CRT: Role of Patient Selection and Device Programming to Optimize Outcomes

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Disclosures

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Honoraria, Speakers Boston Scientific, Research Grants
Honoraria, Speakers St. Jude Medical, Research Grants
Cardiac Resynchronization Therapy: Weight of Evidence

- >6,000 patients evaluated in randomized controlled trials of advanced HF
- Consistent improvement in quality of life, functional status, and exercise capacity
- Strong evidence of changes in LV structure
  - ↓ LV volumes and dimensions
  - ↑ LVEF
  - ↓ Mitral regurgitation
- Reduction in HF and all-cause morbidity and mortality
Corner Stones for Optimal CRT Therapy

- Patient Selection
- LV Lead Placement
- Device Programming
- Team Management including Remote Follow Up
1. Modified recommendation (specifying CRT in patients with LBBB of 150 ms; expanded to include those with NYHA class II symptoms).

2. New Recommendation

CRT is indicated for patients who have left ventricular ejection fraction (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).¹

¹ Modified recommendation (specifying CRT in patients with LBBB of 150 ms; expanded to include those with NYHA class II symptoms).

² New Recommendation
CRT can be useful for patients who have LVEF less than or equal to 35%, sinus rhythm, LBBB with a QRS duration 120 to 149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT.²

CRT can be useful for patients who have LVEF less than or equal to 35%, sinus rhythm, a non-LBBB pattern with a QRS duration greater than or equal to 150 ms, and NYHA class III/ambulatory class IV symptoms on GDMT.²

1. Modified recommendation (specifying CRT in patients with LBBB of 150 ms; expanded to include those with NYHA class II symptoms).
2. New Recommendation
Cardiac Resynchronization Therapy in Patients With Systolic Heart Failure

1. Modified recommendation (wording changed to indicate benefit based on ejection fraction rather than NYHA class; level of evidence changed from C to B).

2. Modified recommendation (wording changed to indicate benefit based on ejection fraction and need for pacing rather than NYHA class; class changed from IIb to IIa).

3. New Recommendation

CRT can be useful in patients with atrial fibrillation and LVEF less than or equal to 35% on GDMT if a) the patient requires ventricular pacing or otherwise meets CRT criteria and b) AV nodal ablation or pharmacologic rate control will allow near 100% ventricular pacing with CRT.¹

CRT can be useful for patients on GDMT who have LVEF less than or equal to 35% and are undergoing new or replacement device placement with anticipated requirement for significant (>40%) ventricular pacing.

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Cardiac Resynchronization Therapy in Patients With Systolic Heart Failure

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3. New Recommendation

CRT may be considered for patients who have LVEF less than or equal to 30%, ischemic etiology of heart failure, sinus rhythm, LBBB with a QRS duration of greater than or equal to 150 ms, and NYHA class I symptoms on GDMT.³

CRT may be considered for patients who have LVEF less than or equal to 35%, sinus rhythm, a non-LBBB pattern with QRS duration 120 to 149 ms, and NYHA class III/ambulatory class IV on GDMT.¹

CRT may be considered for patients who have LVEF less than or equal to 35%, sinus rhythm, a non-LBBB pattern with a QRS duration greater than or equal to 150 ms, and NYHA class II symptoms on GDMT.¹

1. Modified recommendation (wording changed to indicate benefit based on ejection fraction rather than NYHA class; level of evidence changed from C to B).
2. Modified recommendation (wording changed to indicate benefit based on ejection fraction and need for pacing rather than NYHA class; class changed from IIb to IIa).
3. New Recommendation
Cardiac Resynchronization Therapy in Patients With Systolic Heart Failure

CRT is not recommended for patients with NYHA class I or II symptoms and non-LBBB pattern with QRS duration less than 150 ms.¹

CRT is not indicated for patients whose comorbidities and/or frailty limit survival with good functional capacity to less than one year.²

1. New Recommendation
2. Modified recommendation (wording changed to include cardiac as well as non-cardiac comorbidities).

No Benefit
Effect of Cardiac Resynchronization Therapy on Composite Clinical Events in Patients with LBBB and Non LBBB

A Meta Analysis

MADIT CRT; CRT-D:ICD
Hazard Ratios for Pre-specified Subgroups

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. events/No. patients</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 yr</td>
<td>142/852</td>
<td></td>
</tr>
<tr>
<td>≥65 yr</td>
<td>230/968</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>294/1367</td>
<td></td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>78/453</td>
<td></td>
</tr>
<tr>
<td><strong>NYHA Class</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic I</td>
<td>53/265</td>
<td></td>
</tr>
<tr>
<td>Ischemic II</td>
<td>186/734</td>
<td></td>
</tr>
<tr>
<td>Nonischemic II</td>
<td>133/821</td>
<td></td>
</tr>
<tr>
<td><strong>QRS ms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;150</td>
<td>147/645</td>
<td></td>
</tr>
<tr>
<td>≥150</td>
<td>225/1175</td>
<td></td>
</tr>
<tr>
<td><strong>LVEF</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤0.25</td>
<td>101/646</td>
<td></td>
</tr>
<tr>
<td>&gt;0.25</td>
<td>271/1174</td>
<td></td>
</tr>
<tr>
<td><strong>LVEDV</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤240ml</td>
<td>184/828</td>
<td></td>
</tr>
<tr>
<td>&gt;240ml</td>
<td>184/969</td>
<td></td>
</tr>
<tr>
<td><strong>LVESV</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤170</td>
<td>190/835</td>
<td></td>
</tr>
<tr>
<td>&gt;170</td>
<td>178/962</td>
<td></td>
</tr>
<tr>
<td><strong>All Patients</strong></td>
<td>372/1820</td>
<td></td>
</tr>
</tbody>
</table>

Moss et al., N Engl J Med 2009;361
Improving CRT Response – Patient Selection

- **High Likelihood of Responds**: Female, LBBB, QRS ≥ 150 ms, Non-ischemic CM

- **Less Likely to Respond**: QRS 120-150 ms, advanced co-morbidities, medical therapy not optimized

- **No Evidence of Benefit**: RBBB, end-stage renal disease, QRS ≤ 120 ms
Improving CRT Response – Patient Selection

- **Less Likely to Respond:** QRS 120-150 ms, advanced co-morbidities, medical therapy not optimized
  - Lead Location/ CS anatomy
  - High LV Scar burden
MADIT-CRT:
- Most common lead position: lateral wall
- Predominant segmental placements: Lateral-mid; Anterior-basal and Posterior-apical

Segmental Distribution
- Apical segment: 14%; Basal: 23%; Mid-ventricular: 63%
  An apical lead position was associated with 2.5 fold increased risk for death as compared to the non-apical region and nearly 5-fold when selectively compared with basal lead position
• Echocardiographic LV end-systolic volume index (LVESVi), QRS duration, and clinical outcomes at 12–24 months of follow-up were evaluated with respect to the lead tip position

• A significantly greater decrease in the powered secondary endpoint of LVESVi was observed with the non-apical vs. the apical LV lead positions

• The incidence of composite endpoint of death and first hospitalization for HF was lower in the LV lateral than in the non-lateral and in the LV non-apical than in the apical group

Quadripolar LV Leads

- 4 pacing configurations available in bipolar leads
- 10 different possible vectors with the SJM quadripolar LV lead
Quadripolar Technology

- A Quadripolar LV lead can be placed distally, but still allow for basal pacing with more proximal electrodes
- Enables LV pacing at the preferred site without compromising lead stability

Problem: Inability to Pace at the Preferred Site

- MADIT-CRT data showed that LV pacing in an apical position could double the propensity for heart failure or death when compared to basal pacing\(^1\)
- Often a distal apical location is the only stable position

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MultiPoint™ Pacing, exclusively from St. Jude Medical, delivers two pulses from the Quartet™ LV lead per pacing cycle, resulting in a more effective uniform ventricular contraction.
MultiPoint™ Pacing

- Pacing from **two** LV sites ("Multipoint LV stimulation") and **one** RV
  - Capture a larger area

- Engage areas around scar tissue
  - Improve pattern of depolarization/repolarization
  - Improve hemodynamics
  - Improve resynchronization

Not Approved in the US
Late-Breaking HRS Trials
Safety and Efficacy of Multipoint Pacing in Cardiac Resynchronization Therapy:
The MultiPoint Pacing (MPP) IDE Study

A. Responder Rate

<table>
<thead>
<tr>
<th>Spatial Separation</th>
<th>% of Patients</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 mm</td>
<td>60</td>
<td>0.003</td>
</tr>
<tr>
<td>≥30 mm &amp; &gt;5 ms Timing Delay</td>
<td>80</td>
<td>0.678</td>
</tr>
<tr>
<td>≥30 mm &amp; 5 ms Timing Delay</td>
<td>100</td>
<td>0.057</td>
</tr>
</tbody>
</table>

B. Conversion Rate (Non-responder to Responder)

<table>
<thead>
<tr>
<th>Spatial Separation</th>
<th>% of Patients</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 mm</td>
<td>20</td>
<td>0.006</td>
</tr>
<tr>
<td>≥30 mm &amp; &gt;5 ms Timing Delay</td>
<td>40</td>
<td>0.447</td>
</tr>
<tr>
<td>≥30 mm &amp; 5 ms Timing Delay</td>
<td>60</td>
<td>0.200</td>
</tr>
</tbody>
</table>
Improving CRT Response – Device Programming

- Use available AV and VV optimization algorithms
- Use rate response when appropriate
- Maintain high % BiV pacing
- Consider specific optimization algorithms
In a cohort of >80,000 patients, 40.7% exhibited less than 98% BiV pacing


A Significant Percentage of Patients Do Not Achieve Optimal BiV Pacing %

Reasons for < 100% pacing

- Atrial fibrillation
- PVCs
- Competitive AV nodal conduction

<90% CRT 11.5%
90-95% CRT 10.5%
95-98% CRT 18.7%
>98% CRT 59.3%
Outcomes Improved in Patients with Near 100% BiV Pacing

Early data showed decline at <93% BiV pacing; Recent, larger cohort data at <98.5% BiV pacing

CRT in AF With or Without AV Junction Ablation

Total Mortality

Cardiac Mortality

Gasparini et al, JACC Heart Failure Vol. 1, No. 6, 2013
LV Reverse Remodeling after CRT

Gasparini et al, JACC Heart Failure Vol. 1, No. 6, 2013
AdaptivCRT™ Concept

LBBB

AVB and LBBB

LVP to fix QRS

BVP to fix PR and QRS

Medtronic Viva XT CRT-D manual.
AdaptivCRT™ LV Pacing Analysis

Patients with Higher Percentage Synchronized LV Pacing in the CRT Arm had a Lower Rate of Death

CRT in 2017

- Smaller size, longer lasting batteries
- Wireless, remote monitoring
- Arrhythmia logbooks, including AF burden
- Monitoring of HF parameters
- Improved rate response technology
- Approved for MRI
- New LV/RV optimization algorithms
- New LV leads
- Multipoint pacing
Conclusion

- Improved Patient Selection
- Improved Device Technology
- Improved CRT Response!
Thank You