sequence of ventricular contraction
  – May be associated with poorer outcomes in patients with heart failure

• **Atrioventricular Nodal Ablation with Pacing**
  – Provides improved symptoms in patients with atrial fibrillation and difficult to control ventricular rates
  – Provides correction of tachycardia-induced cardiomyopathy
The PAVE Study

- Prospective, randomized study evaluating biventricular pacing after atrioventricular nodal ablation for patients with atrial fibrillation
- Regardless of left ventricular systolic function or NYHA Classification
- Devices:
  - BV patients implanted with SJM BV pacing system (Frontier Model 5508* and Aescula Left Heart Lead Model 1055K*)
  - RV patients implanted with legally marketed SJM single chamber devices

*Caution: For Investigational use only in the US
Inclusion/Exclusion Criteria

• Inclusion Criteria
  – Chronic AF for at least 1 month
  – Electively undergoing AVN ablation procedure and permanent pacemaker implant
  – NYHA class I, II, or III
  – Walk < 450 meters during 6 minute walk test
  – Stable CV medication regimen for 5 drug half lives prior to enrollment

• Exclusion Criteria
  – NYHA class IV
  – Walk > 450 meters during 6 minute walk test
  – Patients with an ICD, being considered for an ICD or considered for cardiac surgery
  – Prosthetic valve replacements
  – Severe Musculoskeletal disorders
Primary & Secondary Endpoints

• Primary Endpoint
  – Exercise capacity as measured by the distance walked during the 6 minute walk test

• Secondary Endpoints
  – Functional capacity as measured by peak VO₂ during cardiopulmonary exercise testing
  – Health related quality of life measured by score of SF-36
Study Overview

- Baseline
- Randomization 2:1
- Ablation and RV Pacing (SJM SR Device)
- Prior to Discharge
- Ablation and BV Pacing (Frontier Device)
- 4-Week Follow-up
- Every 6-months thereafter
- 6-Months Follow-up
- 3-Months Follow-up
- 6-Week Follow-up
- 4-Week Follow-up
- Base Rate Pacing
- High Rate Pacing
Attempted Implants $N = 252$

- Remaining Dataset $N = 102$
- Unsuccessful Implant $N = 21$
- $< 6 \text{ mo. Follow up} = 14$
- Death $N = 6$
- Invalid Test Data $N = 0$
- Pt./Family/MD Request for Withdrawal $N = 2$
- System Explant $N = 1$

- Remaining Dataset $N = 82$
- RV $N = 106$

- Attempted Implants $N = 146$

Analyzable Population
## Patient Demographics

<table>
<thead>
<tr>
<th>Demographic Variables</th>
<th>RV (N=106)</th>
<th>BV (N=146)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr.)</td>
<td>68.6 ± 9.8</td>
<td>69.9 ±10.4</td>
<td>0.31</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>67.9</td>
<td>62.3</td>
<td>0.42</td>
</tr>
<tr>
<td>NYHA Class I / II / III (%)</td>
<td>21 / 40 / 39</td>
<td>12 / 54 / 34</td>
<td>0.87</td>
</tr>
<tr>
<td>EF (%)</td>
<td>45.7 ± 15.4</td>
<td>46.5 ± 16.8</td>
<td>0.75</td>
</tr>
<tr>
<td>QRS duration (msec.)</td>
<td>100.0 ± 21.5</td>
<td>104.3 ± 27.7</td>
<td>0.24</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>52</td>
<td>63</td>
<td>0.10</td>
</tr>
<tr>
<td>CAD (%)</td>
<td>30</td>
<td>37</td>
<td>0.35</td>
</tr>
<tr>
<td>Valvular (%)</td>
<td>16</td>
<td>16</td>
<td>1.00</td>
</tr>
<tr>
<td>Non-Ischemic cardiomyopathy (%)</td>
<td>21</td>
<td>16</td>
<td>0.41</td>
</tr>
<tr>
<td>Receiving ACE inhibitors (%)</td>
<td>44.3</td>
<td>50.7</td>
<td>0.39</td>
</tr>
<tr>
<td>Receiving Beta blockers (%)</td>
<td>53.8</td>
<td>55.5</td>
<td>0.89</td>
</tr>
</tbody>
</table>

## Results: 6-Minute Walk Test

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>6 weeks</th>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Distance (m)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BV</td>
<td>263.27</td>
<td>333.38</td>
<td>350.97</td>
<td>345.64</td>
</tr>
<tr>
<td></td>
<td>± 114.62</td>
<td>± 113.46</td>
<td>± 107.93</td>
<td>± 118.08</td>
</tr>
<tr>
<td>RV</td>
<td>266.75</td>
<td>319.57</td>
<td>341.38</td>
<td>323.57</td>
</tr>
<tr>
<td></td>
<td>± 110.18</td>
<td>± 111.87</td>
<td>± 117.33</td>
<td>± 110.53</td>
</tr>
<tr>
<td></td>
<td>Improvement from Baseline (m)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BV</td>
<td>N/A</td>
<td>70.11</td>
<td>83.48</td>
<td>82.37</td>
</tr>
<tr>
<td></td>
<td></td>
<td>± 94.18</td>
<td>± 95.29</td>
<td>± 93.00</td>
</tr>
<tr>
<td>RV</td>
<td>N/A</td>
<td>52.82</td>
<td>72.88</td>
<td>56.82</td>
</tr>
<tr>
<td></td>
<td></td>
<td>± 94.87</td>
<td>± 101.65</td>
<td>± 88.92</td>
</tr>
</tbody>
</table>
Results: 6-Minute Walk Test

- **RV (n=75)**
  - Baseline: 17.29
  - 6 weeks: 10.60
  - 3 months: 10.60
  - 6 months: 25.55
  - *p* = 0.03

- **BV (n=91)**
  - Baseline: 25.55
  - 6 weeks: 25.55
  - 3 months: 25.55
  - 6 months: 25.55
Results: Improvement in Peak VO$_2$

- RV (n=20): $\Delta 1.02$ ml/kg/min ($p<0.01$)
- BV (n=51): $\Delta 0.09$ ml/kg/min ($p=0.43$)

Time Frame:
- 6 weeks
- 6 months
Results: Exercise Duration during CPET

Δ 41.6 seconds (p< 0.01)

Δ 19.8 seconds (p=0.19)

<table>
<thead>
<tr>
<th>Time Frame</th>
<th>RV (n=20)</th>
<th>BV (n=51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>430</td>
<td>449</td>
</tr>
<tr>
<td>6 months</td>
<td>450</td>
<td>469</td>
</tr>
</tbody>
</table>
Results: QOL via SF-36

Scale

VT
SF
RE
MH
MCS
PCS
PF
RP
BP
GH

Improvement
(Baseline to 6 months)

RV (n=81)
BV (n=97)

BV over RV p=0.03
BV over RV p=0.07
Left Ventricular Ejection Fraction

<table>
<thead>
<tr>
<th>Time Frame</th>
<th>LVEF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Implant</td>
<td>45.6</td>
</tr>
<tr>
<td>6 months</td>
<td>40.7</td>
</tr>
</tbody>
</table>

RV (n=67) BV (n=76)

p=0.03
Kaplan-Meier Curve

![Kaplan-Meier Curve Graph]

- Survival rates are plotted against time in days.
- The graph shows two survival curves, one for RV and another for BV.
- The p-value, which is a measure of statistical significance, is 0.21.

Survival data:
- BV: 111, 73, 36, 22, 3, 0
- RV: 88, 66, 48, 22, 2, 0

Time (days): 0, 200, 400, 600, 800, 1000, 1200
Conclusions

• In patients with chronic AF treated with AV nodal ablation, BV pacing produces a statistically significant improvement in functional capacity over RV pacing as measured by the 6-minute walk test, peak VO₂ and exercise duration.

• This improvement reflects a sustained benefit in the BV group as compared to a deterioration in the RV group.

• Therefore, the results of the PAVE study suggest that BV pacing should be the preferred mode of therapy in patients undergoing AV nodal ablation for control of chronic atrial fibrillation.
Thank You

The PAVE Study Group
Question and Answer Session

The Left Ventricular-Based Cardiac Stimulation Post AV Nodal Ablation Evaluation Study

Rahul N. Doshi, MD, FACC
Sunrise Hospital and Medical Center
Las Vegas, NV
For the PAVE Study Group