Response of Right Ventricular Size to Treatment with Cardiac Resynchronization Therapy and the Risk of Ventricular Tachyarrhythmias in MADIT-CRT

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Colin L. Doyle, BA,* Ilan Goldenberg, MD,* David T. Huang, MD,* Scott D. Solomon, MD,† Scott McNitt, MS,* Slava Polonsky, MS,* Alon Barsheshet, MD,* Mehmet Aktas, MD,* Christine Tompkins, MD,* Wojciech Zareba, MD, PhD,* Arthur J. Moss, MD*

*Cardiology Division, University of Rochester Medical Center, Rochester, New York
†Cardiovascular Division, Brigham and Women’s Hospital, Harvard Medical School, Boston, Massachusetts
Background

- Sudden cardiac death 1/3 or more of deaths in heart failure
  - Majority from ventricular tachycardia/fibrillation (Shiga and Kasanuki. 2007)


- Possibly due to remodeling: focus on left ventricle (LV) (Solomon, et al. 2010, Barsheshet, et al. 2011)

- Severe right ventricular (RV) dysfunction in low LVEF predicted ICD shocks or death (Aktas, et al. 2009)
Study Questions

• Relationship between RV size and VA

• Relationship between RV size and CRT response

• Risk reduction with RV remodeling
Methods

• MADIT-CRT (Moss, et al. 2005)
  • 1820 patients at 110 sites in North America and Europe over 4.5 years
  • Ischemic and non-ischemic cardiomyopathy
  • LVEF $\leq 30\%$
  • QRS $> 130$ msec
  • NYHA class I or II
  • 3:2 randomization for CRT-D or ICD

• Echocardiograms (according to ASE, Lang, et at. 2005)
  • Prior to device implantation ($n = 1809$)
  • At one year ($n = 626$ in ICD group; $n = 752$ in CRT-D group)
  • Paired studies in 1372 patients
• Group Categorization
  • RV size $\rightarrow$ RVEDA/BSA
  • Baseline RVEDA/BSA first quartile $< 13 \, \text{cm}^2/\text{m}^2$
  • RVEDA change at 1 year- % change
  • RV responders to CRT-D $> 1^{\text{st}}$ quartile change ($> 3\%$ reduction)
• Primary endpoints: $1^{\text{st}}$ VT/VF or death and $1^{\text{st}}$ VT/VF or death after 1 year
## Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>RVEDA/BSA &lt;13 cm²/m²</th>
<th>RVEDA/BSA ≥13 cm²/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>61.7±10.5</td>
<td>65.6±10.6</td>
</tr>
<tr>
<td>Female sex</td>
<td>14%</td>
<td>29%</td>
</tr>
<tr>
<td>LBBB</td>
<td>65%</td>
<td>72%</td>
</tr>
<tr>
<td>LVEF</td>
<td>30.0±3.4</td>
<td>28.8±3.4</td>
</tr>
<tr>
<td>Diabetes</td>
<td>38%</td>
<td>28%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>69%</td>
<td>61%</td>
</tr>
<tr>
<td>BMI</td>
<td>32.4±5.4</td>
<td>27.5±4.7</td>
</tr>
</tbody>
</table>

*All p-values < 0.005*
Cumulative probability of VA by baseline RVEDA/BSA in ICD-only patients

Unadjusted P=0.04

Patients at Risk
Q1 153
Q2-Q4 451

Follow-up Time
0.00  1.00  2.00  3.00

Cumulative Probability of VT/180/VF

Q1
Q2-Q4
Cumulative probability of VA or death by treatment in patients with greater RVEDA (Q2-4)
Cumulative probability of VA or death by treatment in patients with smaller RVEDA (Q1)
Multivariate analysis: CRT-D vs. ICD-only risk of VT/VF or death by baseline right ventricular size

<table>
<thead>
<tr>
<th>BASELINE RV SIZE (RVEDA/BSA)</th>
<th>HR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q2-Q4 (n=1121)</td>
<td>0.73</td>
<td>0.59-0.90</td>
<td>0.003</td>
</tr>
<tr>
<td>Q1 (n=374)</td>
<td>1.00</td>
<td>0.68-1.48</td>
<td>0.998</td>
</tr>
</tbody>
</table>

*All findings are adjusted for left ventricular end diastolic volume adjusted for body surface area, left ventricular ejection fraction, left bundle branch block, female sex, QRS, history of ventricular arrhythmias, and current smoking status*
Relationship between RV response to CRT-D and Outcome

Cumulative probability of ventricular tachyarrhythmias by RVEDA response to CRT-D and in ICD-only patients

<table>
<thead>
<tr>
<th>Patients at Risk</th>
<th>Follow-up Time After 1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-responders</td>
<td>124 (0.14) 71 (0.26) 21 (0.37)</td>
</tr>
<tr>
<td>Responders</td>
<td>404 (0.07) 226 (0.15) 66 (0.19)</td>
</tr>
<tr>
<td>ICD-only</td>
<td>397 (0.15) 243 (0.24) 110 (0.32)</td>
</tr>
</tbody>
</table>
Multivariate analysis: Risk of subsequent VA according to RV response

<table>
<thead>
<tr>
<th>Percent change in RVEDA after 1 year</th>
<th>HR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRT-D: &gt;1st quartile RVEDA response vs. ICD-only</td>
<td>0.55</td>
<td>0.41-0.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRT-D: ≤ 1st quartile RVEDA response vs. ICD-only</td>
<td>1.16</td>
<td>0.82-1.64</td>
<td>0.39</td>
</tr>
<tr>
<td>CRT-D: 2nd-4th quartile response vs. 1st quartile response*</td>
<td>0.59</td>
<td>0.38-0.91</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Findings are adjusted for baseline left ventricular end diastolic volume adjusted for body surface area, left ventricular ejection fraction, left bundle branch block, female sex, QRS, history of ventricular arrhythmias, and current smoking status

*Adjusted for percent change in left ventricular end systolic volume,
Conclusions

• Patients with larger right ventricles at baseline have greater risk of VA

• CRT-D therapy reduces risk of VT/VF or death in patients with enlarged right ventricles

• In patients who achieve RV remodeling from CRT-D therapy, subsequent risk for VT/VF or death is reduced

• Quantification of the RV may be useful in determining who will benefit from CRT-D therapy
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• Wojciech Zareba, MD, PhD
• Lang, RM, Bierig, M, Devereux, RB, et al: Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography 2005; 18:1440-1463.
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