



National Imaging Associates, Inc.	
Clinical guidelines CARDIAC RESYNCHRONIZATION THERAPY (CRT)	Original Date: February, 2013 Page 1 of 10
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INTRODUCTION

(Epstein 2012; Brignole 2013; Russo 2013; Yancy 2013; Ponikowski 2016)

- Cardiac resynchronization therapy (CRT), which paces two ventricular sites in rapid sequence, also known as biventricular pacing, improves coordination of ventricular contraction in the presence of a wide QRS complex in the setting of systolic heart failure.
- CRT improves cardiac function and quality of life, and it decreases cardiac events and mortality among appropriately chosen patients. The improved survival in patients with CRT is greater than that provided by ICD insertion alone.
- Guiding principles in the consideration of CRT:
 - NYHA class is an important qualifying factor, with candidacy ranging from New York Heart Association (NYHA) class I to *ambulatory* NYHA class IV (See Additional information for NYHA class descriptions)
 - Bundle branch block/intraventricular conduction delay should be persistent, not rate-related (Russo 2013)
 - Guideline directed medical therapy (GDMT) should have been in place continuously for at least 3 months (Epstein 2012; Yancy 2013; Ponikowski 2016), unless a non-elective permanent pacemaker and/or ICD is indicated prior to completion of the 3 months, and CRT would have been likely required even after 3 months of GDMT. Otherwise, recovery of left ventricular ejection fraction (LVEF) from myocardial infarction (40 days) and reversible causes (e.g. ischemia) should be allowed (Katsumoto 2014; Marine 2018) (See Additional Information section regarding GDMT definition).
 - The patient should have expected survival with reasonably good functional status for more than a year (Epstein 2012; Ponikowski 2016; Hernandez-Madrid 2018; Khairy 2014).

- If CRT is indicated, use of an ICD with CRT should be considered (Epstein 2012), and biventricular pacing should occur nearly 100% the time (Yancy 2013, Ponikowski 2016).
- There are no accepted guidelines for CRT in the pediatric population (Motonaga 2014). Available guidelines are extensions of adult indications.
- Elective CRT generator replacement indicators support generator change (Russo 2013).

Indications for Cardiac Resynchronization Therapy (CRT)

(Epstein 2012; Brignole 2013; Yancy 2013; Ponikowski 2016; Russo 2013; Adelstein 2018)

- LVEF $\leq 35\%$, sinus rhythm, left bundle branch block (LBBB) with a QRS ≥ 130 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT (guideline-directed medical therapy) (Ponikowski 2016; Adelstein 2018).
- LVEF $\leq 35\%$, sinus rhythm, a non-LBBB pattern with a QRS duration ≥ 130 ms, and NYHA III or ambulatory class IV symptoms on GDMT (Epstein 2012; Yancy 2013; Ponikowski 2016).
- Atrial fibrillation and LVEF $\leq 35\%$ on GDMT if:
 - the patient requires ventricular pacing or otherwise meets CRT criteria (as with sinus rhythm)
 - AND**
 - AV nodal ablation or pharmacologic rate control allows nearly 100% ventricular pacing with CRT, or else the patient is expected to return to sinus rhythm (Yancy 2013).
- LVEF $< 50\%$ with heart failure (HF) on GDMT, regardless of NYHA class, when patient will require new ventricular pacing that would be $\geq 40\%$ (Brignole 2013; Yancy 2013; Ponikowski 2016; Adelstein 2018; Curtis 2013)
- LVEF $< 50\%$ with HF, with worsening HF, despite GDMT, subsequent to implantation of a conventional pacemaker or ICD that is pacing $\geq 40\%$ (Ponikowski 2016; Adelstein 2018; Curtis 2013)
- LVEF $\leq 30\%$, ischemic etiology of HF, sinus rhythm, LBBB with a QRS duration ≥ 150 ms, and NYHA class I symptoms on GDMT
- LVEF $\leq 35\%$, sinus rhythm, a non-LBBB pattern with a QRS duration ≥ 150 ms, and NYHA class II on GDMT

NOT Indications for Cardiac Resynchronization Therapy (CRT)

- NYHA class I or II symptoms and non-LBBB pattern with QRS duration < 150 ms (Epstein 2012)
- Comorbidities and/or frailty expected to limit survival with good functional capacity to < 1 year.

Indications for CRT in Adult Congenital Heart Disease (Hernandez-Madrid 2018; Khairy 2014)

- Systemic LVEF $\leq 35\%$, sinus rhythm, wide QRS complex ≥ 120 ms with complete left bundle branch block QRS morphology (spontaneous or paced) and NYHA function Class II—ambulatory IV.
- Systemic ventricle, regardless of ejection fraction (EF), intrinsic narrow QRS complex, NYHA function Class I— ambulatory IV and undergoing new device placement or replacement with anticipated requirement for significant ($\geq 40\%$) ventricular pacing (single site pacing from the systemic ventricular apex or mid-lateral wall may be considered as alternative).
- Systemic right ventricle (RV) with an EF $\leq 35\%$, NYHA function Class II - ambulatory IV, and wide QRS complex ≥ 150 ms with a complete right bundle branch block QRS morphology (spontaneous or paced).
- Single ventricle with an EF $\leq 35\%$, NYHA function Class II—ambulatory IV and wide QRS complex ≥ 150 ms due to intraventricular conduction delay causing either a complete right or left bundle branch block QRS morphology (spontaneous or paced).
- Systemic RV with an EF $\geq 35\%$, **sinus rhythm**, wide QRS complex (120–149 ms) with complete right bundle branch block QRS morphology (spontaneous or paced) and NYHA function Class II—ambulatory IV (Hernandez-Madrid 2018).
- Single ventricle with an EF $\geq 35\%$, **sinus rhythm**, wide QRS complex (120–149 ms) due to intraventricular conduction delay causing either a complete right or left bundle branch block QRS morphology (spontaneous or paced) and NYHA function Class II—ambulatory IV (Hernandez-Madrid 2018).
- Cardiac surgery (especially if thoracotomy access is needed for lead implantation) with an intrinsic or paced QRS duration ≥ 150 ms, complete bundle branch block morphology ipsilateral to the systemic ventricle (left or right), NYHA class I - ambulatory IV, and progressive systolic systemic ventricular dysfunction and/or dilatation or expectation of such development regardless of the ejection fraction value, especially if epicardial access is required to implement CRT.
- Systemic RV and significant tricuspid valve regurgitation without a specific EF limit, NYHA function Class I—ambulatory IV, wide QRS complex ≥ 150 ms with a complete right bundle branch block QRS morphology (spontaneous or paced) undergoing surgery for significant tricuspid valve regurgitation.
- Severe subpulmonary RV dysfunction and dilatation despite interventions to decrease RV volume overload (as in Tetralogy of Fallot), NYHA function Class II— ambulatory IV and wide QRS complex ≥ 150 ms due to a complete right bundle branch block.
- Selected adults with CHD, NYHA class IV, and severe systemic ventricular dysfunction in an attempt to delay or avert cardiac transplantation or mechanical support.

NOT an Indication for CRT in Adult Congenital Heart Disease

- CRT is not indicated in patients with a narrow QRS complex (<120 ms) without major electrical activation delay within the failing ventricle.
- CRT is not indicated for patients whose co-morbidities and/or frailty limit survival with good functional capacity to less than 1 year.

Exemption for < 3 Months GDMT
Indications for CRT as the Appropriate Pacing Modality in Special Situations
(Marine 2018; Katsumoto 2014; Russo 2013)

- Criteria are met for a non-elective implantable cardioverter defibrillator (ICD) or a non-elective pacemaker, either initial or replacement, and based upon the low likelihood of improvement in symptoms and adequate recovery of LVEF, despite less than 3 months GDMT for heart failure or < 40 days post myocardial infarction, criteria for CRT are otherwise met.*

*Based on ICD status, in a setting that would warrant CRT as the appropriate pacing modality. This enables avoidance of a second implantation procedure within less than 3 months.

ADDITIONAL INFORMATION

NYHA Class Definitions
(Russo 2013; Colucci 2018)

- Class I: No limitation of functional activity or only at levels of exertion that would limit normal individuals (patient can carry 24 pounds up 8 stairs, play basketball, and shovel soil).
- Class II: Slight limitation of activity. Fatigue, palpitation, or dyspnea with moderate exercise (patient able to dance, garden, walk 4 MPH on level ground, and have sexual intercourse).
- Class III: Marked limitation of activity. Fatigue, palpitation, or dyspnea with minimal activity (patient able to shower, make bed, bowl or golf, dress, and walk 2.5 MPH on level).
- Class IV: Severe limitation of activity. Symptoms even at rest, worse with activity (patient unable to comfortably perform any significant activity).
- Ambulatory Class IV: Class IV heart failure with:
 - no active acute coronary syndrome,
 - no inotropes, AND
 - on GDMT.

Heart Block Definitions
(Epstein 2012)

- First Degree: All atrial beats are conducted to the ventricles, but with a delay of > 200 ms.
- Second Degree: Intermittent failure of conduction of single beats from atrium to ventricles.
 - Type I: Conducted beats have variable conduction times from atrium to ventricles.

- Type II: Conducted beats have uniform conduction times from atrium to ventricles.
- Advanced: Two or more consecutive non-conducted beats (premature atrial beats might not normally be conducted).
- Third Degree: No atrial beats are conducted from atrium to ventricle

Guideline Directed (or Optimal) Medical Therapy in Heart Failure
(Yancy 2013; Yancy 2017)

- Angiotensin converting enzyme inhibitor (ACE-I), angiotensin receptor blocker (ARB), or combined angiotensin receptor inhibitor and neprilysin inhibitor (ARNI)
- Beta blocker (might be less critical in permanent atrial fibrillation, still recommended) (Kotecha 2017)
- Addition of loop diuretic for all NYHA class II – IV patients
- Addition of hydralazine and nitrate for persistently symptomatic African Americans
- Addition of an aldosterone antagonist, provided eGFR is > 30 ml/min and K+ < 5.0
- Not required for consideration of CRT: Ivabradine for NYHA class II – III, when a beta blocker has failed to reduce a sinus rate to < 70 bpm. Ivabradine listed as a class IIa recommendation, while others are class I recommendations. CRT trials antedated routine use of ivabradine.

Pediatric respiratory rate and heart rate by age*

Age group	Respiratory rate	Heart rate
	Median (1st-99th percentile)	Median (1st-99th percentile)
0 to 3 months	43 (25-66)	143 (107-181); term newborn at birth: 127 (90-164)
3 to 6 months	41 (24-64)	140 (104-175)
6 to 9 months	39 (23-61)	134 (98-168)
9 to 12 months	37 (22-58)	128 (93-161)
12 to 18 months	35 (21-53)	123 (88-156)
18 to 24 months	31 (19-46)	116 (82-149)

2 to 3 years	28 (18-38)	110 (76-142)
3 to 4 years	25 (17-33)	104 (70-136)
4 to 6 years	23 (17-29)	98 (65-131)
6 to 8 years	21 (16-27)	91 (59-123)
8 to 12 years	19 (14-25)	84 (52-115)
12 to 15 years	18 (12-23)	78 (47-108)
15 to 18 years	16 (11-22)	73 (43-104)

* The respiratory and heart rates provided are based upon measurements in awake, healthy infants and children at rest. Many clinical findings besides the actual vital sign measurement must be taken into account when determining whether a specific vital sign is normal in an individual patient. Values for heart rate or respiratory rate that fall within normal limits for age may still represent abnormal findings that are caused by underlying disease in a particular infant or child (Fleming 2011; Fleegler, 2018).

Abbreviations

ACE-I	Angiotensin converting enzyme inhibitor
ARNI	combined angiotensin receptor inhibitor and neprilysin inhibitor
AV	Atrioventricular
CAD	Coronary artery disease, same as ischemic heart disease
CHF	Congestive heart failure
CRT pacing)	Cardiac resynchronization therapy (also known as biventricular
CHD	Congenital heart disease
ECG	Electrocardiogram
eGFR	Estimated glomerular filtration rate
EPS	Electrophysiologic Study
GDMT	Guideline-Directed Medical Therapy
HF	Heart Failure
HRS	Heart Rhythm Society
HV	His-ventricular
ICD	Implantable cardioverter-defibrillator
LBBB	left bundle-branch block

LV	Left ventricular/left ventricle
LVEF	Left ventricular ejection fraction
MI	Myocardial infarction
ms	milliseconds
NYHA	New York Heart Association
STEMI	ST-elevation Myocardial Infarction
SND	Sinus node dysfunction
VT	Ventricular tachycardia

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Reviewed / Approved by

A handwritten signature in black ink, appearing to read 'CCCarney', is positioned between the text 'Reviewed / Approved by' and 'Caroline Carney, MD, Chief Medical Officer'.

Caroline Carney, MD, Chief Medical Officer