

Blue Cross Blue Shield of Massachusetts is an Independent Licensee of the Blue Cross and Blue Shield Association

# Medical Policy Biventricular Pacemakers (Cardiac Resynchronization Therapy) for the Treatment of Heart Failure

## **Table of Contents**

- Policy: Commercial
- Policy: Medicare
- <u>Authorization Information</u>
- Coding Information

Policy History

Description

Policy Number: 101

BCBSA Reference Number: 2.02.10 (For Plan internal use only) NCD/LCD: N/A

•

## **Related Policies**

- Implantable Cardioverter Defibrillator (ICD), #070
- Cardiac Hemodynamic Monitoring for the Management of Heart Failure in the Outpatient Setting, #287

## **Policy**

# Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue<sup>SM</sup> and Medicare PPO Blue<sup>SM</sup> Members

Biventricular pacemakers with or without an accompanying implantable cardiac defibrillator (ie, a combined biventricular pacemaker plus implantable cardiac defibrillator) may be considered <u>MEDICALLY</u> <u>NECESSARY</u> as a treatment of heart failure in patients who meet **all** the following criteria:

- New York Heart Association (NYHA) Class III or IV,
  - Left ventricular ejection fraction  $\leq 35\%$
  - o Sinus rhythm
  - Patients treated with guideline-directed medical therapy\* AND
  - Either left bundle branch block **OR** QRS duration of ≥150 ms.
- New York Heart Association (NYHA) Class II,
  - Left ventricular ejection fraction ≤30%, AND
  - o Sinus rhythm
  - Patients treated with a guideline-directed medical therapy\* AND
  - Either left bundle branch block **OR** QRS duration of ≥150 ms.

Information Pertaining to All Policies

References

Guideline-directed medical therapy for heart failure is outlined in the 2022 American Heart Association, American College of Cardiology, and Heart Failure Society of America guidelines for the management of heart failure (Heidenreich et al [2022]).

For patients who do not meet the criteria outlined above, but have an indication for a ventricular pacemaker or biventricular pacemakers with or without an accompanying implantable cardiac defibrillator (ie, a combined biventricular pacemaker/implantable cardiac defibrillator) may be considered **MEDICALLY NECESSARY** as an alternative to a right ventricular pacemaker in patients who meet all of the following criteria:

- New York Heart Association class I, II, III, or IV heart failure;
- Left ventricular ejection fraction ≤50%;
- The presence of atrioventricular block with requirement for a high percentage of ventricular pacing\*; **AND**
- Patients treated with guideline-directed medical therapy.\*

\*Atrioventricular block with a requirement for a high percentage of ventricular pacing is considered to be present when there is either:

- Third-degree atrioventricular block; or
- Second-degree atrioventricular block or a PR interval of ≥300 ms when paced at 100 beats per minute.

Guideline-directed medical therapy for heart failure is outlined in the 2022 American Heart Association, American College of Cardiology, and Heart Failure Society of America guidelines for the management of heart failure (Heidenreich et al [2022]).

Biventricular pacemakers, with or without an accompanying implantable cardiac defibrillator (ie, a combined biventricular pacemaker plus implantable cardiac defibrillator), are considered **INVESTIGATIONAL** as a treatment for patients with NYHA class I heart failure who do not meet the above criteria.

Biventricular pacemakers, with or without an accompanying implantable cardiac defibrillator (i.e., a combined biventricular pacemaker plus implantable cardiac defibrillator), are considered **INVESTIGATIONAL** as a treatment for heart failure in patients with atrial fibrillation who do not meet the above criteria.

Triple-site (triventricular) cardiac resynchronization therapy, using an additional pacing lead, is considered **INVESTIGATIONAL**.

Intrathoracic fluid monitoring sensor is considered **INVESTIGATIONAL** as a component of a biventricular pacemaker.

Cardiac resynchronization therapy with wireless left ventricular endocardial pacing is considered **INVESTIGATIONAL**.

## **Prior Authorization Information**

Inpatient

 For services described in this policy, precertification/preauthorization <u>IS REQUIRED</u> for all products if the procedure is performed <u>inpatient</u>.

Outpatient

 For services described in this policy, see below for products where prior authorization <u>might be</u> <u>required</u> if the procedure is performed <u>outpatient</u>.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is <b>not required</b> .

Commercial PPO and Indemnity	Prior authorization is <b>not required</b> .
Medicare HMO Blue <sup>sM</sup>	Prior authorization is <b>not required</b> .
Medicare PPO Blue <sup>SM</sup>	Prior authorization is <b>not required</b> .

# CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above <u>medical necessity criteria MUST</u> be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

## CPT Codes

CPT Codes	Description
33224	Insertion of pacing electrode, cardiac venous system, for left ventricular pacing, with attachment to previously placed pacemaker or pacing cardioverter-defibrillator pulse generator (including revision of pocket, removal, insertion, and/or replacement of existing generator)
33225	Insertion of pacing electrode, cardiac venous system, for left ventricular pacing, at time of insertion of pacing cardioverter-defibrillator or pacemaker pulse generator (including upgrade to dual chamber system and pocket revision) (List separately in addition to code for primary procedure)

ICD-10-PCS	
procedure	
codes:	Code Description
02H40JZ	Insertion of Pacemaker Lead into Coronary Vein, Open Approach
02H43JZ	Insertion of Pacemaker Lead into Coronary Vein, Percutaneous Approach
02H43KZ	Insertion of Defibrillator Lead into Coronary Vein, Percutaneous Approach
02H43MZ	Insertion of Cardiac Lead into Coronary Vein, Percutaneous Approach
02H44JZ	Insertion of Pacemaker Lead into Coronary Vein, Percutaneous Endoscopic Approach
02H60JZ	Insertion of Pacemaker Lead into Right Atrium, Open Approach
02H63JZ	Insertion of Pacemaker Lead into Right Atrium, Percutaneous Approach
02H64JZ	Insertion of Pacemaker Lead into Right Atrium, Percutaneous Endoscopic Approach
02HK0JZ	Insertion of Pacemaker Lead into Right Ventricle, Open Approach
02HK0KZ	Insertion of Defibrillator Lead into Right Ventricle, Open Approach
02HK3JZ	Insertion of Pacemaker Lead into Right Ventricle, Percutaneous Approach
02HK3KZ	Insertion of Defibrillator Lead into Right Ventricle, Percutaneous Approach
02HK4JZ	Insertion of Pacemaker Lead into Right Ventricle, Percutaneous Endoscopic Approach
02HK4KZ	Insertion of Defibrillator Lead into Right Ventricle, Percutaneous Endoscopic Approach
02HL0JZ	Insertion of Pacemaker Lead into Left Ventricle, Open Approach
02HL0KZ	Insertion of Defibrillator Lead into Left Ventricle, Open Approach

# ICD-10 Procedure Codes

02HL3JZ	Insertion of Pacemaker Lead into Left Ventricle, Percutaneous Approach
02HL3KZ	Insertion of Defibrillator Lead into Left Ventricle, Percutaneous Approach
02HL4JZ	Insertion of Pacemaker Lead into Left Ventricle, Percutaneous Endoscopic Approach
02HL4KZ	Insertion of Defibrillator Lead into Left Ventricle, Percutaneous Endoscopic Approach
02PA0MZ	Removal of Cardiac Lead from Heart, Open Approach
02PA3MZ	Removal of Cardiac Lead from Heart, Percutaneous Approach
02PA4MZ	Removal of Cardiac Lead from Heart, Percutaneous Endoscopic Approach
0JH607Z	Insertion of Cardiac Resynchronization Pacemaker Pulse Generator into Chest Subcutaneous Tissue and Fascia, Open Approach
0JH609Z	Insertion of Cardiac Resynchronization Defibrillator Pulse Generator into Chest Subcutaneous Tissue and Fascia, Open Approach
0JH637Z	Insertion of Cardiac Resynchronization Pacemaker Pulse Generator into Chest Subcutaneous Tissue and Fascia, Percutaneous Approach
0JH639Z	Insertion of Cardiac Resynchronization Defibrillator Pulse Generator into Chest Subcutaneous Tissue and Fascia, Percutaneous Approach
0JH807Z	Insertion of Cardiac Resynchronization Pacemaker Pulse Generator into Abdomen Subcutaneous Tissue and Fascia, Open Approach
0JH809Z	Insertion of Cardiac Resynchronization Defibrillator Pulse Generator into Abdomen Subcutaneous Tissue and Fascia, Open Approach
0JH837Z	Insertion of Cardiac Resynchronization Pacemaker Pulse Generator into Abdomen Subcutaneous Tissue and Fascia, Percutaneous Approach
0JH839Z	Insertion of Cardiac Resynchronization Defibrillator Pulse Generator into Abdomen Subcutaneous Tissue and Fascia, Percutaneous Approach
0JPT0PZ	Removal of Cardiac Rhythm Related Device from Trunk Subcutaneous Tissue and Fascia, Open Approach
0JPT3PZ	Removal of Cardiac Rhythm Related Device from Trunk Subcutaneous Tissue and Fascia, Percutaneous Approach

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT and ICD Procedure codes above if <u>medical necessity criteria</u> are met:

ICD-10-CM	
Diagnosis	
codes:	Code Description
150.20	Unspecified systolic (congestive) heart failure
150.1	Left ventricular failure, unspecified
150.21	Acute systolic (congestive) heart failure
150.22	Chronic systolic (congestive) heart failure
150.23	Acute on chronic systolic (congestive) heart failure
150.33	Acute on chronic diastolic (congestive) heart failure
150.40	Unspecified combined systolic (congestive) and diastolic (congestive) heart failure
150.41	Acute combined systolic (congestive) and diastolic (congestive) heart failure
150.42	Chronic combined systolic (congestive) and diastolic (congestive) heart failure
150.43	Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure
150.810	Right heart failure, unspecified
150.811	Acute right heart failure
150.812	Chronic right heart failure
150.813	Acute on chronic right heart failure
150.814	Right heart failure due to left heart failure
150.82	Biventricular heart failure
150.83	High output heart failure
150.84	End stage heart failure

150.89	Other heart failure
150.9	Heart failure, unspecified

#### The following CPT and HCPCS codes are considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

#### **CPT Codes**

0861T	Removal of pulse generator for wireless cardiac stimulator for left ventricular pacing; both components (battery and transmitter)
0862T	Relocation of pulse generator for wireless cardiac stimulator for left ventricular pacing,
	including device interrogation and programming; battery component only
0863T	Relocation of pulse generator for wireless cardiac stimulator for left ventricular pacing,
	including device interrogation and programming; transmitter component only

## Description

#### Heart Failure

An estimated 6.7 million adults in the United States 20 years of age and older had heart failure between 2017 to 2020. The prevalence continues to increase over time with the aging of the population. Prevalence of disease is higher in women than men 80 years of age and older. Overall prevalence is especially high in Black individuals. A 2008 study demonstrated that Black individuals had the highest risk of developing heart failure, followed by Hispanic, White, and Chinese individuals in the United States.<sup>2</sup>. Higher risk reflected differential prevalence of hypertension, diabetes, and lower socioeconomic status. Black individuals also had the highest proportion of incident heart failure not preceded by myocardial infarction (75%). Additionally, Black individuals have a greater 5-year case fatality rate associated with heart failure compared to White individuals.<sup>3</sup>. It is estimated that 20% to 30% of patients with heart failure have intraventricular conduction disorders resulting in a contraction pattern that is not coordinated and a wide QRS interval on the electrocardiogram. This abnormality appears to be associated with increased morbidity and mortality.

#### Treatment

Biventricular pacemakers using 3 leads (1 in the right atrium, 1 endocardial in the right ventricle, 1 epicardial for the left ventricle), also known as cardiac resynchronization therapy (CRT), have been investigated as a technique to coordinate the contraction of the ventricles, thus improving patients' hemodynamic status. Originally developed CRT devices typically used 2 ventricular leads for biventricular pacing. Devices and implantation techniques have been developed to allow for multisite pacing, with the goal of improving CRT response. This may be accomplished in 1 of 2 ways: through the use of multiple leads within the coronary sinus (triventricular pacing) or through the use of multipolar left ventricular pacing leads, which can deliver pacing stimuli at multiple sites. Wireless left ventricular endocardial pacing is also being evaluated for patients who are not candidates for or do not respond to standard epicardial pacing leads.

#### Summary

#### Description

Cardiac resynchronization therapy (CRT), which consists of synchronized pacing of the left and right ventricles, is intended to treat patients with heart failure and dyssynchronous ventricular contractions. Treatment involves placement of a device that paces both ventricles and coordinates ventricular pacing to maximize cardiac pumping function and left ventricular ejection fraction (LVEF).

#### Summary of Evidence

For individuals who have New York Heart Association (NYHA) class III or IV heart failure with a left ventricular ejection fraction (LVEF) of 35% or less who are in sinus rhythm, treated with guideline-directed medical therapy, and have either left bundle branch block (LBBB) or a QRS interval of 150 ms or more who receive cardiac resynchronization therapy (CRT) with or without defibrillator, the evidence includes randomized controlled trials (RCTs) and systematic reviews of RCTs. Relevant outcomes are overall survival (OS), symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. There is a large body of clinical trial evidence supporting the use of CRT in patients with

NYHA class III or IV heart failure. The RCTs have consistently reported that CRT reduces mortality, improves functional status, and improves quality of life for patients with NYHA class III or IV heart failure. Multiple subgroup analyses of RCTs have demonstrated that the benefit of CRT is mainly restricted to patients with LBBB or QRS interval greater than 150 ms. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have NYHA class II heart failure with an LVEF of 30% or less who are in sinus rhythm, treated with guideline-directed medical therapy, and have either LBBB or a QRS interval of 150 ms or more who receive CRT with or without defibrillator, the evidence includes RCTs and systematic reviews of RCTs. Relevant outcomes are OS, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. For patients with NYHA class II heart failure, at least 4 RCTs assessing CRT have been published. A mortality benefit was reported in 1 of the 4 trials, the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT). None of the other 3 RCTs reported a mortality difference, but a subgroup analysis of the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT) trial reported a mortality benefit for patients with LBBB. Among other outcome measures, hospitalizations for heart failure showed consistent reductions, but quality of life and functional status did not improve. Multiple subgroup analyses of RCTs have demonstrated that the benefit of CRT is mainly restricted to patients with LBBB or a QRS interval greater than 150 ms. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have NYHA class I heart failure who receive CRT with or without defibrillator, the evidence includes RCTs and systematic reviews of RCTs. Relevant outcomes are OS, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. Few patients with NYHA class I heart failure have been included in RCTs. The MADIT-CRT trial included 265 patients with class I heart failure. While the treatment effect on death and hospitalization favored combined implantable cardioverter-defibrillator (ICD) plus CRT devices versus ICD alone for class I patients, the confidence interval was large and included a 25% to 30% increase in events. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have NYHA class I, II, III or IV heart failure with LVEF of 50% or less and atrioventricular (AV) nodal block with requirement for a high percentage of ventricular pacing, treated with guidelinedirected medical therapy, who receive CRT with or without defibrillator, the evidence includes RCTs. Relevant outcomes are OS, symptoms, functional outcomes, quality of life, hospitalizations, and treatmentrelated morbidity. For patients who have AV nodal block, some degree of left ventricular (LV) dysfunction, and who would not necessarily meet conventional criteria for CRT but would require ventricular pacing, a large RCT has demonstrated improvements in heart failure-related hospitalizations and urgent care visits among patients treated with CRT instead of right ventricular (RV) pacing alone. For patients who require ventricular pacing is associated with improved measures of cardiac function, but the trial was small and underpowered to detect differences in clinical outcomes. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have heart failure and atrial fibrillation who receive CRT with or without defibrillator, the evidence includes 6 RCTs and a registry study. Relevant outcomes are OS, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. Results from RCTs have been conflicting, with 3 reporting improvements for patients with atrial fibrillation, including an all-cause mortality benefit, and others reporting no significant improvements. A registry study reported significant improvements in mortality and hospitalizations for patients with heart failure and atrial fibrillation treated with CRT plus defibrillator compared with implantable cardioverter-defibrillator alone. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have heart failure and AV nodal block who receive CRT, the evidence includes RCTs. Relevant outcomes are OS, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. One large RCT demonstrated that CRT led to reductions in heart failure-related hospitalizations and urgent care visits among patients with heart failure and AV block who would not necessarily meet conventional criteria for CRT. For patients who require ventricular pacing but have no LV

dysfunction, results of a small RCT have suggested that biventricular pacing is associated with improvement in cardiac function, but the trial was small and underpowered to detect differences in clinical outcomes. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have heart failure who receive triple-site CRT, the evidence includes small RCTs and a meta-analysis that included nonrandomized studies. Relevant outcomes are OS, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. The available RCTs have reported improved outcomes on at least 1 measure of functional status or quality of life with triple-site CRT compared with conventional CRT. However, the trials were small and had methodologic limitations. Also, outcomes reported differed across studies. Triple-site CRT was also associated with higher radiation exposure and a greater number of additional procedures postimplantation. Larger, high-quality RCTs are needed to better define the benefit-risk ratio for triple-site CRT compared with conventional CRT. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have heart failure who receive CRT combined with remote fluid monitoring, the evidence includes 3 RCTs. Relevant outcomes are OS, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. Three RCTs have reported no improvement in outcomes associated with remote fluid monitoring for patients with heart failure. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Date	Action
1/2024	Clarified coding information.
7/2023	Annual policy review. 2 references added. Policy statements unchanged.
6/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
6/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
7/2020	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
6/2019	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
10/2018	Annual policy review. Policy statement added that cardiac resynchronization therapy with wireless left ventricular endocardial pacing is considered investigational. Effective 10/1/2018.
1/2018	Clarified coding information.
10/2017	Clarified coding information.
7/2017	Annual policy review.
	Medically necessary criteria clarified. 7/1/2017.
6/2017	Clarified coding information.
7/2016	New references added from Annual policy review.
9/2015	Annual policy review. Policy statements for CRT in class II and II/IV heart failure changed to include presence of LBBB (and QRS >120-130 ms) OR QRS >150 ms as medically necessary criteria. New medically necessary indications described. Clarified coding information. Effective 9/1/2015.
5/2015	Clarified coding information
7/2014	New references added from Annual policy review.
5/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
4/2014	Coding information clarified
10/2013	Annual policy review. New investigational indications described. Effective 10/1/2013.

## **Policy History**

3/2013	Annual policy review. New investigational indications described. Cardiac
	Resynchronization Therapy" added to policy title. Effective 3/1/2013
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No
	changes to policy statements.
12/1/2011	Annual policy review. Changes to policy statements.
4/2011	Medical Policy Group - Cardiology and Pulmonology. No changes to policy
	statements.
6/2009	New policy, effective 6/2009, describing covered and non-covered indications.

# Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information: <u>Medical Policy Terms of Use</u> <u>Managed Care Guidelines</u> <u>Indemnity/PPO Guidelines</u> <u>Clinical Exception Process</u> <u>Medical Technology Assessment Guidelines</u>

## References

- 1. Tsao CW, Aday AW, Almarzooq ZI, et al. Heart Disease and Stroke Statistics-2023 Update: A Report From the American Heart Association. Circulation. Feb 21 2023; 147(8): e93-e621. PMID 36695182
- Bahrami H, Kronmal R, Bluemke DA, et al. Differences in the incidence of congestive heart failure by ethnicity: the multi-ethnic study of atherosclerosis. Arch Intern Med. Oct 27 2008; 168(19): 2138-45. PMID 18955644
- Loehr LR, Rosamond WD, Chang PP, et al. Heart failure incidence and survival (from the Atherosclerosis Risk in Communities study). Am J Cardiol. Apr 01 2008; 101(7): 1016-22. PMID 18359324
- Food and Drug Administration. Summary of Safety and Effectiveness Data (SSED): Cardiac Resynchronization Therapy Defibrillator (CRT-D). 2010; https://www.accescadate.fda.gov/adm..docs/adf/D010012S220h.pdf\_Accescad\_March.8, 2022
- https://www.accessdata.fda.gov/cdrh\_docs/pdf/P010012S230b.pdf. Accessed March 8, 2023. 5. Food and Drug Administration. Approval Order: Biotronic PMA P050023. 2013;
- https://www.accessdata.fda.gov/cdrh\_docs/pdf5/P050023S058A.pdf. Accessed March 9, 2023. 6. Al-Majed NS, McAlister FA, Bakal JA, et al. Meta-analysis: cardiac resynchronization therapy for
- patients with less symptomatic heart failure. Ann Intern Med. Mar 15 2011; 154(6): 401-12. PMID 21320922
- Ezekowitz JA, Rowe BH, Dryden DM, et al. Systematic review: implantable cardioverter defibrillators for adults with left ventricular systolic dysfunction. Ann Intern Med. Aug 21 2007; 147(4): 251-62. PMID 17709759
- 8. McAlister FA, Ezekowitz JA, Wiebe N, et al. Systematic review: cardiac resynchronization in patients with symptomatic heart failure. Ann Intern Med. Sep 07 2004; 141(5): 381-90. PMID 15353430
- Adabag S, Roukoz H, Anand IS, et al. Cardiac resynchronization therapy in patients with minimal heart failure: a systematic review and meta-analysis. J Am Coll Cardiol. Aug 23 2011; 58(9): 935-41. PMID 21851882
- 10. Bertoldi EG, Polanczyk CA, Cunha V, et al. Mortality reduction of cardiac resynchronization and implantable cardioverter-defibrillator therapy in heart failure: an updated meta-analysis. Does recent evidence change the standard of care?. J Card Fail. Oct 2011; 17(10): 860-6. PMID 21962425
- Nery PB, Ha AC, Keren A, et al. Cardiac resynchronization therapy in patients with left ventricular systolic dysfunction and right bundle branch block: a systematic review. Heart Rhythm. Jul 2011; 8(7): 1083-7. PMID 21300176
- Tu R, Zhong G, Zeng Z, et al. Cardiac resynchronization therapy in patients with mild heart failure: a systematic review and meta-analysis of randomized controlled trials. Cardiovasc Drugs Ther. Aug 2011; 25(4): 331-40. PMID 21750900
- Santangeli P, Di Biase L, Pelargonio G, et al. Cardiac resynchronization therapy in patients with mild heart failure: a systematic review and meta-analysis. J Interv Card Electrophysiol. Nov 2011; 32(2): 125-35. PMID 21594629

- 14. Wells G, Parkash R, Healey JS, et al. Cardiac resynchronization therapy: a meta-analysis of randomized controlled trials. CMAJ. Mar 08 2011; 183(4): 421-9. PMID 21282316
- 15. Chen S, Ling Z, Kiuchi MG, et al. The efficacy and safety of cardiac resynchronization therapy combined with implantable cardioverter defibrillator for heart failure: a meta-analysis of 5674 patients. Europace. Jul 2013; 15(7): 992-1001. PMID 23419662
- 16. Woods B, Hawkins N, Mealing S, et al. Individual patient data network meta-analysis of mortality effects of implantable cardiac devices. Heart. Nov 2015; 101(22): 1800-6. PMID 26269413
- 17. Sun WP, Li CL, Guo JC, et al. Long-term efficacy of implantable cardiac resynchronization therapy plus defibrillator for primary prevention of sudden cardiac death in patients with mild heart failure: an updated meta-analysis. Heart Fail Rev. Jul 2016; 21(4): 447-53. PMID 27043219
- Ali-Hassan-Al-Saegh S, Mirhosseini SJ, Karimi-Bondarabadi AA, et al. Cardiac resynchronization therapy in patients with mild heart failure is a reversal therapy. Indian Heart J. 2017; 69(1): 112-118. PMID 28228294
- Lozano I, Bocchiardo M, Achtelik M, et al. Impact of biventricular pacing on mortality in a randomized crossover study of patients with heart failure and ventricular arrhythmias. Pacing Clin Electrophysiol. Nov 2000; 23(11 Pt 2): 1711-2. PMID 11139906
- Cazeau S, Leclercq C, Lavergne T, et al. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. N Engl J Med. Mar 22 2001; 344(12): 873-80. PMID 11259720
- Garrigue S, Bordachar P, Reuter S, et al. Comparison of permanent left ventricular and biventricular pacing in patients with heart failure and chronic atrial fibrillation: prospective haemodynamic study. Heart. Jun 2002; 87(6): 529-34. PMID 12010933
- Leclercq C, Walker S, Linde C, et al. Comparative effects of permanent biventricular and rightuniventricular pacing in heart failure patients with chronic atrial fibrillation. Eur Heart J. Nov 2002; 23(22): 1780-7. PMID 12419298
- 23. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med. Jun 13 2002; 346(24): 1845-53. PMID 12063368
- Auricchio A, Stellbrink C, Sack S, et al. Long-term clinical effect of hemodynamically optimized cardiac resynchronization therapy in patients with heart failure and ventricular conduction delay. J Am Coll Cardiol. Jun 19 2002; 39(12): 2026-33. PMID 12084604
- Auricchio A, Stellbrink C, Butter C, et al. Clinical efficacy of cardiac resynchronization therapy using left ventricular pacing in heart failure patients stratified by severity of ventricular conduction delay. J Am Coll Cardiol. Dec 17 2003; 42(12): 2109-16. PMID 14680736
- Higgins SL, Hummel JD, Niazi IK, et al. Cardiac resynchronization therapy for the treatment of heart failure in patients with intraventricular conduction delay and malignant ventricular tachyarrhythmias. J Am Coll Cardiol. Oct 15 2003; 42(8): 1454-9. PMID 14563591
- Young JB, Abraham WT, Smith AL, et al. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD Trial. JAMA. May 28 2003; 289(20): 2685-94. PMID 12771115
- Bristow MR, Saxon LA, Boehmer J, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. May 20 2004; 350(21): 2140-50. PMID 15152059
- Abraham WT, Young JB, León AR, et al. Effects of cardiac resynchronization on disease progression in patients with left ventricular systolic dysfunction, an indication for an implantable cardioverterdefibrillator, and mildly symptomatic chronic heart failure. Circulation. Nov 02 2004; 110(18): 2864-8. PMID 15505095
- 30. Cleland JG, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med. Apr 14 2005; 352(15): 1539-49. PMID 15753115
- 31. Gasparini M, Bocchiardo M, Lunati M, et al. Comparison of 1-year effects of left ventricular and biventricular pacing in patients with heart failure who have ventricular arrhythmias and left bundlebranch block: the Bi vs Left Ventricular Pacing: an International Pilot Evaluation on Heart Failure Patients with Ventricular Arrhythmias (BELIEVE) multicenter prospective randomized pilot study. Am Heart J. Jul 2006; 152(1): 155.e1-7. PMID 16824846
- Kindermann M, Hennen B, Jung J, et al. Biventricular versus conventional right ventricular stimulation for patients with standard pacing indication and left ventricular dysfunction: the Homburg Biventricular Pacing Evaluation (HOBIPACE). J Am Coll Cardiol. May 16 2006; 47(10): 1927-37. PMID 16697307

- Piccirillo G, Magrì D, di Carlo S, et al. Influence of cardiac-resynchronization therapy on heart rate and blood pressure variability: 1-year follow-up. Eur J Heart Fail. Nov 2006; 8(7): 716-22. PMID 16513420
- Rao RK, Kumar UN, Schafer J, et al. Reduced ventricular volumes and improved systolic function with cardiac resynchronization therapy: a randomized trial comparing simultaneous biventricular pacing, sequential biventricular pacing, and left ventricular pacing. Circulation. Apr 24 2007; 115(16): 2136-44. PMID 17420340
- 35. Leclercq C, Cazeau S, Lellouche D, et al. Upgrading from single chamber right ventricular to biventricular pacing in permanently paced patients with worsening heart failure: The RD-CHF Study. Pacing Clin Electrophysiol. Jan 2007; 30 Suppl 1: S23-30. PMID 17302711
- 36. Beshai JF, Grimm RA, Nagueh SF, et al. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. N Engl J Med. Dec 13 2007; 357(24): 2461-71. PMID 17986493
- 37. Brignole M, Auricchio A, Baron-Esquivias G, et al. 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). Eur Heart J. Aug 2013; 34(29): 2281-329. PMID 23801822
- Linde C, Abraham WT, Gold MR, et al. Randomized trial of cardiac resynchronization in mildly symptomatic heart failure patients and in asymptomatic patients with left ventricular dysfunction and previous heart failure symptoms. J Am Coll Cardiol. Dec 02 2008; 52(23): 1834-1843. PMID 19038680
- 39. Moss AJ, Hall WJ, Cannom DS, et al. Cardiac-resynchronization therapy for the prevention of heart-failure events. N Engl J Med. Oct 01 2009; 361(14): 1329-38. PMID 19723701
- Pinter A, Mangat I, Korley V, et al. Assessment of resynchronization therapy on functional status and quality of life in patients requiring an implantable defibrillator. Pacing Clin Electrophysiol. Dec 2009; 32(12): 1509-19. PMID 19765233
- 41. Boriani G, Kranig W, Donal E, et al. A randomized double-blind comparison of biventricular versus left ventricular stimulation for cardiac resynchronization therapy: the Biventricular versus Left Univentricular Pacing with ICD Back-up in Heart Failure Patients (B-LEFT HF) trial. Am Heart J. Jun 2010; 159(6): 1052-1058.e1. PMID 20569719
- 42. Martinelli Filho M, de Siqueira SF, Costa R, et al. Conventional versus biventricular pacing in heart failure and bradyarrhythmia: the COMBAT study. J Card Fail. Apr 2010; 16(4): 293-300. PMID 20350695
- 43. Tang AS, Wells GA, Talajic M, et al. Cardiac-resynchronization therapy for mild-to-moderate heart failure. N Engl J Med. Dec 16 2010; 363(25): 2385-95. PMID 21073365
- 44. Thibault B, Ducharme A, Harel F, et al. Left ventricular versus simultaneous biventricular pacing in patients with heart failure and a QRS complex ≥120 milliseconds. Circulation. Dec 20 2011; 124(25): 2874-81. PMID 22104549
- 45. van Geldorp IE, Vernooy K, Delhaas T, et al. Beneficial effects of biventricular pacing in chronically right ventricular paced patients with mild cardiomyopathy. Europace. Feb 2010; 12(2): 223-9. PMID 19966323
- 46. Foley PW, Patel K, Irwin N, et al. Cardiac resynchronisation therapy in patients with heart failure and a normal QRS duration: the RESPOND study. Heart. Jul 2011; 97(13): 1041-7. PMID 21339317
- Gillis AM, Kerr CR, Philippon F, et al. Impact of cardiac resynchronization therapy on hospitalizations in the Resynchronization-Defibrillation for Ambulatory Heart Failure trial. Circulation. May 20 2014; 129(20): 2021-30. PMID 24610807
- Goldenberg I, Hall WJ, Beck CA, et al. Reduction of the risk of recurring heart failure events with cardiac resynchronization therapy: MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy). J Am Coll Cardiol. Aug 09 2011; 58(7): 729-37. PMID 21816309
- 49. Goldenberg I, Kutyifa V, Klein HU, et al. Survival with cardiac-resynchronization therapy in mild heart failure. N Engl J Med. May 01 2014; 370(18): 1694-701. PMID 24678999
- Hosseini SM, Moazzami K, Rozen G, et al. Utilization and in-hospital complications of cardiac resynchronization therapy: trends in the United States from 2003 to 2013. Eur Heart J. Jul 14 2017; 38(27): 2122-2128. PMID 28329322
- 51. Yu CM, Abraham WT, Bax J, et al. Predictors of response to cardiac resynchronization therapy (PROSPECT)--study design. Am Heart J. Apr 2005; 149(4): 600-5. PMID 15990740

- 52. Chung ES, Leon AR, Tavazzi L, et al. Results of the Predictors of Response to CRT (PROSPECT) trial. Circulation. May 20 2008; 117(20): 2608-16. PMID 18458170
- 53. Thibault B, Harel F, Ducharme A, et al. Cardiac resynchronization therapy in patients with heart failure and a QRS complex 120 milliseconds: the Evaluation of Resynchronization Therapy for Heart Failure (LESSER-EARTH) trial. Circulation. Feb 26 2013; 127(8): 873-81. PMID 23388213
- 54. Sipahi I, Carrigan TP, Rowland DY, et al. Impact of QRS duration on clinical event reduction with cardiac resynchronization therapy: meta-analysis of randomized controlled trials. Arch Intern Med. Sep 12 2011; 171(16): 1454-62. PMID 21670335
- Bryant AR, Wilton SB, Lai MP, et al. Association between QRS duration and outcome with cardiac resynchronization therapy: a systematic review and meta-analysis. J Electrocardiol. 2013; 46(2): 147-55. PMID 23394690
- 56. Stavrakis S, Lazzara R, Thadani U. The benefit of cardiac resynchronization therapy and QRS duration: a meta-analysis. J Cardiovasc Electrophysiol. Feb 2012; 23(2): 163-8. PMID 21815961
- Sipahi I, Chou JC, Hyden M, et al. Effect of QRS morphology on clinical event reduction with cardiac resynchronization therapy: meta-analysis of randomized controlled trials. Am Heart J. Feb 2012; 163(2): 260-7.e3. PMID 22305845
- Kang SH, Oh IY, Kang DY, et al. Cardiac resynchronization therapy and QRS duration: systematic review, meta-analysis, and meta-regression. J Korean Med Sci. Jan 2015; 30(1): 24-33. PMID 25552880
- 59. Shah RM, Patel D, Molnar J, et al. Cardiac-resynchronization therapy in patients with systolic heart failure and QRS interval ≤130 ms: insights from a meta-analysis. Europace. Feb 2015; 17(2): 267-73. PMID 25164431
- Friedman DJ, Al-Khatib SM, Dalgaard F, et al. Cardiac Resynchronization Therapy Improves Outcomes in Patients With Intraventricular Conduction Delay But Not Right Bundle Branch Block: A Patient-Level Meta-Analysis of Randomized Controlled Trials. Circulation. Mar 07 2023; 147(10): 812-823. PMID 36700426
- 61. Peterson PN, Greiner MA, Qualls LG, et al. QRS duration, bundle-branch block morphology, and outcomes among older patients with heart failure receiving cardiac resynchronization therapy. JAMA. Aug 14 2013; 310(6): 617-26. PMID 23942680
- 62. Kutyifa V, Stockburger M, Daubert JP, et al. PR interval identifies clinical response in patients with non-left bundle branch block: a Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy substudy. Circ Arrhythm Electrophysiol. Aug 2014; 7(4): 645-51. PMID 24963007
- Stockburger M, Moss AJ, Klein HU, et al. Sustained clinical benefit of cardiac resynchronization therapy in non-LBBB patients with prolonged PR-interval: MADIT-CRT long-term follow-up. Clin Res Cardiol. Nov 2016; 105(11): 944-952. PMID 27318807
- Friedman DJ, Bao H, Spatz ES, et al. Association Between a Prolonged PR Interval and Outcomes of Cardiac Resynchronization Therapy: A Report From the National Cardiovascular Data Registry. Circulation. Nov 22 2016; 134(21): 1617-1628. PMID 27760795
- 65. Hawkins NM, Petrie MC, MacDonald MR, et al. Selecting patients for cardiac resynchronization therapy: electrical or mechanical dyssynchrony?. Eur Heart J. Jun 2006; 27(11): 1270-81. PMID 16527827
- 66. Muto C, Solimene F, Gallo P, et al. A randomized study of cardiac resynchronization therapy defibrillator versus dual-chamber implantable cardioverter-defibrillator in ischemic cardiomyopathy with narrow QRS: the NARROW-CRT study. Circ Arrhythm Electrophysiol. Jun 2013; 6(3): 538-45. PMID 23592833
- 67. Ruschitzka F, Abraham WT, Singh JP, et al. Cardiac-resynchronization therapy in heart failure with a narrow QRS complex. N Engl J Med. Oct 10 2013; 369(15): 1395-405. PMID 23998714
- Brignole M, Pokushalov E, Pentimalli F, et al. A randomized controlled trial of atrioventricular junction ablation and cardiac resynchronization therapy in patients with permanent atrial fibrillation and narrow QRS. Eur Heart J. Dec 01 2018; 39(45): 3999-4008. PMID 30165479
- 69. Brignole M, Pentimalli F, Palmisano P, et al. AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: the APAF-CRT mortality trial. Eur Heart J. Dec 07 2021; 42(46): 4731-4739. PMID 34453840

- Brignole M, Botto G, Mont L, et al. Cardiac resynchronization therapy in patients undergoing atrioventricular junction ablation for permanent atrial fibrillation: a randomized trial. Eur Heart J. Oct 2011; 32(19): 2420-9. PMID 21606084
- Kalscheur MM, Saxon LA, Lee BK, et al. Outcomes of cardiac resynchronization therapy in patients with intermittent atrial fibrillation or atrial flutter in the COMPANION trial. Heart Rhythm. Jun 2017; 14(6): 858-865. PMID 28323173
- 72. Healey JS, Hohnloser SH, Exner DV, et al. Cardiac resynchronization therapy in patients with permanent atrial fibrillation: results from the Resynchronization for Ambulatory Heart Failure Trial (RAFT). Circ Heart Fail. Sep 01 2012; 5(5): 566-70. PMID 22896584
- 73. Khazanie P, Greiner MA, Al-Khatib SM, et al. Comparative Effectiveness of Cardiac Resynchronization Therapy Among Patients With Heart Failure and Atrial Fibrillation: Findings From the National Cardiovascular Data Registry's Implantable Cardioverter-Defibrillator Registry. Circ Heart Fail. Jun 2016; 9(6). PMID 27296396
- 74. Curtis AB, Worley SJ, Adamson PB, et al. Biventricular pacing for atrioventricular block and systolic dysfunction. N Engl J Med. Apr 25 2013; 368(17): 1585-93. PMID 23614585
- 75. Curtis AB, Worley SJ, Chung ES, et al. Improvement in Clinical Outcomes With Biventricular Versus Right Ventricular Pacing: The BLOCK HF Study. J Am Coll Cardiol. May 10 2016; 67(18): 2148-2157. PMID 27151347
- 76. Yu CM, Chan JY, Zhang Q, et al. Biventricular pacing in patients with bradycardia and normal ejection fraction. N Engl J Med. Nov 26 2009; 361(22): 2123-34. PMID 19915220
- 77. Chan JY, Fang F, Zhang Q, et al. Biventricular pacing is superior to right ventricular pacing in bradycardia patients with preserved systolic function: 2-year results of the PACE trial. Eur Heart J. Oct 2011; 32(20): 2533-40. PMID 21875860
- 78. Yu CM, Fang F, Luo XX, et al. Long-term follow-up results of the pacing to avoid cardiac enlargement (PACE) trial. Eur J Heart Fail. Sep 2014; 16(9): 1016-25. PMID 25179592
- Doshi RN, Daoud EG, Fellows C, et al. Left ventricular-based cardiac stimulation post AV nodal ablation evaluation (the PAVE study). J Cardiovasc Electrophysiol. Nov 2005; 16(11): 1160-5. PMID 16302897
- Anselme F, Bordachar P, Pasquié JL, et al. Safety, feasibility, and outcome results of cardiac resynchronization with triple-site ventricular stimulation compared to conventional cardiac resynchronization. Heart Rhythm. Jan 2016; 13(1): 183-9. PMID 26325531
- Bencardino G, Di Monaco A, Russo E, et al. Outcome of Patients Treated by Cardiac Resynchronization Therapy Using a Quadripolar Left Ventricular Lead. Circ J. 2016; 80(3): 613-8. PMID 26821688
- Lenarczyk R, Kowalski O, Sredniawa B, et al. Implantation feasibility, procedure-related adverse events and lead performance during 1-year follow-up in patients undergoing triple-site cardiac resynchronization therapy: a substudy of TRUST CRT randomized trial. J Cardiovasc Electrophysiol. Nov 2012; 23(11): 1228-36. PMID 22651239
- Pappone C, Ćalović Ž, Vicedomini G, et al. Improving cardiac resynchronization therapy response with multipoint left ventricular pacing: Twelve-month follow-up study. Heart Rhythm. Jun 2015; 12(6): 1250-8. PMID 25678057
- Rogers DP, Lambiase PD, Lowe MD, et al. A randomized double-blind crossover trial of triventricular versus biventricular pacing in heart failure. Eur J Heart Fail. May 2012; 14(5): 495-505. PMID 22312038
- 85. Gould J, Claridge S, Jackson T, et al. Standard care vs. TRIVEntricular pacing in Heart Failure (STRIVE HF): a prospective multicentre randomized controlled trial of triventricular pacing vs. conventional biventricular pacing in patients with heart failure and intermediate QRS left bundle branch block. Europace. May 03 2022; 24(5): 796-806. PMID 35079787
- 86. Zhang B, Guo J, Zhang G. Comparison of triple-site ventricular pacing versus conventional cardiac resynchronization therapy in patients with systolic heart failure: A meta-analysis of randomized and observational studies. J Arrythmia. 2018;34:55-64. PMID
- 87. Domenichini G, Rahneva T, Diab IG, et al. The lung impedance monitoring in treatment of chronic heart failure (the LIMIT-CHF study). Europace. Mar 2016; 18(3): 428-35. PMID 26683599
- Lüthje L, Vollmann D, Seegers J, et al. A randomized study of remote monitoring and fluid monitoring for the management of patients with implanted cardiac arrhythmia devices. Europace. Aug 2015; 17(8): 1276-81. PMID 25983310

- 89. Böhm M, Drexler H, Oswald H, et al. Fluid status telemedicine alerts for heart failure: a randomized controlled trial. Eur Heart J. Nov 01 2016; 37(41): 3154-3163. PMID 26984864
- 90. Kusumoto FM, Schoenfeld MH, Barrett C, et al. 2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines, and the Heart Rhythm Society. J Am Coll Cardiol. Aug 20 2019; 74(7): 932-987. PMID 30412710
- 91. Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices): developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. Circulation. May 27 2008; 117(21): e350-408. PMID 18483207
- 92. Tracy CM, Epstein AE, Darbar D, et al. 2012 ACCF/AHA/HRS focused update of the 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. [corrected]. Circulation. Oct 02 2012; 126(14): 1784-800. PMID 22965336
- 93. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation. Oct 15 2013; 128(16): 1810-52. PMID 23741057
- 94. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. May 03 2022; 79(17): e263-e421. PMID 35379503
- 95. Lindenfeld J, Albert NM, Boehmer JP, et al. HFSA 2010 Comprehensive Heart Failure Practice Guideline. J Card Fail. Jun 2010; 16(6): e1-194. PMID 20610207
- 96. National Institute for Health and Care Excellence (NICE). Implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure [TA314]. 2014; https://www.nice.org.uk/guidance/ta314. Accessed March 9, 2023.