CCS Guidelines: Update on the Use of Cardiac Resynchronization Therapy

Disclosures

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ACC Rockies 2014
Session Overview

Focus on provision of a framework in which to implement cardiac resynchronization therapy (CRT)

Based on the GRADE system

Review of recommendations relating to patient selection, delivery and optimization of CRT
CCS CRT Guidelines Panel 2013

Primary Panel
• Francois Philippon
• Derek Exner (co-chair)
• Miriam Shanks
• Bernard Thibault
• Jafna Cox
• Aaron Low
• Vidal Essebag
• Jamil Bashir
• Gordon Moe

Secondary Panel
• David Birnie
• Eric LaRose
• Ratika Parkash (co-chair)
• Raymond Yee
• Elizabeth Swiggum
• Padma Kaul
• Damian Redfearn
• Anthony Tang
• Malcolm Arnold
• Jeff Healey
• Jonathan Howlett
• Francois Marcotte
• Finlay McAlister
• John Sapp
• Mario Talajic
• Lyall Higginson
• Michel White
• Robert McKelvie
GRADE Approach

Development of guidelines through:

– Critical evaluation of literature
– Expert consensus
– Use of Grading of Recommendations Assessment, Development, and Evaluation (GRADE)

1. Quality of Evidence:
   - High, Moderate, Low or Very Low

2. Strength of Recommendations
   - Strong or Weak

Guyatt 2011 J Clin Epi 64: 383-94
Case Mr. Pace

80 year old gentleman

- Non-ischemic cardiomyopathy
- Most recent EF on wall motion study 27%
- Permanent pacemaker in place, pacing 100% of the time (ventricular escape of 30 bpm)
- Over the last few months, he has developed NYHA III dyspnea
- No PND, orthopnea or chest pain
- Recent cardiac catheterization revealed minor wall irregularities
Details

- Permanent atrial fibrillation (CHADS$_2$ = 3, age, HF & HTN)
- Known pacemaker dependence
- Due for pulse generator change in the next 2 months
- Abdominal aortic aneurysm
- COPD
- Polymyalgia Rheumatica

Medications:
- Warfarin 6 mg po od
- Furosemide 40 mg po od
- Carvedilol 25 mg po bid
- Prednisone 5 mg po od
- Atorvastatin 10 mg po od
- Ramipril 5 mg po bid
- Rabeprazole 20 mg po od
- Puffers
**CRT Guidelines – Evidence and Patient Selection**

<table>
<thead>
<tr>
<th>Prior Recommendation</th>
<th>Strength</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate medical therapy be implemented prior to the initiation of CRT, that each patient’s suitability for CRT be thoroughly assessed, and the details of that assessment be recorded in their medical record.</td>
<td>Strong</td>
<td>Low</td>
</tr>
</tbody>
</table>

CJC 2013;29:182-195
Electrocardiogram
What do you recommend?

1. Arrange for pacemaker generator change
2. Arrange for ICD upgrade
3. Arrange for CRT + pacemaker upgrade
4. Arrange for CRT + ICD upgrade
5. Other
<table>
<thead>
<tr>
<th>Prior Recommendation</th>
<th>Strength</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CRT may be considered</strong> for patients in permanent AF who are otherwise suitable for this therapy.</td>
<td>Weak</td>
<td>Low</td>
</tr>
<tr>
<td><strong>CRT may be considered</strong> for patients who are chronically RV-paced or are likely to be chronically paced, have signs and/or symptoms of heart failure, and a LVEF ≤ 35%.</td>
<td>Weak</td>
<td>Low</td>
</tr>
</tbody>
</table>
We recommend that all patients with HF who are planned for a CIED system revision should be considered for their eligibility for upgrade to CRT.

Practical Tip: Given the expanding indications for CRT and the changes over time that may occur in a patient’s condition, the need for CRT should be considered at the time of CIED change, as risk/benefit of adding an LV lead when a procedure is being performed may be favourable.
Prior CIED with NYHA II/III CHF

Planned System Revision:
- Pulse generator change
- Lead Revision
- Infection

ECG

QRS <130 ms and no RV pacing
No upgrade to CRT indicated

QRS ≥130 ms
Assessment of LV function
EF ≤ 35%
Consider CRT upgrade

High % RV pacing
Decline in LV function or worsening heart failure
<table>
<thead>
<tr>
<th>New Recommendation</th>
<th>Strength</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>We <strong>recommend</strong> that the prescription of CRT and the choice of platform (CRT-P vs CRT-D) should take into account clinical factors that would affect the overall goals of care.</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prior Recommendation</th>
<th>Strength</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>A CRT pacemaker is recommended for patients who are suitable for resynchronization therapy, but not for an ICD.</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
</tbody>
</table>
Patient Factors and Comorbidities

Age

Mean age of patients in the major CRT trials = 62-66 years

Wells G. et al. CMAJ 2011 March 8;183(4):421-9

Prevalence of heart failure increases with age

• 1-2% under 65 years; >10% over 65 years of age

• 49% of those with newly diagnosed HF are ≥80 years

McMurray J, Stewart S. Heart 2000;83:596-602

Limited non-randomized evidence for CRT in the elderly

• Similar outcomes ≥80 (n=85) vs. <80 years (n=1096)

• Similar device related complication rates

CRT-D in 36% (ICD shocks only in younger group)

Patient Factors and Comorbidities

Frailty

– Loss of reserves (energy, physical ability, cognition, health) that gives rise to vulnerability
– 10-27% in those >65 years and 26-45% if >85 years

Arch Intern Med 2002;162:2333-41

– Variables important in predicting death, use of acute health care services and long-term care:
  • Dependence on others for the activities of daily living
  • Restricted mobility
  • Poor self rated health
  • Lack of social resources or stress on the caregiver
  • Socioeconomic factors
  • Cognitive impairment

Rockwood K, et al. CMAJ 1994;150:489-95
The Phenotype Model

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Unintentional weight loss (&gt;4.5 kg or ≥5% per year)</td>
</tr>
<tr>
<td>1</td>
<td>Self reported exhaustion (≥3-4 days per week)</td>
</tr>
<tr>
<td>1</td>
<td>Low energy expenditure (&lt;383 in men or &lt;270 in women; kcal/week)</td>
</tr>
<tr>
<td>1</td>
<td>Slow gait speed</td>
</tr>
<tr>
<td>1</td>
<td>Weak grip strength</td>
</tr>
</tbody>
</table>

0 = robust  
1-2 = pre-frail  
≥ 3 = frail

Model excluded cognitive impairment

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><strong>Very Fit</strong> - robust, active, energetic, well motivated and fit; commonly exercise regularly and are in the most fit group for their age.</td>
</tr>
<tr>
<td>2</td>
<td><strong>Well</strong> - without active disease, but less fit than category 1.</td>
</tr>
<tr>
<td>3</td>
<td><strong>Well, with treated co-morbid disease</strong> - disease symptoms are well controlled compared with category 4.</td>
</tr>
<tr>
<td>4</td>
<td><strong>Apparently vulnerable</strong> - although not frankly dependent, commonly complain of being “slowed up” or have disease symptoms.</td>
</tr>
<tr>
<td>5</td>
<td><strong>Mildly frail</strong> - limited dependence on others for instrumental ADL.</td>
</tr>
<tr>
<td>6</td>
<td><strong>Moderately frail</strong> – need help with instrumental &amp; non-instrumental ADL.</td>
</tr>
<tr>
<td>7</td>
<td><strong>Severely frail</strong> - completely dependent on others for ADL; terminally ill.</td>
</tr>
</tbody>
</table>

**ADL** - activities of daily living

*CMAJ* 2005;173:489-95
Patient Factors and Comorbidities

Comorbidities
- Risk factor for frailty
- May interact with HF symptoms (anemia, arthritis, depression, COPD)
- May increase risk of death from non-cardiac conditions

- ≥3 comorbid conditions in 81% CRT-D recipients
  - Renal disease, DM, cerebrovascular disease, COPD
- Most large CRT trials excluded patients with severe renal disease, severe hepatic dysfunction, severe COPD and life expectancy <1 year

# Charlson Co-morbidity Index

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MI, CHF, PVD, Cerebrovascular disease, Dementia</td>
<td>COPD, CT Disease, PUD, Mild Liver Disease, Diabetes</td>
</tr>
<tr>
<td>2</td>
<td>Hemiplegia, Moderate or severe CKD (creatinine &gt;230mmol/L), Diabetes with end organ damage</td>
<td>Any tumor, Leukemia, Lymphoma</td>
</tr>
<tr>
<td>3</td>
<td>Moderate or severe liver disease</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Metastatic solid tumor</td>
<td>AIDS</td>
</tr>
</tbody>
</table>
Charlson Co-morbidity Index (CCI)

High comorbidity burden is associated with an increased risk of mortality, in particular non-sudden cardiac death

- **CCI >4** associated with 49% risk of non-sudden death at 5 years in heart failure patients ¹
- **CCI >5** associated with 42% risk of all cause mortality at 7 years in CRT-D recipients ²
- Risk of sudden death relatively constant with increasing CCI ¹,²

¹ Clarke et al. Can J Cardiol 2011;27:25-61
Patient Factors and Comorbidities

Chronic kidney disease (CKD)

– ~ 1/3 of heart failure patients
  • 50% mortality 2 years after ICD implant

– Severe CKD (GRF<30) was exclusion in landmark trials

– Observational data (N = 787)
  • CRT-D vs. controls with unsuccessful LV lead implant
  • Improved survival for each 10 ml/min/1.73m$^2$ in GFR
  • CRT-D in patients with GFR 30-59 was associated with better survival (HR 2.2, 95% CI 1.3-1.7; p=0.002) plus improved renal / cardiac function versus controls.

Practical Tips

• Objective evaluation of the pre-CRT implantation functional capacity and symptoms is important, particularly in patients in whom there is disparity between the reported symptoms and the clinical assessment, or to distinguish the non-HF related causes of functional limitation

• Comorbid conditions and clinical factors (eg, age, renal function, frailty) should be considered together, and 1 alone should not preclude a patient from CRT implantation

• Therapy should be individualized in accordance with the overall goals of care and patient preference.

• Potential for procedural complications should be considered

• Main focus may be improvement in quality of life rather than longevity
Question One

What do you recommend ?

1. Arrange for pacemaker generator change
2. Arrange for ICD upgrade
3. Arrange for CRT + pacemaker upgrade
4. Arrange for CRT + ICD upgrade
5. Other
Decision is made to upgrade Mr. Pace to CRT-P
The additional risk with an LV lead at the time of PG change is accordingly minimized
Evaluation Process at the Time of Pulse Generator change

- A change in the clinical status of the patient might occur between the time of the original implant and the time of generator replacement.

- Clinical deterioration, alteration in cognitive function, other illnesses (eg, cancer), and QOL should also be considered in the decision-making process.

- A multidisciplinary approach (HF team, geriatrician, family) might be of value in the decision-making process.
Question Two

What would you manage his anticoagulation peri-procedurally?

1. Stop warfarin 5 days prior
2. Stop warfarin 5 days prior / Start LMW Heparin when INR < 2.0
3. Do not stop warfarin (INR 2.0 – 3.0)
4. Stop warfarin / Start Novel OAC prior
5. Other
## Preparation for Procedure

<table>
<thead>
<tr>
<th>New Recommendation 5</th>
<th>Strength</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>We <strong>recommend</strong> that in patients on warfarin for whom perioperative anticoagulation is deemed necessary, continued warfarin is recommended over the use of heparin-based bridging</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

**Values and Preferences.** Places great value on safely preventing peri-operative bleeding and the quality of the evidence.
## Bruise Control

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Heparin Bridging (N=338)</th>
<th>Continued Warfarin (N=343)</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically significant hematoma – # (%)</td>
<td>54 (16.0)</td>
<td>12 (3.5)</td>
<td>0.19 (0.10-0.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Components of Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematoma prolonging hospitalization – # (%)</td>
<td>16 (4.7)</td>
<td>4 (1.2)</td>
<td>0.24 (0.08-0.72)</td>
<td>0.006</td>
</tr>
<tr>
<td>Hematoma requiring interruption of OAC – # (%)</td>
<td>48 (14.2)</td>
<td>11 (3.2)</td>
<td>0.20 (0.10-0.39)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hematoma requiring evacuation – # (%)</td>
<td>9 (2.7)</td>
<td>2 (0.6)</td>
<td>0.21 (0.05-1.00)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Birnie et al. NEJM 2013 May 30;368: 2084-93
Practical Tip

- Perioperative OAC is usually deemed necessary in those patients at high risk of thromboembolism (CHADS$_2$ $\geq$ 3, mechanical mitral valve or $> 5\%$ annual risk).
- No data is presently available on the use of novel oral anticoagulants (NOACs) in this population.
- The rapidity of onset and offset make NOACs more facile to control peri-procedurally.
- Discontinuation of OAC in patients at lower risk of thromboembolism should be considered to minimize the risk of bleeding.
Question Three

What do you do to manage him peri-procedurally?

1. IV antibiotics immediately prior to skin incision
2. IV antibiotics 30 minutes prior to skin incision
3. Hold diuretics the day of his procedure
4. 1 & 3
5. 2 & 3
## Operative Issues

<table>
<thead>
<tr>
<th>New Recommendation 6</th>
<th>Strength</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>We <strong>recommend</strong> that CRT implantation be performed only in facilities that have strict infection prevention control standards.</td>
<td>Strong</td>
<td>Low</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>New Recommendation 7</th>
<th>Strength</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>We <strong>recommend</strong> that appropriate fluoroscopic equipment, radiation shielding and radiation reduction imaging methods be used to minimize radiation exposure to the operator, patient and other staff.</td>
<td>Strong</td>
<td>Low</td>
</tr>
</tbody>
</table>
## Factors to Consider Prior to CRT Implantation

<table>
<thead>
<tr>
<th>Factors</th>
<th>Recommended</th>
<th>For consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Selection</strong></td>
<td>NYHA II, III or ambulatory IV HF, LVEF ≤ 35%, QRS &gt;130 ms if LBBB; sinus rhythm, and absence of severe CKD</td>
<td>QRS &gt;150 ms if non-LBBB; presence of AF; elderly age; evidence of frailty; chronic RV pacing with LVEF &lt; 45%</td>
</tr>
<tr>
<td>Imaging</td>
<td>Evaluation of LVEF: echocardiogram, nuclear imaging, CMR</td>
<td>Imaging for assistance in LV lead placement</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>Continue warfarin if high risk for thromboembolism</td>
<td>NOACs will need to be considered on an individual basis</td>
</tr>
<tr>
<td>Renal Insufficiency</td>
<td>Adequate hydration; hold or decrease diuretics</td>
<td></td>
</tr>
<tr>
<td>Complication</td>
<td>Incidence</td>
<td>Suggested methods to prevent</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>------------</td>
<td>-------------------------------------------------------------------</td>
</tr>
<tr>
<td>Contrast-induced nephropathy</td>
<td>7-43%</td>
<td>Pre-hydration; ↓ dose of diuretics; ↓ dose of contrast, dilution of contrast</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>0.6-1.0%</td>
<td>Extrathoracic puncture, echo or contrast-guided venous puncture, axillary preferred to subclavian; use of cephalic vein</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>1.5%</td>
<td>Use of soft tip guides and access tools</td>
</tr>
<tr>
<td>Phrenic nerve stimulation</td>
<td>up to 13%</td>
<td>Conscious sedation; no paralytic agents; identify all available coronary vein branches; use of multi-polar leads</td>
</tr>
<tr>
<td>Lead related</td>
<td>3.5-18.7%</td>
<td>Appropriate training and adequate procedural volumes</td>
</tr>
<tr>
<td>Device infection</td>
<td>1.3-2.6%</td>
<td>Appropriate antibiotic prophylaxis; chlorhexidine skin preparation; limited shaving</td>
</tr>
</tbody>
</table>
Presented to Device Clinic 3 months later

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Strength</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>We <strong>recommend</strong> that alterations in clinical parameters after versus before CRT be assessed within 6 to 12 months after CRT implantation to guide ongoing HF management.</td>
<td>Strong</td>
<td>Low</td>
</tr>
</tbody>
</table>

**Values and Preferences.** Based on the importance of ensuring optimal medical therapy and deriving important benefit in improvement in reverse remodeling and quality of life with CRT delivery.
Defining Benefit from (Response to) CRT

Lack of consensus

Agreement between methods:

- Poor 75% of the time
- Strong 4% of the time.

Follow up of CRT Implants

Collaboration between heart rhythm specialist, heart failure specialist and other caregivers

Optimization of medications should be done first, as patients may be able to tolerate higher doses of ACE inhibitors/ARBs, beta blockers or aldosterone antagonists with pacing support and improved hemodynamics with CRT delivery

*Evaluation of response (~ 6 months)*
Follow-up & Optimization of CRT Delivery

Throughout Patient Follow-up

- **Optimize Heart Failure Therapy**

  - **Assessment of Response**
    - Functional Capacity (3-12 months)
      - No improvement
    - % Biventricular pacing immediately after implant and at each follow up
      - <95%

  - **Optimize CRT programming**
    - Consider further interventions for non-response
    - Modify LV pacing (turn off, change site, etc)
    - Treatment for AF
    - Assessment of PVC burden

---

CRT Guidelines

www.ccs.ca
## Limited Evidence – Enhancing CRT Response

**Elimination of PVCs**  
AV nodal ablation for rate control  

**OPT of AV & VV timing**  
LV only pacing

<table>
<thead>
<tr>
<th>Study</th>
<th>Comparison</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>RHYTHM ID</td>
<td>Echo OPT vs. nominal VV.</td>
<td>Similar clinical response</td>
</tr>
<tr>
<td>DECREASE-HF</td>
<td>Simultaneous vs. EGM OPT VV.</td>
<td>Similar LV remodeling</td>
</tr>
<tr>
<td>FREEDOM</td>
<td>Usual vs. serial EGM AV &amp; VV OPT.</td>
<td>Similar clinical outcomes</td>
</tr>
<tr>
<td>CLEAR</td>
<td>Echo vs. automatic AV &amp; VV OPT via contractility sensor</td>
<td>Modest to no clinical benefit with contractility sensor</td>
</tr>
<tr>
<td>SMART AV</td>
<td>Echo OPT vs EGM OPT vs fixed AV &amp; VV settings.</td>
<td>Similar clinical outcomes &amp; LV remodeling</td>
</tr>
</tbody>
</table>

**OPT** - optimized
Case 2 Mrs. Block

78 yr old woman

Syncope

CAD
– CABG (1994)
– PCI (2011)

DM

HTN

NYHA II

Echo: LVEF 40%

ASA 81mg OD
Plavix 75mg OD
Lipitor 40mg OD
Gliclazide 30mg
Saxagliptin 2.5mg
Lasix 40mg daily
Candesartan 16 mg OD
Carvedilol (12.5 mg²) stopped
Holter Monitor
Question Four: What do you do next?

1. Implant a single chamber pacemaker
2. Implant a dual chamber pacemaker
3. Implant a dual chamber ICD
4. Implant a CRT pacemaker
5. Implant a CRT defibrillator
<table>
<thead>
<tr>
<th>New Recommendation</th>
<th>Strength</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>We <strong>suggest</strong> that CRT might be considered for patients with new-onset high-degree AV block requiring chronic RV pacing, signs and/or symptoms of heart failure, and LVEF ≤ 45%</td>
<td>Conditional</td>
<td>Moderate</td>
</tr>
</tbody>
</table>
Bi-ventricular versus RV pacing in patients with

– Class I or IIa pacing indication
– NYHA Class I, II or III
– LVEF ≤ 50%
– 2nd or 3rd degree AV block or 1st degree AV block
  + symptoms of PM syndrome or Wenckebach or
  PR > 300 ms during A pace (100 bpm)

1° Endpoint: Death, IV Tx, or ≥ 15% ↑ LVESV

NEJM; 2013: 368:1585-93
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pacemaker (N = 484)</th>
<th>ICD (N = 207)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Biventricular Pacing (N = 243)</td>
<td>Right Ventricular Pacing (N = 241)</td>
</tr>
<tr>
<td>Male sex — no. (%)</td>
<td>181 (74.5)</td>
<td>168 (69.7)</td>
</tr>
<tr>
<td>Age — yr</td>
<td>74.4±10.2</td>
<td>73.8±10.8</td>
</tr>
<tr>
<td>Left ventricular ejection fraction — %</td>
<td>43.4±6.5</td>
<td>42.5±6.6</td>
</tr>
<tr>
<td>Left ventricular ejection fraction &gt;35% — no. (%)</td>
<td>213 (87.7)</td>
<td>215 (89.2)</td>
</tr>
<tr>
<td>Heart rate — beats/min</td>
<td>68.7±23.4</td>
<td>68.7±23.9</td>
</tr>
<tr>
<td>QRS duration — msec</td>
<td>125.4±32.8</td>
<td>124.5±31.1</td>
</tr>
<tr>
<td>NYHA class — no. (%)†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>35 (14.4)</td>
<td>47 (19.5)</td>
</tr>
<tr>
<td>II</td>
<td>141 (58.0)</td>
<td>126 (52.3)</td>
</tr>
<tr>
<td>III</td>
<td>66 (27.2)</td>
<td>68 (28.2)</td>
</tr>
<tr>
<td>Atrioventricular block — no. (%)§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st degree</td>
<td>39 (16.0)</td>
<td>35 (14.5)</td>
</tr>
<tr>
<td>2nd degree</td>
<td>84 (34.6)</td>
<td>70 (29.0)</td>
</tr>
<tr>
<td>3rd degree</td>
<td>120 (49.4)</td>
<td>135 (56.0)</td>
</tr>
<tr>
<td>Bundle-branch block — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>86 (35.4)</td>
<td>75 (31.1)</td>
</tr>
<tr>
<td>Right</td>
<td>52 (21.4)</td>
<td>55 (22.8)</td>
</tr>
</tbody>
</table>
Primary Endpoint

Estimated HR (95% CI)
0.73 (0.59, 0.89)
PP=0.999

Event-Free Rate (%)

Number of Months

Number at Risk
BiV Arm 349
RV Arm 342

0 12 24 36 48 60 72

0 20 40 60 80 100
HF Urgent Care/Mortality

CRT-P
- BiV Arm
- RV Arm

Estimated HR (95% CI)
0.74 (0.57, 0.95)

Number of Months:
- BiV: 243, 198, 146, 105, 71, 48, 24
- AV: 241, 183, 137, 86, 65, 43, 21

CRT-D
- BiV Arm
- RV Arm

Estimated HR (95% CI)
0.74 (0.55, 1.03)

Number of Months:
- BiV: 106, 86, 60, 37, 29, 14, 6
- AV: 101, 73, 52, 38, 29, 16, 6
Who Should Receive CRT in the presence of atrioventricular block?

<table>
<thead>
<tr>
<th>Factor</th>
<th>Favours RV based Pacing</th>
<th>Favours CRT based pacing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Failure Symptoms</td>
<td>No heart failure or NYHA I</td>
<td>NYHA II, III or ambulatory IV heart failure</td>
</tr>
<tr>
<td>LVEF</td>
<td>LVEF &gt; 45%</td>
<td>LVEF ≤ 45%</td>
</tr>
<tr>
<td>Rhythm</td>
<td>Persistent or Permanent AF</td>
<td>Sinus rhythm or paroxysmal AF</td>
</tr>
<tr>
<td>Life Expectancy</td>
<td>&lt; 1 year</td>
<td>&gt; 1 year</td>
</tr>
<tr>
<td>Frailty</td>
<td>Higher frailty index or comorbidity score</td>
<td>Lower frailty index or comorbidity score</td>
</tr>
</tbody>
</table>
Most patients in BLOCK HF had reduced LV systolic function (LVEF ≤ 45%) and symptomatic (NYHA class II/III) HF.

BLOCK HF enrolled patients with de novo implants and the same considerations might not apply in patients who are chronically RV-paced.

There is insufficient randomized data related to CRT upgrade.

The potential benefits of CRT upgrade must be balanced with the significantly higher risk of CRT upgrade versus a generator replacement alone.
US and European guidelines - CRT implantation performed only when LVEF meets guideline criteria for patients with:

- Non-ischemic: ≥ 3 months of appropriate medical therapy
- Ischemic: ≥ 3 months of appropriate medical therapy post-revascularization or ≥ 40 days with no revascularization.

Patient wait times will vary depending on a variety of factors including patient access and service availability

- Invariably, access and hence waits for procedures can vary by physician, centre and, in Canada, by province

No published CRT wait times data, including in Canada.

McMurray JJ, *Eur Heart J* 2012; 33: 1787-847.
Question Five: What is an Acceptable Wait Time for CRT?

1. It should be done in hospital, when indicated.
2. It should be done within 7 days.
3. It should be done within one month of assessment.
4. It should be done within two months of assessment.
5. It should be done within 3 months of assessment.
6. None of the above.
<table>
<thead>
<tr>
<th>New Recommendation</th>
<th>Strength</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>We <strong>suggest</strong> that CRT implantation occur within 6-8 weeks from the decision to implant to avoid preventable adverse events, such as HF hospitalizations and death.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
</tbody>
</table>

Based on data from prior CRT trials and advocating for an acceptable wait-list mortality < 0.5% and HF hospitalization rate < 10%

## Cost Effectiveness of CRT

<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Horizon</th>
<th>Per QALY gained</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linde (2011)</td>
<td>Simulation: REVERSE (NYHA I-II)</td>
<td>10 year</td>
<td>€14 278</td>
<td>CRT vs control</td>
</tr>
<tr>
<td>Neyt (2011)</td>
<td>COMPANION (NYHA III-IV)</td>
<td>Lifetime</td>
<td>€11 200 €56 600</td>
<td>CRT-P vs control CRT-D vs CRT-P</td>
</tr>
<tr>
<td>Noyes (2012)</td>
<td>MADIT-CRT, (NYHA I-II)</td>
<td>4 year</td>
<td>$58 330 With LBBB $16 640</td>
<td>CRT-D vs ICD</td>
</tr>
<tr>
<td>Wells (2013)</td>
<td>RAFT (NYHA II-III)</td>
<td>8 year</td>
<td>$29 869 With QRS ≥150 ms $18 072</td>
<td>CRT-D vs ICD</td>
</tr>
</tbody>
</table>
CRT Cost-Effectiveness

Several analyses of CRT cost-effectiveness of CRT have now been published, including from a Canadian perspective. Although wide ranges have been estimated, improved experience with device insertion resulting in fewer procedural complications and lower rates of post-implantation hospitalization, as well as unit reductions in device costs, has led to more favourable recent estimates. Most studies now suggest that CRT in comparison with optimal medical therapy appears consistently to meet the traditional $50,000/QALY benchmark. Increased utilization of CRT-pacemakers may further improve the cost effectiveness of this therapy, in expanded indications.
Summary

Strong evidence for CRT, as per prior guidelines

Implementation of CRT is difficult but there are key principles that are evidence-based to guide therapy delivery

Given expanding indications, in less-severe forms of heart failure, judicious use and implementation is necessary

Incorporation of the current guidelines into practice is a challenge, with many current programs running at capacity

- Knowledge translation programs regionally will be key
- Evaluation and feedback of CRT utilization
- Expansion of programs to meet unmet need