Cardiac Resynchronization Therapy Optimization: Still Have a Role?!

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Cardiac Resynchronization Therapy Optimization: Still Have a Role?!

Yes
“Your Eyes See What Your Mind Knows”

Hippocrates (c. 460 BC – c. 370 BC)

Objectives of CRT

Table 2. The results from the CARE-HF (Cardiac Resynchronization in Heart Failure) program demonstrated that, in comparison with a control group, CRT had the following effects [7,8,21]. However, the analysis failed to identify any patient subgroup who did not respond.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased mean left ventricular ejection fraction by 6.9%</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Improved symptoms and quality of life</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Reduced the rate of hospitalization for WHF by 52%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Reduced the rate of all-cause mortality by 40%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Reduced the rate of death due to WHF by 45%</td>
<td>p=0.003</td>
</tr>
<tr>
<td>Reduced the rate of sudden death by 46%</td>
<td>p=0.006</td>
</tr>
</tbody>
</table>

WHF: worsening heart failure.
CRT Optimization

- Device (PM/ICD) Optimization
- CRT (HF therapy) Optimization
- Patient Optimization

CRT Follow Up

- Device (PM/ICD) Optimization
- CRT (HF therapy) Optimization
- Patient Optimization
Device Optimization

- Rhythm
- Percent pacing
- Battery
- Lead status
- Sensing
- Threshold
- Events
- Diagnostics
- Programming

Look for Complications of CRT

The most common complication

- Inability to implant the LV pacing lead successfully in the coronary vein

Additional complications include

- Coronary sinus or coronary vein trauma
- Pneumothorax
- Diaphragmatic/phrenic nerve pacing
- Infection
CRT Follow Up

- Device (PM/ICD) optimization
- CRT (HF therapy) optimization
- Patient Optimization

CRT Optimization

- CRT Promotion
- CRT Optimization
Promoting CRT

- Unlike conventional pacing (where the goal is to minimize unnecessary ventricular pacing), CRT should pace both ventricles as close to 100% of the time as possible.
- Percentage of LV pacing (as high as 90% or more) = Optimal CRT delivery
- **Lower pacing %**
  - LV lead dislocation
  - Paroxysmal or permanent atrial fibrillation
  - Frequent ventricular ectopic beats

Promoting CRT- MTR

- The Maximum Tracking Rate sets the highest rate at which the ventricles will be paced in response to intrinsic atrial activity
- If the patient has high intrinsic atrial rates >MTR with good conduction, it is possible that the ventricle will not be paced some of the time
- Make sure the MTR is high enough so that even in the presence of high intrinsic atrial rates, the patient will have V pacing as much as possible
CRT Optimization

- Why do we optimize CRT?
- How do we optimize CRT?
- When should we optimize CRT?
- Does optimizing CRT benefit patients?

Why Do We Optimize CRT?

- Proper CRT depends on precise timing of the ventricular contractions.
- Timing should allow:
  - Adequate time for the filling of the ventricles (i.e. diastolic optimization).
  - Proper contraction of the right and left ventricles with respect to each other (i.e. systolic optimization).
Who Should Be Optimized

Any CRT recipient should be optimized

Any CRT Patient who didn’t show:

- NYHA Class Improvement
- 6 Minutes walking distance Improvement
- BNP improvement
- Echocardiographic parameters Improvement
- Reduction of Hospitalization
How Should Non-Responders to CRT be Managed?

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Department of Cardiology, University of Hull, Kingston upon Hull, UK

CRT, applied according to existing guidelines, is an effective therapy for heart failure patients who are refractory to conventional medical treatment. No adequate definition of “response” or “non-response” to the therapy exists, and there is little evidence that electrocardiographic or cardiac imaging criteria are useful in selecting patients who are more or less likely to have a good clinical response to CRT. It is estimated from CRT studies that approximately one third of patients who receive the therapy do not exhibit an adequate response. Accordingly, it is important to develop strategies to enhance the effectiveness of CRT for patients who do not receive optimal benefit from the therapy. This review aims to discuss clinical approaches to managing heart failure patients who are labeled as non-responders. Ensuring that the CRT device is pacing and capturing both ventricles, and that the atrioventricular delay is optimal at rest and during exercise, is essential in all patients who have an inadequate response. The burden of atrial fibrillation, should it arise, requires quantification and management. Careful attention should also be paid to pharmacological therapy following the deployment of CRT. Finally, left ventricular lead re-positioning, or other cardiac procedures, will be occasionally required. Device Therapy for Heart Failure 2008;2(1):2-9.
What is a „responder“?

„soft“ end-point:
- NYHA improvement >1

„hard“ end-points:
- survival
- ↑ 6 MWD > 10 ... 25%
- ↑ EF > 5 ... 25%
- ↓ ED Volume > 15%
- ↓ ES Volume > 10 ... 15%
- ↑ Stroke Volume > 15%

Table 4. Authors’ summary of questions to be answered by the clinician before labeling an HF patient with a CRT device as a “non-responder”.

1. Have all correctable cardiac causes of HF (including ischemia, valvular abnormalities, hypertension, or dysrhythmias) been identified and managed?
2. Have all correctable non-cardiac abnormalities (including anemia, renal, thyroid, or other hormonal abnormalities) that cause or worsen HF been identified and managed?
3. Have drugs that cause or worsen HF (including class I and III anti-arrhythmic agents, nonsteroidal anti-inflammatory drugs, or cancer chemotherapeutic agents) been stopped or substituted as appropriate?
4. Has optimal medical management (including angiotensin-converting enzyme inhibitors, β-blockers, angiotensin receptor blockers, aldosterone antagonists, digoxin, and diuretics) been initiated at an optimal dose based on current evidence? Is the patient compliant with this regimen?
5. Is the patient on an appropriate health education program (including salt intake restriction, avoidance of excessive alcohol consumption, regular exercise, and weight reduction)? Is he or she compliant with it?
6. Is the CRT device functioning properly (for example, has optimal left ventricular lead position been ensured during CRT implantation? Have the atrioventricular and interventricular delay intervals been programmed to provide the best hemodynamic response?)

HF: heart failure.
CRT Optimization

• Why do we optimize CRT?

• How do we optimize CRT?

• When should we optimize CRT?

• Does optimizing CRT benefit patients?
Echocardiographic Parameters For Patient Selection and Response Prediction

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>View</th>
<th>Cut-off</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apical rocking</td>
<td>Visual assessment of apical transverse motion</td>
<td>Apical 4-chamber view</td>
<td>Yes/No</td>
<td>Highly reproducible method, high specificity for response prediction</td>
<td>Affected by RV function</td>
</tr>
<tr>
<td>Septal flash</td>
<td>Visual assessment of short inward septal motion during beginning of systole</td>
<td>Apical 4-chamber view</td>
<td>Yes/No</td>
<td>Highly reproducible method, high specificity for response prediction</td>
<td>Translation of continuous process to on/off phenomenon, observer differences</td>
</tr>
<tr>
<td>IVMD</td>
<td>Interventricular mechanical delay, difference in onset of outflow of LV (LVPEP) and RV (RVPEP)</td>
<td>PW Doppler of LVOT and RVOT</td>
<td>40 msec</td>
<td>Highly reproducible method</td>
<td>Affected by both LV and RV function</td>
</tr>
<tr>
<td>Septal strain patterns</td>
<td>Strain pattern of the septum during systole</td>
<td>Apical 4-chamber view</td>
<td>3 types (1:2 responder: 3 non-responder)</td>
<td>Prediction of volumetric response and outcome</td>
<td>Technically demanding</td>
</tr>
<tr>
<td>SD-TTP</td>
<td>Standard deviation of time to peak shortening (strain) or velocity (TDI) of all myocardial segments</td>
<td>Apical 4-chamber view, 2-chamber view, PLAX view</td>
<td>&gt; 32 msec</td>
<td>Offline analysis</td>
<td>Requires high quality image, confounded by passive motion tetherting</td>
</tr>
<tr>
<td>SL delay</td>
<td>Difference of time to peak velocity of septal and lateral view</td>
<td>Apical 4-chamber view</td>
<td>&gt; 65 msec</td>
<td>Prediction of volumetric response and outcome</td>
<td>Confounded by passive motion tetherting</td>
</tr>
<tr>
<td>SAb</td>
<td>Time to minimal systolic volume of 16 segments</td>
<td>3D</td>
<td>9.9%</td>
<td>High value for response prediction</td>
<td>Limited spatial and temporal resolution</td>
</tr>
<tr>
<td>SRS sept (Systolic rebound stretch of the septum)</td>
<td>All positive deflections after initial shortening of the septum during systole</td>
<td>Apical 4-chamber view</td>
<td>4.7%</td>
<td>Prediction of volumetric response and outcome</td>
<td>Technically demanding, observer differences</td>
</tr>
</tbody>
</table>
Optimization Techniques

AV optimization
- Echocardiography
  - Ritter method
  - Simplified inflow method
  - Iterative method
  - Maximal filling time
  - Mitrail VTI
  - Aortic VTI
- Finger plethysmography
- Impedance cardiography
- Device algorithms
  - PEA
  - AV/EGM-based algorithm

VV optimization
- Echocardiography
  - Aortic VTI
  - TDI
- Radionuclide ventriculography
  - LVEF
- Finger plethysmography
- Device algorithms
  - PEA

PEA = peak endocardial acceleration; VTI = velocity-time integral; TDI = tissue Doppler imaging.

Summary of the various methods of AV and VV interval optimization.

<table>
<thead>
<tr>
<th></th>
<th>AV optimization</th>
<th>VV optimization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echocardiography</td>
<td>Mitrail inflow (Ritter method, iterative method; “Fast and Simple”), aortic VTI</td>
<td>LV M-mode (Septal-posterior wall motion delay), tissue Doppler imaging, aortic VTI</td>
</tr>
<tr>
<td>Alternative techniques</td>
<td>Impedance cardiography, finger plethysmography, acoustic cardiography, peak endocardial acceleration</td>
<td>Intracardiac echocardiography, elektromanatonic mapping, radionuclide angiography, finger plethysmography, peak endocardial acceleration, surface ECG</td>
</tr>
<tr>
<td>Intracardiac electrogram-based algorithms</td>
<td>Boston Scientific SmartDelay™, St. Jude Medical QuickOpt™, Medtronic Adaptive Algorithm</td>
<td>Boston Scientific Expert Ease™, St. Jude Medical QuickOpt™, Medtronic Adaptive Algorithm</td>
</tr>
</tbody>
</table>
AV Optimization: Iterative Method

Objective: Identify the AV Delay that maximizes LV filling using mitral velocity echocardiographic measurements

Procedure

• Obtain transmitral Doppler echo at a “long” programmed AV Delay during ventricular pacing
• Shorten the programmed AV Delay by 10-20 ms until the echo Doppler A-wave becomes truncated (A wave is atrial contraction)
• Lengthen the programmed AV Delay back to the value where there is no A-wave cutoff. This timing should enable ventricular contraction to occur just at the end of atrial systole
Optimal AV delay is

1. E and A wave separated.
2. Termination of the A wave at 40-60 msec before the onset of the QRS.
3. Stage I diastolic filling pattern i.e A > E pattern.

Optimize AV Delay to Permit 100% BiV Pacing During Exercise
Timing of Optimization

• Best evidence-based practice is to follow the CARE-HF protocol and optimize AV delay using the iterative method at:
  
  • Baseline (predischarge)
  
  • 3 months,
  
  • every 6 months thereafter.
**V-V Optimization**

- The best V-V setting is by measuring the RVOT & LVOT PW Doppler signals

- V-V above 40 ms is considered abnormal

- Normally: the RV will contract after the LV by 20 ms

CRT Optimization

- Why do we optimize CRT?
- How do we optimize CRT?
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## Major Randomized Trials of CRT AV/VV Optimization

### Major trials of AV/VV delay optimization

<table>
<thead>
<tr>
<th>N</th>
<th>Technique</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Abraham et al. (FREEDOM)</strong> [74] 1525</td>
<td>Optimization at implant with standard of care vs. QuickOpt™ AV/VV optimization every 3 months</td>
</tr>
<tr>
<td></td>
<td><strong>Ellenbogen et al. (SMART-AV)</strong> [17] 980</td>
<td>Fixed AV delay (120 ms), iterative method, or SmartDelay™ AV optimization</td>
</tr>
<tr>
<td></td>
<td><strong>Martin et al. (adaptive CRT)</strong> [70] 522</td>
<td>Echo optimized AV/VV delays (iterative and aortic VTI) vs. Adaptive CRT algorithm</td>
</tr>
<tr>
<td></td>
<td><strong>Ritter et al. (CLEAR)</strong> [30] 238</td>
<td>Standard of care optimization (mostly echo) vs. PEA AV/VV optimization algorithm</td>
</tr>
</tbody>
</table>

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**A Prospective Randomized Evaluation of VV Delay Optimization in CRT-D Recipients: Echocardiographic Observations from the RHYTHM II ICD Study**

V-V delay optimization was associated
- with better immediate hemodynamic function than simultaneous biventricular stimulation,
- did not promote additional reverse remodeling at 6 Mos
- did not increase the proportion of echocardiographic responders to CRT

**PACE 2009; 32:S120–S125**
CRT Optimization

- Device (PM/ICD) optimization
- CRT (HF therapy) optimization
- Patient Optimization

Patient Optimization

- Device Interrogation
- NYHA Class
- 6 minute walking test
- BNP
- Echocardiography
- Responder status
- Overall wellbeing and Activity
**Patient Follow-up: HR trend**

- With worsening of HF, HR increases during the day and night.
- This is indicative of increased SNS activity
  - Patients with increased average HR need to be seen more frequently until HR return to baseline/normal
  - Assess for signs/symptoms of decompensation
  - Verify adherence to low sodium diet and medication regimen
  - BNP levels may be useful in diagnosing decompensation
- Correlate with HRV and activity for more insight into overall status

**Patient Follow-up: Activity**

- Goal: 30 minutes 5x/week
- Patient physically active -> Encourage continued or increased activity
- Activity levels decreased -> Correlate with symptoms, clinical exam, and other trend data to identify possible cause, e.g. decompensation, arrhythmias
- Patient remains inactive and is clinically stable -> encourage increased activity
CRT OPTIMIZATION IN THE GUIDELINES

- 2013 ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR CRT guidelines:
  - Posterolateral LV lead position, the target of latest activated area and avoidance of apical position.
  - A shortest AV delay without truncation of the A-wave (Ritter's method) or change in LV systolic function
  - The largest stroke volume by Echo Doppler is recommended as CRT optimization about VV delay

- The 2016 ESC guidelines suggest that echocardiography may be considered for patients who have had a disappointing response to CRT

CONCLUSIONS

Who wants to implant CRT? Who wants to Optimize CRT?
Conclusion

• CRT could be implanted by a cardiologist who has good invasive skills

• However, only few who could precisely follow-up their patients post implantation to maximize & optimize their benefits from CRT

• CRT Optimization aims to increase the likelihood of being a good, or even super, responder to this impotent HF therapy

• It should be tailored to the patient

• This includes: Device, CRT, and Patient HF status Optimization

Cardiac Resynchronization Therapy Optimization: Still Have a Role?!

Yes