PROPOSED Local Coverage Determination (LCD): Cardiac Resynchronization Therapy (CRT) (DL39080)

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CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
Palmetto GBA	10111 - MAC A	10111 - MAC A	J - J	Alabama
Palmetto GBA	10112 - MAC B	10112 - MAC B	J - J	Alabama
Palmetto GBA	10211 - MAC A	10211 - MAC A	J - J	Georgia
Palmetto GBA	10212 - MAC B	10212 - MAC B	J - J	Georgia
Palmetto GBA	10311 - MAC A	10311 - MAC A	J - J	Tennessee
Palmetto GBA	10312 - MAC B	10312 - MAC B	J - J	Tennessee
Palmetto GBA	11201 - MAC A	11201 - MAC A	J - M	South Carolina

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Palmetto GBA	11202 - MAC B	11202 - MAC B	J - M	South Carolina
Palmetto GBA	11301 - MAC A	11301 - MAC A	J - M	Virginia
Palmetto GBA	11302 - MAC B	11302 - MAC B	J - M	Virginia
Palmetto GBA	11401 - MAC A	11401 - MAC A	J - M	West Virginia
Palmetto GBA	11402 - MAC B	11402 - MAC B	J - M	West Virginia
Palmetto GBA	11501 - MAC A	11501 - MAC A	J - M	North Carolina
Palmetto GBA	11502 - MAC B	11502 - MAC B	J - M	North Carolina

Proposed LCD Information

Document Information

Source LCD ID
N/A

Proposed LCD ID
DL39080

Proposed LCD Title
Cardiac Resynchronization Therapy (CRT)

AMA CPT / ADA CDT / AHA NUBC Copyright

Statement

CMS National Coverage Policy

This Local Coverage Determination (LCD) supplements but does not replace, modify, or supersede existing Medicare applicable National Coverage Determinations (NCDs) or payment policy rules and regulations for Biventricular Pacing/Cardiac Resynchronization Therapy (CRT) or Implantable Cardiac Defibrillators. Relevant Centers for Medicare and Medicaid Services (CMS) manual instructions and policies may be found in the following Internet-Only Manuals (IOMs) published on the CMS website.

Title XVIII of the Social Security Act, §1862(a)(1)(A) states that no Medicare payment shall be made for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury

CMS Internet-Only Manual, Pub. 100-03, Medicare National Coverage Determinations (NCD) Manual, Chapter 1, Part 1, §20.4 Implantable Cardioverter Defibrillators (ICDs) and §20.8 Cardiac Pacemakers

CMS Internet-Only Manual, Pub. 100-08, Medicare Program Integrity Manual, Chapter 13, §13.5.4 Reasonable and Necessary Provisions in LCDs

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

Heart failure (HF) is common and carries a poor prognosis. It is also associated with a high burden of illness, high resource utilization, and frequent hospitalizations.

A proportion of patients with HF exhibit dyssynchronous contractions of the left and right ventricles due to conduction system disease. Dyssynchrony further depresses the already impaired pumping ability of the heart.

CRT is a form of cardiac pacing used in patients with systolic HF and dyssynchronous ventricular activation. CRT involves pacing of the left ventricle (LV) and usually simultaneous or nearly simultaneous pacing of the right ventricle (RV) to restore ventricular synchrony and thus improve LV systolic function and clinical outcomes for selected patients.

Electrical dyssynchrony (prolonged QRS on electrocardiogram (ECG)) is associated with adverse clinical outcomes. One-third of patients with HF with reduced ejection fraction (EF) have a QRS complex > 120 ms.[1] Many studies have demonstrated that LV electromechanical activation in patients with baseline or pacing-induced left bundle branch block (LBBB) is hemodynamically impacting in an adverse way. In the patient with cardiomyopathy, this hemodynamic inefficiency further reduces cardiac output, makes functional mitral regurgitation worse, and causes even more adverse LV remodeling.[2]

For those who respond to CRT, this therapy provides immediate hemodynamic benefits such as improved LV systolic function, LV reverse remodeling, increased systolic blood pressure, increased cardiac output, and increased contractility. The CARE-HF trial noted that CRT was associated with increases in LVEF and decreases in LV end systolic volume indices.[3] Clearly CRT has progressive cardiac structural benefits. CRT increases myocardial contractility without increasing myocardial oxygen consumption.

Candidacy for CRT is based on LVEF, QRS duration, QRS pattern, New York Heart Association (NYHA) functional class, and need for ventricular pacing.

Some patients with HF are also at high risk for life-threatening heart rhythms such as ventricular tachycardia and ventricular fibrillation. Most patients being considered for CRT due to EFs $\leq$ 35% should also be considered for implantable cardioverter-defibrillator (ICD) placement.

This LCD does not address the decision-making between CRT-pacemaker (CRT-P) or CRT-defibrillator (CRT-D) options other than to emphasize that those patients receiving CRT-D must not only meet coverage criteria in this policy but also meet the NCD for Implantable Automatic Defibrillators (20.4) criteria for the defibrillator portion of their therapy in order to be considered for coverage.

This LCD provides for CRT coverage with a few identified limitations.

Covered Services:

CRT will be considered medically necessary when the following criteria for a given beneficiary are met:

- LVEF ≤ 35%, with ischemic or non-ischemic cardiomyopathy, on maximally tolerated guideline-directed medical therapy (GDMT) for at least 3 months and with no reversible causes; *and*
    a. QRS ≥ 150 ms; and
    b. Any type bundle branch block with evidence of dyssynchrony; and
    c. NYHA class III or ambulatory IV HF
- LVEF ≤ 35%, on maximally tolerated GDMT for at least 3 months and with no reversible causes; *and*
    a. QRS ≥ 150 ms; and
    b. LBBB; and
    c. NYHA classes II, III or ambulatory IV HF
- LVEF ≤ 35%, on maximally tolerated GDMT for at least 3 months and with no reversible causes; *and*
    a. QRS 130-149 ms; and
    b. LBBB; and
    c. NYHA class II, III or ambulatory IV HF
- In patients with atrial fibrillation (AF) or in sinus rhythm who have an indication for pacemaker implant for second or third degree atrioventricular (AV) block (including those who have or will have AV nodal ablation), or very prolonged first degree block with PR > 300 ms, *and*:
    a. with an EF < 50%; and
    b. with NYHA I, II or III class; and
    c. anticipated frequent ventricular pacing
- Patients who are being paced from the RV frequently (generally considered at least > 40% of the time) and who develop worsening HF symptoms (NYHA class II-IV) with a decline in LVEF to a value < 40% may be considered for upgrade to CRT.*

*For an upgrade from standard pacing to CRT, this A/B Medicare Administrative Contractor (MAC) would expect documentation narrative regarding the risk-benefit balance for that individual patient and his/her degree of HF, QRS duration/morphology, etc. A "stand-alone" upgrade in patients with an existing pacemaker or implanted cardiac defibrillator should be considered carefully and based on the individual patient's unique circumstances. Upgrades to CRT from conventional RV pacing at the time of a needed generator change will be covered per the usual criteria as noted in all preceding coverage bullets.

In patients with AF and HF for whom CRT is planned, narrative in the medical record is expected regarding plans for AF control so that CRT may be most effective. It is understood that the future for such patients cannot be predicted and thus future therapy cannot be defined precisely; however, a reference to the need for focus on AF control is desirable.

HF patients with concomitant moderate-severe chronic obstructive pulmonary disease (COPD) should have documentation related to a reasonable hope for CRT response with a clinically guided rationale that the dyspnea is at least in part significantly related to HF.

Patients with end stage or advanced renal disease may benefit less from CRT. Documentation regarding the risk-benefit balance in these patients would also be expected.

Patients who meet all CMS coverage requirements for cardiac pacemakers, and who meet the criteria in the NCD for

Implantable Automatic Defibrillators (20.4), may receive the combined devices in 1 procedure, at the time the biventricular pacemaker is clinically indicated.

Patients with an existing CRT device may receive a generator replacement if it is required due to the end of battery life, elective replacement indicator (ERI), or device/lead malfunction.

Limitations:

Noncovered Services: (CRT is unlikely to offer benefit and is probably associated with harm)

1. Patients with a QRS < 130 ms (Exception to this non-coverage criterion would be in the case of patients undergoing AV nodal ablation or in need of RV pacing (due to second- or third-degree block or very long first degree block) that is expected to occur a majority of the time.)
2. Patients with an EF $\geq$ 50%
3. CRT in patients with non-ambulatory NYHA IV HF symptoms or on chronic inotropic HF therapy or with LV assist devices in place

Summary of Evidence

For purposes of this LCD, international society guidelines were reviewed as well as evidence-based literature.

Major international society guidelines (for a period spanning 2011-2017) for CRT implantation were also reviewed and are noted in the various tables below for reference purposes. The American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guidelines published in 2013 agreed with the 2012 focused update of the 2008 guidelines published by the ACCF/AHA/Heart Rhythm Society. These documents, considered together, can be referred to as the ACC/AHA/HRS guidelines. Since these guidelines in 2013, there have been several focused updates of HF published by ACC/AHA/Heart Failure Society of America (HFSA). None of these updates changed the CRT recommendations. Additional guidelines reviewed were the European Society of Cardiology (ESC) guidelines for HF of 2016 and the 2013 ESC European Heart Rhythm Associate guidelines for cardiac pacing and CRT, 2014 National Institute of Health and Care Excellence (NICE) guidelines for ICD and CRT, and the 2017 Canadian Cardiovascular Society Guidelines for the management of HF. Although the international societies provide consistent recommendations for most CRT indications, key differences are noted related to QRS duration, bundle branch block morphology, patient populations with AF, and the patient population likely to be dependent on RV pacing. It is important to note that the timing of the various publications must be considered as the lag time between evidence development and guideline work toward publication no doubt explains some of the discrepancies that currently exist.

Evidence Related to CRT

Cazeau, et al. conducted 1 of the earliest single blind, randomized, controlled crossover studies to examine 67 patients with severe HF (NYHA class III) with normal sinus rhythm (NSR) and a QRS duration > 150 ms who had received a transvenous atrio-biventricular pacemaker. Responses of the patients were compared during 2 periods: a 3-month period of inactive pacing and a 3-month period of active pacing. The primary end point was distance walked in 6 minutes and secondary end points were quality of life by questionnaire, peak oxygen consumption, hospitalization for HF, patients' treatment preference, and mortality rate. Forty-eight patients completed both phases. The mean distance walked in 6 minutes was 22% greater with active pacing ($P<0.001$), the quality-of-life score improved by 32% ($P<0.001$), peak oxygen uptake increased by 8% ($P<0.03$), hospitalizations were decreased by two thirds ($P<0.05$), and active pacing was preferred by 85% of the patients ($P<0.001$).[4]

Similarly, Abraham, et al. conducted a double-blind trial with 453 patients with moderate-to-severe symptoms of HF associated with an EF of 35% or less and a QRS interval of 130 ms or more and randomly assigned them to a CRT group (228 patients) or to a control group (225 patients) for 6 months, while continuing their conventional therapy for HF. Primary end points were the NYHA functional class, quality of life, and distance walked in 6 minutes. As compared to the control group, the patients assigned to CRT experienced an improvement in the distance walked in 6 minutes (P=0.005), functional class (P<0.001), quality of life (P=0.001), time on a treadmill during exercise testing (P=0.001), and EF (+4.6% vs. -0.2%, P<0.001). Fewer patients in the CRT group required hospitalization (8% vs. 15%) or intravenous medications (7% vs. 15%) treatment of HF (P<0.05 for both comparisons).[5]

In 2005 Cleland, et al. (CARE-HF) published results which looked at morbidity and mortality via a multicenter, international randomized trial involving 813 patients with HF and cardiac dyssynchrony. The patients had NYHA class III or IV HF and were receiving standard pharmacologic therapy. They were randomly assigned to either medical therapy alone or with cardiac resynchronization. The primary end point was the time to death from any cause or an unplanned hospitalization for a major cardiovascular event. The principal secondary end point was death from any cause. These patients were followed for a mean of 29.4 months. The primary end point was reached by 159 patients in the CRT group, as compared with 224 patients in the medical-therapy group (39% vs. 55%; hazard ratio (HR), 0.63; 95% confidence interval (CI), 0.51 to 0.77; P<0.001). There were 82 deaths in the CRT group, as compared with 120 in the medical-therapy group (P<0.002). As compared with medical therapy, CRT reduced the interventricular mechanical delay, the end-systolic volume index (by 16.7% at 3 months and 29.6% at 18 months), and the area of the mitral regurgitant jet; increased the LVEF (by 3.7% at 3 months and 6.9% at 18 months); and improved symptoms and the quality of life (P<0.01 for all comparisons).[3]

The REVERSE study of 2008 by Linde, et al. looked at the impact of CRT in NYHA class I and II patients with previous HF symptoms. Six hundred and ten patients with class I or II NYHA HF and a QRS duration ≥ 120 ms and an EF ≤ 40% received a CRT-D device and were randomly assigned to CRT-ON (N=419) or a CRT-OFF control group (N=191) for 12 months. The primary end point was a HF response which could be improved, unchanged or worsened. The prospectively powered secondary end point was LV end-systolic volume index. Hospitalization for worsening HF was evaluated in a prospective secondary analysis of health care use. Results showed that 16% of the CRT-ON group reported worsening as compared with 21% in the CRT-OFF group (P=0.10). Patients in the CRT-ON group experienced a greater improvement in LV end-systolic volume index (-18.4 +/- 29.5 ml/m^2 vs. -1.3 +/- 23.4 ml/m^2, P<0.0001) and other measures of LV remodeling. Time-to-first HF hospitalization was significantly delayed in the CRT-ON on group (P=0.03). The results led to the conclusion that CRT in combination with optimal medical therapy (+/- defibrillator) reduced the risk for HF hospitalization and improved ventricular structure and function in NYHA functional class II and NYHA functional class I patients with previous HF symptoms.[6]

As published in 2004, Bristow, et al. studied whether prophylactic CRT with or without a defibrillator would reduce the risk of death and hospitalization among patients with advanced chronic HF and intraventricular conduction delays. A total of 1520 patients who had advanced HF (NYHA class III or IV) due to ischemic or non-ischemic cardiomyopathies and a QRS interval of at least 120 ms were randomly assigned in a 1:2:2 ratio to receive optimal medical management (diuretics, angiotensin-converting-enzyme inhibitors, beta-blockers, and spironolactone) alone or in combination with CRT with either a pacemaker or a pacemaker-defibrillator. The primary end point was the time to death from or hospitalization for any cause. As compared with optimal medical management alone, CRT with a pacemaker decreased the risk of the primary end point (HR, 0.81; P=0.014), as did CRT with a pacemaker-defibrillator (HR, 0.80; P=0.01). The risk of the combined end point of death from or hospitalization for HF was reduced by 34% in the pacemaker group (P<0.002) and by 40% in the pacemaker-defibrillator group (P<0.001 for the comparison with the pharmacologic-therapy group). A pacemaker reduced the risk of the secondary end point of death from any cause by 24% (P=0.059), and a pacemaker-defibrillator reduced the risk by 36% (P=0.003).[7]

An observational registry study compared outcomes in patients with HF with QRS duration of ≥ 120 ms and LVEF of ≤ 35% receiving CRT (n=4471) versus those who got no device therapy (n=4888). The first cohort was gathered

from the National Cardiovascular Data Registry's ICD Registry and the second cohort was pulled from the Acute Decompensated Heart Failure National Registry (ADHERE) and then both registries were linked with Medicare claims to evaluate long term outcomes. After multi-variable adjustment, CRT-D use was associated with lower 3-year risks of death (HR, 0.52; 95% CI, 0.48-0.56; P<0.001), all-cause readmission (HR, 0.69; 95% CI, 0.65-0.73; P<0.001), and cardiovascular readmission (HR, 0.60; 95% CI, 0.56-0.64; P<0.001).[8]

Evidence based literature overlaps considerably in terms of various important subgroup patient population characteristics such as LVEF, QRS duration, QRS morphology, NYHA functional class, etc. All the evidence noted below has importance in a variety of different ways regardless of its inclusion within any particular section. International specialty society guidance for various categories of patients is also noted below.

Additional Evidence Pertinent to QRS Duration and/or QRS Morphology

McAlister, et al. (2007)

A meta-analysis of 14 randomized trials including 4420 patients looked at the evidence base at that time regarding the efficacy of CRT in patients with LV systolic dysfunction. Nearly all these patients had NYHA class III or IV symptoms and all had EFs between 21-30%. The mean QRS range was 155-209 ms. The analysis revealed that CRT increased the likelihood of improvement by at least 1 NYHA class in 59% of recipients. In addition to the randomized trials, this same meta-analysis also included 106 studies with 9209 patients for CRT effectiveness review and 89 studies with 9677 patients for safety outcomes. The same NYHA class, EF, and QRS duration characteristics were present. CRT improved LVEF (weighted mean difference, 3.0%; 95% CI, 0.9%-5.1%) and quality of life (weighted mean reduction in Minnesota Living With Heart Failure Questionnaire, 8.0 points; 95% CI, 5.6-10.4 points). CRT decreased hospitalizations by 37% (95% CI, 7%-57%), and all-cause mortality decreased by 22% (95% CI, 9%-33%). Implant success rate was 93.0% (95% CI, 92.2%-93.7%) and 0.3% of patients died during implantation (95% CI, 0.1%-0.6%). During a median 11-month follow-up, 6.6% (95% CI, 5.6%-7.4%) of CRT devices exhibited lead problems and 5% (95% CI, 4%-7%) malfunctioned.[9]

Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT)

This trial was done to determine whether QRS morphology identifies patients who benefit from CRT with a defibrillator. HF event or death was the primary end point of the trial. Death, HF event, ventricular tachycardia, and ventricular fibrillation were secondary end points. Among 1817 patients with NYHA class I or II HF, 1281 (70%) had LBBB, 228 (13%) had right bundle branch block (RBBB), and 308 (17%) had nonspecific intraventricular conduction disturbances. The latter 2 groups were defined as non-LBBB groups. HRs for the primary end point for CRT-D patients versus patients who only received an ICD were significantly (P<0.001) lower in LBBB patients (0.47; P<0.001) than in non-LBBB patients (1.24; P=0.257). The risk of ventricular tachycardia, ventricular fibrillation, or death was decreased significantly in CRT-D patients with LBBB but not in non-LBBB patients. Echocardiographic parameters showed significantly (P<0.001) greater reduction in LV volumes and increases in EF with CRT-D in LBBB than in non-LBBB patients. The primary finding of this study was that HF patients with a wide QRS complex (≥ 130 ms) and with an LBBB pattern derived significantly more benefit from CRT than patients with non-LBBB QRS morphologies (RBBB and intraventricular conduction delay (IVCD)). Non-LBBB patients did not benefit clinically from CRT-D therapy, with some trends toward a nonsignificant increase in primary and secondary end points. And the findings regarding the clinical benefit of CRT-D in LBBB but not in non-LBBB patients were consistent throughout the MADIT-CRT population evaluated by age, sex, NYHA class, ischemic or non-ischemic origin, QRS duration, and baseline hemodynamic status. The findings also showed that the echocardiographically measured remodeling effect of CRT in LBBB patients was significantly more pronounced than in non-LBBB patients. Interestingly, CRT in non-LBBB patients also contributed to a significant reduction in the measured volumes and an increase in EF; however, reduction in volumes and improved EF in non-LBBB patients did not translate to a reduction in HF events. In

conclusion, the MADIT-CRT trial demonstrated that HF patients with NYHA class I (ischemic only) or NYHA class II (both ischemic and non-ischemic) and EF ≤ 30% who presented with LBBB derived substantial clinical benefit from CRT-D: a reduction in HF progression and a reduction in the risk of ventricular tachyarrhythmias. No evidence of clinical benefit was observed in patients with a non-LBBB QRS pattern (RBBB or IVCD).[10]

Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction (REVERSE)

Continuing analysis of this study's results (Gold, et al. 2012) assessed the impact of baseline QRS duration and morphology and the change in QRS duration with pacing on CRT outcomes in mild HF. Baseline and CRT-paced QRS durations and baseline QRS morphology were evaluated by blinded core laboratories. The mean baseline QRS duration was 151+/-23 ms, and 60.5% of subjects had LBBB. Paired baseline and 12-month echocardiographic data were available for 509 patients, with an overall LV end-diastolic volume index (LVESVi) reduction of 18.3±28.9 mL/m^2 in the CRT-ON arm. Patients with LBBB experienced a 25.3 mL/m^2 mean reduction in LV end-systolic volume index (P<0.0001), whereas non-LBBB patients had smaller, nonsignificant decreases (6.7 mL/m^2; P=0.18). Similarly, the clinical composite score (CCS) improved with CRT for LBBB subjects (odds ratio, 0.530; P=0.0034) but not for non-LBBB subjects (odds ratio, 0.724; P=0.21). For clarification, the CCS was based on response groups of worsened, unchanged, or improved. Patients were judged to be worsened if they died, were hospitalized for worsening HF, crossed over to or permanently discontinued double-blind treatment owing to worsening HF, or demonstrated worsening in NYHA class or moderate to marked worsening of patient global assessment. Patients were judged to be improved if they had not worsened and had demonstrated improvement in NYHA class and/or a moderate to marked improvement in patient global assessment. Patients who were not worsened or improved were classified as unchanged. A significant increase in EF was observed only in the LBBB cohort. This analysis suggested that the benefit of CRT in mild HF is strongly dependent on QRS morphology and duration. Specifically, echocardiographic changes in volumes and EF were noted only in the LBBB cohort, and the magnitude of this response was strongly dependent on baseline QRS duration. Similarly, improvement in the CCS with CRT was larger in the LBBB cohort, and again it was related strongly to baseline QRS duration.[11]

Stavrakis, et al. (2012)

This was a meta-analysis of 5 randomized clinical trials to evaluate the impact of QRS duration on the efficacy of CRT. Only trials that reported subgroup data according to QRS duration were included. Three of the trials enrolled patients with mild to moderate HF and then compared those treated with CRT-D versus CRT alone. The other 2 trials also included patients with advanced HF and compared those who received CRT versus those managed only by medical therapy. This total of 5 trials involved 6501 patients (4437 with QRS ≥ 150 ms and 2064 with QRS < 150 ms). Based on the pooled data of all 5 trials, CRT significantly decreased the primary endpoint of death or hospitalization for HF in patients with QRS ≥ 150 ms by 42% (HR = 0.58, 95% CI: 0.50-0.68; P<0.00001), but not in patients with QRS < 150 ms (HR = 0.95, 95% CI: 0.83-1.10; P = 0.51). These results were consistent across all degrees of HF severity.[12]

Cleland, et al. (2013)

This study group conducted a meta-analysis of 5 randomized trials (CARE-HF, MIRACLE, REVERSE, MIRACLE-ICD and RAFT) comparing CRT either with no active device or with a defibrillator. Many baseline variables were also examined: age, sex, NYHA class, etiology, QRS morphology, QRS duration, LVEF, and systolic blood pressure. Outcomes were all-cause mortality and first hospitalization for HF or death. The total number of patients was 3782 and all were in sinus rhythm. For this group, the median age was 66 (58–73) years, the median QRS duration was 160 (146–176) ms, the median LVEF was 24 (20–28)%, and 78% had LBBB. A multivariable model suggested that only QRS duration predicted the magnitude of the effect of CRT on outcomes. Further analysis suggested increasing benefit with increasing QRS duration. The 95% confidence bounds excluding 1.0 at ☐140 ms for each endpoint

suggested a high probability of substantial benefit from CRT when QRS duration exceeded 140 ms. The overall conclusion was that QRS duration is a powerful predictor of the effects of CRT on morbidity and mortality in patients with symptomatic HF and LV systolic dysfunction who are in sinus rhythm. QRS morphology did not provide additional information about clinical response.[13]

Zusterzeel, et al. 2014

Much of the evidence-based literature related to CRT is notably underrepresented by female study subjects. This meta-analysis examined that specific issue with regard to LBBB morphology and QRS duration treated by CRT. Individual patient data were pooled from 3 CRT-D vs. ICD trials (4076 patients) predominated by class II HF. Follow up occurred up to 3 years. The main outcome measured was time to HF event or death (primary) and death alone (secondary). The results demonstrated that women benefited from CRT-D more than men. The main difference occurred in patients with LBBB and a QRS of 130 to 149 ms. In this group, women had a 76% reduction in HF or death (absolute CRT-D to ICD difference, 23%; HR, 0.24, [95% CI, 0.11-0.53]; P<0 .001) and a 76% reduction in death alone (absolute difference 9%; HR, 0.24, [95% CI, 0.06-0.89]; P=0.03), while there was no significant benefit in men for HF or death (absolute difference 4%; HR, 0.85 [95% CI, 0.60-1.21]; P=0.38) or death alone (absolute difference 2%; HR, 0.86 [95% CI, 0.49-1.52]; P=0.60). Neither women nor men with LBBB benefited from CRT-D at QRS shorter than 130 ms, while both sexes with LBBB benefited at QRS of 150 ms or longer.[14]

Cunnington, et al. 2015

This meta-analysis was done to better define the effect of CRT within randomized controlled trials that reported outcomes in patients with non-LBBB QRS morphology. Five randomized controlled trials were analyzed with a total number of patients at 6523 of whom 1766 had non-LBBB QRS morphology. CRT was not associated with a reduction in death and/or HF hospitalization in patients with non-LBBB QRS morphology (HR 0.99 95% CI 0.82 to 1.20).[15]

Peterson, et al. 2013

This retrospective cohort study was done on Medicare beneficiaries in the National Cardiovascular Data Registry's ICD Registry between 2006 and 2009 who had received CRT-D. This group was then also stratified for the presence/absence of LBBB and QRS $\geq$ 150 ms or 120-149 ms. Outcomes measured included all-cause mortality; all-cause, cardiovascular, and HF readmission; and complications. Patients underwent follow-up for up to 3 years. Among 24,169 patients, both the unadjusted rate and adjusted risk of 3-year mortality were lowest among patients with LBBB and QRS duration of 150 ms or greater (20.9%), compared with LBBB and QRS duration of 120 to 149 ms (26.5%; adjusted HR, 1.30 [99% CI, 1.18-1.42]), no LBBB and QRS duration of 150 ms or greater (30.7%; HR, 1.34 [99% CI, 1.20-1.49]), and no LBBB and QRS duration of 120 to 149 ms (32.3%; HR, 1.52 [99% CI, 1.38-1.67]). The unadjusted rate and adjusted risk of 1-year all-cause readmission were also lowest among patients with LBBB and QRS duration of 150 ms or greater (38.6%), compared with LBBB and QRS duration of 120 to 149 ms (44.8%; adjusted HR, 1.18 [99% CI, 1.10-1.26]), no LBBB and QRS duration of 150 ms or greater (45.7%; HR, 1.16 [99% CI, 1.08-1.26]), and no LBBB and QRS duration of 120 to 149 ms (49.6%; HR, 1.31 [99% CI, 1.23-1.40]). The stated conclusion noted that amongst fee-for-service Medicare beneficiaries undergoing CRT-D in community clinical practice who had LBBB and QRS $\geq$ 150 ms compared with LBBB and QRS < 150 ms or no LBBB regardless of QRS duration, there was lower risk of all-cause mortality and of all-cause cardiovascular and HF readmissions.[16]

Echocardiography Guided Cardiac Resynchronization Therapy (EchoCRT)

This study by Ruschitzka, et al. (2013), as an international, multicenter (115) randomized clinical trial, was done to evaluate the effect of CRT in patients with NYHA class III or IV HF on optimized medical therapy, an LVEF of 35% or

less, a QRS duration of less than 130 ms, an LV end-diastolic diameter ≥ 55 mm, and echocardiographic evidence of LV dyssynchrony. All patients underwent CRT-D device implantation and were randomly assigned to have CRT capability turned on or off. After randomization, patients underwent follow-up at 1 month and 3 months and then every 3 months thereafter. Echocardiography was done at 6 and 12 months. The primary efficacy outcome was the composite of death from any cause or first hospitalization for worsening HF. The study, begun in 2008, was stopped for futility and a potential for harm in 2013. At that time, the 809 patients who had undergone randomization (404 to CRT and 405 to control) had been followed for a mean of 19.4 months. The mean QRS duration measured by the centers was 105.0 ms for the CRT group and 105.4 ms for the control group. The primary outcome occurred in 116 of 404 patients in the CRT group as compared with 102 of 405 in the control group (28.7% vs. 25.2%; HR, 1.20; 95% CI, 0.92 to 1.57; P=0.15). There were 45 deaths in the CRT group and 26 in the control group (11.1% vs. 6.4%; HR, 1.81; 95% CI, 1.11 to 2.93; P=0.02). The use of CRT did not reduce the rate of death from any cause or first hospitalization for HF and mortality may have been increased among patients with symptomatic HF, an LVEF of 35% or less, and a QRS duration of less than 130 ms.[17]

Evaluation of Resynchronization Therapy for Heart Failure (LESSER-EARTH)

This trial was a randomized, double-blind, 12-center study that was designed to compare the effects of active and inactive CRT in patients with severe LV dysfunction and a QRS duration < 120 ms. Only 85 patients were randomized before the trial was stopped due to futility and safety concerns. Changes in exercise duration after 12 months were no different in patients with and without active CRT. Similarly, no significant differences were observed in LV end-systolic volumes (-6.4 mL [95% CI, -18.8 to 5.9] versus 3.1 mL [95% CI, -9.2 to 15.5]; P=0.28) and EF (3.3% [95% CI, 0.7-6.0] versus 2.1% [95% CI, -0.5 to 4.8]; P=0.52). CRT was associated with a significant reduction in the 6-minute walk distance (-11.3 m [95% CI, -31.7 to 9.7] versus 25.3 m [95% CI, 6.1-44.5]; P=0.01), an increase in QRS duration (40.2 ms [95% CI, 34.2-46.2] versus 3.4 ms [95% CI, 0.6-6.2]; P<0.0001), and a nonsignificant trend toward an increase in HF-related hospitalizations (15 hospitalizations in 5 patients versus 4 hospitalizations in 4 patients). The conclusion was drawn that in patients with an LVEF </= 35%, symptoms of HF, and a QRS duration < 120 ms, CRT did not improve clinical outcomes or LV remodeling and was associated with potential harm.[18]

Patients with LBBB-International Specialty Society Guidance[19]

Guideline (Year)	QRS ≥ 150 ms	QRS ≥ 150 ms	QRS 130-149 ms	QRS 130-149 ms	QRS 120-129 ms	QRS 120-129 ms
	NYHA Functional Class III/IV	NYHA Functional Class II	NYHA Functional Class III/IV	NYHA Functional Class II	NYHA Functional Class III/IV	NYHA Functional Class II
ESC HFA (2016)	I, A	I, A	I, B	I, B	III, A	III, A
ESC EHRA (2013)	I, A	I, A	I, B	I, B	I, B	I, B
ACC/AHA/HRS (2013)	I, A	I, B	IIa, B	IIa, B	IIa, B	IIa, B
CCS (2017)	I, High	I, High	I, High	I, High	III, Moderate	III, Moderate

Patients with non-LBBB-International Specialty Society Guidance[19]

Guideline (Year)	QRS ≥ 150 ms	QRS ≥ 150 ms	QRS 130-149 ms	QRS 130-149 ms	QRS 120-129 ms	QRS 120-129 ms
	NYHA Functional	NYHA Functional	NYHA Functional	NYHA Functional	NYHA Functional	NYHA Functional

	Class III/IV	Class II	Class III/IV	Class II	Class III/IV	Class II
ESC HFA (2016)	IIa, B	IIa, B	IIb, B	IIb, B	III, A	III, A
ESC EHRA (2013)	IIa, B	IIa, B	IIb, B	IIb, B	IIb, B	IIb, B
ACC/AHA/HRS (2013)	IIa, A	IIb, B	IIb, B	III, B	IIb, B	III, B
CCS (2017)	IIb, Low	IIb, Low	—	—	III, Moderate	III, Moderate

EHRA guidelines provide a Class III recommendation, Level of Evidence: B, for a QRS duration <120 ms; whereas the HFA provides a III recommendation, Level of Evidence: A, for QRS duration <130 ms; and CCS states that CRT should not be used in patients with QRS duration <130 ms. NICE guidelines clearly state that a CRT is not indicated in NYHA functional class IV with a QRS <120 ms. The other guidelines only provide guidance for patients with QRS >120 ms rather than specifically mentioning not to implant in cases with a narrower QRS.[19]

Additional Evidence Pertinent to NYHA Functional Class

For NYHA class III -ambulatory class IV HF

Al-Majed, et al. 2011

This meta-analysis demonstrated that CRT reduced all-cause mortality by 19%. In the 19 trials enrolling predominantly patients with NYHA class III or IV symptoms, CRT reduced the risk for all-cause mortality (RR, 0.78 [CI, 0.67 to 0.91]; I^2=0%). Repeating this analysis for the 11 studies that included exclusively patients with NYHA class III or IV symptoms (in addition to the subgroup of patients with NYHA class III symptoms from the RAFT study) showed similar results (666 deaths in 3805 patients; RR, 0.80 [CI, 0.70 to 0.92]; I^2=0%). Overall, CRT was associated with a reduction in the risk for hospitalization with HF (RR, 0.69 [CI, 0.58 to 0.82]; I^2=50%); no appreciable difference was found between trials enrolling predominantly patients with NYHA class III or IV symptoms (RR, 0.65 [CI, 0.50 to 0.86]; I^2= 57%) and those enrolling predominantly patients with NYHA class I or II symptoms (RR, 0.71 [CI, 0.57 to 0.87]; I^2=37%), although the absolute rate of HF hospitalization was higher in the former trials (22% vs. 17% in the NYHA class I or II trials).[20]

Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT) Tang, et al. 2010

This was a randomized controlled trial attempting to determine if adding CRT therapy to an ICD, along with optimized medical therapy, would reduce morbidity and mortality amongst patients with NYHA class II or III HF, an EF of 30% or less and a wide QRS > 120 ms (or a paced QRS duration > 200 ms). The primary outcome was death from any cause or hospitalization for HF. In total, 1798 patients were followed for a mean of 40 months. The primary outcome occurred in 297 of 894 patients (33.2%) in the ICD-CRT group and 364 of 904 patients (40.3%) in the ICD group (P<0.001). In the ICD-CRT group, 186 patients died, as compared with 236 in the ICD group (P=0.003), and 174 patients were hospitalized for HF, as compared with 236 in the ICD group (P<0.001). However, at 30 days after device implantation, adverse events had occurred in 124 patients in the ICD-CRT group, as compared with 58 in the ICD group (P<0.001). Thus, it was concluded that in patients with NYHA class II or III HF, a wide QRS complex, and LV systolic dysfunction, the addition of CRT to an ICD reduced rates of death and hospitalization for HF. However, this improvement was accompanied by more adverse events.[21]

CARE-HF trial Cleland, et al. 2005

The effects of CRT on the risk of complications and death for patients receiving standard medical therapy for moderate or severe HF and cardiac dyssynchrony were evaluated. As detailed above already, this study concluded that CRT (as compared to medical therapy) reduced the interventricular mechanical delay, the end-systolic volume index, and the area of the mitral regurgitant jet; increased the LVEF; and improved symptoms and the quality of life (P<0.01 for all comparisons).[3]

For NYHA class I or II

Al-Majed, et al. 2011

As mentioned above, this meta-analysis included 25 randomized controlled trials. In the 6 specific trials that predominantly included patients with NYHA class I or II symptoms, CRT reduced the risk for all-cause mortality (RR, 0.83 [CI, 0.72 to 0.96]; I^2=0%). Repeating this analysis for the 3 studies that exclusively included patients with NYHA class I or II symptoms (in addition to the subgroup of patients with NYHA class II symptoms from the RAFT study) showed similar results (407 deaths in 4054 patients; RR, 0.80 [CI, 0.67 to 0.96]; I^2=0%). CRT improves LVEF and reduces all-cause mortality and HF hospitalization in patients with milder symptoms of HF (NYHA class I or II), LV systolic dysfunction, and prolonged QRS duration. The relative magnitude of these benefits (risk reductions of 17% for mortality and 29% for HF hospitalization) is similar to that seen in patients with NYHA class III or IV symptoms, LV systolic dysfunction, and prolonged QRS duration.[20]

Adabag, et al. 2011

A systematic review and meta-analysis of 5 prospective randomized clinical trials (RAFT, MADIT-CRT, REVERSE, MIRACLE ICD II, and CONTAK CD) was conducted to evaluate CRT-D versus ICD only in patients with reduced EF $\leq$ 40%, QRS $\geq$ 120 ms, and NYHA class I and II HF. This meta-analysis encompassed 4317 patients- 2429 for CRT-D and 1888 for ICD only. Follow up ranged from 6-40 months. The average age of the patients was 65 years, 80% were male, 60% had ischemic cardiomyopathy, and 9% were asymptomatic (NYHA class I). Frequency of all-cause mortality for CRT versus ICD was 8% versus 11.5% (risk ratio [RR]: 0.81; 95% CI: 0.65 to 0.99, P=0.04); for HF hospitalization, it was 11.6% versus 18.2% (RR: 0.68; 95% CI: 0.59 to 0.79, P<0.001). Patients assigned to CRT had a significantly greater improvement in LVEF (+5.9% vs. +2.2%, P<0.001) and LV volume than ICD patients. Among mildly symptomatic (NYHA functional class II) patients, there was a 22% reduction in mortality (9.6% CRT vs. 13.1% ICD; RR: 0.78, 95% CI: 0.65 to 0.95; P=0.01) and a 33% reduction in HF events or hospitalization (14.6% CRT vs. 21.5% ICD; RR: 0.67, 95% CI: 0.57 to 0.79; P<0.001). CRT was associated with significantly lower mortality and HF hospitalization. In asymptomatic (NYHA functional class I) patients, there was a 43% reduction in HF hospitalization between patients assigned to CRT versus ICD (11.9% CRT vs. 20.5% ICD; RR: 0.57, 95% CI: 0.34 to 0.97; P=0.04). However, there was no difference in mortality. Twelve asymptomatic HF patients needed to be treated with CRT to prevent 1 hospitalization.[22]

MADIT-CRT trial

This trial did include NYHA Class I ischemic HF patients, but the numbers were too low to provide enough evidence to show benefit of CRT in this subgroup. Eighty-five percent of the enrollees in that trial were class II patients.

REVERSE Study Group, Linde, et al. 2008

Published results from this study noted the effects of CRT in NYHA class I and II patients with previous HF symptoms. This was an international 73 center randomized controlled trial. Six hundred and ten patients with NYHA class I or II HF on optimal medical therapy with a QRS $\geq$ 120 ms, an LVEF $\leq$ 40%, and an LV end-diastolic diameter

≥ 55 mm received a CRT device (+/- defibrillator) and were randomly assigned to active CRT (CRT-ON; n=419) or control (CRT-OFF; n=191) for 12 months. Mean age for patients was ~ 62 and ~ 80% were male. Mean LVEF was 27%. The primary end point was the HF clinical composite response, which scores patients as improved, unchanged, or worsened via the Kansas City Cardiomyopathy Questionnaire and the Minnesota Living with Heart Failure Questionnaire. The prospectively powered secondary end point was LV end-systolic volume index. Hospitalization for worsening HF was evaluated in a prospective secondary analysis of health care use. Patients were evaluated at 1, 3, 6, and 12 months. The HF clinical composite response end point, which compared only the percent worsened, indicated 16% worsened in CRT-ON compared with 21% in CRT-OFF (P=0.10). Patients assigned to CRT-ON experienced a greater improvement in LV end-systolic volume index (-18.4 +/- 29.5 ml/m^2 vs. -1.3 +/- 23.4 ml/m^2, P<0.0001) and other measures of LV remodeling. Time-to-first HF hospitalization was significantly delayed in CRT-ON (HR: 0.47, P=0.03). It was concluded that the REVERSE trial demonstrated that CRT, in combination with optimal medical therapy (+/- defibrillator), reduced the risk for HF hospitalization and improved ventricular structure and function in NYHA functional class II and NYHA functional class I patients with previous HF symptoms.[6]

Moss, et al. 2009

A randomized control trial was conducted to determine whether CRT would reduce the risk of death or HF events in patients with mild cardiac symptoms, a reduced EF, and a wide QRS complex. During a 4.5-year period, 1820 patients with ischemic or non-ischemic cardiomyopathy, an EF of 30% or less, a QRS duration of 130 ms or more, and NYHA class I or II symptoms were enrolled and followed. Patients were randomly assigned in a 3:2 ratio to receive CRT plus an ICD (1089 patients) or an ICD alone (731 patients). The primary end point was death from any cause or a nonfatal HF event (whichever came first). HF events were diagnosed by physicians who were aware of the treatment assignments, but they were adjudicated by a committee that was unaware of assignments. The average follow-up was 2.4 years. The primary end point occurred in 187 of 1089 patients in the CRT-ICD group (17.2%) and 185 of 731 patients in the ICD-only group (25.3%) (HR in the CRT-ICD group, 0.66; 95% CI, 0.52 to 0.84; P=0.001). The benefit did not differ significantly between patients with ischemic cardiomyopathy and those with non-ischemic cardiomyopathy. The superiority of CRT was driven by a 41% reduction in the risk of HF events, a finding that was evident primarily in a prespecified subgroup of patients with a QRS duration of 150 ms or more. CRT was associated with a significant reduction in LV volumes and improvement in the EF. There was no significant difference between the 2 groups in the overall risk of death, with a 3% annual mortality rate in each treatment group. Serious adverse events were infrequent in the 2 groups.[23]

None of the ESC guidelines, CCS, or Australian guidelines provide recommendations for patients in NYHA functional class I. The ACC/AHA/HRS guidelines, on the other hand, provide a Class IIb recommendation, evidence level C, on condition that the patients have LBBB with a QRS ≥ 150 ms, HF caused by ischemia, and an LVEF ≤ 30% on GDMT. They do not recommend CRT implantation in NYHA functional class I patients if they do not have LBBB and a QRS ≤ 150 ms, providing this indication with a Class III recommendation. NICE guidelines recommend implantation in patients with a QRS ≥ 150 ms in NYHA functional class I, regardless of the morphology of the bundle branch block. CCS guidelines state that there is insufficient evidence to recommend CRT to patients with NYHA functional class I status.[19]

Additional Evidence Pertinent to EFs Between 35-50%

There is indirect evidence, derived from large pacing mode selection trials and observational studies, that conventional RV apical pacing may have detrimental effects on cardiac structure and LV function, which are associated with the development of HF.[24]

Doshi, et al. (PAVE Study Group) primarily studied biventricular pacing compared to RV pacing in patients undergoing AV node ablation for AF management. Subset analysis indicated patients with an EF ≤ 45% or with NYHA Class II/III

symptoms receiving a biventricular pacemaker appeared to have a greater improvement in 6-minute walk distance compared to patients with normal systolic function or Class I symptoms.[34]

The evidence base for this category related to EF in excess of 35% is limited. There are studies which support use of CRT with an EF between 35-50% when frequent ventricular pacing is expected. For patients with an EF between 35-50% with a QRS ≥ 150 ms, LBBB (native or paced), and NYHA class III or IV despite optimal medical therapy for at least 3 months, the efficacy of CRT has not been established.

BLOCK-HF trial (Curtis, et al. 2013)

This was a multicenter, prospective, randomized and double blinded trial which enrolled patients who had indications for pacing with AV block; NYHA class I, II, or III HF; and an LVEF of 50% or less. Patients received a CRT-P or a CRT-ICD (the latter if the patient had an indication for defibrillation therapy) and were randomly assigned to standard RV pacing or biventricular pacing. The premise question focused on whether biventricular pacing might reduce mortality, morbidity, and adverse LV remodeling in such patients. The primary outcome was the time to death from any cause, an urgent care visit for HF that required intravenous therapy, or a 15% or more increase in the LV end-systolic volume index. Of 918 patients enrolled, 691 underwent randomization and were followed for an average of 37 months. The primary outcome occurred in 190 of 342 patients (55.6%) in the RV-pacing group, as compared with 160 of 349 (45.8%) in the biventricular-pacing group. Patients randomly assigned to biventricular pacing had a significantly lower incidence of the primary outcome over time than did those assigned to RV pacing (HR, 0.74; 95% credible interval, 0.60 to 0.90); results were similar in the pacemaker and ICD groups. LV lead–related complications occurred in 6.4% of patients. Biventricular pacing was felt to be superior to conventional RV pacing in patients with AV block and LV systolic dysfunction with NYHA class I, II, or III HF.[24]

In patients with systolic HF who need a pacemaker and are likely to be dependent on chronic RV pacing, there is a strong Class I, Level of Evidence: A recommendation from the ESC HFA guidelines (2016) for patients with an indication for ventricular pacing and high-degree AV block. This includes patients with AF. These guidelines were published post BLOCK-HF trial publication. The EHRA and ACC/AHA/HRS guidelines provide a Class IIa recommendation. It is notable that these recommendations were issued BEFORE the BLOCK-HF trial results were published. The ACC/AHA/HRS guidelines specify that the degree of anticipated RV pacing must be > 40%. This figure is based on the DAVID (Dual Chamber and VVI Implantable Defibrillator) trial, which suggested a worse outcome in patients who were paced at > 40%. None of the other guidelines specify the exact degree of anticipated pacing for this recommendation.[19]

Additional Evidence Pertinent to EFs ≥ 50%

Patients with an EF ≥ 50% represent a group of patients for which there are no clinical trials that demonstrate CRT benefit. The PACE study noted that CRT preserved LVEF as compared to RV pacing amongst 177 patients, but there were no beneficial functional outcomes such as improved 6-minute walk distances or quality of life measures at 12 months.[25] Dickstein responded to this fact by noting that these patients in the PACE study did not have symptomatic HF or reduced EF in the first place. The RV paced group did lose EF over the course of 2 years, changing from 61.5% at baseline to 53%, but remained well within a preserved EF range thus perhaps explaining the lack of functional outcome impact. Fang, et al.[26] provided additional comment in 2015 on the subject noting that patients with normal EFs seem more resistant to the adverse effects of RV pacing and yet LV dysfunction still ends up commonly observed in patients with frequent long-term pacing. However, despite the results of the PACE trial, there have been conflicting results as well. The PREVENT-HF trial found little difference in LV volumes, LVEF, mitral regurgitation, or the combination of HF events and cardiovascular hospitalization at 1-year follow-up between biventricular and RV pacing groups. The larger (n=1810) Biventricular pacing for Atrioventricular Block to prevent Cardiac Desynchronization (BioPace) study randomized patients with AV block and a mean age of 73.5 to either RV pacing (n=908) or

biventricular pacing (n=902) to determine if the latter approach could prevent deleterious LV effects. After a mean follow-up of 5.6 years, the groups had a similar rate of the composite endpoint that included time-to-death or first hospitalization due to HF, with a non-significant trend in favor of biventricular (HR 0.87; P=0.08). This trend persisted, still without reaching statistical significance, when patients were stratified according to their LVEF. For patients with an LVEF of 50% or less, the HR was 0.92 (P=0.47) and for patients with an LVEF of more than 50% it was 0.88 (P=0.21).[27]

Additional Evidence Pertinent to Patients with Advanced HF

Non-randomized single center studies suggest a lack of benefit of CRT in the population of patients with non-ambulatory class IV HF. Patients on chronic inotropic therapy for HF have a poor prognosis even with CRT-D and there is likely no survival benefit conferred by CRT-D as compared to ICD alone.[28] A meta-analysis by Hernandez, et al. 2018 was reviewed. Eight studies were included for a total of 151 patients who all had EFs < 30% and QRS durations > 130 ms. Eighty percent of these patients were classified as NYHA class IV. The pooled analysis demonstrated that 93% of the reported patients (95% CI: 86% to 100%) were weaned from inotropic support after CRT, and the overall 12-month survival rate was 69% (95% CI: 56% to 83%). These results suggest that rescue CRT-D in inotrope dependent patients may allow for weaning of the inotropes, an improved quality of life, and reduction in mortality. It is hypothesized that rescue CRT could be a bridging strategy toward heart transplant or left ventricular assist device (LVAD). At present, there are no randomized trials evaluating the benefit of CRT in patients who require inotropic support.[29]

Additional Evidence Pertinent to Patients with Non-Ischemic Cardiomyopathy and Pacemaker Dependency

Patients with non-ischemic cardiomyopathy and pacemaker dependency may receive benefit from CRT by normalizing LV function. Smaller LV dimensions (LV end-diastolic dimension < 58 mm, LV end-systolic dimension < 48 mm) and shorter time from their cardiomyopathy diagnosis (< 24 months) had a higher chance for normalization of LVEF.[30] This finding has relevance for patients who develop LV dysfunction with RV pacing in the setting of complete heart block (spontaneous or iatrogenic). Pacemaker-dependent patients with non-ischemic cardiomyopathy undergoing CRT upgrade had a lower risk of device therapy for ventricular tachyarrhythmias.[31] These studies have small sample sizes. There is not randomized control trial evidence available.

Additional Evidence Pertinent to Patients with Non-Ischemic Cardiomyopathy and LBBB

NEOLITH study (Wang, et al. 2016)

It is a not an uncommon scenario for patients to be diagnosed with a new-onset idiopathic non-ischemic cardiomyopathy in the setting of LBBB. Currently CRT is recommended if the EF remains ≤ 35% after at least 3 months of optimal medical therapy. A retrospective cohort study was performed in subjects with new-onset idiopathic non-ischemic cardiomyopathy, LVEF ≤ 35%, and LBBB or narrow (<120 ms) QRS complex morphology. LVEF response between groups was evaluated. In 102 subjects (70 with narrow QRS complex and 32 with LBBB), post-optimal medical therapy of 3 months, EF was > 35% in 39 narrow QRS complex subjects (56%) and 2 LBBB subjects (6%) (P<0.0001). The absolute difference between post-GDMT LVEF and initial LVEF was greater in the narrow QRS complex group (16.1% ± 14.6% vs. 3.3% ± 10.7%; P<0.0001). Narrow QRS complex, as compared to those with LBBB, was significantly associated with post-GDMT LVEF > 35% (relative risk 10.30; 95% CI 2.63-40.27; P=0.0008) and absolute difference between post-optimal medical therapy LVEF and initial LVEF (β = 16.296; standard error = 2.977; P<0.0001). CRT super-response, defined as post-CRT LVEF ≥ 50%, was observed in 8 of LBBB subjects (35%) who received CRT. It was concluded that optimal medical therapy did not significantly improve LVEF in new onset LBBB-associated non-ischemic cardiomyopathy at 3 months. Most remained candidates for CRT and after receiving it, a high percentage were super responders.[32]

In Atrial Fibrillation (AF)

AF is quite common in HF and so the question related to CRT effectiveness in this population is a clinically relevant one. Unfortunately, no prospective randomized trial exists that has studied the specific impact of CRT on AF patients and end points such as mortality and hospitalizations. However, there is sufficient data to evaluate the role of CRT in patients with AF, as discussed below. Some major clinical trials evaluating the benefit of CRT have included subgroups of patients with AF. There are also small, randomized trials with functional end points, observational trials and meta-analyses that can serve as viable references. In a chronic AF population, 3 overlapping clinical settings must be considered: AV block due to conduction system disease, post AV node ablation, and in patients with systolic HF and evidence of ventricular dyssynchrony (generally based on QRS duration and morphology). While patients with AF and concomitant HF may benefit from CRT, the evidence to support this therapy in patients with AF is not as strong or as comprehensive as it is for patients in sinus rhythm. Another point for practical consideration with this policy is the fact that a high rate of biventricular pacing is required to achieve maximum benefit from CRT, which may be difficult to achieve in patients with AF without AV block.

Evidence for patients in need of a pacemaker for AV block

While RV pacing provides an adequate heart rate in patients with AV block, it is also known that high percentages of RV apical pacing may promote LV systolic dysfunction. The BLOCK HF trial (Curtis, et al. 2013) evaluated whether biventricular pacing might reduce mortality, morbidity, and adverse LV remodeling in such patients. Nine hundred and eighteen patients who had indications for pacing due to AV block, NYHA class I, II or III HF, and an EF of 50% or less were enrolled. It is also noteworthy that over 50% of study participants had AF at baseline. Six hundred and ninety-one of these patients underwent randomization to an RV paced group (n=342) or to biventricular paced group (n=349). The primary outcome was the time to death from any cause, an urgent care visit for HF that required intravenous therapy, or a 15% or more increase in the LV end-systolic volume index. The randomized patients were followed for an average of 37 months. The primary outcome occurred in 190 of 342 patients (55.6%) in the RV-paced group, as compared with 160 of 349 (45.8%) in the biventricular-paced group. Patients randomly assigned to biventricular pacing had a significantly lower incidence of the primary outcome over time (HR, 0.74; 95% credible interval, 0.60 to 0.90). This was true whether the patient had a CRT-P or a CRT-D. LV lead-related complications occurred in 6.4% of patients. The conclusion of the study was that biventricular pacing was superior to conventional RV pacing in patients with AV block and LV systolic dysfunction with NYHA class I, II, or III HF.[24]

Evidence for patients undergoing AV node ablation for AF

Observational studies and small randomized trials support the value of CRT in patients with AF who undergo AV node ablation, particularly for patients with reduced LV systolic function or HF.

Leon, et al. in 2002

This group studied the effects of biventricular pacing on ventricular function, functional status, quality of life and hospitalization in patients with HF, prior AV junction ablation and RV pacing for chronic AF. Twenty consecutive patients with severe HF (EF $\leq$ 35%), NYHA class III or IV, a prior AV junction ablation and RV pacing for at least 6 months duration were studied. ECGs, echocardiograms, functional status evaluations and quality of life surveys were completed before and at 3 to 6 months after implant. The results of this small study demonstrated improvement in the NYHA class by 29% (P<0.001), increased EF by 44% (P<0.001), decreased LV diastolic diameter by 6.5% (P<0.003) and decreased end-systolic diameter by 8.5% (P<0.01). The number of hospitalizations decreased by 81% (P<0.001). The scores on the Minnesota Living with Heart Failure survey improved by 33% (P<0.01).[33]

PAVE study (Doshi, et al. 2005)

This randomized trial compared chronic biventricular pacing to RV pacing in patients undergoing ablation of the AV node for management of AF with rapid ventricular rates. One hundred and eighty-four patients requiring AV node ablation were randomized to receive a biventricular pacing system (n=103) or an RV pacing system (n=81). The study endpoints were based on the 6-minute hallway walk test, quality of life, and EF. Patient characteristics were similar (64% male; average age 69, average EF 46%, and 83% with NYHA Class II or III). At 6 months post-ablation, patients treated with CRT had a significant improvement in 6-minute walk distance, 31% above baseline (82.9 +/- 94.7 m), compared to patients receiving RV pacing, 24% above baseline (61.2 +/- 90.0 m) (P=0.04). There were no significant differences in the quality-of-life parameters. At 6 months post-ablation, the EF in the biventricular group (0.46 +/- 0.13) was significantly greater in comparison to patients receiving RV pacing (0.41 +/- 0.13, P=0.03). Patients with an EF $\leq$ 45% or with NYHA Class II/III symptoms receiving a biventricular pacemaker appeared to have a greater improvement in 6-minute walk distance compared to patients with normal systolic function or Class I symptoms. Thus, for patients undergoing AV node ablation for AF, CRT offered significant improvement with the 6-minute walk test and with EF compared to RV pacing. These benefits were greatest in patients with impaired systolic function or with symptomatic HF.[34]

Brignole, et al. (2011)

This group conducted a prospective, multi-center study with random assignment of 186 patients, in whom AV junction ablation and CRT device implantation had occurred, to receive CRT (97 patients) or RV apical pacing (89 patients). The data were analyzed according to the intention-to-treat principle. During a median follow-up of 20 months, the primary composite endpoint of death from HF, hospitalization due to HF, or worsening HF occurred in 11 (11%) patients in the CRT group and 23 (26%) patients in the RV group [CRT vs. RV group: sub-hazard ratio (SHR) 0.37 (95% CI 0.18-0.73), P=0.005]. In the CRT group, fewer patients had worsening HF [SHR 0.27 (95% CI 0.12-0.58), P=0.001] and hospitalizations for HF [SHR 0.20 (95% CI 0.06-0.72), P=0.013]. Total mortality was similar in both groups. The beneficial effects of CRT were consistent in patients who had EFs ≤ 35%, NYHA class ≥ III and QRS width ≥ 120 and in those who did not. At multi-variable Cox regression, only CRT mode remained an independent predictor of absence of clinical failure during the follow-up [HR = 0.23 (95% CI 0.08-0.66), P=0.007]. The conclusion was drawn that in patients with an ”Ablate and Pace” strategy for severe symptomatic AF, CRT was superior to RV pacing in reducing the consequences of HF.[35]

Evidence for AF and Concomitant HF

Data on CRT in patients with HF and AF is limited but suggests a benefit from CRT (especially in patients with high rates of ventricular pacing). Patients with atrial dysrhythmias were excluded from most of the major CRT trials. In the CARE-HF trial which compared CRT with drug therapy alone, the mean duration of follow-up was 29.4 months and AF was noted in 66 patients in the CRT group compared with 58 who got medical therapy alone. There was no difference in the time until first onset of AF between the groups. Although mortality was higher among patients who developed new AF during follow-up, this subgroup did benefit from CRT with reduced risk of all-cause mortality, all the other major study endpoints, and improved EF and symptoms (all P>0.2). So, while CRT did not decrease the incidence of AF, it did improve outcome regardless of whether AF developed.[36]

In the RAFT trial which compared ICD alone to CRT plus ICD, CRT-D provided no incremental benefit in the subgroup of 229 patients with AF. However, less than one-third of patients treated with CRT received ≥ 95% ventricular pacing during the first 6 months of follow-up.[21]

The MUSTIC-AF trial included 59 patients with HF and chronic AF with wide QRS complex requiring a permanent pacemaker because of a slow ventricular rate; the patients were randomly assigned to either single site RV pacing or biventricular pacing in a crossover design. Sixty-three percent had undergone AV node ablation. Only 37 patients completed the 6-month crossover trial, which limits interpretation. In the intention-to-treat analysis, there were no

significant differences in exercise tolerance or peak oxygen consumption. However, among the patients who received effective therapy (97 to 100% paced), biventricular pacing was associated with a 9.3% improved 6-minute walk distance and peak oxygen uptake increased by 13%. Hospitalizations decreased by 70% and 85% of the patients preferred the biventricular pacing.[37]

Guideline (Year)	Atrial Fibrillation and HF	Expected High % of Ventricular Pacing With Reduced LVEF and Symptomatic HF
ESC HFA (2016)	IIa, B	I, A
ESC EHRA (2013)	IIa, B	IIa, B
ACC/AHA/HRS (2013)	IIa, B	IIa, C
CCS (2017)	IIb, Low	IIb, Moderate

The ESC HFA and EHRA guidelines and the ACC/AHA/HRS guidelines all provide a Class IIa recommendation for CRT in patients with HF and AF. The Canadian guidelines state it "may be considered" (Class IIb). The European guidelines also specify EFs ≤ 35% and NYHA class III or IV. The ACC/AHA/HRS and Canadian guidelines do not really specify other than to state eligible patients must otherwise qualify for CRT.

The 2010 REVERSE substudy by Linde, et al. examined the effects of CRT with respect to HF etiology. In this randomized controlled trial, a total of 277 patients with non-ischemic heart disease and 333 patients with ischemic heart disease, all with NYHA class I or II HF and all with QRS duration ≥ 120 ms and LVEFs ≤ 40% received CRT-D and were randomized to CRT-ON or CRT-OFF for 12 months. The primary end point was the percentage of patients with worsened HF. Results showed that at baseline, ischemic heart disease patients were significantly older and had more comorbidities and less dyssynchrony than non-ischemic heart disease patients. In non-ischemic heart disease patients, 10% worsened in CRT-ON compared with 19% in CRT-OFF (P=0.01). In ischemic heart disease patients, 20% worsened in the CRT-ON compared with 24% in the CRT-OFF group (P=0.10). Non-ischemic heart disease patients assigned to CRT-ON improved more in LV end-systolic volume index than ischemic heart disease patients. Randomization to CRT, LBBB, and wider QRS duration independently predicted response to both end points, whereas non-ischemic heart disease etiology was an independent predictor only for LV end-systolic volume index. CONCLUSIONS: This substudy of REVERSE shows that CRT reverses LV remodeling with a more extensive effect on non-ischemic patients. Etiology was, however, not an independent predictor of clinical response.[38]

Effective CRT delivery in patients with AF is inherently more difficult. Often AV node ablation is needed for rate control. Gasparini, et al. studied the effects of CRT in HF patients with AF. Forty-eight patients with permanent AF had their ventricular rates controlled by drugs resulting in biventricular pacing > 85% of the pacing time. One hundred and fourteen permanent AF patients had undergone AV junction ablation and thus had biventricular pacing achieved 100% of the time. Within this group of permanent AF patients, only the ones who had ablation showed a significant increase in EF (P<0.001), positive reverse remodeling (P<0.001) and improved exercise tolerance (P<0.001). No improvements were observed in the AF patients who were not ablated.[39]

The various literature that is available, as noted above, suggests that patients with reduced LV function requiring AV

nodal ablation for rapid AF are best served with CRT compared to conventional RV pacing. Functional capacity, hospitalization rates and even HF death rates are improved. But meta-analysis suggests that while these patients get EF preservation or improvement like those in sinus rhythm, their response is not as functionally beneficial and they still remain at higher risk for non-response to the CRT and for death.[40] Thus CRT is indicated in AF patients with reduced LV function if they have an indication for pacing (including those who have AV nodal ablation) regardless of NYHA class (Class I, Level of Evidence: A). CRT can be considered in AF patients with class III-IV HF, an EF < 35%, a QRS > 130 ms (Class IIa, Level of Evidence: B) (ESC 2016) provided there is a good strategy to ensure biventricular capture or the patient is expected to get back to a NSR. In the guidelines that provide recommendations for CRT in patients with AF there is consensus that ventricular rate must be adequately controlled by pharmacologic intervention or AV nodal ablation in order to ensure a high degree of CRT pacing.[19]

Contractor Advisory Committee (CAC) Evidentiary Meeting 3/23/2021

This A/B MAC hosted a CAC meeting to review the evidence regarding CRT on 3/23/2021. Panelists from general cardiology and electrophysiology specialized cardiology were represented. Key questions regarding the following topics were posed with full panel discussion regarding the applicability of relevant evidence. The panelists agreed there was sufficient evidence (average of 4/5, range 4) supporting lack of benefit for CRT in a patient population with a QRS duration < 130 ms. However, all made the point that a need for chronic RV pacing would create an exception to a broad application based upon a QRS duration < 130 ms.

Regarding the use of CRT in HF patients with EF measurement < 35%, a QRS duration in a 130-149 ms range, and a non-LBBB pattern, all panelists voted the quality of the evidence at 4.5/5 for generally avoiding CRT in a RBBB population with a QRS duration between 130-149 ms. However, a few panelists did note that a left bundle branch predominant interventricular conduction delay might be considered for CRT with other sound clinical reasoning, such as, a high probability for HF or QRS prolongation progress to occur or within the setting of pacemaker dependence. There was no firm high quality evidence for or against this approach.

The key question regarding evidence quality for the use of CRT in patients with LBBB, QRS duration > 150 ms and NYHA class II-ambulatory IV was posed. The average score of 4/5 was agreed by all and mostly based on the MADIT trial. A few panelists noted their opinions regarding the use of CRT in Class I HF with QRS > 150 ms and based those opinions on the evidence of the MADIT trial. They admitted the number of Class I HF patients included in that study was small but felt the potential for benefit was significant. Such patients would benefit greatly from the standpoint of LV remodeling post CRT therapy. These patients, if not offered CRT early in their HF would be highly likely to proceed to classes II and III without device intervention. Four panelists rated this MADIT subgroup evidence quality at 4/5. Furthermore, they felt the same regardless of any hypothesized ischemic or non-ischemic origins for the LV dysfunction. One of the panelists opined, with the others agreeing, that it was also unlikely that any data better than the small Class I HF subset data of MADIT would ever be obtained in the future. Later, 2 panelists returned with opinions that the MADIT subset numbers were simply too small to be used as a high quality evidentiary basis for inclusion of Class I HF patients in a coverage population for CRT.

The BLOCK-HF trial was also extensively discussed. The evidence from this trial was highly valued by all panelists with a unanimous vote of 4/5 quality of that evidence. Specifically, patients with EFs between 30-50% and HF symptoms and a need for pacing were felt to be CRT eligible per the weight of this evidence. It was felt that any patient who meets inclusion/excision criteria for the BLOCK-HF trial has an indication for CRT.

Other key questions were asked and discussed in general fashion without complete evidence quality voting due to a general lack thereof. These questions with the discussion are noted below:

Regarding the importance of NYHA class as a differentiating factor for CRT candidacy: The panelists uniformly

agreed that NYHA classification is a very subjective assignment with much inter-rater unreliability. Also, the NYHA class can vary over time for a given patient. The point was made that many characteristics in addition to NYHA class are utilized for CRT candidacy and included QRS morphology/duration, LV dimensions and EF, etc. 4/5 panelists did agree that based on ubiquitous use of NYHA classification within most study parameters, the NYHA class symptomatology was of value to document and did represent a "measuring stick."

Regarding the applicability of a 40% pacing standard or greater as a criterion for "anticipated high burden RV pacing": The data quality per the DAVID trial was voted 5/5 per all panelists regarding the detrimental impact of > 40% RV pacing. However, the panelists did not feel this particular percentage carried more weight than any other chosen percentage. Any documentation that RV pacing would be frequent was sufficient in the panelists' minds to cause great concern for loss of LV function over time.

Regarding the issue of CRT upgrades: The panelists knew of no definitive evidence but generally felt that EF decreases of 10% or more or to an absolute value of 40% would be reasonable standards supporting a need for upgrade to CRT pacing from standard pacing.

Analysis of Evidence
(Rationale for Determination)

The evidence certainly supports the fact that CRT, with its positive effect on ventricular synchrony, promotes progressive cardiac structural benefits with improved contractility. In selected patients, HF symptoms and LV systolic function can be positively impacted. It is well established that indications for CRT are based upon LVEF, QRS duration, QRS morphology, NYHA functional class and the need for ventricular pacing, if applicable. The importance of shared decision making and documentation detailing the risk-benefit equation for any given patient is also clear.

Randomized clinical trials have demonstrated that CRT reduces mortality, reduces hospitalizations, and improves functional status in patients with LVEF $\leq$ 35 and QRS $\geq$ 150 ms (mostly with LBBB) with NYHA class II, III or ambulatory IV HF. The benefits of CRT have been firmly established in HF patients who remain in NYHA functional classes II and III, despite optimal medical therapy, with a wide QRS complex and reduced LVEF (≤ 30-35%).

In patients with LBBB and a QRS duration > 150 ms, all international guidelines and the preponderance of evidence supports use of CRT in this population. For patients with LBBB and a QRS between 120-129 ms, there is a marked discrepancy between the 2 ESC guidelines of 2013 and 2016. The EHRA 2013 provides a Class I recommendation ("is recommended"); the ESC HFA 2016 guidelines note a Class III recommendation ("is not recommended"). The 2017 Canadian guidelines clearly state that CRT should not be used for patients with QRS < 130 ms. For purposes of this LCD, this A/B MAC believes the ESC discrepancies are based on publication timing which lags the evidence. The ECHO CRT study is felt to be compelling and has already contributed to the ESC HFA and Canadian guidelines which reset their cutoffs for CRT to > 130 ms. Beshai, et al. with the RethinQ trial studied patients with narrow QRS complexes and echocardiographic evidence of LV mechanical dyssynergy related to CRT benefit. Rather surprisingly they found that CRT did not improve peak oxygen consumption in patients with moderate-to-severe HF. They concluded that patients with HF and narrow QRS (< 120 ms) may not benefit from CRT.[41] This A/B MAC has determined that beneficial health outcomes likely do not exist in the setting of narrow QRS complexes and therefore supports coverage for CRT in a population of patients only with a QRS duration $\geq$ 130 ms. The exception to this coverage element is for patients who otherwise have LV dysfunction with EFs < 50% but who require a pacemaker with anticipated high frequency pacing.

The benefit of CRT does seem to be dependent on QRS duration. Available data suggest a significant benefit associated with CRT in patients with QRS ≥ 150 ms but is less clear for patients with QRS < 150 ms. While subgroup analyses from the various large randomized control trials should be interpreted with some caution, a consistent finding in the trials and meta-analyses is that subgroups with shorter QRS durations or non-LBBB morphology

appeared to benefit less from CRT than patients meeting more stringent QRS duration and morphology criteria.

In patients with non-LBBB and a QRS < 150 ms, the European and American guideline recommendations vary from Classes IIb to III. The Canadian guidelines do not provide a formal recommendation for this group, but do state there is no clear evidence of benefit with CRT in this demographic. Since 2011, increasing evidence has shown better outcomes for CRT in LBBB patients versus non-LBBB patients in subgroup analysis of randomized control trials.

With an eye toward subgroup analysis and with CAC input regarding those subgroups, it is clear there are mixed views of the value of LBBB in driving CRT response. Cleland's 2013 meta-analysis of 5 randomized trials offers valuable information by showing QRS duration to be a powerful predictor of CRT effect, but also indicating QRS morphology did not provide any additional information about clinical response.

This A/B MAC has determined that beneficial health outcomes likely exist and therefore supports coverage for CRT in a population of patients with HF of NYHA class II, III, or ambulatory IV and QRS duration $\geq$ 130 ms with LBBB and for CRT in a population of patients with HF of NYHA class III-ambulatory IV with left bundle predominant non-LBBB and QRS duration $\geq$ 130 ms.

This A/B MAC cannot currently provide coverage for CRT in patients with only RBBB and a QRS < 150 ms in any HF functional class due to a current lack of compelling evidence.

Regarding NYHA functional class I patients, most of the international specialty society guidelines do not discuss patients with NYHA functional class I. Those that do, either provide a III recommendation or a weak recommendation for those with a wide QRS. Although both the MADIT CRT and REVERSE studies included NYHA functional class I patients, the total number of these patients included was small, and the subgroup analysis was not meaningful. With careful analysis of pooled data from randomized controlled trials as conducted by Adabag, the benefits were robust for patients with NYHA class II symptoms. However, the number of NYHA functional class I patients analyzed was < 300 as access was not granted for data of NYHA class I patients in the REVERSE trial. Such a small number limits the power of analysis. While it was promising that there was a significant reduction in HF events and hospitalizations with CRT in asymptomatic HF patients (NYHA functional class I); the overall small numbers and lack of mortality impact begs for more research.

This A/B MAC has determined there is insufficient evidence to recommend CRT to patients with NYHA functional class I status unless evidence of LV dysfunction (an EF < 50%) exists and the patient has an indication for pacing.

This A/B MAC cannot currently provide coverage for CRT in patients with QRS < 130 ms (despite echocardiographic evidence of LV dyssynchrony) in any HF functional class due to a current lack of compelling evidence. The only exception to that statement is in the case of patients with AV nodal ablation or in need of RV pacing (due to second- or third-degree block or very long first degree block) that is expected a majority of the time. Again, documentation to that expectation would be expected from the CRT implanting physician.

For patients with HF who need a pacemaker and are likely to be dependent on chronic RV pacing, there is international guideline support for CRT-pacing in patients who need a pacemaker due to high-degree AV block. Most randomized control trials of CRT excluded patients with AF, and those trials that did include patients with AF were small. Choice of device—a conventional pacemaker or a CRT—is a rapidly evolving issue, and guidelines concerning the patient categories likely to benefit from CRT are not yet clearly defined. Although the complication rate is greater with an increasing number of leads implanted, a later upgrade from a permanent standard RV pacemaker to 1 with CRT is also associated with added risk. This A/B MAC sees this clinical scenario as an important and common one and thus feels a policy that avoids mention of a category with limited evidence misses an opportunity to support potentially meaningful health outcomes for Medicare beneficiaries. While evolving evidence may yet develop and

should be understood to potentially change this initial coverage decision, due to the common occurrence of AF in patients with moderate or severe HF, this A/B MAC has decided that while evidence is limited, there is enough consensus for the following coverage decision: this A/B MAC will cover CRT in patients with AF or NSR who have NYHA class I-III HF and an EF < 50% who need a pacemaker due to documented high-grade AV block (including those who will be treated with AV nodal ablation). Subsequent medical record documentation should certainly manifest ongoing efforts to ensure biventricular capture via AF control.

In patients with HF and an ICD indication, international professional society guidelines support the use of CRT therapy. Regarding upgrades from a standard pacemaker or ICD, in patients with worsening HF symptoms, a continuing or new need for pacing, and an EF < 50%, this A/B MAC believes supporting evidence from the BLOCK-HF trial and input from the CAC supporting such practices to be compelling. However, the threshold for upgrading an existing device to CRT is higher than for a de novo implant. A stand-alone "upgrade" procedure in patients with an existing pacemaker or ICD should be considered only after careful consideration of the risk-benefit balance. Documentation of that risk-balance consideration should be evident in a medical record that may be requested by this A/B MAC.

Proposed Process Information

Synopsis of Changes

CHANGES	FIELDS CHANGED
Not Applicable	**N/A**

Associated Information

Factors associated with less benefit from CRT are recognized by this A/B MAC based on the evidence analysis.

- Greater scar burden, as assessed by either myocardial perfusion or cardiac magnetic resonance imaging (MRI), is associated with less improvement in LVEF, less reverse remodeling, and higher mortality among patients treated with CRT. However, there are no randomized trials assessing whether patients with high scar burden benefit less from CRT.
- Non-LBBB QRS patterns, particularly RBBB, are associated with less reverse remodeling and higher mortality compared with LBBB.
- A native QRS duration between 120 and 149 ms predicts less clinical benefit from CRT than QRS duration 150 ms or greater.
- Milder HF symptoms are associated with a lower baseline risk of morbidity and mortality and so the estimated absolute risk reduction from CRT is less.
- Patients with severe COPD may not derive symptomatic benefit from CRT if their symptoms are predominantly caused by COPD.
- Patients with severe renal insufficiency may benefit less from CRT and may also not benefit from ICDs. Hemodialysis is associated with a high rate of device complications, including hematoma, pocket infection, bacteremia with endovascular lead infection, and compromise of hemodialysis access.

For patients with weaker indications or in patients for whom CRT would be a stand-alone upgrade procedure rather than a de novo implant, NYHA class is recognized as an important factor in decision making along with many other factors. It is important that medical record documentation reflecting a risk-benefit balance favoring CRT be present. This A/B MAC reserves the right to request medical record documentation and to adjust any or all coverage decisions based on content of that record regarding a reasonable and necessary standard for any CRT procedure.

Likewise, CRT implementation performed outside the above coverage indications can be appealed if denied. The medical record would be requested and the quality of the documentation regarding risk-benefit balance for a given patient would be considered in rendering a redetermination.

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N/A

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Open Meetings

MEETING DATE	MEETING STATE(S)	MEETING INFORMATION
08/02/2021	**Alabama** **Georgia** **North Carolina** **South Carolina** **Tennessee** **Virginia** **West Virginia**	Teleconference

Contractor Advisory Committee (CAC) Meetings

MEETING DATE	MEETING STATE(S)	MEETING INFORMATION
03/23/2021	**Alabama** **Georgia** **North Carolina** **South Carolina** **Tennessee** **Virginia** **West Virginia**	Teleconference

MAC Meeting Information URL(s)

CAC Meeting Information

Open Meeting Information

Proposed LCD Posting Date

N/A

Comment Period Start Date

07/22/2021

Comment Period End Date

09/04/2021

Released to Final LCD Date

Not yet released.

Reason for Proposed LCD

- Provider Education/Guidance

Contact for Comments on Proposed LCD

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Associated Documents

Attachments

N/A

Related Local Coverage Documents

N/A

Related National Coverage Documents

N/A

Public Version(s)

N/A

Keywords

- Cardiac Resynchronization Therapy
- CRT