Update on Cardiac Resynchronization Therapy

Nitish Badhwar, MD, FACC, FHRS
Associate Chief, Cardiac Electrophysiology
Director, Cardiac Electrophysiology Training Program
Stone-Chamberlain Endowed Chair in Cardiology
University of California, San Francisco

Innovative Procedures, Devices, and State of the Art Care for Arrhythmias, Heart Failure and Structural Heart Disease

October 8, 2015

Disclosures

Honoraria - St. Jude, Biosense, Senterheart
Fellowship Support – Medtronic, St. Jude, Boston Scientific, Biotronik

- Update on indications
- CRT optimization
- Role of imaging
**Burden of Heart Failure**

- Annual incidence: 550,000
- Incidence 10/1000 population > 65 years
- Prevalence: 4.7 million
- Acute HF hospitalization: 3 million
- Annual mortality: 250,000

---

**LBBB and Heart Failure**

Narrow QRS EF 47%  
LBBB EF 30%

---

**Deleterious Effects of Ventricular Dyssynchrony**

- Reduced diastolic filling time
- Weakened contractility
- Protracted mitral regurgitation
- Post-systolic regional contraction
- Diminished stroke volume

Cardiac Resynchronization Therapy (CRT)

Baseline qrs 160 ms

Biv pacing qrs 120 ms

Effects on Remodeling

Pre CRT

Post CRT
Effects on Remodeling

Pre CRT

Post CRT

Benefits of CRT in Advanced Heart Failure

• Clinical outcomes
  – Exercise capacity
  – Quality of life
  – Heart failure hospitalization
• CRT leads to reverse remodeling
• Mortality benefit (COMPANION, CARE-HF)

Indications for CRT

• Sinus rhythm
• Advanced heart failure (NYHA Class III or IV)
• QRS complex duration > 120 ms (Electrical dyssynchrony assumed to be a correlate of mechanical dyssynchrony)
• Left Ventricle Ejection Fraction (LVEF) ≤ 35%
• Ischemic or non-ischemic cardiomyopathy
• Optimal drug therapy for heart failure

QRS Duration and Morphology

- QRS morphology
  - LBBB
  - RBBB
  - Non LBBB
- QRS duration
  - > 150 ms
  - 120-150 ms
  - < 120 ms

RV Pacing

PAVE: BiV vs RV pacing in pts with AF and AVN ablation

Block HF: CRT in pts with AV block and mild LV dysfunction (EF ≤50%)

Indications for CRT

- Sinus rhythm class I indication
- RV pacing induced class IIa indication
- Atrial fibrillation class IIa indication

Can CRT benefit patients with early heart failure
CRT and mild HF (NYHA II)

- MADIT CRT, RAFT, MIRACLE-ICD II, REVERSE
- Improved mortality and hospitalization
- Lead to LV reverse remodeling


QRS Morphology and CRT

MADIT-CRT: Outcome by LBBB & Non-LBBB

<table>
<thead>
<tr>
<th>Group</th>
<th>Event Free of HF (%)</th>
<th>HR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBBB</td>
<td>50</td>
<td>0.45</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Non-LBBB</td>
<td>65</td>
<td>1.25</td>
<td>0.25</td>
</tr>
</tbody>
</table>

QRS Morphology and CRT

MADIT-III: MADIT-CRT

Hazard Ratio = 0.66
P = 0.001
N = 1820

Elig:
IHD or NIHD, NYHAI/II,
EF < 0.30, QRS > 130 ms


CRT-D Better          ICD-only Better

CRT-D:ICD Hazard Ratios for Prespecified Subgroups

Significant Sex-Rx Interaction
Significant QRS-Rx Interaction

QRS duration and CRT
2012 CRT Guideline Update

2012 CRT Guideline Update

Class I: Recommended
1. CRT is indicated for patients who have LVEF less than or equal to 35%, sinus rhythm, a non-LBBB pattern with QRS duration less than 150 ms, and NYHA class II symptoms on GDMT. (Level of Evidence: A)

To Test the Hypothesis that CRT Can Help Heart Failure Patients With Narrow QRS if they have a positive Dyssynchrony Echo

CRT in narrow QRS patients: Negative study
• Update on indications
• CRT optimization
• Role of imaging

Cardiac Resynchronization Therapy
• 30% patients with HF NYHA III-IV qualify for CRT based on EKG criteria
• 30-40% patients with HF NYHA III-IV and narrow QRS who do not qualify for EKG criteria for CRT have evidence of mechanical dyssynchrony by imaging
• 30% patients do not respond to CRT
• 10-29% patients show super or hyper response with EF > 50% and NYHA I

Poor Responders to CRT
• RBBB
• Ischemic cardiomyopathy
• NYHA IV
• Advanced age
• Discordant LV lead and myocardial scar
“Non responders”: Medical causes

- Suboptimal HF therapy
- Mitral regurgitation +/- ischemia
- Comorbidities (COPD, anemia, arthritis, amiodarone)
- End stage heart disease
  - Restrictive pattern on echo
  - RV dysfunction

“Non responders”: Device causes

- Lower % BiV pacing due to
  - AT/AFib/Aflutter with rapid ventricular rates
  - Higher threshold with loss of LV capture
  - Lead dislodgement
  - Phrenic stimulation
  - Anodal stimulation
- Inadequate rate response
- Suboptimal PV or AV delay
- Suboptimal V-V timing
- LV lead position
- LV dyssynchrony

ECG to Assess BiV Pacing

- BiV capture produces a rightward axis (negative or initial negative in leads I, AVL and positive in aVR) and R>S in lead V1.

- R–S ratio ≥ 1 in lead V1, q in lead I, R-S ratio of ≤ 1 in lead I suggest BiV pacing.

- 12 lead ecg in basal post lat vein does not give complete negative complex in 1, avL ..it looks like LBBB with narrower QRS.
Maximizing Biventricular Pacing

Options for patients at risk of rapid intrinsic conduction?
• Maximizing beta-blocker therapy
• Negative AV/PV hysteresis ensures constant ventricular pacing by shortening the AV/PV delay if intrinsically conducted R waves are sensed.
• Biv trigger pacing, adaptive CRT
• AV Junction ablation in patients with Atrial fibrillation and rapid ventricular conduction (< 85% biv pacing)

AV and VV optimization

• Echo based (Mitral inflow and Aortic VTI)
• EKG based
• EGM based (through the device)

AV and V-V Optimization

• Statistically speaking: the average optimal AV delays were between 170-190 ms, and the average optimal V-V delays were between 20-30 ms.
• In almost all studies, approximately 60% of all patients were paced LV first.
• Update on indications
• CRT optimization
• Role of imaging

Mechanical Dyssynchrony

- Electrical dyssynchrony (wide QRS) → Mechanical dyssynchrony
- Some patients with wide QRS may not have mechanical dyssynchrony
- Narrow QRS patients with heart failure may have mechanical dyssynchrony
**Equilibrium Radionuclide Angiogram (ERNA)**

- **Dyssynchrony -**
  - Lao amplitude
  - Lao phase
- **Dyssynchrony +**
  - Lao amplitude
  - Lao phase

---

**The Solution**

- Need imaging modality that reliably measures mechanical dyssynchrony
  - Echo
  - MRI / CT
  - ERNA (Equilibrium radionuclide angiogram)

---

**Role of ERNA to select patients for CRT**

A combined preoperative value of $S \leq 0.88$ and $E > 0.69$ predicted clinical improvement in 86% of the patients after CRT. The remainder showed clinical improvement only in 56% of the patients.

Levophase for Coronary Sinus Anatomy

Coronary Sinus Anatomy

LV lead position and Clinical Outcomes

- No difference among Anterior, Posterior and Lateral lead positions
- Apical lead positions associated with a significantly worse clinical outcome
LV Lead Concordance with Latest Activated Segment by ERNA Predicts Improvement after CRT

<table>
<thead>
<tr>
<th>Concordant Lead Placement</th>
<th>Discordant Lead Placement</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean NYHA 0.8 ± 0.41 (n=20)</td>
<td>0.47 ± 0.52 (n=15)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Mean Change ESVI -77% ± 132 (n=14)</td>
<td>+9% ± 24 (n=9)</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

CRT Non-Response: Postlateral Aneurysm by Echo

LV pacing in scar region

- Long delay from stimulus to LV capture
- No benefit derived from BiV pacing, can even lead to worsening of symptoms due to RV pacing
- Rarely can lead to ventricular tachycardia in patients with ischemic heart disease (inferoposterior MI)
- Role of viability assessment (PET scan, MRI)
Role of Imaging in CRT

- Dyssynchrony evaluation
  - Predict response in patients with QRS >150 ms
  - Select patients with QRS 120-150 ms and < 120 ms (pending results of ECHO CRT)
  - Select patient with non LBBB and RBBB
- Guiding LV lead placement
- Assessment of coronary sinus anatomy
- Assessment of scar and viability
- Optimization of CRT with echo

Virtual CRT

- Baseline ECG
- Imaging to assess mechanical dyssynchrony, scar and area of latest LV contraction
- Body surface map to assess latest electrical activation
- CT / MRI to assess coronary sinus anatomy
- Heart model to predict response to CRT
- Plan coronary sinus vs endocardial LV vs surgical epicardial LV lead placement based on imaging

Thank you