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2023 HRS/APHRS/LAHRS guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure.

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2023 HRS/APHRS/LAHRS guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure

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Abstract

Cardiac physiologic pacing (CPP), encompassing cardiac resynchronization therapy (CRT) and conduction system pacing (CSP), has emerged as a pacing therapy strategy that may mitigate or prevent the development of heart failure (HF) in patients with ventricular dyssynchrony or pacing-induced cardiomyopathy. This clinical practice guideline is intended to provide guidance on indications for CRT for HF therapy and CPP in patients with pacemaker indications or HF, patient selection, pre-procedure evaluation and preparation, implant procedure management, follow-up evaluation and optimization of CPP response, and use in pediatric populations. Gaps in knowledge, pointing to new directions for future research, are also identified.

Keywords

Guideline; Cardiac resynchronization therapy; Conduction system pacing; His bundle pacing; Left bundle branch area pacing

Section 1 Introduction

1.1. Preamble

The Heart Rhythm Society (HRS) has developed scientific and clinical documents that have guided clinical care in the management of cardiac arrhythmias since 1996. This HRS-led clinical practice guideline was developed in partnership with the Asia Pacific Heart Rhythm Society (APHRS) and the Latin American Heart Rhythm Society (LAHRS) and in collaboration with the American College of Cardiology (ACC), the American Heart Association (AHA), the Pediatric and Congenital Electrophysiology Society (PACES), the

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Appendix

Supplementary data

Supplementary data (Appendix 3) associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2023.03.1538.

International Society of Holter and Noninvasive Electrocardiology (ISHNE), and the Heart Failure Society of America (HFSA).

This clinical practice guideline provides recommendations applicable to patients who have or are at risk of heart failure (HF) who are being considered for or who are undergoing a cardiac physiologic pacing (CPP) implantation procedure. Although the term "physiologic pacing" has been used to describe sensor-driven rate response pacing or variable atrioventricular (AV) delay pacing, this guideline utilizes a contemporary definition of CPP that refers to *cardiac pacing intended to restore or preserve ventricular synchrony, including cardiac resynchronization therapy* (*CRT*) *utilizing left ventricular stimulation, His bundle pacing* (*HBP*), *or left bundle branch area pacing* (*LBBAP*). Scientific evidence was systematically reviewed and translated into clinical practice guidelines with recommendations to improve the quality of care in the use of CPP. The guideline was developed in international collaboration and is intended to be relevant to medical practice worldwide. Although guidelines may be used to inform regulatory or payer decisions, the intent is to improve quality of care, support appropriate use of therapeutics, and align with patients' interests. Guidelines are intended to define practices that meet the needs of patients in most, but not all, circumstances and are not meant to replace clinical judgment.

1.2. Document scope, objectives, and assumptions

Since the publication of the *2012 EHRA/HRS Expert Consensus Statement on Cardiac Resynchronization Therapy in Heart Failure: Implant and Follow-up Recommendations and Management*[1] and the *2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients with Bradycardia and Cardiac Conduction Delay*,[2] extensive data have emerged regarding optimization of pacing techniques and new pacing-related therapies, including CPP, for patients with pacing indications or HF. The purpose of this guideline is to evaluate these new advances with the goal of creating recommendations to guide electrophysiology practice in the use of CPP in patients with pacing or HF indications.

Although right ventricular (RV) apical pacing has long been a standard treatment for symptomatic AV block, it has become clear that in a proportion of patients, right ventricular pacing (RVP) can lead to dyssynchronous left ventricular (LV) contraction and HF. With the introduction of biventricular (BiV) pacing for CRT, studies have shown that CRT can lead to improvements in LV function, HF, and survival in selected patients with decreased LV function in the setting of conduction system disease or RVP. However, the impact of an unfavorable response to CRT has become apparent. Over the past decade, data have emerged that may enable improvements in response rate, including refinement of selection criteria (eg, patient populations, conduction disorder type, and expected RVP burden), improvements in implant practices (eg, anatomical lead position, quadripolar leads, and new software technology to increase response to CRT pacing), and management of postimplant care (eg, follow-up evaluation of CRT patients, identification and treatment of nonresponders, and shared decision-making at generator replacement or revision). More recently, the field of physiologic pacing has been greatly expanded by technological advances to directly target the conduction system, including HBP, LBBAP, and direct LV pacing. These advances bring additional questions, including those regarding patient

selection, indications, and follow-up for conduction system pacing (CSP) vs CRT via BiV pacing.

This guideline is not intended to be a comprehensive review of pathophysiology but to provide guidance for the use of CPP, which we define as an umbrella term that encompasses CRT with BiV pacing and CSP, including HBP and LBBAP. The guideline includes indications for CRT for HF therapy, guidance on indications for CPP in patients with pacemaker indications or HF, patient selection, preprocedure evaluation and preparation, implant procedure management, follow-up evaluation and optimization of CPP response, and use in pediatric populations. We identify significant gaps in knowledge pointing to new directions for future research. This guideline does not address topics related to other forms of ventricular pacing (including cardiac contractility modulation pacing), indications for bradycardia pacing, implantable cardioverter-defibrillator (ICD) implantation, or lead extraction.

The intended audience includes practicing clinical cardiac electrophysiologists, cardiologists or other clinicians caring for or referring patients for cardiovascular implantable electrical devices (CIEDs), and researchers or industry personnel involved in the development of CIED technologies.

The writing committee recognizes that clinical scenarios and operator and institutional capabilities may vary widely. Recommendations assume that procedures are performed by an operator with appropriate training and experience and in a properly equipped hospital or other facility. In addition, it is assumed that restorative treatment is the patient's (or designator's) goal. There may be scenarios where therapy other than pacing may be more concordant with the patient's wishes and priorities. Scenarios for which evidence is sparse or absent will require clinicians to rely on their expertise and clinical judgment.

1.3. Editorial independence

This guideline was sponsored by HRS and was developed without commercial support; writing committee members volunteered their time to the writing and review efforts.

1.4. Organization of the writing committee and stakeholder involvement

The writing committee consisted of experts from 15 countries in the fields of electrophysiology, cardiology, pediatric electro-physiology and cardiology, and biostatistics and epidemiology. Each writing committee member served as a representative of either HRS or partner/collaborator society and was nominated according to each organization's processes. HRS strives to ensure that the writing committee contains bothrequisite expertise and diverse representation from the broader medical community. This is achieved by selecting participants from a wide range of backgrounds representing different geographic regions, genders, races, ethnicities, intellectual perspectives, and scopes of clinical practice and by inviting organizations and professional societies with related interests and expertise to participate as partners or collaborators. In addition, a patient partner was included in the writing committee to ensure a focus on delivering optimal patient care that is in alignment with patients' wants, needs, and preferences.

HRS has rigorous policies and methods to ensure that documents are developed without bias or improper influence. The HRS policy on relationships with industry and other entities (RWI) can be found in the HRS Code of Ethics and Professionalism: Appendix C and in the HRS Clinical Document Development Methodology Manual and Policies. A majority of the writing committee was free of relevant RWI throughout the development of the document, and sections with recommendations were written by the writing committee members who were free of relevant RWI. For full transparency, Appendix 1 is a comprehensive list of RWI (both relevant and nonrelevant to the document topic) disclosed by the writing committee members. Appendix 2 is a comprehensive list of RWI disclosed by the peer reviewers.

1.5. Evidence review and formulation of recommendations

This clinical practice guideline was developed in accordance with the clinical practice methodology processes detailed in the *HRS Clinical Document Development Methodology Manual and Policies: Executive Summary*[3] and with the standards issued in 2011 by the Institute of Medicine (now National Academy of Medicine).[4]

The writing committee reviewed evidence gathered by electronic literature searches (MEDLINE, PubMed, Embase, and Cochrane Library). No specific year was chosen for the oldest literature. Some literature databases allow the use of certain symbols to search for different forms or spellings of a word. The asterisk (*) was used for truncation to search for all forms of a word, the plus (+) symbol was used to search for plural and singular forms of a word, and the hash symbol (#) was used as a wildcard to search for variant spellings or hyphenation of a word. Search terms included, but were not limited to, the following: *12 lead ECG*, *abandon**, *ACHD*, *adaptive pacing*, *adult congenital heart disease*, *adverse effects*, *alternative site**, *ambulation*, *apex*, *artificial*, *atrial fibrillation*, *AV block*, *AV node ablation*, *bipolar lead**, *BIV*, *biventricular pacing*, *bleed**, *bundle of his*, *cardiac echocardiography*, *cardiac magnetic resonance*, *cardiac pacing*, *cardiac resynchroniz**, *cardiac resynchronization therap**, *CHD*, *clinical outcomes*, *combin**, *complete AV block*, *complication**, *congenital heart disease*, *coronary sinus*, *cost**, *crossover**, *CRT*, *CRT indication*, *device clinic management*, *ECG*, *Echo*, *echocardiograph**, *echocardiography guided*, *ejection fraction*, *emergen**, *epicardial left ventricular*, *epicardial LV lead*, *feasibility*, *fft*, *guide**, *guiding*, *heart block*, *heart ventricle**, *hematoma**, *hemorrhage*, *his bundle*, *his bundle*, *His bundle pacing*, *his optimized*, *hospital admission**, *HOT-CRT*, *HBP*, *Image**, *Imaging**, *impact**, *improv**, *infection**, *lateral wall*, *LBBAP*, *lead placement*, *lead placement failure*, *left bundle area pacing*, *left bundle branch*, *Left bundle branch area pacing*, *left bundle branch block*, *left bundle branch pacing*, *left bundle pacing*, *left ventricular*, *left ventricular pacing*, *long term adverse effects*, *LV*, *LV Epi lead*, *LV epicardia*, *LV pacing*, *magnetic resonance imaging*, *mild*, *mortality*, *multi point pacing*, *multisite pacing*, *narrow QRS*, *New York Heart Association*, *non LBBB*, *non-LBBB*, *non#left bundle branch*, *non-selective*, *NYHA*, *optimal lead location**, *optimal lead position**, *optimization*, *optimized CRT*, *outcome**, *pace**, *pacemaker*, *pacing**, *patient readmission*, *pediatric**, *placements*, *pneumothorax*, *pre-procedural imaging*, *QLV*, *QRS duration*, *quadripolar lead**, *quality of life*, *QOL*, *randomized control trial*, *RBBB*, *RCT*, *respond**, *response*, *resynchronization*, *reverse remodeling*, *RV pacing*, *selective*, *septal pacing*, *shared decision*, *shared decision-making*, *survival*, *testing*, *treatment outcome*,

troubleshooting, *ventricularization*, *ventricularized lead*, *walk**. Literature searches focused whenever possible on randomized controlled trials (RCTs), but systematic reviews, nonrandomized and registry studies, cohort studies, and case series were included. Case reports were not used to support recommendations. Evidence tables are included in Appendix 3 and summarize the evidence used by the writing committee to formulate recommendations. References are representative of the totality of data and are not meant to be all-inclusive. Limitations of the evidence base are discussed in individual sections.

The writing committee discussed all recommendations with the consideration of the risk vs benefit of an intervention and the strength of the evidence. To assess consensus after discussions, the writing committee members participated in surveys. A predefined threshold of 80% approval for each recommendation was required, with a quorum of two-thirds of the writing committee. An initial failure to reach consensus was resolved by subsequent discussions, revisions as needed, and revoting. Writing committee members with RWI did not vote on recommendations concerning relevant topics. The final mean consensus over all recommendations was 97.3%, with 32 of 73 recommendations reaching 100% consensus.

1.6. Class of recommendation and level of evidence

Recommendations in this guideline are designated with a class of recommendation (COR) and a level of evidence (LOE). The COR denotes the strength of the recommendation based on an assessment of the magnitude and certainty of the benefits in proportion to the risks. The LOE reflects the quality of the evidence that supports the recommendation based on type, quantity, and consistency of data from clinical trials and other sources (Table 1).[5]

For clarity and usefulness, each recommendation is linked to the supportive evidence through the specific references from the literature used to justify the LOE rating, which are also summarized in the evidence tables (Appendix 3). Each recommendation is accompanied by supportive text. Algorithms and tables provide a summary of the recommendations, intended to assist clinicians at the point of care.

1.7. Document review and approval

The HRS invites public and stakeholder involvement in document development. In addition to patient representation on the writing committee, draft recommendations were posted for public comment, and contribution was solicited from regulatory agencies and patient organizations.

This guideline was approved by the writing committee and underwent internal review by the HRS Scientific and Clinical Documents Committee. The document underwent external peer review by reviewers appointed by HRS and each of the collaborating societies, and revisions were made by the chairs. A record of writing committee response to reviewer comments and rationale is maintained by the HRS.

1.8. Document updates

The HRS Scientific and Clinical Documents Committee reviews each clinical practice document for currency at least every 5 years, or earlier in the event of newly published data. Literature is routinely monitored to evaluate the continued validity of recommendations.

1.9. Other guideline documents and systematic reviews

Clinical practice documents and systematic reviews relevant to the topic of CPP were used to inform the development of this guideline. Table 2 lists applicable clinical practice documents (eg, guidelines and consensus statements) that the writing committee considered as fundamental to the development of this document, and Table 3 lists systematic reviews that informed the clinical practice guideline development. Other systematic reviews used to support specific recommendations are referenced in respective sections.

Section 2 Definitions, epidemiology, and pathophysiology

In this section we define CPP as distinct from RV septal pacing, distinguish between HBP and LBBAP, and provide guidance on what constitutes a high percentage of RVP that may result in iatrogenic HF due to ventricular dyssynchrony. We present the range of objective criteria (echocardiographic parameters and increase in peak oxygen uptake [VO_2]) and clinical criteria (reduction in heart failure hospitalization [HFH], mortality, and others) that can be used to define response to CPP. We review the physiology of ventricular dyssynchrony and how it is promoted by left bundle branch block (LBBB). Finally, we review the concept of HF produced by intrinsic ventricular electrical dyssynchrony or chronic RVP and how it might be corrected by CPP.

2.1. Definitions

The terms used in this guideline are defined in Table 4. The criteria for defining the clinical and echocardiographic response to CRT are listed in Table 5.

2.2. Epidemiology, pathophysiology, and detection of electrical dyssynchrony–induced cardiomyopathy and rationale for CPP

During RV apical pacing and LBBB, regions that are electrically activated early also contract early, while the late-activating segments of the LV contract late. This asynchronous electrical activation of the RV and LV leads to dyssynchronous mechanical contraction that is referred to as ventricular dyssynchrony. The hemodynamic consequences of this electromechanical dyssynchrony can be a reduction in LV contraction and impaired relaxation, which in turn may lead to adverse remodeling in the long term. As a result, a proportion of patients with long-term RVP or LBBB may develop dyssynchrony-induced cardiomyopathy (reduction in left ventricular ejection fraction [LVEF]) and HF.

Recommendations for detection of electrical dyssynchrony-induced cardiomyopathy

COR	LOE	Recommendations	References
1	B-NR	**1. In patients who have substantial RVP that cannot be minimized with programming, periodic assessment of ventricular function is recommended to detect pacing-induced cardiomyopathy.**	13–20
2a	B-NR	**2. In patients with chronic LBBB, periodic assessment of ventricular function is reasonable to detect cardiomyopathy.**	21–27

Synopsis—RVP and LBBB result in similar electromechanical dyssynchrony and can be associated with subsequent dyssynchrony or pacing-induced cardiomyopathy (PICM). Several factors, such as the degree of electromechanical dyssynchrony, percentage of RVP, functional mitral regurgitation, and underlying substrate (preexisting LV dysfunction) contribute to the development of cardiomyopathy. A systematic review[20] of 26 studies (6 prospective) on nearly 58,000 patients showed a pooled prevalence of 12% of PICM using 15 unique definitions from 23 publications. Reported incidence has ranged widely from 5.9% to 39% over a similarly variant follow-up time of 0.7 to 16 years.[13,14,16,17,28] These studies have used an RVP burden of 20% (4 studies), 40% (1 study), 70% (1 study), and 90% (1 study) as substantial pacing percentages associated with PICM; 18 studies did not report percent pacing. The true incidence of PICM and the time required to develop cardiomyopathy in this population are unclear. Nonetheless, dyssynchrony-induced/associated cardiomyopathy has been shown to be reversible with CPP. Hence, periodic assessment of ventricular function in patients with substantial RVP or LBBB is helpful in identifying dyssynchrony-induced cardiomyopathy.

Recommendation-specific supportive text—1. High RVP burden (>40%) has been associated with an increased risk of HFH as observed in the Mode Selection Trial (MOST).[15] The incidence of PICM in observational cohorts has ranged from 5.9% to 39%.[13,14,16,17,28] All these studies were retrospective, had differences in the definition of cardiomyopathy and percentage of RVP as inclusion criteria, and were prone to selection bias. A systematic review[20] of PICM studies found a pooled estimate of 12% with data limited by variable definitions of PICM and duration of follow-up. In a prospective, randomized, double-blind study[18] of 177 patients, RVP was associated with a significant reduction in LVEF compared to BiV pacing and 9% of patients with RVP (1% in BiV pacing) developed PICM at 12 months. In a retrospective observational study[16] of 198 patients undergoing RVP vs HBP, PICM was observed in 22% of RVP patients (1% in HBP) during 5-year follow-up. The incidence of PICM was observed in 12.3% of 823 patients with complete heart block undergoing RVP during a mean of 4.3 years of follow-up; when treated with BiV pacing, PICM was reversible in 84%.[14] In a retrospective study[19] of 60 patients with PICM, HBP was successful in 95% of patients and associated with improvement in LVEF from 34.3% to 48.2% ± 9.8% ($P < .001$). Based on these observations, in patients with a substantial burden of RVP that cannot be minimized by programming, periodic assessment of LV function is recommended to detect PICM. Once detected, PICM may be reversible with CPP.[29] A suggested time frame for LVEF assessment is every 1–2 years in patients with high-risk features (eg, QRS duration >115 ms at baseline

and paced QRS duration >150 ms) and with reduced frequency if LV function has been stable.

2. In the general population, the prevalence of LBBB ranges from 0.2% to 1.1%.[30] Approximately 30% of patients with dilated cardiomyopathy have interventricular conduction delay, with LBBB being the most common.[31] Although LBBB can result in LV dysfunction and HF from dyssynchronous contraction and is associated with an increased mortality risk in the elderly and those with underlying structural heart disease, not all patients with LBBB develop electrical dyssynchrony–mediated cardiomyopathy and it has minimal effects on younger healthy individuals.[32] Moreover, there is no formal consensus definition of LBBB-mediated cardiomyopathy. Vaillant et al[21] defined LBBB-mediated cardiomyopathy as (1) a history of typical LBBB >5 years, (2) LVEF >50% at the time of diagnosis of LBBB, (3) decrease in LVEF to <40% and the development of HF with New York Heart Association (NYHA) class II–IV over several years, (4) major mechanical dyssynchrony, (5) no known etiology of cardiomyopathy, and (6) super-response to CRT with an increase in LVEF to >45% and decrease in NYHA class at 1 year. By these criteria, they identified 8 patients (2%) in a 375-patient cohort of CRT-eligible patients.[21] Other studies[22–24] have noted a varying percentage of patients with LBBB who developed cardiomyopathy. However, these studies were all retrospective and the differences could be attributed to varying definitions. Currently, the true incidence and prevalence of electrical dyssynchrony–induced HF and cardiomyopathy remain unclear. The relationship between LBBB and LV dysfunction and HF is complex and not well understood. LBBB can reduce diastolic filling time and the septal contribution to LV ejection.[33] LBBB can be the cause or consequence of cardiomyopathy and HF. Several retrospective observational studies[21,24,25] have demonstrated that CPP can reverse LBBB-induced cardiomyopathy in a very high percentage of patients. In patients with chronic LBBB, a suggested time frame for LVEF assessment is every 1–2 years to detect LBBB-associated cardiomyopathy and with reduced frequency if LV function has been stable.

Section 3 Indications for CPP

This section outlines the consensus recommendations on indications for CPP, divided by indications for pacing, anticipated requirement for ventricular pacing, LVEF, and presence of HF, LBBB, and AF.

3.1. Patients with indications for pacemaker therapy

This section provides recommendations for pacing strategies in patients undergoing pacemaker implantation for bradycardia indications, as outlined in Figure 1. Subgroups addressed include patients who are anticipated to require substantial (<20%–40%) vs less than substantial (<20%–40%) ventricular pacing, and those with normal LVEF vs LVEF >35% (see definitions in Section 2.1). Recommendations for patients with reduced LV function (< 35%) or PICM are addressed in Section 3.2.

3.1.1. Substantial ventricular pacing

Recommendations for substantial ventricular pacing

COR	LOE	Recommendations	References
2a	B-R (CRT) B-NR (HBP, LBBAP)	**1. In patients with an indication for permanent pacing with an LVEF 36%−50% who are anticipated to require substantial ventricular pacing, CPP is reasonable to reduce the risk of PICM.**	CRT[9,10,34–39] HBP[9,10,16,40–44] LBBAP[45–48]
2b	B-NR	**2. In patients with normal LVEF who are anticipated to require substantial ventricular pacing, it may be reasonable to treat patients with CPP to reduce the risk of PICM.**	14,16,34,38–41,43, 49–54
2b	C-LD	**3. In patients who are ventricular pacing-dependent undergoing HBP pacemaker implantation, placement of an additional backup lead may be reasonable to mitigate the risk of high pacing capture thresholds, lead dislodgment, loss of capture, or oversensing.**	16,42

Synopsis: The type of pacing strategy selected will have a greater impact on patients who require substantial amounts of ventricular pacing compared to those who require minimal ventricular pacing. In addition, the impact of pacing strategy will vary based on the pre-pacing LVEF. In patients with ejection fraction (EF) 36%–50%, physiologic pacing (CRT, HBP, and LBBAP) is most likely to preserve or improve the LVEF when pacing requirements are substantial. It is not yet clear which patients with normal LVEF will develop PICM from RVP; therefore, it may be acceptable to choose CPP when pacing requirements will be substantial to prevent PICM in patients with normal LVEF. It is reasonable to implant a “backup” lead when the primary pacing lead is a His bundle lead and the patient will require substantial pacing because His bundle leads have a substantial incidence of rising thresholds.

Recommendation-specific supportive text: 1. For the 2018 bradycardia clinical practice guideline,[55] a systematic review[10] was performed assessing physiologic pacing (CRT and HBP) vs RVP in patients with moderately reduced LV function (LVEF 35%–50%) expected to require significant ventricular pacing. This review included 3 randomized or crossover studies of CRT vs RVP (total n = 335). The main finding was that RV PICM can be avoided in patients with reduced LVEF needing significant ventricular pacing by delivering CRT or HBP pacing.[10] The Biventricular Versus Right Ventricular Pacing in Heart Failure Patients With Atrioventricular Block (BLOCK HF) trial[35] assessed CRT in patients with reduced LV function (≤ 50%) and an expected high burden of ventricular pacing. Subjects randomized to CRT had fewer HFH. However, some patients in BLOCK HF had LVEF ≤35%, so it was not included in the systematic review discussed above. LBBAP was also not commonly performed at the time of that review.

LBBAP can reduce QRS duration and preserve ventricular synchrony, which, based on existing evidence, may benefit patients with reduced LVEF needing substantial ventricular pacing. Compared with HBP, LBBAP has a higher rate of successful implantation, and LBBAP leads demonstrate excellent medium-term lead stability and electrical characteristics.[46,56,57] Longer-term data are recently emerging, and randomized data are limited to patients with AV block and reduced LVEF. In prospective observational cohorts[45,47,58] of CRT-eligible patients receiving LBBAP, echocardiographic measures

including LVEF were improved from baseline. Furthermore, when compared to traditional CRT, early and mid-term echocardiographic and functional outcomes are favorable for LBBAP.[59] A recent retrospective analysis[60] also suggests that LBBAP reduces the incidence of AF when compared to RVP. Complications of LBBAP (eg, septal perforation), extraction considerations for deep septal leads, and long-term consequences of delayed RV activation, among other factors, are concerns for which long-term data are lacking.

2. The detrimental effects of chronic RVP have been well detailed since the publication of the Dual Chamber and VVI Implantable Defibrillator (DAVID) trial and others.[13–15,61] To avoid PICM, CPP strategies have been successful at preserving synchronous ventricular contraction and improving clinical outcomes.

HBP vs RVP: Many small observational studies have compared HBP to RVP. Among 34 patients with high-grade AV block, QRS duration <120 ms, and LVEF ≥40%, LVEF was slightly lower during RV septal pacing vs HBP ($P = .005$).[41] In 192 patients with >40% pacing, HFH was less in the HBP group (2%) compared to the RVP group (15%) ($P = .02$).[43] In 192 consecutive patients with normal LVEF referred for permanent pacemaker implantation, the subgroup of patients requiring >40% ventricular pacing had significantly more death and HFH in the RVP group (53%) than in the HBP group (28%) (hazard ratio [HR] 2.1; $P = .02$).[16] In 332 consecutive patients who underwent HBP compared to 442 similar patients who underwent RVP in a sister hospital, the combined endpoint of death from any cause, HFH, or upgrade to BiV pacing was significantly lower in the HBP group (25%) than in the RVP group (32%) (HR 0.71; $P = .02$).[40] In a meta-analysis[50] of 2349 patients with normal or mildly reduced EF who required >20% ventricular pacing, HBP or BiV pacing was superior to RVP and associated with lower all-cause death and HFH. There was no significant difference between BiV pacing and HBP.[50] HBP is technically more difficult to achieve than RVP with widely variable (80%–100%) reported rates of HBP procedural success even by experienced implanters.[16,40,41,43]

LBBAP vs RVP: In an observational registry[52] of 703 patients who underwent pacemaker implantation with LBBAP (321) or RVP (382) for bradycardia indications with mean baseline LVEF 58%, the primary composite outcome of all-cause mortality, HFH, or upgrade to BiV pacing was significantly lower with LBBAP (10.0%) compared to RVP (23.3%) (HR 0.46; $P < .001$). The endpoint was driven by patients with ventricular pacing burden >20%. In a study[51] of AV block patients (LVEF >50%) who received LBBAP or RVP, patients with LBBAP had significantly lower occurrences of HFH and upgrade to BiV pacing than patients with RVP (2.6% vs 10.8%; $P < .001$). Differences in outcome were driven by patients with ventricular pacing >40%. In a retrospective review[48] of 70 patients who underwent RVP vs LBBAP, HFH and AF incidences were less in the LBBAP group. A recent retrospective analysis[60] also suggests that LBBAP reduces the incidence of AF when compared to RVP.

CRT vs RVP: Two studies, 1 with 50 patients[34] and the other with 149 patients,[39] followed patients with normal LVEF and found BiV pacing was associated with preserved LVEF and avoidance of adverse remodeling during long-term follow-up when compared to RVP. The Progressive Ventricular Dysfunction Prevention in Pacemaker Patients (PREVENT-HF)

trial[38] randomized 108 patients with anticipated ventricular pacing at least 80% to BiV pacing (n = 50) vs RV apical pacing (n = 58). Subjects had nearly normal LVEF at baseline (57.5% ± 11.8% BiV pacing and 54.9% ± 12.9% RVP). The study did not show benefit of BiV pacing over RVP but did not show harm.

3. Data regarding long-term outcomes are scarce, but most series reflect a relatively higher risk of revision in His bundle leads compared with RV leads due to suboptimal outcomes, including risk of unacceptably high His bundle lead capture threshold, dislodgment, loss of capture, and oversensing (of atrial or His potentials). Revisions are reported in the medium term in approximately 5%–7% of acutely successful implants.[8,16,42,62] Thus, for HBP, after weighing the risks and benefits of additional hardware, procedural duration, programming complexity, and cost, it may be reasonable to place a “backup” ventricular lead in scenarios in which ventricular capture is critical (eg, pacemaker dependency).[8] Short- and medium-term outcomes demonstrate LBBAP lead stability and lead revision risk to be similar to those of traditional RVP.[52]

3.1.2. Less than substantial ventricular pacing

Recommendations for less than substantial ventricular pacing

COR	LOE	Recommendations	References
2a	B-R	**1. In patients with an indication for permanent pacing with LVEF >35% who are anticipated to require less than substantial ventricular pacing, it is reasonable to choose a traditional RV lead placement and minimize RVP.**	14,40,52
2b	C-LD	**2. In patients with an indication for permanent pacing with LVEF 36%−50% who are anticipated to require less than substantial ventricular pacing, a CSP lead with HBP or LBBAP may be considered as an alternative to an RVP lead.**	40,52
2b	C-LD	**3. In patients with an indication for permanent pacing, LVEF 36%−50% and LBBB, and who are anticipated to require less than substantial ventricular pacing, CPP may be considered to potentially improve symptoms and LVEF.**	25,45,52,58,63–66
2b	C-LD	**4. In patients who are undergoing permanent pacing with normal LVEF and are anticipated to require less than substantial ventricular pacing, an LBBAP lead may be considered as an alternative to an RVP lead.**	46,52
3: No Benefit	B-R	**5. In patients with normal LVEF who are anticipated to require less than substantial ventricular pacing, CRT with BiV pacing is not indicated.**	14,34,38,39,53,54,67,68

Synopsis: Patients who require less than substantial amounts of ventricular pacing will have a smaller clinical impact of the pacing strategy selected compared to those who require substantial ventricular pacing. Therefore, RV lead placement with minimization of RVP, as well as CSP, are acceptable strategies for patients with normal or mildly depressed LVEF. CRT with BiV pacing has not been found to be of benefit in patients who are not anticipated to require substantial pacing and who have normal LVEF.

Recommendation-specific supportive text: 1. Patients with a normal QRS complex and LVEF 36%–50% in whom expected pacing is minimal account for <40% of the studied population in observational comparative studies of broad populations of patients with indications for de novo pacemaker implantation.[16,40,43,46,52,57] Despite the narrower QRS

complex in CSP groups, these studies failed to demonstrate a significant difference in clinical outcomes (mortality or HFH) between CSP and RVP in the group for whom expected pacing is minimal.[16,40,41,43,52,69] There are proven benefits to choose a traditional RV lead and minimize RVP as evidenced by the Evaluation of the SafeR Mode in Patients With Dual-Chamber Pacemaker Indication (ANSWER) trials.[70,71]

2. To date, the clinical benefits of CSP in terms of mortality, HFH, and reduction of PICM have been observed only in patients who require substantial pacing.[16,40,43,46,52,57] It is difficult to predict which patients may progress from requiring minimal RVP at the time of implant to needing substantial pacing in the future; therefore, CSP may be considered in selected cases where it is suspected that RVP requirements might increase over time. Follow-up clinical data are emerging to establish safety for CSP,[40,52] but additional data from multiple centers are needed to establish longer-term clinical outcomes and safety.

3. Some patients who already meet indications for a conventional pacemaker but are anticipated to require less than substantial pacing (< 20%–40%) might still benefit from CPP. Patients with impaired LV function, evidenced by LVEF between 36% and 50%, and electrical dyssynchrony, evidenced by LBBB, may benefit from CPP. Three relatively large observational studies[52,58,66] and several smaller cohort studies[25,45,63–65] have shown that CPP can significantly improve symptoms and LVEF in this population.

4. A prospective observational study[46] of 632 consecutive patients showed that LBBAP was successful in 98%, had stable pacing parameters over 2 years of follow-up, and improved the LVEF in patients who had a QRS duration .120 ms at baseline (48% to 58%; $P < .0s01$). Rising thresholds occurred in only 1% of patients, and only 2 patients required lead revision. An observational registry[52] of 703 patients who underwent PPM implant for bradycardia indications compared outcomes of LBBAP to RV apical pacing (321 LBBAP and 382 RVP). The primary composite outcome (all-cause mortality, HFH, or upgrade to BiV pacing) was significantly lower with LBBAP compared to RVP (10.0% vs 23.3%; $P < .001$). Among patients with ventricular pacing burden >20%, LBBAP was associated with an even greater reduction in the primary outcome compared to RVP (8.4% vs 26.1%; $P < .001$). LBBAP was also associated with a significant reduction in mortality (7.8% vs 15%; $P = .03$) and HFH (3.7% vs 10.5%; $P = .004$). The Multicentre European Left Bundle Branch Area Pacing Outcomes Study (MELOS)[66] of LBBAP outcomes in 2533 patients, however, noted a learning curve for LBBAP lead implantation with LBBAP lead complication rate of 8.3%, though this included acute perforation to the LV in 3.7% that typically would be managed with repositioning of the lead during the procedure. Capture threshold rise occurred in 0.7%, lead dislodgment in 1.5%, acute chest pain in 1%, acute coronary syndrome in 0.4%, delayed perforation to the LV in 0.1%, and trapped/damaged helix in 0.4%. These data support the need for continued surveillance over the long-term safety of LBBAP leads.

5. Worsening of LVEF in patients who do not require substantial ventricular pacing has not been shown. Several studies[14,54] reported that PICM (defined as LVEF <40% or CRT upgrade) occurred in patients with lower preprocedure LVEF and RVP >20%. The randomized PREVENT-HF trial[38] of 108 patients with mean baseline normal LVEF did not show benefit of BiV pacing over RVP but did not show harm. Additional LV lead placement

is associated with longer procedure time, higher procedure-related complications (eg, venous occlusion and infection), and an increased risk of an additional lead to extract should that be required.[72–75] Since the incidence of PICM is low after several years of follow-up and has a higher incidence when the baseline LVEF is low and percent RVP is high, the consensus recommendation is that there is no apparent benefit of CRT in patients with preserved LVEF without a need for substantial RVP.

3.1.3. At time of surgery

Recommendations for at time of surgery

COR	LOE	Recommendations	References
2a	B-R	**1. In patients undergoing cardiac surgery who will likely require future CRT, intraoperative placement of a permanent epicardial LV lead can be useful.**	[76–78]
2b	C-EO	**2. In patients undergoing cardiac surgery who will likely require substantial ventricular pacing, intraoperative placement of a permanent epicardial LV lead may be considered to potentially reduce the risk of PICM.**	

Synopsis: An epicardial lead placed at the posterolateral or lateral wall of the LV can be performed at the time of cardiac surgery, or as a stand-alone procedure, usually by mini-thoracotomy or a minimally invasive thoracoscopic approach. A large observational study[79] demonstrated equivalent survival and improvements in LVEF for patients who received a CRT device utilizing either a surgical epicardial LV lead or a transvenous coronary sinus (CS) lead over a mean follow-up of 5.1 years. Two small RCTs[80,81] comparing surgically placed LV leads to percutaneous CS leads showed equivalence in clinical outcomes, LV function, and LV size. Furthermore, a surgically placed lead can be superior to a CS lead if there are no suitable posterolateral or lateral CS branches. In a small randomized study[82] of patients deemed to have unfavorable CS anatomy by preprocedure computerized tomography (CT) imaging, those who were randomized to a surgically placed epicardial lead had improved NYHA class, LVEF, LV volume, and peak VO_2 max by cardiopulmonary exercise testing compared to those randomized to a CS lead, for which the CS lead was then placed either in a posterior vein or the great cardiac vein. Therefore, surgically placed epicardial LV leads offer a viable alternative to CRT and a feasible option at the time of cardiac surgery. It is worth noting that placement of an epicardial LV lead that is not connected to a generator might preclude future magnetic resonance imaging (MRI) at many institutions.

Recommendation-specific supportive text: 1. In the RESCUE trial,[78]178 patients undergoing coronary artery bypass graft (CABG) surgery with an LVEF of ≤35%, NYHA class III or IV, and either a QRS duration >120 msor echocardiographic evidence of dyssynchrony were randomized to receive an epicardial CRT pacing system at time of CABG vs CABG alone. Over a mean follow-up of 55 months, patients randomized to CABG with CRT had decreased all-cause mortality (HR 0.43; $P = .012$) and reduced hospital readmission rates (9.9% vs 28.7%; $P = .001$). A trial[76] of 23 patients, who underwent CABG with implant of an epicardial CRT system and were randomized in a crossover fashion to a 3-month period with CRT programmed either on or off, found that during the CRT on period, there were significant improvements in LVEF, LV volumes, mitral

regurgitation, NYHA class, and 6-minute walk distance (6MWD).Finally, in a retrospective analysis[77] of 18 patients who had undergone implant of epicardial leads at the time of cardiac surgery as an upgrade to a prior transvenous system, there was improvement in NYHA class. These studies support implanting a permanent epicardial LV pacing lead at the time of cardiac surgery in patients likely to require future CRT.

2. In patients who are likely to require ventricular pacing but without an indication for CRT, there remains the concern that RV apical pacing may expose the patient to the potential risk of developing PICM. This risk might be avoided by taking advantage of the opportunity to place a permanent epicardial LV lead at the time of cardiac surgery. Epicardial leads placed at time of cardiac surgery have been shown to maintain good durability over time and stable lead performance parameters.[78]

3.1.4. New LBBB after transcatheter aortic valve implantation—Transcatheter aortic valve implantation (TAVI) can be complicated by AV block (see Sections 3.1.1 and 3.1.2) and LBBB. The latter occurs in approximately 10% of procedures when patients with preexisting LBBB or pacemakers and those with complete AV block postprocedure are excluded.[83] Although studies on the consequences of LBBB after TAVI have yielded mixed results, overall there appears to be an increased risk of adverse outcomes, including mortality.[84] Patients who develop new-onset persistent LBBB after TAVI have an increased risk of pacemaker implantation, which is likely influenced by multiple factors including physician and patient preference. Whether pacemaker implantation necessarily avoids any adverse consequences of LBBB is unknown–indeed, unnecessary RVP might result in deleterious effects on LV function. A prospective multicenter study[83] of 103 patients who developed new-onset LBBB after TAVI procedures and who received an implantable loop monitor before discharge found that 9 (9%) received a pacemaker for high-grade AV block at 12 months follow-up. A recent guideline[55] addressed the indications for pacing after TAVI.

Few data have been published on the optimal type of pacemaker to implant after TAVI and even less among those patients without a bradycardia indication for pacing. A study[85] of 16 patients assessed the feasibility of HBP in patients undergoing pacemaker implantation in the setting of new-onset persistent LBBB after TAVI. LBBB correction was achieved in 11 patients (69%). In over half, 2 ventricular leads were used with the second in the RV or LV via the CS. A concern with HBP in this setting is that AV block or bundle branch block (BBB) might develop at a site distal to the site of His bundle capture subsequent to pacemaker implant. Data[85–87] on LBBAP for new LBBB post-TAVI are limited to small subgroups or those with a traditional bradycardia indication for pacing (eg, complete heart block), and data on CRT are limited to case reports. Given this, the writing committee did not feel that sufficient data existed to make recommendations on the type of device to use after TAVI, beyond those for AV block or LBBB in other settings.

3.2. Indications for CPP in patients with HF

This section provides recommendations for pacing strategies in patients who do not have an a priori indication for pacing due to bradycardia but who have HF (NYHA class I–IV) across

variable QRS durations and LBBB/non-LBBB morphologies or who are expected to have a substantial burden of anticipated RVP, portending a risk of PICM, as outlined in Figure 2.

3.2.1. LBBB—This subsection focuses on recommendations for patients with LBBB morphologies with variable QRS durations and NYHA classification of HF.

3.2.1.1. LBBB, sinus rhythm, QRS duration ≥150 ms, NYHA class I–IV symptoms

Recommendations for LBBB, sinus rhythm, QRS duration ≥ 150 ms, NYHA class I–IV symptoms

COR	LOE	Recommendations	References
1	A	**1. In patients with LVEF ≤ 35%, sinus rhythm, LBBB with QRS duration ≥ 150 ms, and NYHA class II-IV symptoms on GDMT, CRT with BiV pacing is indicated to improve symptoms and reduce morbidity and mortality.**	9,88–97
2a	C-LD	**2. In patients with LVEF ≤35%, sinus rhythm, LBBB with QRS duration ≥150 ms, and NYHA class II-IV symptoms on GDMT, CSP with HBP with LBBB correction or LBBAP is reasonable if effective CRT cannot be achieved with BiV pacing based on anatomical or functional criteria.**	HBP[42,98–103] LBBAP[24,45,47,58,65,104]
2b	B-R	**3. In patients with LVEF ≤30%, sinus rhythm, LBBB, QRS duration ≥150 ms, and NYHA class I symptoms on GDMT, CRT with BiV pacing may be considered to reduce the risk of worsening HF and potentially improve LV remodeling.**	92,94
2b	C-LD	**4. In patients with LVEF 36%−50%, sinus rhythm, LBBB with QRS duration ≥ 150 ms, and NYHA class II-IV symptoms on GDMT, CPP may be considered to maintain or improve LVEF.**	CRT[63,105–107] HBP[42,98–103] LBBAP[24,45,47,58,65]
2b	C-LD	**5. In patients with LVEF ≤35%, sinus rhythm, LBBB with a QRS duration ≥150 ms, and NYHA class II-IV symptoms on GDMT, CSP with HBP or LBBAP may be considered as an alternative to CRT with BiV pacing.**	HBP[42,98–103] LBBAP[24,45,47,58, 65,104]

Synopsis: Patients with systolic HF with LVEF ≤35% who have chronic NYHA class II–IV symptoms despite guideline-directed medical therapy (GDMT) and an LBBB with wide QRS duration ≥150 ms constitute a patient population at high risk of progression of HF and other adverse cardiac events. They constituted a majority of patients in original trials for CRT, which showed significant improvements in functional status, quality of life, and mortality.[9,88,90,91,97] There is a paucity of data to support CRT implantation in patients with severe cardiomyopathy, wide QRS duration, and NYHA class I symptoms. Trials that included NYHA class I patients within this category generally included NYHA class I and II patients and did not distinguish outcomes between the 2 NYHA classes. Subsequent analyses[9,88,95] have shown that the subset of patients with LBBB and wider QRS duration derived the greatest benefit from CRT.

More recent studies[24,42,45,47,58,65,98–103,108] of CSP with HBP with LBBB correction and LBBAP have demonstrated potential to serve as alternatives to CRT with BiV pacing. In addition, there is some evidence for utility of CRT or CSP in patients with HF and mild-to-moderate reduction in LVEF.[63,105–107] If an HBP lead is chosen in an ICD or cardiac resynchronization therapy–defibrillator (CRT-D), it should not be used for tachycardia detection, as smaller R-waves and/or atrial oversensing may compromise tachycardia

detection/discrimination and result in inappropriate shocks or undertreatment of ventricular tachycardia/ventricular fibrillation.

Recommendation-specific supportive text: 1. The use of CRT with BiV pacing has been supported by long-established evidence showing improvement in clinical outcomes and extensive experience in well-selected patients. The Multicenter InSync Randomized Clinical Evaluation (MIRACLE) trial[88] studied 453 patients with NYHA class III and IV symptoms with LVEF ≤35% and QRS duration ≥130 ms implanted with a cardiac resynchronization therapy–pacemaker (CRT-P) who were then randomized to CRT off or on for 6 months. The CRT-on group had significantly greater improvement in distance walked in 6 minutes, NYHA class, quality of life, and LVEF than the CRT-off group. Additional studies[90,97] showed similar benefits in patients implanted with CRT-D devices. The Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial[90] additionally demonstrated significant survival advantage to CRT-D over medically treated patients. The Cardiac Resynchronization in Heart Failure (CARE-HF) trial[91] randomized 813 patients with NYHA class III and IV congestive heart failure (CHF), LVEF ≤35%, and QRS duration ≥120 ms to CRT-P or medical therapy and found improved survival in the CRT-P arm as well as improved LVEF, symptoms, and quality of life. Subsequent meta-analyses[9,95,109] of these studies showed that patients with LBBB and those with longer QRS duration (> 140–150 ms) were most likely to derive clinical benefit from CRT. Additional studies[88,92–94,96] in patients with LVEF ≤35% and prolonged QRS duration with only NYHA class II symptoms showed improvement in symptoms and quality of life with CRT. Two independent meta-analyses[9,95] of these studies additionally showed improved survival with CRT in this population.

2. HBP has demonstrated the potential to correct LBBB and serve as an alternative to CRT with BiV pacing. In a randomized crossover study[100] of 29 patients referred for CRT, implanting all patients with an HBP lead and a CS lead, 21 of 29 patients (72%) had significant QRS narrowing, and HBP delivered an equivalent clinical response to CRT over 6 months. Subsequent case series[42,98,99,101,102] demonstrated LBBB correction with permanent HBP in 70%–90% of patients. The Direct His-pacing as an Alternative to BiV-pacing in Symptomatic HFrEF Patients With True LBBB (His-Alternative) trial[103] randomized 50 patients to HBP vs BiV pacing. In the HBP group, 72% achieved successful LBBB correction, and HBP provided comparable clinical and echocardiographic improvement, though with higher pacing thresholds. When LBBB correction can be achieved with HBP, it is reasonable for it to serve as an alternative to CRT with BiV pacing when effective CRT cannot be achieved with an LV/CS lead.

Given limits of HBP for LBBB correction, pacing the more distal conduction system (LBBAP) may provide an alternative means of effective LV resynchronization. Small cohort studies[24,45,58,65] demonstrated the feasibility and potential utility of this approach. The LBBAP Collaborative Study Group multicenter cohort study[47] of 325 patients showed successful LBBAP in 85% of patients with low/stable pacing thresholds and good clinical and echocardiographic outcomes at 6 months. An analysis[110] of 200 patients in this cohort who were implanted for a “rescue” indication showed similar improvement. A pilot study[104] of 40 patients with LBBB, CHF, and LVEF ≤40% randomized to either LBBAP or standard

CRT with LV lead found that patients assigned to LBBAP had greater improvement in LVEF and reduction in left ventricular end-systolic volume (LVESV) with similar improvement in functional status. Therefore, LBBAP is reasonable to perform as an alternative to CRT with BiV pacing when effective CRT cannot be achieved with an LV/CS lead.

3. Trials that specifically address CRT implantation in patients with cardiomyopathy, QRS duration ≥150 ms, and NYHA class I HF are limited. Careful query of patient symptoms may uncover limitations or symptoms such as fatigue, palpitations, or dyspnea during ordinary physical activity that would reclassify a patient from NYHA class I and II HF. The Multicenter Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy (MADIT-CRT) trial[94] assessed endpoints of death from any cause or nonfatal HF events in 1089 patients with LVEF ≤30%, QRS duration ≥130 ms, and NYHA class I and II symptoms by randomizing 3:2 for CRT-D or ICD only. The primary endpoint was lower in patients in the CRT-D group (17.2%) compared to the ICD group (25.3%; $P = .001$). The primary endpoint was driven by HF events, as there was no difference in mortality. In the Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction (REVERSE) trial,[92] 610 patients who received CRT for NYHA class I and II symptoms with QRS duration ≥120 ms, LVEF ≤40%, and left ventricular end-diastolic diameter (LVEDD) ≥55 mm while on GDMT were randomized 2:1 to CRT-on and CRT-off with observation of the clinical composite endpoints left ventricular end-systolic volume index (LVESVI) and hospitalization for worsening HF. There was no significant difference in clinical response for patients with CRT-on vs CRT-off (16% vs 21% respectively; $P = .10$). LVESVI and intraventricular mechanical delay improved in the CRT-on compared to CRT-off group ($P < .0001$ and $P = .0007$, respectively). There was a statistically significant delay in the first HFH in the CRT-on group (HR 0.47; $P = .03$).[90] The 5-year follow-up analysis of the REVERSE trial[109] showed sustained improvement in functional and LV remodeling as well as 6MWD in those randomized to CRT-on.

4. Two pilot studies[106,107] of systolic HF patients with LVEF 36%–45% showed clinical and functional improvement with CRT. A retrospective analysis[63] of the Predictors of Response to Cardiac Re-Synchronization Therapy (PROSPECT) study found that 86 patients initially determined to have LVEF ≤35% had adjudicated LVEF ≥35% after core laboratory review of echocardiograms, and this subset of patients had similar clinical and structural benefit from CRT as patients adjudicated to have LVEF ≤35%. An additional small study[105] of 27 patients had similar findings. However, the randomized MIRACLE EF Clinical Study (MIRACLE EF)[111] had to be terminated due to futility after enrollment of 44 patients. On the basis of these smaller studies, as well as of clinical experience, CRT with BiV pacing may be considered in patients with LBBB, QRS duration ≥150 ms, LVEF 36%–50%, and NYHA class II–IV symptoms to maintain or improve LVEF when such patients are undergoing CIED implantation for other indications. These patients may include those undergoing pacemaker implantation for sinus node dysfunction or ICD implantation for primary or secondary prevention of sudden cardiac death who would otherwise not have an indication for ventricular pacing. Patients with more prolonged QRS duration, more impaired LV systolic function (ie, LVEF 36%–40%), and more severe HF symptoms may derive greater benefit from CRT than this group. For selected patients in this group, HBP or LBBAP may be utilized as an alternative to CRT, particularly when effective

CRT cannot be achieved due to inability to place an LV/CS lead in a suitable stable location.[24,42,45,47,58,65,98–103,108]

5. Several clinical studies[24,42,45,47,58,65,98–103,108] provide a rationale for utilizing HBP or LBBAP when effective CRT cannot be obtained with a CS LV lead due to anatomical or functional considerations. In a randomized crossover study[100] of 29 patients referred for CRT, implanting all patients with an HBP lead and a CS lead, 21 of 29 patients (72%) had significant QRS narrowing, and HBP delivered an equivalent clinical response to CRT over 6 months. Subsequent case series[42,98,99,101,102] demonstrated LBBB correction with permanent HBP in 70%–90% of patients. The His-Alternative study[103] randomized 50 patients to HBP vs BiV pacing. In the HBP group, 72% achieved successful LBBB correction, and HBP provided comparable clinical and echocardiographic improvement, though with higher pacing thresholds. The LBBAP Collaborative Study Group's multicenter cohort study[47] reported successful LBBAP in 85% of patients with low/stable pacing thresholds and good clinical and echocardiographic outcomes at 6 months. A pilot study[104] of 40 patients with LBBB, CHF, and LVEF ≤40% randomized to either LBBAP or standard CRT with LV lead found that patients assigned to LBBAP had greater improvement in LVEF and reduction in LVESV with similar improvement in functional status. Operators with experience and skill in placement of HBP or LBBAP leads may in select circumstances prefer to try this option preferentially. The rationale may include limited vascular access and/or desire to reduce the total number of leads (when only pacing and not defibrillator capacity is needed). When neither HBP nor LBBAP can be achieved when attempted first, the operator may then choose to implant a CS LV lead for conventional CRT.

3.2.1.2. LBBB, sinus rhythm, QRS duration 120–149 ms, NYHA class II–IV symptoms

Recommendations for LBBB, sinus rhythm, QRS duration 120–149 ms, NYHA class II–IV symptoms

COR	LOE	Recommendations	References
1	A	**1. In patients with select characteristics (eg, female sex) who have LVEF ≤35%, sinus rhythm, LBBB with QRS duration 120–149 ms, and NYHA class II-IV symptoms on GDMT, CRT with BiV pacing is recommended to reduce mortality and HF events and to improve LVEF.**	9,90–92,94–96, 112–124
2a	B-R	**2. In patients who have LVEF ≤35%, sinus rhythm, LBBB with QRS duration 120–149 ms, and NYHA class II-IV symptoms on GDMT, CRT with BiV pacing is reasonable to reduce mortality and HF and to improve LVEF.**	9,90–92

Synopsis: Women appear to derive more benefit from CRT across QRS durations compared to men, despite being underrepresented in most clinical trials.[9] This benefit is seen even at narrower QRS durations (120–149 ms). The reasons for these sex-specific differences may be related to anthropometric differences, particularly LV size. More favorable baseline characteristics of women in RCTs may also play a role. It is important to recognize sex-specific differences when evaluating CRT response and outcomes at narrower QRS durations, given that meta-analyses looking at broader populations suggest that a QRS duration <150 ms is of lesser benefit overall. Although female sex is associated with more benefit from CRT at narrower QRS durations, there remains very limited data in patients

with QRS duration 120–129 ms. The evidence for HBP or LBBAP is extremely limited for these patients, and as such, there is no recommendation for CSP as an alternative to CRT for QRS duration 120–149 ms.

Recommendation-specific supportive text: 1. Female patients are underrepresented in many of the seminal RCTs with CRT in HF, with approximately 20%–30% of enrollees being women.[88,90–92,94,96] In a 2015 systematic review[125] of CRT trials, approximately one-third of enrollees were women in 90% of the studies. No sex-specific differences in CRT benefit were noted in CARE-HF or COMPANION. However, the results from 2 subanalyses[126] from MADIT-CRT (25% women) and 1 subanalysis[127] from the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT) (17% women) demonstrated sex-related differences in response to CRT compared to ICD. In MADIT-CRT,[128] women had a significant 69% reduction in the combined endpoint of death or nonfatal HF compared to 28% in men. When limited to approximately 1300 patients with LBBB and stratified by QRS duration (<150 or ≥150 ms), women (31% of this population) had a greater reduction in mortality and HF compared with men, despite shorter baseline QRS durations. When stratified by QRS duration, women had a significant reduction in HF or mortality at all ranges of QRS duration, while men exhibited more benefit at ≥150 ms (although trending toward significance with QRS duration <150 ms).[9,128]

A meta-analysis[120] of 4076 patients from the RAFT, MADIT-CRT, and REVERSE trials —comparing CRT-D to ICD therapy in patients with predominantly NYHA class II HF— reported the sex-specific benefit in HF or mortality in those with LBBB stratified by QRS durations in 10-ms increments from 120 to ≥180 ms. While no differences were noted at 120–129 ms, a significant benefit for women was found at 130–139 and 140–149 ms (85% and 69% relative risk reduction, respectively), with no significant differences in men.[120] Above 150 ms, both groups had significant reductions in the combined endpoint of HF and mortality, or in death alone.

Similar results were seen in a single-center retrospective analysis[117] of approximately 200 patients with nonischemic cardiomyopathy (NYHA class III and IV) and an LBBB that explored the probability of CRT response (pre- and post-CRT echocardiography) based on QRS duration and gender. Overall, both groups had an improvement in LVEF beginning at QRS duration 120–130 ms and peaking at 150–175 ms—specifically, 58% and 76% at QRS duration <150 and ≥150 ms, respectively. However, women had a much more robust and continued response compared with men at both narrow and wide QRS: 86% and 83% with QRS duration <150 and ≥150 ms, compared to 36% and 69%, respectively.

The potential mechanisms for sex differences in CRT response in terms of QRS duration may be related to anatomic differences, especially patient height, with a greater CRT benefit seen in shorter patients.[112,113,115–118,121,129,130] In a meta-analysis,[122] longer QRS duration and shorter height (mean 163.8 cm [64 in] in the shortest tercile), but not sex, were independent predictors of CRT benefit, suggesting that body measurements more common in women may explain some of the greater benefit of CRT. The same meta-analysis found that shorter height across QRS durations conferred greater CRT benefit in mortality and first HFH, particularly at QRS duration 160–190 ms. However, the effect was seen even at QRS

duration 120–149 ms in shorter heights (Figure 3). Specifically, a benefit (HR ≤0.8) was seen in patients with a QRS duration of 120 ms at ≤152 cm (60 in), a QRS duration of 135 ms at ≤165 cm (65 in), and a QRS duration of 149 ms at ≤181 cm (71 in).

Men who were in the shortest tercile (median 167.6 cm [66 in]) with QRS duration <130 ms also appeared to derive benefit from CRT.[123] Height was most influential in the moderately prolonged (120–149 ms) range. This was supported by a separate analysis that observed. >20% increment in CRT response rates among Asian patients with QRS duration 120–149 ms (mean height 163 cm [64 in]) compared to non-Asian patients (mean height 172 cm [68 in]).[124]

It should be noted that the number of patients studied in the QRSduration120–129 ms range is small and the data are limited. The writing committee debated whether to include the QRS duration 120–129 ms range in this recommendation, and after multiple rounds of discussions and consensus voting, the writing committee reached consensus on the QRS duration 120–149 ms range. Additional studies are needed to better understand the sex-specific differences in CRT response among patients with HF, LBBB, and QRS duration <150 ms.

2. Two meta-analyses[95,114] focused onQRS duration found no benefit in any of the 5 trials studied with QRS durations <150 ms, though CARE-HF showed a trend toward significance for QRS duration 120–159 ms.[90–92,94,96] However, the other trials did not directly report HRs for all QRS durations, and QRS durations did not always correlate with true LBBB. Of note, a QRS duration ranging from 120 to 149 ms may not align with the same benefit, given that a meta-analysis[120] of 3 CRT-D vs ICD trials in patients with predominantly NYHA class II HF suggested that there is no benefit of CRT-D in patients with QRS durations <130 ms.

3.2.2. Non-LBBB—The incidence of non-LBBB is lower than that of typical LBBB in the HF population but is still frequently encountered. In a cohort study[131] of 2254 Spanish patients with NYHA class II–IV symptoms, 7.6% had right bundle branch block (RBBB), 8.7% had intraventricular conduction delay (IVCD), and 30.2% had LBBB. Some studies report greater mortality in patients with non-LBBB compared to patients with LBBB. One study[132] showed a 29% increase in mortality at 4-year follow-up for patients with RBBB when compared to those with LBBB, and the risk ratio increased further in those with LVEF <30%. This subsection focuses on recommendations for patients with non-LBBB morphologies with variable QRS durations and NYHA classification of HF.

3.2.2.1. Non-LBBB, sinus rhythm, QRS duration ≥150 ms, NYHA class II–IV symptoms

Recommendations for non-LBBB, sinus rhythm, QRS duration ‡150 ms, NYHA class II–IV symptoms

COR	LOE	Recommendations	References
2a	A	**1. In patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with QRS duration ≥150 ms, and NYHA class III or**	90,91,96,133,134

COR	LOE	Recommendations	References
		ambulatory class IV symptoms on GDMT, CRT with BiV pacing can be useful to improve functional class, cardiac structure, and LVEF.	
2b	**B-R (CRT)**	**2. In patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with QRS duration ≥150 ms, and NYHA class II symptoms on GDMT, CPP may be considered to potentially improve mortality, HFH, LVEF, and/or functional class.**	CRT[94,96] HBP, LBBAP[47,108]
	C-LD (HBP, LBBAP)		
2b	**C-LD**	**3. In patients with LVEF ≤35%, sinus rhythm, non-LBBB with QRS duration ≥150 ms, and NYHA class II-IV symptoms on GDMT, CSP with HBP or LBBAP may be reasonable if effective CRT cannot be achieved with BiV pacing based on anatomical or functional criteria.**	[42,47,108,110]

Synopsis: CRT has been shown to improve heart function and clinical outcomes among patients with reduced LVEF, HF, and prolonged QRS duration. Studies have shown significant improvements in exercise capacity, NYHA class, quality of life, and cardiac structure and function with CRT. However, fewer patients with non-LBBB have been included in these studies and results have been mixed. There was no significant reduction in the combined clinical outcome of mortality or HFH in patients without LBBB. More significant benefit was shown with CRT in patients with NYHA class III or IV, while only modest benefit was seen in patients with NYHA class II. The strength of evidence for CSP is more limited than CRT. Two studies of CSP did include substantial proportions of patients with non-LBBB IVCD and reported their results separately from patients with LBBB, supporting the use of CSP in this population. Finally, several studies in patients who would have been candidates for CRT and in those who had failed coronary venous lead placement or did not respond to CRT support significant QRS narrowing and improvement in the functional class and LVEF in a mixed patient population using CSP, many of whom did not have an LBBB pattern at baseline.

Recommendation-specific supportive text: 1. Although most clinical trials enrolled predominantly subjects with LBBB, several included subjects with IVCD or RBBB. Patients without LBBB made up 47% of patients in CONTAK CD,[135] 30% of patients in MADIT-CRT,[94] 29% of patients in COMPANION,[90] 26% of patients in REVERSE,[92] 20% of patients in MIRACLE,[133] 20% of patients in RAFT,[96] and 6% of patients in CARE-HF.[91] While the interaction between non-LBBB pattern and QRS duration is difficult to discern, QRS duration in each of the studies exceeded 150 ms, and findings supported improvement in NYHA class, cardiac structure, and function with CRT. CRT reduced mortality in RAFT and CARE-HF.[91,96] A meta-analysis[95] confirmed the benefit of CRT in patients with QRS duration >150 ms across NYHA classes. The combined data[136] from COMPANION, CARE-HF, MADIT-CRT, RAFT, and REVERSE showed no significant reduction in the composite outcome of mortality or HFH in patients without LBBB, with RBBB, or with IVCD. No clinical benefit was initially reported in patients without LBBB in MADIT-CRT,[137] but a later analysis[138] did support benefit in patients with non-LBBB and PR interval in excess of 230 ms. In RAFT, clinical benefit was observed only in patients without LBBB with QRS duration >160 ms.[72] Real-world data and post hoc analyses[139] support this finding, demonstrating benefit of CRT among patients with IVCD and QRS duration ≥150 ms but not among patients with RBBB and QRS duration ≥150 ms.

2. Several studies, MADIT-CRT, RAFT, REVERSE, and Multicenter InSync ICD Randomized Clinical Evaluation II (MIRACLE ICD II) included patients with NYHA class II HF symptoms. MADIT-CRT[94] and RAFT[96] support reduction in mortality and HFH with CRT in this population including patients with non-LBBB and a prolonged QRS duration in the case of RAFT[96] or a prolonged PR interval in the case of MADIT-CRT.[94] On the other hand, REVERSE[92] and MADIT-CRT[94] showed a more modest benefit with no reduction in mortality but significant improvement in the echocardiographic parameters. A limited number of small studies[47,108] of CSP have included patients with non-LBBB IVCD and reported their results separately from patients with LBBB. The results are discussed in detail below; the studies showed improvements in QRS duration, LVEF, and NYHA class, though the strength of evidence is notably limited by an absence of control groups.

3. Three small nonrandomized studies[47,108,110] assessed the use of CSP among patients with CHF, non-LBBB, and reduced EF. HBP used in 39 such patients was associated with a significant narrowing of the QRS duration (158 ± 24 to 127 ± 17 ms), increase in LVEF (31% ± 10% to 39% ± 13%), and improvement in NYHA class (average class 2.8 ± 0.6 to 2.0 ± 0.6) over a mean follow-up of 15 ± 23 months.[108] In another observational study,[47] 103 of 325 patients who were treated with LBBAP for CRT indication had a non-LBBB QRS pattern. Patients experienced significant narrowing of the QRS duration (160 ± 28 to 143 ± 23 ms), improvement in LVEF (33% ± 0.1% to 43% ± 0.12%), and improvement in NYHA class (average class 2.7 ± 0.7 to 1.8 ± 0.6). In the third study,[110] 200 of 212 patients who had either failed coronary venous lead placement or did not respond to CRT were successfully implanted with LBBAP leads. This was a heterogeneous population with 45% of patients having a non-LBBB QRS pattern (5% RBBB, 14% IVCD, and 22.5% RV paced). This study showed significant QRS narrowing in LBBAP-treated patients by 31 ms with 11% improvement in LVEF. All 3 studies were limited by the lack of a comparator group. Therefore, improvements in outcomes could have occurred because of background medical therapy or other factors, rather than CSP.

3.2.2.2. Non-LBBB, QRS duration <150 ms, NYHA class I–IV symptoms

Recommendations for non-LBBB, QRS duration <150 ms, NYHA class I–IV symptoms

COR	LOE	Recommendations	References
2b	B-NR (CRT) C-LD (HBP, LBBAP)	**1. In patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with QRS duration 120–149 ms, and NYHA class III or IV symptoms on GDMT, the usefulness of CPP is not well established.**	CRT[94,96,140] HBP, LBBAP[42,46,47,108]
3: No Benefit	B-R	**2. In patients with LVEF ≤35%, NYHA class II-IV symptoms on GDMT, and QRS duration <120 ms, CRT with BiV pacing is not recommended.**	141–144
3: No Benefit	B-R	**3. In patients who have LVEF ≤35%, sinus rhythm, a non-LBBB pattern with QRS duration <150 ms, and NYHA class I or II symptoms on GDMT, CRT with BiV pacing is not recommended.**	94,96,139

Synopsis: Among patients with non-LBBB, shorter QRS duration (<150 ms), and more advanced HF (NYHA class III and IV), there is very limited evidence of potential benefit from CPP.[42,46,47,94,96,108,140] For patients with non-LBBB and shorter QRS duration (<120

ms) or less severe HF (NYHA class I and II), there is evidence of no benefit from CPP.[94,96,139,141–144] The limited role for physiologic pacing in these contexts is most likely due to the fact that while prolonged LBBB usually reflects delay within the conduction system with latest activation in the posterolateral LV (more amenable to correction with CPP), shorter non-LBBB conduction abnormalities reflect intrinsic myocardial disease or variable sites of delayed LV activation (less amenable to correction with CPP).[145–149]

Recommendation-specific supportive text: 1. There is uncertain and unpredictable efficacy of BiV pacing among patients with non-LBBB. In an observational study[140] of 99 patients with RBBB (22.2%) or IVCD (77.8%) who had LVEF <35%, NYHA class II–IV symptoms, and QRS duration >/120 ms, the average LVEF increased 4% with BiV pacing during a mean follow-up of 13 months. Only longer QRS duration was independently associated with improved ventricular remodeling. However, in 2 large RCTs,[94,96] subgroup analysis found no clinical outcome benefit from BiV pacing in patients with non-LBBB, QRS duration 130–150 ms, NYHA class I and II, and LVEF ≤30% or patients with non-LBBB, QRS duration 120–150 ms, NYHA class II and III, and LVEF ≤30%.

There is even less certainty regarding the evidence supporting the use of CSP (vs BiV pacing) for patients with non-LBBB morphology. Some observational studies[42,108] with small sample sizes show that the QRS duration can be narrowed with HBP in patients with RBBB and advanced HF. Subanalysis from 1 study[108] showed the improvement by 1 NYHA class, no HFH noted in 15 of 19 patients (79%), and ≥5% increase in LVEF during follow-up in 11 of 16 (69%) patients. In patients with RBBB, IVCD, or RVP with suboptimal QRS narrowing by HBP, an additional LV/RV pacing lead can be used to maximize electrical resynchronization.[150,151] A study[46] showed that LBBAP can improve LV cardiac function in patients with RBBB (QRS duration 120–150 ms and LVEF ≤50%) with bradycardia pacing indications. Another study,[47] which included patients with CRT indications, showed that NYHA class improved from a baseline of 2.7 ± 0.7 to 1.8 ± 0.7 and LVEF increased from 33% ± 10% to 43% ± 12% in patients with non-LBBB (RBBB, IVCD, or RVP) morphology; however, the clinical benefits of CSP for patients with non-LBBB, if any, need further investigation.

Novel echocardiography techniques, electrocardiographic (ECG) mapping, advanced ECG analytics, and vectorcardiography, potentially with the use of artificial intelligence/machine learning methodology, are future directions that may enhance prediction of response to CRT or CSP and guidance of optimization of programming.

2. Several trials[141–144] have addressed the role of CRT in patients with HF and QRS duration <120 ms, given that some degree of dyssynchrony may still be present. Most were parallel controlled trials comparing CRT pacing programmed on or off. One trial[141] was terminated after 85 patients with symptomatic LV dysfunction and QRS duration <120 ms were randomized and no significant differences in LV reverse remodeling, a significant reduction in exercise capacity, and an increase in QRS duration were noted with CRT pacing programmed on vs off. In another trial[143] of 809 patients with QRS duration <130 ms, after a median of 19 months, a nonsignificant trend toward higher all-cause death or HFH in the CRT group was demonstrated; there were significantly more deaths in the CRT group.

However, a subsequent study[123] suggested that the risk was concentrated among patients with larger LV dimensions, and that patients with a longer QRS duration and smaller LV size indexed to height appeared to benefit from CRT. In a trial[142] of 120 patients with ischemic cardiomyopathy with QRS duration <120 ms, randomized to CRT-D or dual-chamber ICD groups, there was a significant reduction in HF clinical composite response after 1 year in the CRT group, with a significantly lower combined endpoint of HFH, HF death, and spontaneous ventricular fibrillation after 16 months.

3. Among patients with non-LBBB and QRS duration <150 ms, CPP has been evaluated in subgroups of randomized trials and in observational research.[94,96,139] In these studies, CRT with BiV pacing was not associated with improved clinical outcomes. The findings are consistent with those in REVERSE,[152] a randomized trial assessing ventricular remodeling among patients with predominantly NYHA class II HF, 39% non-LBBB, and 50% QRS duration <150 ms. In REVERSE, investigators randomized 610 patients to CRT with BiV pacing on vs off, with echocardiographic assessment of LV size and function after 12 months. Patients with non-LBBB did not experience beneficial remodeling. Among patients with LBBB, benefit was significantly related to degree of QRS prolongation. CSP has been inadequately studied among patients with non-LBBB, QRS duration <150 ms, and NYHA class I and II to warrant recommendations at this time.

3.2.3. PICM with high-burden RVP

Recommendations for PICM with high-burden RVP

COR	LOE	Recommendations	References
1	B-NR	**1. In patients with a CIED with a decline in LV function or worsening of HF symptoms attributed to substantial ventricular pacing, CRT with BiV pacing is recommended to improve LV function and improve HF symptoms.**	29
2a	B-NR	**2. In patients with a CIED with a decline in LV function or worsening of HF symptoms attributed to substantial ventricular pacing, revision of CIED to a CSP device can be beneficial to improve LV function and symptoms of HF.**	19,29,153,154

Synopsis: A subset of patients with normal preimplant LVEF who require RV apical or nonapical pacing will develop PICM characterized by a reduction in LVEF and symptoms of systolic HF.[14,155,156] While there is no single definition of PICM, most studies have included patients identified as having (1) a decline in LVEF of ≥10% with a baseline LVEF >50% prior to RVP, (2) pacing percentage ≥20%, and (3) no alternative explanation for the decline in LVEF following RVP.[14,19,153,156] Physiologic pacing with CRT, HBP, and LBBAP have each been demonstrated to result in significant recovery of LVEF and improvement in HF symptoms among most patients.

Recommendation-specific supportive text: 1. Among patients with PICM, upgrading to CRT with BiV pacing has demonstrated improvement in symptoms related to HF and reverse remodeling of the LV.[14,155,156] Studies are limited in that most were not randomized, most of the randomized studies had a crossover design confounding assessments of survival, and HF outcomes assessed and entry criteria were heterogeneous. However, a meta-analysis[29] of 6 RCTs (161 patients; 5 of 6 were crossover studies) and 47 observational studies (2644 patients) of BiV pacing upgrade demonstrated improvements in LVEF,

LVESV, NYHA class, quality of life, peak exercise oxygen capacity as measured by peak VO_2 max, and QRS duration. Among complications associated with device upgrades, infection rates averaged 3.7%, pneumothorax 2.0%, cardiac perforation or tamponade in 1.4%, and lead-related complications in 3.3%.

2. Physiologic pacing with HBP and LBBAP has been associated with significant improvement in LVEF and HF symptoms among patients identified as having PICM.[19,29,153,154] A retrospective observational multicenter study[19] of 60 patients with PICM referred for upgrade to HBP revealed successful HBP in 57 (95%) of the patients, which was associated with an improvement in LVEF from 34.3% ± 9.6% to 48.2% ± 9.8% ($P < .001$). Among the 57 patients, 95% experienced ≥5% improvement in LVEF and 75% had >10% increase in LVEF. A prospective study[153] examined the effect of HBP among 18 patients with either PICM or CRT nonresponse. HBP lead fixation was successful in 16 (88.9%) of the patients (11 had PICM and 5 were CRT nonresponders). At 1-year follow-up, LVEF increased from 35.7% ± 7.9% to 52.8% ± 9.6% ($P< .01$).

Another retrospective multicenter study[154] evaluated the efficacy of LBBP to reverse PICM among patients with infranodal block who had previously received a standard RVP lead. Permanent LBBP upgrade was successful in 19 of 20 patients. Over a median follow-up duration of 12 months, LVEF increased from 36.3% ± 6.5% to 51.9% ± 13.0% ($P < .001$) with LVESV reduced from 180.1 ± 43.5 to 136.8 ± 36.7 mL ($P< .001$). Furthermore, there were no lead dislodgments and the mean LBBP threshold was 0.7 ± 0.3 mV at 0.4 ms at implant and remained stable during follow-up.

A systematic review and meta-analysis[29] of the upgrade of RV pacemakers to CSP included 8 observational studies (217 patients) and reported improvements in LVEF, LVESV, NYHA class, VO_2 max, quality of life, and QRS duration with lead-related complications in 1.8%. To date, there have been no randomized trials of upgrade to CSP for PICM.

3.2.4. Survival < 1 year

Recommendations for survival <1 year

COR	LOE	Recommendations	References
1	C-EO	**1. In patients with a life expectancy of < 1 year, the decision to implant a CPP device should incorporate shared decision-making, taking into account the potential improvement in quality of life balanced against the risk of procedural complications.**	

Synopsis: When considering device implantation to improve quality of life, selected patients nearing the end of life may derive benefit from CPP. Thus, the decision to place a physiologic pacemaker to alleviate HF symptoms should incorporate shared decision-making incorporating discussion of prognosis, the patient's values, and consideration of potential benefits and procedural risks.

Recommendation-specific supportive text: 1. There are very little or no data on the implantation of pacemakers in patients with cardiac or noncardiac morbidities limiting life span to <1 year.[157–161] Most clinical trials used noncardiac mortality <1 year as an exclusion

criterion. However, clinical trials are not the same as clinical practice, in which shared decision-making regarding risks and benefits is critical, especially in patients with end-stage HF in whom procedural risks are higher.[162] If CPP could reasonably be expected to improve quality of life, even in patients with severe noncardiac comorbidities, then CPP implant may be reasonable.[2,162]

3.3. Combination CRT with LV (CS LV or LV epicardial) lead plus HBP or LBBP

During conventional CRT implantation, failure ranges from 5% to 10%. During follow-up, clinical nonresponders can be as high as 30%–40%. Multiple factors are associated with these failures or suboptimal responses to conventional CRT. HBP and LBBAP are rapidly evolving with regard to their implantation techniques, optimization of lead location, acute assessment of "physiologic" response, long-term pacing thresholds, lead longevity, and patient outcomes. Combining the conventional CRT with HBP (CRT + HBP) or CRT with LBBAP (CRT + LBBAP) is intriguing or even mechanistically desirable based on the ultimate goal to achieve pacing-mediated contractile synchrony, whether it is performed during the de novo implantation, as a "rescue" when the initial approach is suboptimal, or as an "upgrade" when the clinical response is inadequate during follow-up. Limited preliminary data from observational study cohorts suggest that CRT + HBP or CRT + LBBAP implantation is technically feasible with favorable acute and short-term outcomes in selected patient populations.

The combined use of LV lead with HBP has been studied in limited mechanistic[151] or clinical[150,163] feasibility studies with short-term outcomes. One case series[164] reported implantation and follow-up outcomes in patients who had an inadequate response to HBP with subsequent implantation of an additional LV lead. Similarly, the combined use of LV lead with LBBAP has been studied only in limited feasibility[165] or case series[166,167] studies. All references in this subsection are observational studies with a wide range of patient selection criteria without comparators. Key findings from the limited observational studies are summarized below. *The writing committee reached a consensus that there is insufficient evidence to make practice recommendations at this time. Outcomes from ongoing and future well-designed studies may enable formal recommendations in the future.*

In a case series study[150] of 27 patients who met class I indications for CRT with either failed HBP (partial or insignificant QRS narrowing) or who were nonresponders to prior conventional CRT, CRT + HBP was implanted successfully in 93% and resulted in significant narrowing of QRS duration (183 ms at baseline, 162 ms by BiV, 151 ms by HBP, and 120 ms by CRT + HBP). At a mean follow-up duration of 14 ± 7 months, LVEF significantly improved from 24% to 38%, NYHA class improved from 3.3 to 2.04, and 84% were clinical responders. In a study of 2 cases,[163] clinical conditions improved in 2 inotrope-dependent patients when conventional CRT was revised to CRT + HBP. Both patients were discharged from the hospital, no longer being inotrope dependent. In an ECG-based nonclinical outcome study[151] of 19 patients, CRT + HBP significantly reduced LV activation time by 21% when compared to HBP, by 24% compared to BiV, and by13% compared to multisite pacing.

In a retrospective study[164] of 21 patients referred for CRT and who consented to HBP as an alternative method for CRT, QRS duration did not narrow to <130 ms by HBP. These patients subsequently had a CS LV lead implanted. CRT + HBP resulted in significant shortening of QRS duration (baseline 170 ± 21 ms, HBP 157 ± 16 ms, BiV pacing 141 ± 15 ms, and CRT + HBP 110 ± 14 ms), increase in LVEF (from 27.6% ± 6.4% to 41.1% ± 12.5%) at a mean follow-up of 25 months, and improvement in NYHA class (from 3.1 ± 0.5 to 2.1 ± 0.8) at a mean follow-up of 32 months.

In a prospective multicenter study[165]of 112 patients, CRT + LBBAP was attempted in patients qualified for CRT or who were CRT nonresponders. The implantation success rate was 81%. Among patients who failed CRT + LBBAP implantation, 16 of 21 failed LBBAP lead placement and 4 of 16 failed CS lead placement. CRT + LBBAP significantly shortened QRS duration (baseline 182 ± 25 ms and CRT 1 LBBAP 144 ± 22 ms). At follow-up of >3 months, LVEF improved from 28.7% to 37%. Clinical improvement was observed in 76% of the total study cohort. Acute complications included 1 LBBAP lead and 1 CS lead dislodgment, 1 septal perforation, and 2 pocket hematomas. Complications at follow-up included 1 infection, 1 CS lead threshold increase, and 1 right atrial lead dislodgment.

3.4. Indications for CPP in AF

Although initial CRT data were minimal for patients with atrial fibrillation (AF), subsequent investigations have shown a benefit in patients with AF. AF should not preclude CRT eligibility; however, ensuring a very high percentage (close to 100%) of BiV pacing is essential to derive benefit.

Patients with treatment-refractory AF undergoing atrioventricular junction (AVJ) ablation with LVEF ≤50% may have improved clinical outcomes with CRT. HBP (with or without a backup RVP lead) or LBBAP may also improve clinical outcomes. The evidence for HBP and LBBAP in AF patients undergoing AVJ ablation is mostly limited to retrospective and prospective observational studies, with 1 small prospective randomized crossover trial[168] showing a modest improvement in LVEF in HBP compared with BiV pacing.

RCTs[169,170] testing the effects of RV apical pacing and the RVP prevention algorithms have shown that a high burden of RVP increases overall AF burden and the risk of AF progression. Although the pathophysiology behind RV apical pacing resulting in an increased risk of AF is not well defined, it is likely related to pacing-induced ventricular dyssynchrony contributing to increased left atrial pressure and size, and possibly related to increased mitral regurgitation due to papillary muscle dyssynchrony. Intrinsic AV conduction (by minimizing RVP), HBP, and LBBAP avoid pacing-induced LV dyssynchrony and result in a decreased incidence of AF compared to RV apical pacing.

Recommendations for CPP in AF

COR	LOE	Recommendations	References
2a	B-R	**1. In patients with AF undergoing AVJ ablation with LVEF ≤50%, CRT with BiV pacing is reasonable to improve HFH, reverse structural remodeling, and improve quality of life, exercise capacity, LVEF, and potentially mortality.**	35,171–176
2a	B-NR	**2. In patients with AF who otherwise meet CRT implantation eligibility criteria, CRT with BiV pacing can be beneficial to improve quality of life, functional capacity, and LVEF.**	35,177–180
2b	C-LD	**3. In patients with AF undergoing AVJ ablation, HBP with or without a backup ventricular pacing lead may be reasonable to improve or preserve LVEF and improve functional class.**	10,168,181–186
2b	C-LD	**4. In patients undergoing AVJ ablation, it may be reasonable to implant an LBBAP lead.**	186–188
2b	C-LD	**5. In patients with a high burden of ventricular pacing, HBP or LBBAP may be reasonable to decrease the risk of AF.**	189–192

Synopsis—Selected patients with AF undergoing CIED implantation may benefit from CPP. RV apical pacing may increase AF burden and the risk of AF progression, and this risk may be mitigated by RVP prevention algorithms, HBP, or LBBAP. For patients with AF undergoing CRT, achieving a high percentage of BiV pacing is critical to achieve maximal benefit. In patients with treatment-refractory AF undergoing AVJ ablation with LVEF ≤50%, several RCTs have demonstrated that CRT improves clinical outcomes. In patients with treatment-refractory AF undergoing AVJ ablation, HBP with or without a backup RVP lead also improves clinical outcomes. However, the evidence is based on retrospective and prospective observational studies and 1 small prospective randomized crossover study. Data are limited on the benefit of implanting an LBBAP lead in patients with treatment-refractory AF undergoing AVJ ablation. Future randomized studies should evaluate the risk of new-onset AF and progression of AF in patients with CSP. An algorithm outlining the indications for CPP in patients with AF is shown in Figure 4.

Recommendation-specific supportive text—1. Several RCTs have demonstrated improved clinical outcomes in patients with refractory AF undergoing AVJ ablation with LVEF ≤50% who received CRT compared with patients who receive pharmacological rate control[174] or compared with patients who received RVP.[171,172,174–176] In the morbidity phase of the Atrioventricular Junction Ablation and Biventricular Pacing for Atrial Fibrillation and Heart Failure (APAF-CRT) trial,[174] 102 HF patients were randomized to AVJ ablation + CRT vs pharmacological rate control. AVJ ablation + CRT was superior in reducing HF, decreasing hospitalization, and improving quality of life in elderly patients with permanent AF and narrow QRS duration. Other RCTs that compared AVJ ablation + CRT to conventional RVP demonstrated that CRT is superior in reducing clinical manifestations of HF in patients with severely symptomatic permanent AF[171] and improving quality of life and exercise capacity.[172] The Post AV-Nodal Ablation Evaluation (PAVE) study[175] was a prospective, randomized, multicenter clinical trial that compared BiV pacing with RVP in 184 patients undergoing AVJ ablation for AF with rapid ventricular response. At 6 months postablation, LVEF in the BiV group (46% ± 13%) was significantly greater compared to patients receiving RVP (41% ± 13%). In a prospective, randomized,

multicenter, single-blinded study[176] comparing CRT to RVP, RVP resulted in a significant increase in left atrial volume, LV mass, and worsening of LV contractility compared to patients receiving BiV pacing post–AVJ ablation for refractory AF. The mortality phase of the APAF-CRT trial[173] was an international blinded study of 133 patients (predominantly elderly with NYHA class ≥III HF) that demonstrated that AVJ ablation + CRT was superior to pharmacological therapy in reducing mortality in patients with permanent AF and narrow QRS who were hospitalized for HF, irrespective of their baseline LVEF.

2. Two meta-analyses[179,180] showed that although the degree of benefit and the percentage of CRT response is less in patients with AF, they did experience an improvement in quality of life and 6MHW and a similar improvement in LVEF compared to patients in sinus rhythm. Although a prespecified subgroup analysis of RAFT looking at subjects with permanent AF did not demonstrate a benefit of CRT over ICD therapy alone, only one-third of permanent AF patients achieved BiV pacing >95% despite appearing rate controlled at enrollment.[177] A real-world observational analysis[178] of almost 9000 patients in the National Cardiovascular Data Registry ICD Registry also supports a benefit of CRT. A reduction of all-cause mortality, all-cause hospital readmission, and HF-related readmission with CRT-D compared to ICD in patients with a history of AF, particularly in patients with LBBB and QRS duration >150 ms, was demonstrated. Lastly, although BLOCK HF, which demonstrated a benefit of CRT in pacing-indicated patients, did not assess outcomes stratified by history of AF, 52.8% of patients had a history of AF.[35]

3. Several retrospective observational studies[10,181,182,184–186] have demonstrated the feasibility of HBP in patients undergoing AVJ ablation. Success rates of HBP were about 95% in this population.[184,185] Observational studies have shown improvement in LVEF and NYHA class[181,185] and stable His capture thresholds.[182,184] One study[185] demonstrated an acute increase in HBP threshold in 7 of 15 patients. In a meta-analysis[10] of 8 studies including 679 patients, CRT or HBP was compared with RVP in patients with LVEF >35% who required permanent pacing due to heart block. LVEF was preserved or increased with CRT or HBP compared with RVP, but no effect on mortality was seen. Clinical benefit seemed to be limited primarily to patients with permanent AF and rapid ventricular rates who underwent AVJ ablation. In ALTERNATIVE-AF, a prospective randomized crossover trial[168] of 50 patients with HF, narrow QRS, and persistent AF who received both HBP and BiV pacing, a small statistically significant improvement in LVEF was seen in HBP compared to BiV pacing in the 38 patients that completed both phases of the study.

4. The data on outcomes in patients with LBBAP and AVJ ablation are limited. One prospective observational study[183] evaluated the feasibility and efficacy of LBBAP in 99 patients, 4 (4%) of whom underwent AVJ ablation. In a single-center, retrospective, cohort study[186] of 86 patients with HBP or LBBAP (9%) with ICD who underwent AVJ ablation compared with ICD only, the incidence of adverse events including HFH or death was higher in the non-AVJ ablation group than in the AVJ ablation group ($P = .01$). Several prospective studies[187,188] showing successful LBBAP implantation and stable lead parameters have included patients undergoing AVJ ablation, supporting feasibility in this population. In a study[190] of 98 patients undergoing AVJ ablation (48 HBP and 50 LBBAP), CSP was associated with preservation or improvement in EF, and LBBAP was associated

with a higher success rate and lower lead-related complications compared with HBP. While feasibility has been shown, mid- and long-term lead performance and clinical outcomes related to LBBAP and AVJ ablation still remain to be demonstrated. Because of the more distal location of LBBAP in the RV compared with HBP, AVJ ablation may be technically easier to perform with LBBAP. In addition, mid- and long-term lead performance is more stable with LBBAP compared with HBP. Prospective randomized studies are needed to further evaluate the outcomes of AVJ ablation in patients with LBBAP.

5. RV apical pacing can increase the risk of new onset and progression of AF. A large prospective study[193] that enrolled patients with sinus node dysfunction indicated for pacemaker implantation found that conventional dual-chamber rate-modulated pacing with an AV delay of 120–180 ms resulted in 99% RVP and a 12.7% incidence of progression from no/paroxysmal AF to persistent AF. The RVP prevention algorithm group had a lower incidence of RVP (9.1%) and persistent AF progression (7.9%) ($P = .004$). Two observational studies[189,191] examined patients with either no prior AF or paroxysmal AF and compared HBP to RVP in terms of AF burden postimplant. One study[191] showed that new-onset AF was significantly lower (20.8% HBP and 40.8% RVP) but AF progression was not, and this was driven by subjects with higher RVP burdens. Similarly, the other study demonstrated less persistent/permanent AF in the HBP subjects. This was due to a significantly lower rate of new-onset AF (7.3% vs 18.8%, 20.4% of patients with RV septal/RV apical pacing) with no significant reduction in AF progression.[189] Compared to RVP, LBBAP was associated with lower new-onset AF risk (relative risk reduction of 59% for AF episodes ≥6 minutes; $P = .035$) in a retrospective cohort[60] of 410 patients and in a prospective cohort[192] of 527 patients, especially if patients required >20% ventricular pacing (relative risk reduction 72%; $P < .001$).

Section 4 Preprocedure evaluation and preparation

Successful and safe device implantation is dependent on preparing for the procedure. Established steps include preoperative antibiotic prophylaxis, careful maintenance of operative room sterility, and appropriate management of perioperative anticoagulation. This section focuses on preprocedure testing that can affect device choice and procedural planning. In particular, the resting ECG is an essential part of the initial evaluation of patients under consideration for CIED implant. Bradyarrhythmia may be readily detected, and potential underlying structural diseases may be suggested by findings such as Q waves, QT prolongation, LV hypertrophy, low QRS voltage, and other abnormalities. In addition, a variety of ambulatory monitors (short term or implanted) may be used to determine transient conduction defects, such as intermittent heart block, or reveal the presence of episodic arrhythmias.

For patients with suspected structural heart disease, pre-procedure imaging is useful to determine LV function and potentially to identify treatable conditions. Noninvasive studies, such as coronary computed tomography angiography, cardiac MRI with late gadolinium enhancement, and echocardiography, can help determine pathology, assess prognosis, and direct specific non-device-related treatments. Other tests, such as laboratory testing and in

certain cases genetic testing, may be useful from a planning and prognostic standpoint but are not immediately helpful for device selection.

Implantation of a CIED requires a patient-centered focus. Implanting a permanent device with multiple permutations and variations in techniques, device choices, and potential outcomes requires a careful partnership between the clinician and the patient. A detailed discussion of choices, risks, benefits, and alternatives should be included for any CIED procedure as part of shared decision-making. Risk factors and comorbidities, such as advanced age and frailty, may need to be considered for specific patients. Use of online tools and other tools for shared decision-making may improve patient-reported outcomes. An algorithm outlining the decision making regarding preprocedural testing and shared decision-making is shown in Figure 5.

4.1. Preprocedure testing

Recommendations for preprocedure testing

COR	LOE	Recommendations	References
1	A	**1. In patients being considered for implantation of a CPP device, a 12-lead ECG is recommended to evaluate the heart rhythm, heart rate, AV conduction, and QRS duration and morphology to determine the appropriate type of CPP.**	136,194–199
1	A (CRT) C-EO (HBP, LBBAP)	**2. In patients planned to undergo implantation of a CPP device, preprocedural echocardiographic screening for LVEF is recommended.**	CRT[92,94,96]
2b	B-R	**3. In patients indicated for CRT, use of an imaging modality (eg, echocardiogram, cardiac MRI, or CT) may be considered to target LV lead placement.**	200–204
3: No Benefit	A	**4. In patients being considered for CRT, preprocedural echocardiographic assessment of ventricular dyssynchrony is not useful to predict outcomes from CRT with BiV pacing.**	205,206

Synopsis—Electrocardiographic evaluation is essential to determine the type of device to be implanted in patients considered as candidates for CPP. In subjects with bradycardia indications for pacing, ECG is used to predict a high percentage of ventricular pacing based on the presence of conduction disturbances and their location. In subjects with decreased LVEF, ECG evaluation of the heart rhythm, heart rate, and QRS duration and morphology is essential to establish the indications for a specific CPP device and to predict the benefit from a given therapy.

Echocardiographic imaging for the assessment of LVEF is essential in patients who are being assessed for consideration of CPP therapy. In addition to LVEF, there is evidence that preprocedural imaging can also be helpful in determining areas of delayed LV activation or scar to guide LV lead placement in CRT patients. On the other hand, there are no consistent data that recommend preprocedural assessment of ventricular dyssynchrony in patients indicated for CRT, as it has not been able to predict clinical response.

Recommendation-specific supportive text—1. CPP techniques are targeted to achieve more physiologic ventricular activation and/or correction of electromechanical

dyssynchrony.[12,207,208] The surface 12-lead ECG with the assessment of QRS duration and morphology is historically the oldest tool in evaluation of electrical dyssynchrony and remains the gold standard in qualifying patients for CRT. Several limitations of ECG have been reported including different definitions of LBBB, different methodologies of the measurement, and inconsistent results of the trials designed to examine the correlation between electrical and mechanical dyssynchrony.[197,209–216] Nevertheless, the results of landmark RCTs in CRT patients, which established the current recommendations, are based on benefits achieved from this therapy in patients enrolled for CRT implantation based on QRS duration.[90–92,94,96] The results of meta-analyses of RCTs showed consistent benefits of CRT in patients with wide QRS. Subsequent post hoc subanalyses of these trials, targeted toward QRS duration and morphology, showed that the most substantial benefit was achieved in patients with LBBB morphology (see Section 3.2).[72,136,137,152,194–196,199,217,218] The debate of whether QRS duration or morphology is more important continues.[129] Further studies showed that PR interval duration may also be useful in the identification of CRT responders.[198] More sophisticated ECG techniques, such as noninvasive ECG mapping or vectorcardiography, have also been reported to predict outcomes.[147,219–221] The evaluation of the percentage of ectopy on preimplantation ambulatory ECG monitoring may identify reduced CRT efficacy due to low BiV pacing during follow-up.[222] Wide baseline and postimplant paced QRS duration were reported to predict PICM.[13,223] A detailed evaluation of LBBB morphology may help to distinguish true BBB from LV intraventricular delay, which is more likely to result from underlying structural heart disease.[146,224,225]

2. In patients who are considered for implantation of a CPP device, the use of cardiac imaging is recommended before implantation to guide appropriate therapy. Echocardiography is the imaging technique of first choice to assess the presence of structural heart disease and to determine the LVEF. Currently, LVEF remains a cornerstone in deciding which cardiac pacing therapy is recommended for the patient. Especially for CRT, the clinical evidence obtained from the large randomized clinical trials is typically based on the LVEF.[92,94,96]

In patients with cardiomyopathy, cardiac MRI and nuclear imaging could also be used to evaluate LV systolic function but are especially helpful before device implantation to evaluate the underlying etiologies of LV dysfunction, presence of ischemia and myocardial scar, and potential causes of conduction disturbances.

3. Mechanical dyssynchrony in patients who are considered suitable for CRT is most often delayed LV activation of the posterolateral wall. This region is therefore targeted during implantation for LV lead position. There is substantial individual variation in the latest activated region as well as in the presence and location of scar that could influence the effect of CRT. Three randomized studies[200–202] reported that an LV lead placement approach targeting the latest activated region free from scar using preprocedural radial strain imaging by echocardiography resulted in a significant improvement in clinical outcome after CRT. However, these results were not consistent for all imaging modalities.[203,204]

4. The clinical effect of CRT varies considerably between patients. Many patients encounter significant improvements after CRT, but there remains a substantial group of patients that has little or no effect from this therapy. Since LV dyssynchrony was considered to be the substrate amenable to CRT, many echocardiographic measurements of LV dyssynchrony have been prospectively evaluated. These observational, mostly single-center, studies had promising results, as they showed that the presence of LV dyssynchronywas associated with reverse remodelling or improved clinical response after CRT. These results, however, were not confirmed in larger multicenter prospective trials.[205,206] In these studies, echocardiographic measurements of ventricular dyssynchrony showed only a modest accuracy to predict response to CRT, suggesting that the echocardiographic parameters of LV dyssynchrony have not been accurate enough for clinical decision-making in CRT. Since then, many other cardiac imaging techniques have been studied in observational studies, generating various new parameters of dyssynchrony that were associated with CRT response. These parameters need to be prospectively confirmed. Therefore, at this time there is still no measure of LV mechanical dyssynchrony with enough predictive power that can be recommended to improve patient selection for CRT beyond current guidelines, and the ECG remains the standard for patient selection in CRT.

4.2. Assessment for other predictive factors associated with CPP response

Although several risk factors may identify patients at an increased risk of PICM, many patients tolerate high-burden RVP without adverse outcomes. The ability to identify those at highest risk remains challenging. Current HBP and LBBAP studies,[226,227] while demonstrating feasibility and safety, do not contribute greatly to determining patient selection. Most studies contain small numbers of patients, the patient population appears younger than those seen clinically, and data are generally lacking on race, sex, and comorbidities. The studied populations include patients with different clinical profiles (such as pacing indications and risk factors), but most lack a control group.

Factors associated with reverse remodeling following CRT are female sex, nonischemic etiology, and LBBB.[228] In the case of HBP and LBBAP, the studies are largely limited to retrospective, observational, single-center or multicenter studies with inherent limitations, such as potential bias in patient selection and patient treatment.[58] Clinical benefits and risks have not been systematically examined. Specific reporting of clinical outcomes also varies, making clear recommendations challenging. Information regarding patients where HBP or LBBAP was not successful is generally also not available. Many groups are underrepresented. For example, women tend to be under-represented and data on race are often not provided.

4.3. Shared decision-making

Recommendations for shared decision-making

COR	LOE	Recommendations	References
1	C-EO	**1. In patients who may benefit from CPP, clinicians and patients should engage in a shared decision-making approach in which (1) information is shared on the evidence base for different types of CPP and (2) treatment decisions are based**	

COR	LOE	Recommendations	References
		not only on the best available evidence but also on the patient's goals of care, preferences, and values.	

Synopsis—For shared decision-making to occur, the following criteria should be met: (1) participation of at least the clinician and the patient, (2) exchange of information between participants, (3) consensus regarding the preferred therapy, and (4) agreement on the therapy to be employed.[229]

Recommendation-specific supportive text—1. The CPP guideline writing committee supports shared decision-making as an integral part of the overall care of patients who may benefit from CPP. When a decision is made that a patient may benefit from CPP, clinicians should engage in a conversation with the patient that applies the principles of shared decision-making. Providing a patient with information related to the risks and benefits of the procedure and letting them make a decision about how to proceed is not shared decision-making.[230] Rather, the conversation should include information on the clinical indication for the procedure, careful consideration of the patient's risks and benefits based on their comorbidities, frailty, and overall prognosis, and the patient's goals of care and preferences. The conversation should also cover the evidence base for CRT vs CSP and the potential effects of these pacing modalities on battery longevity and short- and long-term complications, as well as potential future lead management issues (if applicable) and potential considerations at the end of life.[10,50,231–233] The conversation about different physiologic pacing options should occur even if CPP strategies other than the chosen one are considered a fallback alternative if the planned procedure is unsuccessful. Having such a conversation with patients might be challenging, as clinicians have to strike a balance between being fully transparent and informative and not overburdening the patient with complex information that may make it difficult for them to make an informed decision. Then a recommendation is made based on the best available evidence and a good understanding of the patient's health goals, preferences, and values. It is important to remember that patient preferences for and perception and acceptance of the risks of invasive therapies vary and are likely to change during the course of their illness.

Section 5 Implant procedure

Although BiV pacing is an established approach that has been widely supported in medical guidelines, obstacles remain in optimizing the technique, whether engaging the CS, finding optimal branches, or determining the best pacing strategies that will maximize cardiac resynchronization. Challenges encountered with HBP have included optimizing the leads and delivery systems that target a small area within the conduction system, achieving long-term anatomic stability, and obtaining stable and durable pacing thresholds. More recently, LBBAP has emerged as a feasible approach at more distal targets within the conduction system but with need for more data regarding appropriate patient selection, definition of intraprocedural success, and longer-term outcomes with respect to lead stability and safety. This section addresses the minimal criteria for successful implantation using each of these

techniques, as well as recommendations regarding alternative strategies should the initial implant approach be unsuccessful, as outlined in Figure 6.

5.1. Tools and techniques for CRT with BiV pacing

Recommendations for tools and techniques for CRT with BiV pacing

COR	LOE	Recommendations	References
1	B-R	**1. In patients undergoing CRT implant, a quadripolar LV lead is recommended to assist with lead stability, lower capture thresholds, avoid phrenic nerve pacing, and decrease need for lead repositioning.**	9,234–237
2a	B-NR	**2. In patients undergoing CRT implant, lead positioning and programming the device to deliver the narrowest QRS duration can be beneficial in improving LV structure and function.**	9,238–244
2a	C-LD	**3. In patients undergoing CRT implant, LV lead placement to allow for pacing from a nonapical position is reasonable to improve CRT clinical and structural response.**	9,245–249
2b	C-LD	**4. In patients undergoing CRT implant, targeting lead placement at sites of late ventricular activation may be considered to improve CRT response.**	134,200,249–258

Synopsis—Lead positioning plays an important role in whether patients implanted with a CRT device derive the desired benefits. The definition of success or failure of CRT has been variably defined due to variations in criteria involving acute hemodynamic response, mechanical remodeling, HFH, or mortality. However, lead positioning seems to consistently be an important factor in CRT response.[250]

There are various means of optimization of LV lead placement. The area of the latest LV activation allowing for adequate threshold without phrenic nerve stimulation is optimal for achieving the best hemodynamic response measuring (LV dP/dt_{max}). Electrical delay or QLV is measured in milliseconds from the beginning of the surface QRS complex to the beginning of the intrinsic local signal on the intracardiac electrogram.[259,260]

Implantation of extendable-retractable helices appear to have a higher dislodgment rate compared to fixed helices.[261]

Recommendation-specific supportive text—1. In a large RCT,[235] use of a quadripolar LV lead, compared to a bipolar lead, reduced intraoperative and postoperative LV lead–related events up to 6 months. This finding was confirmed by observational studies.[234,236] Quadripolar leads also needed less fluoroscopy for implantation, allowed for better distal vein positioning, and had lower pacing thresholds and impedances, compared to bipolar leads.[9,237] Even though phrenic nerve stimulation can be more common, there is less need for lead repositioning given the ability to switch vectors to avoid phrenic stimulation.[234] There was also a statistically significant decrease in lead placement failure, but no difference in procedural complication rates with quadripolar leads, compared to unipolar and bipolar leads in a large analysis[237] using the National Cardiovascular Data Registry database.

2. In a small observational study,[239] optimization of interventricular pacing delay using electrocardiographic and echocardiographic parameters with achievement of the narrowest

QRS duration allowed better hemodynamic response. In another study,[238] the best fusion-optimized AV interval was one that achieved the narrowest QRS duration during LV pacing, and fusion-optimized intervals (FOI) shortened the QRS duration more compared to nominal settings. A subset of these patients also showed improvement in LV dP/dt_{max} with FOI pacing. The finding of FOI further reducing QRS duration compared to nominal groups was confirmed in an RCT[240] that included patients with ischemic cardiomyopathy, NYHA class II–IV symptoms, LVEF ≤35%, and LBBB with successful CRT implantation. There was more reverse remodeling observed in the FOI group, with a correlation between narrowing QRS duration and the reverse remodeling. There were more super-responders and fewer negative responders in the FOI group in this study as well.[240] In the multicenter, prospective, observational Sync-AV study,[241] a device-based algorithm that automatically adjusted AV delay according to intrinsic AV conduction led to narrower QRS duration compared to nominal CRT settings. Narrowing the QRS duration was associated with favorable echocardiographic and clinical responses.[9,242,243] QRS area independent of QRS duration also predicted combined clinical outcomes of all-cause mortality, cardiac transplant, and left ventricular assist device (LVAD) implantation in patients with LBBB who were receiving CRT.[244] A systematic review and meta-analysis[242] showed an association between QRS shortening with improvement in electrical dyssynchrony and NYHA class reduction ≥1 or LVESV reduction ≥15% response to CRT. Survival benefit over a 9-year period was observed in patients with LBBB who had QRS narrowing following CRT implant.[243]

3. A single-center prospective observational study[246] demonstrated that event-free survival was lower with apical LV pacing compared to basal and midventricular LV lead positions. There was also less LV reverse remodeling and improvement in NYHA class with apical pacing.[246] A large subgroup analysis[247] of MADIT-CRT showed that LV lead location classified by radiographic positioning in the short and long axis showed a higher propensity for HFH and mortality among those with apical lead positioning compared to midventricular or basal positions. A subgroup observational study[248] of the REVERSE trial of the LV lead position reported more responders to CRT in the nonapical position group. Among echocardiographic parameters, LVESVI decreased more in the nonapical position group compared to the apical position group. The composite endpoint of death and first HFH was lower in the nonapical position group compared to the apical position group and in the LV lateral position group compared to the non-lateral position group.[248]

Another study[249] showed that improvement in hemodynamic response was guided by pacing site using echocardiographic parameters. In contrast, a large retrospective observational study[245] showed no difference in mortality or HFH between apical and nonapical positioning on the basis of fluoroscopic CS lead positioning at implant. Although the apical position group had higher mortality and pump failure, there was a lower risk of sudden cardiac death.[245] Quadripolar leads allow for more choices regarding pacing sites regardless of positioning, including ability to pace from nonapical sites despite apical lead placement.[9]

4. Compared to anatomic locations, placement of LV leads in areas of electrical delay can confer a greater benefit.[262] In a post hoc analysis of a large multicenter RCT,[252] HF clinical composite outcomes were assessed relative to interventricular electrical delay (short delay being <67 ms and long delay being ≥67 ms) in patients who underwent CRT placement.

The long interventricular electrical delay group had more clinical improvement, less clinical deterioration, and higher freedom from HFH or mortality.[252] QLV is the time from the onset of QRS on the ECG to local activation at the site of the LV lead. RV to LV lead activation can serve as a surrogate in pacing-dependent patients.[251,254,255] Generally, sites with QLV >95 ms or >50% of total QRS duration favor optimal response with CRT. QLV .120 ms further improves chances of CRT having an optimal response.[250,259] In a substudy[250] of the Comparison of AV Optimization Methods Used in Cardiac Resynchronization Therapy (SMART-AV) trial, high QLV was associated with higher reverse remodeling, statistically significant decreases in LVESVI, and improved quality of life measurements. Observational studies[255,256] and 1 prospective study[249] have shown that longer QLV corresponded to higher LV dP/dt_{max}. Acute hemodynamic response using stroke volume using pressure volume loops showed a large variation between electrodes in a quadripolar lead. An antero-lateral or lateral electrode placement with high QLV/QRS duration was shown to have the highest association with change in stroke volume in univariate analysis acutely.[258] Speckle tracking with echocardiographic guidance to place the LV leads at sites closest to the regions of latest activation has also conferred a benefit for event-free survival.[200]

5.1.1. Other tools and techniques for CRT

Multipoint pacing, multisite pacing, and quadripolar leads: Ventricular multisite pacing (MSP) can be performed using triventricular pacing from 3 ventricular leads, with 2 of the leads being in RV and LV and the third lead being in 1 of the ventricles. Occasionally, the term MSP refers to pacing using multipolar LV leads.[263,264] Multipoint pacing (MPP) traditionally refers to pacing from multiple poles from an LV lead.[241,265] When BiV pacing is suboptimal, MSP/MPP can improve response when 2 LV leads are spaced at least 30 mm apart with a minimal delay of 5 ms.[251,266,267] MSP can be performed with use of a Y adapter or with a BiV device, as there are no specific devices for MSP. The 3 leads in MSP can also be connected to a BiV device using the atrial channel for 1 of the ventricular leads if the patient is in AF. Programming for MPP leads is easier, but there is still no BiV pacing device that can deliver varied outputs in accordance with individual thresholds for each pole. MPP is preferred to MSP due to ease of implantation and programming as well as safety during implant (20% adverse events with MSP).[268–270]

Since optimal lead placement can have anatomical or technical challenges, quadripolar leads (with a distal tip and 3-ring electrodes) can help with stability, optimal threshold obtainment, and avoidance of phrenic nerve stimulation, leading to decreases in LV lead–related intraoperative or postoperative events. Quadripolar LV pacing has less LV lead–related events intraoperatively and at 6 months compared to bipolar LV CS pacing.[235] Active fixation LV pacing leads may also help reduce lead dislodgment.[271,272]

Adaptive algorithms: Given the high rate of suboptimal responders to CRT, algorithms to optimize AV and interventricular (VV) intervals have been created by various device companies. These algorithms vary in their optimization technique and acute hemodynamic responses in comparison to echocardiography-guided optimization. Some algorithms take only a few minutes and are based on timing cycles of intracardiac ECGs.[273] Others adjust sensed and paced AV delays to maximize LV dP/dt_{max} based on intrinsic AV interval,

RV-LV timing, and LV lead location. Optimization of CRT to allow for triple wavefront fusion of intrinsic conduction and BiV pacing can help with response rates with CRT.[274] One algorithm adjusts AV pacing intervals and synchronously paces LV to intrinsic RV activation with improved responder rates and clinical outcomes, including reduction in AF in patients with long AV delays; with this algorithm, LV-only pacing occurs when HR is <100 bpm, and BiV pacing occurs when HR is .100 bpm or there is a long AV delay.[275,276] LV pacing linked to the RVP or BiV pacing during normal AV delay of <200 ms is a basis of this algorithm for adaptive CRT. AV and VV delays are adjusted by intrinsic conduction interval timing to allow for more physiologic ventricular activation and decrease in RVP (and subsequently increase in battery life).[276] Another algorithm was developed to optimize intrinsic RV and LV electrical and mechanical synchrony. In addition to manual programming with the use of ECG, this algorithm alters AV delay up to 350 ms continuously to allow for fusion between native conduction and BiV pacing[277] and was reported to narrow the QRS duration more than conventional CRT pacing and improve electrical dyssynchrony by narrowing the QRS duration further during BiV pacing compared to conventional CRT pacing, including with assessment by vectorcardiography.[246,278]

Various other optimization algorithms have also been developed and compared to echocardiography-guided optimization. An algorithm[279] that automated AV and VV intervals each week using an accelerometer in NYHA class III and IV patients was noninferior compared to echocardiography-guided AV and VV optimization. Another AV optimization method[273] was studied in patients receiving CRT-D devices with NYHA class III and IV symptoms despite optimal medical therapy, LVEF ≤35%, and QRS duration ≥120 ms. LVESV, NYHA class, quality of life, and 6MWD were assessed at implantation, 3 months, and 6 months with no difference in LVESV or secondary endpoints observed between the AV optimization algorithm and the echocardiography-guided optimization groups.[273]

Another trial[280] categorized patients who had programming optimized using an echocardiogram, an ECG, an algorithm that optimized AV and VV delays, or nominal device programming. Although there was a significant reduction in LVEDD, shorter 6MWD, and more improvement in LVEF in all groups compared to the nominal programming group at 6 months, there were no significant long-term differences between the groups at 12, 24, and 48 months.[280]

LV epicardial pacing: Surgical epicardial LV lead pacing is a reasonable alternative when CS lead placement fails.[253] In addition to a small operative risk, the largest operative challenge is achieving an optimal lead position on the posterolateral aspect of the LV.[281] Video-assisted thoracoscopic epicardial LV lead placement can be guided by mapping the maximum QLV using a multipolar electrophysiological mapping catheter (such as a decapolar catheter) intraoperatively.[253]

LV endocardial pacing: LV endocardial pacing has been explored as an alternative to LV epicardial lead placement when CS lead placement fails. Various methods for endocardial non-CS LV pacing include an atrial trans-septal approach, hybrid surgical/endocardial trans-ventricular apical pacing, and nonapical trans-septal ventricular pacing. All endocardial

non-CS LV lead techniques require systemic anticoagulation with international normalized ratio (INR) goals around 2.5–3.5, with a continued risk of thromboembolic events and difficulties with subtherapeutic INRs or holding anticoagulation due to thromboembolic events.[282]

Scar: Compared to patients with ischemic cardiomyopathy, patients with nonischemic cardiomyopathy have more improvement in LV function and reverse remodeling with CRT placement. Assessment of myocardial viability can be performed using contrast echocardiography with perfusion score index (PSI) for summed segmental perfusion. The PSI correlates with improvement in LVEF, stroke volume, end-systolic volume, and global myocardial performance in those undergoing CRT implantation.[283] Cardiac MRI scan can also assess scar burden and transmurality. Significant scar burden on contrast-enhanced cardiac MRI correlates well with change in LVESV with CRT in patients with ischemic cardiomyopathy. Higher scar burden is associated with lower response rates to CRT.[284]

Pacing in areas of LV scar during BiV pacing can lead to longer QRS duration and higher capture thresholds. Incorporation of cardiac MRI–based scar map using a segmental heart model on the CS venogram can help with avoidance of areas with myocardial scar and guide the CS lead to areas of true mechanical dyssynchrony during implantation.[284,285]

5.2. Tools and techniques for CSP

CSP requires specialized tools and techniques for successful implantation. Recommendations are based on expert opinion and findings from several prospective and retrospective studies involving CSP.

HBP was initially reported in the year 2000 with traditional active fixation leads.[286] Subsequent studies[287] have demonstrated greater success with the use of a dedicated lead with an electrically active, exposed screw and specialized delivery systems. While early studies used an electrophysiology catheter to map the His bundle region, the His region can be successfully mapped using the pacing lead in unipolar fashion.[43] Although associated with a significant learning curve and longer procedure/fluoroscopy duration, 3-dimensional mapping systems have been used to facilitate CSP lead implantation with shorter fluoroscopy times and reasonable success.[40,288–291] Use of contrast injection to delineate the tricuspid valve and the septal region can be helpful during both HBP and LBBP.[292,293] While His and left bundle electrograms can be recorded using the pacing system analyzer, high-resolution recording system at sweep speeds of 100 mm/s can be more helpful to record and confirm conduction system capture.[294,295]

HBP can result in selective capture of the His bundle alone or capture of surrounding RV myocardium in addition to the His bundle, resulting in nonselective capture (Figure 7). Nonselective HBP can be difficult to differentiate from RV myocardial–only capture. A 12-lead ECG can help differentiate nonselective HBP from RV septal–only pacing. In addition, BBB correction (Figure 8) can be more readily recognized with 12-lead ECG.[294] During threshold testing, output (voltage)–dependent changes in ECG morphology are helpful in identifying and accurately documenting His bundle capture and BBB correction thresholds. In up to 10% of patients, both His bundle and RV myocardial capture thresholds can be

identical. In such patients, change in pulse width, programmed stimulation, or rapid pacing can help confirm conduction system capture.[296,297] Various criteria to define His bundle capture in patients with normal and diseased His-Purkinje conduction are provided in Table 6.[12]

HBP can be associated with higher capture thresholds compared to RVP. Additionally, during longer-term follow-up, late rise in capture thresholds requiring lead revisions are seen in 7%–11% of patients.[16,298,299] During HBP lead implantation, it is suggested to achieve capture thresholds of <2.5 V at 1 ms.[12,294] Injury current recorded in the HBP and LBBP lead electrogram during lead implantation has been shown to be associated with excellent acute and long-term thresholds.[300–302] Adjusting the high-pass filter in the high-resolution recording system (0.5–1 Hz from 30 Hz) can be helpful in recording the HB current of injury.[295] HBP lead placement in the proximal His bundle region can be associated with atrial oversensing and ventricular undersensing.[303,304] It is preferable to target the distal His bundle region during implantation to avoid sensing issues and threshold increases after AV node ablation.[185,305] While programming devices with HBP, AV delay should be shortened by 40–50 ms compared to conventional parameters to allow for His-ventricular conduction times.[294,303] Current automatic threshold assessment algorithms do not allow for accurate assessment of His bundle capture thresholds and should generally be turned off.[12,294]

LBBAP was initially described using a lead with an electrically active, exposed screw.[306] Other active fixation leads with an extendable-retractable screw and dedicated delivery sheaths have also been used to achieve LBBAP.[307] During LBBAP, 12-lead ECG characteristics help confirm placement of the lead in the LV septal subendocardial region and assess capture of the left conduction system (Figure 9 and Table 7).[308,309] Transition from nonselective to selective LBB or LV septal capture is highly specific for LBB capture, while recording LBB potentials (LB-V intervals of 15–35 ms) is highly sensitive.[310] A 2-lead technique (lead in the HB location and LBB area) can be helpful in recording retrograde His in non-LBBB and recording of LBB potential during corrective HBP in LBBB to confirm LBB capture.[310] Recently, physiology-based criteria using native V_6 R-wave peak time (RWPT) have been proposed to assess LBB capture.[311] While no single criterion has high sensitivity and specificity to confirm LBB capture, a stepwise algorithm has recently been proposed to assess LBB capture during LBBAP.[312]

Recommendations for tools and techniques for CSP

COR	LOE	Recommendations	References
1	C-EO	**1. In patients undergoing CSP with HBP or LBBAP, 12-lead ECG is useful during implantation to assess conduction system capture most accurately.**	
1	C-EO	**2. In patients undergoing CSP with HBP or LBBAP, accurate demonstration of conduction system capture thresholds (including BBB correction) and myocardial capture thresholds at implant is useful for appropriate programming of the device.**	
2a	C-LD	**3. In patients undergoing CSP with HBP or LBBAP, assessment of His bundle/left bundle current of injury using appropriate filter settings can be beneficial in achieving acceptable capture thresholds and lead stability.**	300–302

Synopsis—During implantation of CSP leads, it is essential to confirm conduction system capture, which can be challenging. The 12-lead ECG is useful to differentiate capture of the conduction system and surrounding myocardium, accurately establish pacing thresholds required to correct the underlying BBB and appropriately program pacing outputs. Similar to the myocardial current of injury observed during atrial and ventricular lead placement, injury current can be recorded from the His bundle and LBB. Demonstration of the current of injury is often associated with excellent CSP thresholds. Recommendations are based on expert opinion and findings from several prospective and retrospective studies involving CSP.

Recommendation-specific supportive text—1. A 12-lead ECG during the implant procedure is recommended to assess the baseline ECG and analyze pacing morphologies to confirm QRS narrowing and conduction system capture, including correction of underlying BBB, differentiation of nonselective HBP from RV septal (para-Hisian) pacing, and confirmation of LV septal and LBB capture. An electrophysiology recording system and/or pacing system analyzer to record His bundle/LBB electrograms can be helpful in identifying conduction system capture. Criteria for HBP and LBBAP, including ECG-based criteria, are listed in Tables 6 and 7. For differentiating nonselective HBP from RV septal pacing, ECG-based criteria of no QRS slur/notch in leads I, V_1, V_4–V_6, and the V_6 RWPT ≤100 ms were associated with 100% specificity.[303,313] Measurement of RWPT is assessed from the stimulation artifact to the peak of the R-wave. Change in V_6 RWPT >12 ms between stimulus to RWPT and His to V_6 RWPT was shown to have 99.1% sensitivity and 100% specificity to confirm lack of His capture.[314] Demonstration of RV conduction delay pattern in lead V_1 (qR, Qr, QR, rSR, etc) is associated with high sensitivity for LBBAP but is not specific for confirming LBB capture.[310] Criteria to distinguish LBBP from LV septal pacing without LBB capture continue to evolve. Abrupt shortening of stimulus to V_6 RWPT ≥10 ms during deep-septal LBBP lead implantation and subsequent short and constant V_6 RWPT during high- and low-output pacing was associated with high specificity for LBB capture.[310] V_6 RWPT <75 ms in non-LBBB and <80 ms in LBBB was associated with 100% specificity for LBB capture but with lower sensitivity in physiology-based series based on a review of transitions in surface ECG morphology.[311] Jastrzebski et al[311] proposed that during LBB capture, QRS onset to RWPT equals the RWPT during native non-LBBB rhythm in lead V_6 and stimulus to RWPT equals the LBB potential to RWPT in lead V_6 during non-LBBB rhythm. Change in V_6 RWPT ≥8 ms (RWPT during corrective HBP – LBBAP) was associated with 100% sensitivity and 93% specificity to confirm LBB capture in a small series of patients with LBBB meeting the Strauss criteria (Figure 10).[315] Similarly, a V_6–V_1 interpeak interval of >44 ms during LBBP had 100% specificity for LBB capture.[316] Importantly, the majority of these criteria have largely been established based on careful review of transitions in ECG morphology rather than invasive assessment, with the exception of abrupt decrease in stimulus to V_6 RWPT of ≥10 ms during lead delivery.[310]

2. The physiology of CSP is dependent on whether the conduction system is captured or not. A low conduction system capture (including BBB correction) threshold is associated with long-term stability and safety of pacing. During CSP for infranodal AV block and BBB, pacing should be performed at ≥120 bpm to confirm distal conduction system

capture and/or BBB correction. Accurate documentation of the His/left bundle capture threshold, BBB correction threshold, and local myocardial capture threshold in patients with nonselective CSP is useful for appropriate programming of the pacing output both at implant and during follow-up.[16,40,42,43,46,99,188,287,290,298,299,312] Several observational studies[298,299] have shown an increase in His bundle capture threshold by >1 V in up to 15%–28% of patients during intermediate-term follow-up. In ventricular pacing–dependent patients with nonselective HBP, RV septal myocardial capture can provide ventricular pacing backup in addition to His bundle capture.

3. Injury current in atrial and ventricular myocardial lead electrograms is associated with low tissue capture thresholds. Recording of His bundle injury current suggests that the lead has penetrated the insulating outer layer of the His bundle or in close proximity. In patients undergoing HBP,[302] demonstration of His bundle current of injury at the time of implant was shown to be associated with low capture thresholds at implant and during 1-year follow-up compared to when injury current was not observed in the His bundle electrogram. In another study,[300] demonstration of deep negative His potential and His bundle injury current was associated with low capture thresholds at implant and 1-year follow-up. In a study[301] of 115 patients with LBBP, 100% of patients with LBB injury current were associated with LBB capture thresholds <1.5 V at 0.5 ms compared to 76% of patients without LBB injury current. Injury current can be recorded in the pacing system analyzer or more clearly using high-resolution recording system by adjusting the high-pass filter settings.

5.3. When to consider alternative CPP sites (intraprocedural crossovers)

During the initial implant of CRT with BiV pacing implantation, implant failure can be up to 10% for the LV lead placement. The key factors for the initial implantation failure are summarized in Table 8. The threshold for abandoning the conventional LV lead implantation to crossover to alternative CPP option is variable depending on the operator, implantation criteria, or available or proven alternatives. Newer lead design from a bipolar to a quadripolar configuration and lead delivery tools have provided more choices for LV lead pacing configurations and have overcome some technical issues; however, challenges remain in some patients.

Similar scenarios can be encountered when the de novo CPP is HBP or LBBAP. HBP or LBBAP implanting failure rates are 10%–40% with the current implanting tools and leads. When suboptimal HBP or LBBAP lead placement occurs, crossover to CRT with BiV pacing LV lead placement could be an option.

Criteria for optimal lead placement (CRT with BiV pacing, HBP, or LBBAP) continue to evolve rapidly. Definitions for failure of lead placement at initial implantation have not been standardized. In the absence of sufficient data on any established criteria for implantation failure requiring crossover to another CPP option, it is important to recognize that the decision on when to abandon the initial approach is operator dependent and variable. The terms “implantation failure” and “crossover” used in this section are qualitative until criteria are established based on future investigations.

Recommendations for when to consider alternative CPP sites (intraprocedural crossovers)

COR	LOE	Recommendations	References
2a	C-LD	**1. In patients undergoing CRT with BiV pacing implantation via the CS, crossover to CSP with HBP or LBBAP is reasonable when the CS LV lead placement is unsuccessful or suboptimal.**	42,47,58,101,103
2b	C-LD	**2. In patients undergoing CRT with BiV pacing implantation via the CS, crossover to surgical epicardial CRT with BiV pacing might be reasonable when the initial approach is unsuccessful or suboptimal.**	317–319

Synopsis—The use of HBP as a crossover approach to failed CRT with BiV pacing or for crossover from HBP to CRT with BiV pacing has been reported in limited small RCTs[101,103] and observational case-cohort studies.[42,58] Limited cohort studies[47,58] have reported crossover to LBBAP from either failed CRT with BiV pacing or HBP. The criteria and decision for crossover were prespecified in 2 reported RCTs, although criteria varied between studies. The decision for crossover was quite variable and operator dependent in the observational cohort studies. When to cross over is an area of rapid change as implantation technology and techniques continue to improve and as long-term data become available. When an anatomical barrier prevents CS LV lead placement, surgical placement of epicardial LV placement has been reported in observational cohort studies.[317–319]

Recommendation-specific supportive text—1. Criteria for crossover between CRT with BiV pacing and HBP were prespecified in a multicenter RCT.[101,103] Based on the prespecified crossover criteria, 10 of 21 patients (48%) randomized to HBP crossed over to CRT with BiV pacing, and 5 of 19 patients (26%) randomized to CRT with BiV pacing crossed over to HBP. This RCT pilot study highlighted the high crossover rates when the crossover criteria were prespecified. In a single-center RCT[103] of 50 patients, 1 of 25 (4%) crossed over from CRT to HBP and 7 of 25 (28%) crossed over from HBP to CRT. Implantation of either LV or HBP leads was successful after crossover in both studies. These preliminary data from 2 small RCTs suggest that it is reasonable to consider HBP when the initial CRT with BiV pacing approach is unsuccessful or suboptimal.

In 3 observational crossover studies,[3–5] the success rates of HBP or LBBAP as a rescue procedure after failed LV lead placement or nonresponders to CRT with BiV pacing ranged from 85% to 91%, suggesting that HBP or LBBAP are technically feasible after failed LV lead placement.

2. When CS LV lead placement is unsuccessful, implant of a BiV generator may be warranted if future crossover to epicardial LV lead placement is anticipated. Surgical epicardial LV lead placement was studied in 3 observational studies.[317–319] In a multicenter study,[317] 44 patients who failed previous CS LV lead placement or had LV lead failure received surgical LV leads for CRT. Similar clinical outcomes and survival rates were noted between surgical LV-CRT and CRT with BiV pacing patients, with age, sex, and etiology of cardiomyopathy matched during a mean follow-up of 57 months. In a single-center study of 1053 subjects, 895 received transvenous LV leads and 158 received epicardial LV leads via thoracotomy or sternotomy (108 failed CS leads and 50 during concomitant

cardiac surgery). During the 5-year observation period, the lead revision rate was 10.2% for transvenous LV leads and 1.9% for epicardial leads. A statistically significant increase in LVEF was observed in both groups.[318] In a single-center study[319] including 100 patients who had failed previous LV lead implant or LV lead failure, surgical epicardial leads were placed via video-assisted thoracoscopy. Compared to 100 patients who had transvenous CRT, surgical CRT had similar outcomes in terms of deaths, cardiovascular hospitalization rate, and complications. Both groups displayed similar improvements in LV reverse remodeling and EF. These investigations demonstrated that surgical LV epicardial lead placement was technically feasible and is an alternative approach for those who cannot achieve meaningful transvenous LV pacing. Surgical LV lead placement had a lower lead revision rate than transvenous LV lead placement with comparable outcomes during follow-up.

Section 6 CPP follow-up and management

Patients implanted with a CPP device require comprehensive follow-up beyond a routine check of device performance. With CSP, appropriate conduction system capture should be confirmed, including BBB correction at the assigned programmed output. In addition, as patients with a CPP device typically have LV systolic dysfunction, multidisciplinary follow-up that incorporates HF management is helpful to ensure that GDMT is continuously assessed and optimized. An ECG and chest X-ray (posterior-anterior and lateral views) are simple tools to assess LV lead capture and placement in CRT patients. Patients who do not appear to have benefited from CRT may have potentially reversible factors, such as suboptimal lead placement position or an inadequate BiV pacing percentage due to premature ventricular contractions (PVCs) or AF. Finally, when approaching the time of generator replacement, shared decision-making is an important component to determine whether to continue defibrillation therapies or to perform lead revisions. This section discusses these patient follow-up issues, and an algorithm outlining the concepts is shown in Figure 11.

6.1. Follow-up evaluations

Recommendations for follow-up evaluations

COR	LOE	Recommendations	References
1	B-NR (CRT)	**1. After implantation of a CPP device in patients with heart failure with reduced ejection fraction (HFrEF), a follow-up echocardiogram within 3–12 months is useful to determine reverse remodeling and the likelihood of improved survival and reduction in HFH.**	CRT[320–322]
	C-EO (HBP, LBBAP)		
1	B-NR	**2. In patients with CPP, remote monitoring is beneficial for device and arrhythmia management.**	[323–328]
2a	B-NR (CRT)	**3. In patients with CPP and HF, multidisciplinary management with HF and device clinics for adjustment of medications and device programming can be useful to improve clinical outcomes.**	CRT[329–334]
	C-EO (HBP, LBBAP)		
2a	C-LD	**4. In patients with CRT and heart failure with improved ejection fraction (HFimpEF), continuation of GDMT is reasonable to reduce the risk of HF relapse and arrhythmias and treat hypertension.**	[335,336]
3: No Benefit	B-R	**5. In patients with CRT and HFrEF, routine use of thoracic impedance alone to manage congestive HF is not recommended.**	[337–339]

Synopsis—Follow-up after device implant should include an echocardiogram to assess changes in LV size and function, persistent valvular disease, such as mitral valve disease that may need intervention, and need for medication titration or device optimization. Continuous evaluation of the patient by a multidisciplinary team, including primary care, HF, device/electrophysiology, and other specialty providers, depending on the underlying pathology, can be helpful. Reassessment of medications, continuation of goal-directed medical therapy, and other disease modification strategies should be assessed in all patients.

Recommendation-specific supportive text—1. There is a lack of consensus regarding when to reassess cardiac function post-CRT since most of the data are derived from retrospective studies with varied clinical outcomes and measurements of LV function. As shown by the 5-year results[93] from the REVERSE trial, there can be a continuous improvement in LV volumes for at least 2 years post-CRT. In patients who have received a CRT device, the volumetric response to CRT assessed by echocardiography with different indices, such as change in left ventricular end-diastolic volume (LVEDV) or LVESV and improvement in EF at 12 months, predicts subsequent death or HF events[320,321] and helps guide further HF management and auxiliary therapies. Further, a lack of echocardiographic response was associated with a 2.8 times higher risk of all-cause mortality after a mean follow-up of 5.6 years in a substudy of the MADIT-CRT trial.[340] The best parameters to follow vary with different studies. However, the benefit of the therapy seems to be directly related to the degree of remodeling, with every 10% decrease in LVEDV or each 5-point increase in LVEF associated with 40% reduction in the risk of death or HFH in the MADIT-CRT study, and an 8% reduction in mortality for every 10% decrease in LVESV reported in the PREDICT-CRT study.[320–322] Successful CSP, including LBBAP and HBP, have been shown to increase LVEF in observational studies[42,99]; however, the relationship between the change in EF and clinical outcomes such as mortality has not been studied. After the initial follow-up echocardiogram, further imaging at follow-up may be guided by changes in clinical status.

2. Studies in patients with CRT and CRT-D have shown that the use of remote monitoring improves arrhythmia management.[323–328] In observational studies, the average time to detection of events is shorter with remote monitoring than in-office device checks,[323] allowing prompt reactions to optimize medical therapy.[324] In the Clinical Evaluation of Remote Notification to Reduce Time to Clinical Decision (CONNECT) trial,[325] the median time from a clinical event to a clinical decision was reduced from 22 days in the in-office arm to 4.6 days in the remote monitoring arm. Further, the use of remote monitoring has been shown to reduce healthcare resources.[326–328,341] Clinical outcomes data are conflicting. While some studies show that remote monitoring leads to decreased hospitalizations and HF exacerbations, improvement in quality of life, and in some studies reduction in all-cause mortality,[326,342,343] other studies, including the Monitoring Resynchronization Devices and Cardiac Patients (MORE-CARE) study,[341] found no significant differences in cardiovascular death and hospitalizations. In the REmote Monitoring and evaluation of implantable devices for management of Heart Failure patients (REM-HF) trial,[344] which included 1650 patients with HF and CIEDs, the use of remote monitoring did not lead to improved death from any cause or unplanned cardiovascular

hospitalization. However, in a meta-analysis[343] of the Influence of Home Monitoring on the Clinical Status of Heart Failure Patients (IN-TIME), Effectiveness and Cost of ICDs Follow-up Schedule with Telecardiology (ECOST), and Lumos-T Safely Reduces Routine Office Device Follow-up (TRUST) trials, home monitoring reduced all-cause mortality and the composite of mortality and HFH, though this was mostly composed of ICD patients with only 1 of the trials including CRT-D therapy.

3. In a study[329] of a protocol-driven approach to HF management including continued uptitration of goal-directed medical therapy, AV optimization, HF education, and arrhythmia management, the multidisciplinary approach led to significant increases in LV remodeling (change in LVEDD 0.7 ± 0.6 cm vs 0.2 ± 1.2 cm; change in LVEF 11% ± 7% vs 7% ± 9%) and decreased all-cause mortality, heart transplant, or readmission for HF (14% vs 53%). Some institutions have proposed HF clinics conjoined with HF providers to avoid fragmenting care.[334] HF management should include downtitration of diuretics when appropriate and uptitration of neurohormonal blockade.[329,332,333]

4. The benefit of CRT in patients with systolic HF has been shown on a background of optimal medical management, while withdrawal of therapy after CRT has only been studied in small cohorts that do not specifically target patients with CRT. In the Advance Cardiac Resynchronization Therapy Registry (ADVANCE-CRT),[345] patients who were determined to have a beneficial impact from CRT were less likely to have their therapy optimized, which may inadvertently lead to suboptimal care in this subset. It is therefore important to continue to treat the underlying pathology including HF management.[329,331] The Pilot Feasibility Study in Recovered Heart Failure (TRED-HF)[335] evaluated the phased withdrawal of HF pharmacological treatment in patients with dilated cardiomyopathy with recovered EF (n = 51); withdrawal of pharmacological treatment led to relapse of HF, but only 1 patient in this study had concomitant CRT. In another study[336] with 80 patients with normalized EF after CRT, withdrawal of neurohormonal blockade increased adverse outcomes, such as hypertension or arrhythmic events.

5. The use of thoracic impedance to detect the gradual accumulation of fluid and increased filling pressure has been proposed to enable timely treatment interventions to avoid HFH. However in the Diagnostic Outcome Trial in Heart Failure (DOT-HF),[337] 335 patients were randomized to usual care and to have the information from thoracic impedance available to their providers; the use of thoracic impedance did not lead to improved mortality or hospitalizations (29% vs 20%; $P = .063$), with patients who had the information available to providers having more outpatient visits. The lack of benefit was consistent in systematic reviews and meta-analyses.[338,339]

6.2. Role of a dedicated CRT clinic

Clinical benefits of dedicated disease management clinics for patients with HF have been well established,[346,347] although their applications in CRT recipients have been largely under-studied. From the multicenter ADVANCE-CRT Registry of CRT nonresponders assessed at 6 months,[345] intensification of in-clinic/remote evaluations and involvement of HF specialists remained minimal and 44% received no additional treatment. Early approaches aimed at referral for troubleshooting of CRT nonresponders demonstrated

opportunities for device optimization as well as identification and management of HF and its comorbidities.[348] An innovation of a dedicated CRT clinic is the intention to see all HF patients who underwent CRT device implantation, as referral bias from symptom-based evaluation may fail to identify those who may benefit from evidence-based treatments. Taking advantage of the improved myocardial efficiency with CRT, case series of dedicated CRT clinics have demonstrated feasibility and potential benefits, especially with scheduled intensification of neurohormonal antagonists[332] and downtitration of diuretic therapy.[333] Recently, a multidisciplinary clinic care model (electrophysiology, cardiac imaging, and HF care) for CRT recipients with simultaneous device optimization and HF disease management has been proposed,[334] with early experience demonstrating that the majority of patients (95%) may benefit from device/drug-related interventions or referral for alternate medical services. Compared to historical controls, enrollment in a post-CRT structured clinic with scheduled echocardiographic surveillance, as well as device and drug optimizations within the first 6 months of implant, was associated with improvement in clinical outcomes.[330] Clinical benefits have also been associated with CRT recipients who underwent postimplant multidisciplinary cardiac rehabilitation.[349] However, in a prospective RCT,[336] full withdrawal of neurohormonal blockade, while deemed safe with low relapse rates (7.5%) in the majority of CRT recipients with full myocardial recovery, may be limited by cardiac comorbidities such as arrhythmias or hypertension. Despite the many potential benefits and expert recommendations,[350] published literature to date include only single-center experiences, and there have been no prospectively conducted studies to conclusively demonstrate incremental clinical benefits of dedicated CRT clinics vs routine follow-up.

6.3. Optimization of CPP response

Recommendations for optimization of CPP response

COR	LOE	Recommendations	References
1	C-EO	**1. In patients with CRT, a 12-lead ECG is useful to confirm LV lead capture and facilitate optimization of LV pacing configurations.**	
1	B-NR	**2. During in-office follow-up of patients with CSP, a multilead or 12-lead ECG is recommended to assess conduction system capture, including BBB correction.**	16,40,42,43,46,47,99,188,290,298,299,304,305,351
2a	B-NR	**3. During in-office follow-up of patients with CSP, a comprehensive assessment that includes documentation of His/left bundle capture, BBB correction, and myocardial capture thresholds can be useful.**	16,40,42,43,46,7,99,188,290,298, 299,304,305,351
2a	C-EO	**4. In patients with HBP who have an increase in threshold of >1 V, more frequent in-office follow-up can be beneficial to determine the need for lead revision, especially in ventricular pacing-dependent patients.**	

Synopsis—Given the surrounding electrically inert membranous septum and fibrous body and the presence of atrial, His bundle, and ventricular tissues in the area, HBP can be technically challenging. An assessment of the appropriate device function after CPP (Table 9) starts with a baseline ECG to evaluate appropriate capture and compares the paced morphology of the QRS with the native QRS. Follow-up of patients after CPP includes in-office assessment of their clinical status, ECG after any device changes, and assurance of capture. Further, device analyses, including battery status, percent pacing in different

chambers, arrhythmias, lead impedance, and sensing and pacing thresholds, are important to ensure persistent BiV or CSP. For HBP and LBBAP, there are no data at present to support the use of echocardiography for optimization. For CRT, the PROSPECT study[206] tested the ability of 12 echocardiographic parameters to predict CRT response. No single echocardiographic parameter could be used to improve patient selection for response. A single study[352] compared CRT response when the interventricular pacing (VV) interval was optimized by tissue Doppler imaging to CRT response when optimized by QRS width. Although echocardiographic response was higher in the QRS width optimized group, the clinical response was similar in both groups. Thus, the tissue Doppler imaging might be a promising parameter for CRT optimization but needs further study.

Recommendation-specific supportive text—1. An ECG can be a practical means to assess if the LV lead is capturing by contributing a positive deflection in lead V_1 and a negative deflection in lead I. An ECG to confirm LV lead capture is particularly helpful if the patient is being seen in a setting where it is not feasible or practical to perform a device interrogation. Optimization of CRT pacing vectors can be facilitated by ECG QRS duration assessments during testing of LV unipolar and bipolar vectors. A baseline ECG obtained at the time of a successful CRT or CSP implant can also be useful as a future template to determine continued successful pacing capture.

2. In patients who have had a CSP device implanted, a 12-lead ECG, including long strips during threshold testing, can help to ensure and optimize maximal conduction system capture. The tracing should be evaluated to determine capture thresholds, LBBB correction when pertinent, and type of capture (selective vs nonselective conduction system capture).[99,351,353,354] The paced QRS duration and morphology should be compared to prior readings and used as a comparison point for future follow-up.[12,42,46,47,308,353]

3. In a small observational study (n = 61),[304] freedom from lead-related complications after 1-year postprocedure was observed in 93% of patients who underwent HBP. Compared with RVP, HBP was associated with higher rates of lead revisions (6.7% vs 3%) and need for generator change (9% vs 1%) over a 5-year follow-up period.[16] Observational data[47,188] on LBBAP suggest that pacing thresholds remain stable in the first 3–6 months. During long-term follow-up (n = 618), a significant increase in capture thresholds occurred in 1%, with 0.3% requiring lead revision due to dislodgment. Given the possibility of late increase in thresholds and gaps in follow-up, comprehensive follow-up of CSP patients documenting appropriate capture and device thresholds is prudent.[12,16,42,43,47,99,188,290,299,304,305,308,354]

4. In an observational study[298] of 294 patients who underwent HBP, 15% had increased capture threshold, the majority occurring in the first 8 weeks (41%), with 6% eventually requiring a lead revision. Pacing thresholds were higher in patients who underwent HBP compared to those who underwent RVP (1.35 ± 0.9 V vs 0.6 ± 0.5 V at 0.5 ms; $P < .001$).[43] In a minority of patients, these may increase over time and lead to capture loss.[99,299,305] In observational studies,[43,290,298,299] the threshold changes depend in part on the experience and technique of the operator and changes in the programming of the pulse width in an effort to maximize battery longevity. There is no absolute cutoff defining an adequate HBP

threshold, but generally an increase in capture threshold of >1 V warrants more frequent monitoring to determine if a lead revision is required.

6.4. Replacement or upgrade considerations

Recommendations for replacement or upgrade considerations

COR	LOE	Recommendations	References
1	C-LD	1. In patients with HFimpEF, continuation of CRT with BiV pacing is recommended at the time of elective generator replacement.	355,356
1	C-EO	2. In patients who are thought to have benefited from CRT (including improvement, stabilization, or partial reversal of natural decline) in terms of symptoms, LVEF, or functional status, continuation of CRT with BiV pacing is recommended at the time of elective replacement based on patient-individualized risks and benefits of the procedure.	
1	B-NR	3. In patients with CRT-D at the time of elective replacement, it is recommended that a decision for replacement vs revision to CRT-P should be based on patient-individualized risks and benefits of the procedure, and such shared decisionmaking should involve consideration of the previous response to CRT, appropriate ICD therapies for ventricular arrhythmias, continued risk of ventricular arrhythmias, inappropriate therapies, current lead performance factors, and the patient's overall goals of care.	357–360
2b	C-EO	4. In patients with CRT or CSP where high lead pacing threshold contributes to rapid battery drain, implantation of a new lead may be considered after shared decision-making with the patient at the time of generator replacement to reduce the risk associated with frequent generator replacements.	

Synopsis—CRT may benefit HF patients to varying extents. Patients may experience improvement in objective and/or subjective parameters, such as LVEF, LV volume, functional status, or symptom improvement. However, in certain patients, the benefit from CRT might manifest not as an overt improvement but as a slowing of the natural progression of HF.[361] This is considered a "disease stabilizing" response to CRT. This response is difficult to adjudicate and/or quantify in routine patient care and clinical trials but nevertheless is important to recognize. In general, if a patient has previously benefited from CRT pacing to any extent, subsequent interruption or discontinuation of CRT can be detrimental.[355,356]

Currently available data appear to support continuation of ICD therapy in patients whose LV function has improved. In general, continuation of ICD therapy is recommended in such patients. However, in certain situations where the risk vs benefits of continuation of ICD therapy is considered adverse (eg, history of multiple inappropriate therapies or dysfunctional ICD), a shared decision-making strategy should be adopted after informing patient of all the risks, benefits, and alternatives of ICDs.

Recommendation-specific supportive text—1. Small randomized and nonrandomized studies[355,356] have shown adverse clinical and echocardiographic outcomes in patients who have interruption of CRT after having experienced improvement with CRT previously. Patients with HFimpEF (with near normalization of LVEF) resulting from superior response to CRT have poor outcomes when CRT pacing is terminated. This was demonstrated in a small single-center randomized study[355] of 19 patients who showed a superior response to CRT (with improvement in LVEF ≥50% and NYHA class I or II) at mid-term follow-up (average 39 months after CRT implant). These patients were

randomized to CRT pacing continuation (On-Pace group) or deactivation (Off-Pace group). The patients in the Off-Pace group deteriorated with poor clinical and echocardiographic outcomes, while the On-Pace group had no change in status, clearly highlighting the benefit of continuation of CRT in these patients despite HFimpEF. Intuitively, this recommendation applies to patients with CSP, but data on device replacement in CSP are not yet available.

2. All patients who have benefited from CRT, regardless of the extent of the benefit, should continue CRT at the time of elective generator replacement interval. This recommendation recognizes that beyond improvement in LVEF, CRT benefit may include stabilization of ventricular function as well as improvement in symptoms or functional status.

3. Multiple studies have examined the risk of ventricular tachyarrhythmias in patients with previously low LVEF who have undergone improvement in LVEF due to any reason including medical management and/or CRT. These include retrospective studies and subanalyses of RCTs. Most studies show that an elevated risk of tachyarrhythmias persists in these patients, although decreased compared to patients whose LVEF did not improve ≥35%.[362–366] In patients with near normalization of LVEF, the risk of ventricular tachyarrhythmias appears to be markedly reduced,[357–359,366,367] yet still persists. Currently the data are inadequate to support discontinuation of ICD therapy at the time of elective replacement interval. An additional consideration is that revision to CRT-P from CRT-D may not be possible without an adapter if a DF-4 defibrillation lead is in place.

4. Certain patients with CRT might have rapid battery depletion due to high LV lead thresholds. This could be a result of suboptimal lead threshold at implant or a subsequent worsening over time. Frequent pacemaker generator replacements carry a statistically significant risk of complications including infection and hematoma. In such a scenario, revision of the LV lead or CPP lead may reduce the frequency of future generator replacements.[368]

6.5. Troubleshooting for unfavorable response

Recommendations for troubleshooting for unfavorable response

COR	LOE	Recommendations	References
1	C-LD	**1. In patients with HFrEF with an unfavorable response to CRT with BiV pacing, continued efforts to optimize medical and device therapies are recommended to improve quality of life and long-term outcomes.**	330,334,348,369
1	C-LD	**2. In patients with an unfavorable response to CRT with BiV pacing, obtaining a posteroanterior and lateral chest X-ray is recommended to assess the LV lead position.**	245–248
2a	C-LD	**3. In patients with an unfavorable response to CRT with BiV pacing and who have less than optimal LV pacing percentage, ablation or pharmacological suppression of frequent PVCs or better rhythm or rate control of AF is reasonable to improve cardiac function and patient symptoms.**	370,371

Synopsis—Many patients who receive CRT do not improve to the degree expected and have been labeled “nonresponders.” However, this definition has come under increased scrutiny as it does not consider the natural history of disease in any individual patient. The term CRT “stabilizer” has evolved to include patients who may not derive significant

reverse remodeling from CRT but seem to realize a blunting of the natural downhill progression of CRT.[361] Recently the superior outcomes of such patients compared to patients with progressive LV remodeling has been demonstrated.[361,372] The terms “favorable responder,” which includes the CRT stabilizer, and “unfavorable responder” have been proposed to account for this. Nevertheless, there are certain best practices that all CRT patients should be subjected to at follow-up, including medication optimization, evaluation of lead position, device troubleshooting, and arrhythmia detection and management. Newer therapies designed to improve outcomes in patients with an unfavorable response to CRT are areas of active research. For example, in the More Response on Cardiac Resynchronization Therapy With MultiPoint Pacing (MORE-CRT MPP) trial,[267] MPP failed to meet its endpoint of converting nonresponders to responders. Whether MPP has a role in the treatment of CRT patients remains unclear. One potential role of MPP may be in patients with a severely enlarged LV. Such patients have increased myocardial mass and may benefit from the increased depolarization wavefront provided by MPP.[373] In addition, whether percutaneous mitral valve repair improves outcomes in CRT patients with an unfavorable response remains unclear.[374] In patients who have undergone CRT but require implantation of an LVAD, inactivation of CRT to preserve device battery longevity has become a common practice[375] given data showing no significant improvements in clinical outcome with continued CRT in the presence of an LVAD.[376,377] However, as small studies show conflicting results with regard to continued CRT vs CRT-off on ventricular arrhythmias and ICD shocks,[377–380] data from larger randomized trials of CRT inactivation vs activation would be needed to inform recommendations in this area.

Recommendation-specific supportive text—1. All patients regardless of CRT response criteria should continue to have optimization of medical therapy at follow-up.[330,334,348] In a dedicated CRT clinic, 74% of “nonresponders to CRT” had opportunities for substantial uptitration of current medications or addition of new HF medications.[334] Even in patients who have normalized their EF with CRT, withdrawal of GDMT has been shown to lead to poor outcomes.[336] In patients considered to be doing poorly with CRT, small nonrandomized studies have suggested that substituting sacubitril-valsartan for an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker may be beneficial.[381,382] In addition, consideration should be given to addition of aldosterone antagonists and sodium-glucose cotrans-porter-2 inhibitors.

2. LV lead position is an important determinant of CRT response such that patients with more septal lead positions respond less favorably compared to those with leads placed in lateral positions.[383] In addition, analysis[247] from the MADIT-CRT trial has suggested that apically placed LV leads may respond less favorably compared to more midor basally placed leads. As such, gaining a rough determination of where an LV lead is located via a posteroanterior and lateral chest X-ray is useful.

3. Reduced BiV pacing percentage has been linked to elevated mortality among CRT recipients. Studies suggest that achieving as close to 100% effective BiV pacing as possible is preferred.[384] A >92% BiV pacing percentage was associated with a 44% reduction in clinical events compared to a ≤92% BiV pacing percentage (HR 0.56; $P < .001$).[370] Common reasons behind diminished BiV pacing percentage include AF, elevated PVC

burden, and long AV delay. In CRT patients with AF, an uncontrolled ventricular rate defined by a mean ventricular rate of >80 bpm and a maximum ventricular rate of >100 bpm was associated with increased HFH and mortality in multivariate analysis and was associated with <95% BiV pacing.[385] In patients who have responded unfavorably to CRT who have AF and <92% BiV pacing, aggressive management of AF with either a rhythm control strategy or a rate control strategy, potentially with AV node ablation, may be reasonable. In such patients with permanent AF, AV node ablation may be superior to medical therapy.[386] Suppression of PVCs either with catheter ablation or medical therapy may be reasonable in patients with an unfavorable response to CRT. ECG to assess PVC morphology and ambulatory monitoring or device assessment to assess PVC burden may be helpful to assess candidacy for and results of suppressive or ablative therapies. In a multicenter registry[371] of 65 patients deemed “nonresponders” to CRT who concomitantly had PVC burden >10,000 per day, acute success of ablation was 91%, with patients realizing significant reverse ventricular remodeling and symptomatic benefit. As such, PVC suppression can be helpful for CRT recipients with an unfavorable response.

6.6. When to cross over to CSP, CRT, or epicardial options

Recommendations for when to cross over to CSP, CRT, or epicardial options

COR	LOE	Recommendations	References
2a	C-LD (HBP, LBBAP) B-NR (surgical epicardial lead)	**1. In patients with a suboptimal response to CRT with BiV pacing, CSP (with HBP or LBBAP) or surgical epicardial lead implantation can be useful when other approaches have been unsuccessful or not feasible.**	HBP, LBBAP[47,58,100,101,103,110,387] Surgical epicardial lead[318,319,388,389]

Synopsis—In some patients with CPP, suboptimal response to CPP may be due to technical limitations of the implant procedure or it may become apparent that the goals to be achieved have not been met in either short- or longer-term follow-up. This may be because the original implant was not acutely successful. In the case of BiV pacing, CS access and anatomical limitations leading to suboptimal LV lead location or dislodgment, unsatisfactory thresholds, and phrenic nerve stimulation are typical challenges. For patients with CSP, obstacles can include an inability to deliver a His bundle lead or achieve stable anatomic position, unacceptable thresholds acutely or over time in the case of HBP, or inability to achieve LBBAP with LBBB correction. At this time, data remain limited regarding crossover options for CSP to CRT during follow-up. Beyond the acute implant, suboptimal lead location or CPP nonresponse or unfavorable response may prompt consideration of crossover to an alternative CPP modality. As there are no randomized studies in this area, most of the recommendations in this section are based on retrospective analyses of populations of patients who during follow-up were crossed over to a different anatomic pacing approach that proved feasible and/or subsequently successful. LV transvenous endocardial approaches were considered,[282,390–393] but the data are preliminary and the associated risk of cardioembolic stroke was felt to be unacceptably high to support a recommendation.

Recommendation-specific supportive text—1. In patients with unsuccessful CRT or an unfavorable response to CRT, HBP can be useful. Most data derive from observational, retrospective, crossover, and/or nonrandomized studies with a small sample size, showing the feasibility of HBP in patients who are candidates for CRT, particularly as rescue for a failed LV lead or an unfavorable response to BiV pacing.[42,394] This has been demonstrated not only for patients with LBBB but for patients with RBBB as well.[108] Three randomized studies,[100,101,103] albeit with small numbers of patients, have also demonstrated the potential benefit of crossing over to HBP when CS lead placement was not achieved or an unfavorable response to BiV pacing was observed. In addition, 1 study[150] demonstrated that HBP could be used in conjunction with BiV pacing to optimize CRT with improvement in QRS narrowing and LVEF compared to BiV pacing alone. Taken together, these studies have shown that HBP could correct LBBB in the majority of patients and achieve a significant narrowing in QRS duration and improvement in EF and/or NYHA class with clinical status comparable, if not superior, to BiV pacing,[42,100,101,103,108,150,394,395] albeit at the expense of elevated pacing thresholds observed for HBP.[42,103]

In patients with unsuccessful CRT, LBBAP can be useful where other approaches have been unsuccessful or not feasible. To date, there are no RCTs assessing when LBBAP may be utilized when either BiV pacing or HBP is neither feasible nor successful in longer-term follow-up. Nonrandomized prospective feasibility studies with a small sample size have demonstrated that LBBAP may serve as rescue from failed LV lead placement or as a primary strategy in CRT-indicated patients, achieving improvement in EF and often a more dramatic shortening of QRS duration.[47,58,188,387,396] High implant success with low thresh olds has been observed. Three studies[47,58,188] analyzed crossover from HBP to LBBAP after HBP attempt or lead failure, indicating that LBBAP offered an alternative to the high thresholds potentially encountered longer term with HBP though with equal degrees of cardiac resynchronization and often with more effective electrical resynchronization as compared with BiV pacing. Most recently, a large observational multicenter study[110] examined LBBAP as a crossover in patients who met standard indications for CRT but who had failure of coronary venous pacing due to lack of access, elevated stimulation thresholds, diaphragmatic pacing, suboptimal lead position, need for CS lead extraction, or lack of clinical responsiveness to BiV pacing. In 200 of 212 patients (94%), LBBAP was successfully achieved and resulted in significant QRS narrowing from 170 ± 28 to 139 ± 25 ms and an improvement in LVEF from 29% ± 10% to 40% ± 12% in the follow-up period. Of interest, the indication of coronary venous lead failure for crossing over to LBBAP was an independent predictor of reduced risk of death or HFH when compared with the indication of BiV pacing nonresponsiveness.

In patients with unsuccessful CRT, surgical epicardial lead implantation can be useful where other approaches have been unsuccessful or not feasible. Only retrospective observational studies have been undertaken to assess the utility of placing epicardial leads surgically in patients where BiV pacing could not be achieved transvenously.[317–319,388,389,397] No randomized clinical trials have been reported. Surgical placement has been shown to be feasible as a first noncrossover option for CRT,[318,397] with no significant differences in improved LVEF or lead performance, though at the expense of a longer hospital stay. In 1

study,[318] the need for reintervention/lead revision was significantly reduced in the surgical approach in both shorter- and longer-term follow-up. As a crossover approach where CS lead implantation failed as a primary approach (whether due to inability to cannulate the CS, CS anomaly, dislodgment, or phrenic nerve stimulation), the surgical approach was feasible and safe, with comparable clinical outcomes with regard to functional status and ventricular reverse remodeling.[317,319,388]

Section 7 Congenital heart disease and pediatric populations

Pacing applications in pediatric populations and in children and adult patients with congenital heart disease (CHD) introduce factors not typically found in other patient populations. Issues of congenital heart anatomy, alterations in systemic ventricular morphologies, and surgical repairs as well as vessel diameters and chamber dimensions can create technical challenges to implants. A prime concern is the concept of lifelong (decades) pacing and the potential of pacing-induced myocellular changes leading to ventricular dysfunction. For this reason, ventricular lead implant at sites that most optimize contractility is advised. To date, no one site has been shown to be optimal for all patients. In this regard, lead implant should be patient specific (select site/targeted) and based on resultant contractility assessments in addition to usual sensing/threshold values; however, limitations are that ideal sites may be unable to be accessed or that pacing thresholds in these areas may be poor. Although BiV/CRT pacing for clinical HF/ventricular dysfunction has been applied to this diverse patient population, results to date have been variable with different definitions of success. Basic echocardiographic values (LVEF and chamber dimensions) and QRS duration have not shown a strong correlation with clinical outcomes. Risks/benefits and potentially adverse issues associated with an additional lead via either the CS or an epicardial site need to be considered when contemplating BiV/CRT pacing.

7.1. CHD

Pediatric and adult patients with CHD often require pacing secondary to intrinsic conduction disease or scarring following palliation or repair. Patients with congenitally corrected transposition of the great arteries (CCTGA) have an annual risk of developing AV block of 2%,[398] including intrinsic conduction disease. Surgical heart block occurs in 1%–6% of CHD patients.[399] These patients have a high risk of developing HF when compared to the general population, and thus careful consideration of type of pacing system is necessary to optimize their outcome.

Recommendations for CHD

COR	LOE	Recommendations	References
2a	C-LD	**1. In patients with CHD on GDMT with a systemic LV, LVEF <45%, and ventricular dyssynchrony (as defined by a QRS duration z score of ≥3 or ventricular pacing ≥40%), CRT with BiV pacing is reasonable to reduce the risk of mortality or need for transplant.**	400–408
2a	C-LD	**2. In patients with CHD and a systemic single ventricle who require pacing, apical pacing is reasonable in preference to nonapical pacing.**	409

COR	LOE	Recommendations	References
2b	C-LD	**3. In patients with CHD and a systemic single ventricle with symptomatic HF on GDMT, CRT with multisite ventricular pacing may be considered to maintain functional class or ventricular function.**	400,402,410,411
2b	C-LD	**4. In patients with CHD and a systemic RV with symptomatic HF on GDMT associated with ventricular electrical delay or requiring substantial ventricular pacing, CRT with BiV pacing may be considered to improve or maintain functional class or ventricular function.**	400–408,412–415
2b	C-LD	**5. In patients with CHD and a subpulmonary RV with RV dysfunction and RBBB, CRT with fusion-based pacing may be considered to improve RV function.**	416–418
2b	C-LD	**6. In patients with CCTGA and AV block in whom anatomic repair has not been performed, CSP with HBP or LBBAP may be considered to improve functional status.**	419,420

Synopsis—Patients with CHD comprise a complex heterogeneous group with varied anatomy, including systemic LV, systemic RV, and even patients with functional single ventricles. All these subpopulations, to differing degrees, have a heightened risk of developing HF in comparison to the general population.[421] CRT has been used in these patients with varying degrees of success. Patients with a systemic LV have shown the greatest response to CRT in comparison to systemic RV and single-ventricle patients.[401,403,411] While the majority of studies of CHD and CRT have found improvements in EF, clinical status, and QRS duration, only recently has a survival benefit been shown.[401]

Additional considerations for use of CRT in these populations include the need to normalize QRS duration for age by the use of z scores[422]; the need for varied approaches to device implantation based on size, access, and anatomy; and the potential for disadvantages of size to outweigh procedural benefits in the smallest of patients.

True CSP therapy has been used in CHD patients with demonstration of feasibility and safety.[419,420,423] In patients with CCTGA and AV block, this therapy has been shown to improve functional status.[420,422]

Follow-up with optimization, remote monitoring, and considerations on replacement or upgrade are important in the pediatric and CHD population. Please refer to Sections 6.1–6.4 for recommendations on follow-up and management after CPP implantation. An algorithm outlining the recommendations for pediatric and adult patients with CHD is shown in Figure 12.

Recommendation-specific supportive text—1. CRT has been found to be most useful in patients with CHD and a systemic LV, with several multisite studies showing improvements in QRS duration, EF, and functional status.[400,402,403] Only recently has there been data to support a survival benefit in a propensity score matched single-site study of patients with CHD.[401] Patients with CHD and systemic EF <45%, QRS duration z score >3, or ventricular pacing >40% had a markedly reduced HR of transplant/death (HR 0.24; 95% CI 0.12–0.46; $P < .001$) with CRT compared to a propensity score matched control group. QRS duration in children changes with age. Normalization using a z score algorithm allows for comparable criteria and longitudinal tracking.[422]

2. Pacemaker therapy in patients with single-ventricle physiology has been associated with impaired ventricular function and an increased risk of need for cardiac transplant.[424–426] In a propensity score matched study[409] of 236 paced single-ventricle patients and 213 matched controls, multivariable HR for death/transplant associated with a pacemaker was 3.8 (95% CI 1.9–7.6; $P < .0001$). Nonapical lead position was also associated with death/transplant with an HR of 2.17.

3. Patients with single-ventricle physiology are known to have a poor outcome if they require ventricular pacing with an increased risk of transplantation or death (odds ratio 4.9; 95% CI 1.05–22.7; $P = .04$).[424] Several investigators have attempted multisite pacing in this vulnerable population with varying success. While patients may not have classic improvement with multisite pacing, it does appear that this therapy may slow the progression of HF.[411]

4. Patients with systemic RV have shown improvement in their EF and clinical status following resynchronization, but not to the extent of patients with a systemic LV.[403] This has been hypothesized as possibly secondary to differing ventricular architecture (right vs left) or decreased myocardial perfusion reserve.[427,428] These patients often have abnormal CS anatomy and can be a challenge when considering transvenous CRT.[406] A systematic review[412] of 14 studies of systemic RV resynchronization found that this therapy can be useful in the failing systemic RV, but the studies to date were all relatively small with long-term outcomes lacking. There was also not a uniform definition for response, which hampered the interpretation and comparison of these studies. In the largest study[414] to date of 80 patients with systemic RV, CRT showed consistent improvement in NYHA functional status, but only a marginal increase in systemic ventricular function.

5. Patients with subpulmonary RV dysfunction and RBBB have shown acute hemodynamic improvement including improvements in cardiac index and blood pressure with short-term selective-site RVP and fusion-based pacing.[418,429] Fusion-based pacing refers to optimizing RV-only pacing by attempting to fuse paced electrical and mechanical activity with the intrinsic QRS complex. Recently there have been some small studies[416,417] looking at long-term use of RV resynchronization in this population, with somewhat promising results. Larger studies are needed to assess the long-term outcome of this patient population. To date, the optimal method to deliver fusion-based RV-CRT has not been determined. The 2 approaches described thus far include static AV timing[416] and triggered pacing,[417] both with potential limitations (ie, variability in AV conduction time over time may lead to loss of CRT in the former and late onset of fusion-based pacing may limit the maximal effect in the latter).

6. There are limited data regarding the use of CSP in patients with CCTGA and AV block. A small multicenter study[420] of patients with CCTGA and AV block who had not undergone anatomic repair showed unchanged QRS duration compared to junctional escape rhythm with functional status improvement in 33% at 8 months.

7.2. Pediatric patients without CHD

In pediatric patients with structurally normal hearts, heart block can be seen with maternal-fetal antibody transmission or infection.[430–435] Approximately 10% of these patients will go on to develop myocardial dyssynchrony and dilated cardiomyopathy.[436] There are specific issues to be considered when pacing a pediatric patient, including small body weight, long-term vascular access, and the need for lifelong pacing. The potential for development of HF with need for long-term pacing has led to consideration for more physiologic pacing. RV lead implant sites that best approximate the normal conduction system (eg, His bundle region, inflow, and mid-septum) and LV (left bundle and apex) appear promising to maintain or improve contractility.[437–440] Due to smaller septal dimensions in a child than in adults, lead implant in the mid-, inflow, or para-His ventricular septum can approximate CSP. However, HBP may be limited in pediatric patients due to higher pacing thresholds and the need for more frequent intervention.[440] Mid- and apical septal thickness dimensions correlate with patient body weight and typically range from 3 to 12 mm after the age of 5 years, an age where transvenous pacing is often applied. Predetermination of septal thickness at any proposed implant site may prevent potential adverse problems, for example, during deep septal pacing or LBBAP. Unfortunately, to date, there are no comparative studies of contractility responses between “best site” RV septal and His bundle or LBB pacing in children. Therefore, at present, risks/benefits of attempted direct CSP in young children must be individualized. In cases of overt HF, CRT has been applied with some positive results. In the young, body size, anatomy, vascular dimensions, growth, and preexisting pacing leads can restrict lead implants. Patient growth–related issues of lead performance and the potential need for eventual extractions are a greater concern among younger than older populations. Surface fibrosis can hinder epicardial lead implant, and elevated pacing thresholds are always a concern.[441] This section provides recommendations for pediatric patients without CHD who have HF or have indications for pacemaker therapy, as outlined in Figure 13.

7.2.1. Indications for CPP in pediatric patients with HF

Recommendations for CPP in pediatric patients with HF

COR	LOE	Recommendations	References
2a	C-LD	**1. In pediatric patients with complete AV block, preexisting ventricular pacing, and symptomatic clinical HF on GDMT, CRT with BiV pacing is reasonable.**	400,402,442
2b	C-LD	**2. In pediatric patients with complete AV block and evidence of clinical HF on GDMT, CPP may be considered.**	401,440,443

Synopsis: CRT pacing for clinical HF therapy has been applied to children as well as young adults with repaired CHD, albeit in much smaller numbers than among older adult populations. Due to the diversity of cardiac anatomies and typical absence of any predefining criteria for implant or definition of actual success, interpretation of results can be challenging. Nevertheless, CRT, if applied appropriately, can still be an effective therapy to improve HF symptoms as well as delay heart transplant listing.

Recommendation-specific supportive text: 1. PICM in young patients with complete AV block and pacemaker dependence has been successfully treated with upgrade to CRT with BiV pacing. Although limited in numbers of patients reported, studies report clinical improvements with increase or stabilization of LVEF, shortening of QRS duration, and/or reduction in LV size.[400,402,442]

2. CRT-related publications in children and young adults with clinical HF, to date, have included patients with both repaired CHD as well as those with isolated congenital complete atrioventricular block (CCAVB). As might be expected due to the utilization of devices in children, study patient numbers have been limited when compared with those from older adult populations. Patient selection criteria have been variable, including patients with and without anatomical heart defects or surgery, and follow-up has been limited, making interpretation of CRT efficacy challenging. Changes in LVEF and QRS duration have typically been utilized to define success. As a result, results from single-center and multicenter studies have been mixed. Patient numbers have ranged from 6 to 103 per study, with 45%–100% having preexisting pacemakers and follow-up from 0.7 to 16 years.[442] Predefined criteria for implant (≥ 15% contractility improvement [dP/dt] with acute BiV pacing) was reported in only 1 study.[444] Actual clinical improvement was reported from 38% to 100% of patients in these studies, regardless of measured EF value changes. In addition, QRS duration shortening was not a consistent variable defining clinical improvement. The typical absence of a pre-CRT LBBB QRS pattern in children, except those with previous RVP, somewhat complicates any interpretation of QRS shortening. There are multiple ways to optimize lead positions. This can be difficult because of anatomy, size, and thresholds. Some methods require repositioning the lead location to optimize the QRS duration or to improve acute hemodynamic measurements in the catheterization laboratory.

In a propensity score matched study[401] of 63 patients who received CRT and 63 matched controls, CRT was associated with a reduced risk of death/heart transplant (HR 0.24; 95% CI 0.12–0.46; $P < .001$) at a median follow-up of 2.7 years. In that study, in deference to empirically placing leads, a positive CRT response was enhanced by specific CRT lead implant showing optimization of mechanical synchrony based on cardiac output, ECG changes, and echocardiography at implant.

Due to the various etiologies of HF among children with CCAVB without preexisting pacemakers, targeting initial pacing sites that may be expected to maintain or improve contractility would be optimal. This may need to be individualized. Targeting RV lead implant sites that best approximate the normal conduction system (eg, His bundle region, inflow, or mid-septum) or LV sites (left bundle or apex) may improve myocardial function without the need for CRT.[401]

7.2.2. CPP considerations for pediatric patients with indications for pacemaker therapy

Recommendations for pediatric patients with indications for pacemaker therapy

COR	LOE	Recommendations	References
2a	C-LD	**1. In pediatric patients undergoing pacemaker implantation for AV block, it is reasonable to either target an RV mid-septal, inflow, or outflow tract transvenous endocardial site, or use apical LV (systemic ventricle) epicardial pacing, in preference to RV apical endocardial or epicardial pacing sites.**	445–449

Synopsis: Lifelong pacing starting in childhood is associated with the propensity to develop myopathic changes due to pacing.[436,450] As a result, in addition to standard evaluations of sensing and pacing thresholds, myocardial response becomes an important factor during implant. The traditional RV apical pacing site, using early lead designs without fixation capabilities, resulted in altered myocellular contractility causing adverse histopathology in children.[431] With the introduction of improved lead designs, implants can now be achieved at most preselected or “targeted” locations that optimize contractility or narrowest QRS duration.

Recommendation-specific supportive text: 1. Lead placement in close proximity to the normal septal conduction system or LV sites may be preferred. Select RV septal pacing sites, typically inflow to mid-septum, are associated with either improved or preserved LV contractility when compared with other RV sites. These sites are also associated with a narrow QRS duration and normalized axis.[445,446] In studies of RVP sites (apex to outflow tract), no demonstrable difference could be seen with “nontargeted” septal sites; however, when assessing sites using contractility (dP/dt), the mid-septal region (moderator band area) was typically associated with the best responses.[450,451] The optimal site, in regard to paced contractility, appears to be patient specific with no one site optimal for all, stressing the need to individualize lead implants. Electroanatomic mapping has been utilized to localize RV transvenous sites with narrowest QRS duration on mid-septum, para-Hisian, or RV outflow tract sites.[445,446] Adverse thresholds and valve problems have not been a concern with septal pacing.

Only a small number of pediatric patients who have undergone HBP or LBBAP have been reported.[423,440,443] One of the studies[423] reported clinical improvements, but EF changes in both studies were variable and QRS duration shortened only among patients with preexisting pacemakers. Elevated pacing thresholds were reported in patients from both studies, with some requiring lead revisions. Therefore, at this time, data are too limited to make recommendations regarding HBP or LBBAP applications in pediatric patients.

Epicardial apical LV pacing has been advocated over RVP to better preserve ventricular contractility among infants and children with isolated CCAVB with reported improvements in echocardiographic parameters of EF as well as strain and synchrony.[445,446,448,449] Of note, QRS duration was not different between sites.

Section 8 Gaps, needs, and future directions

CPP carries the potential to mitigate or prevent HF in select patients undergoing implantable device therapies. The strongest evidence for CPP has been with randomized clinical trials showing improvement in clinical outcomes, including improved survival and HFH, for select populations undergoing CRT, particularly for patients with LVEF ≤35%, LBBB, and QRS duration ≥150 ms, and NYHA functional class II–IV symptoms. For patients with LVEF 36%–50% expected to require substantial RVP, randomized trials support use of CRT or HBP to avoid PICM if substantial RVP is anticipated. However, there remain significant gaps with limited randomized data for other CPP indications and for CSP (HBP or LBBAP). Identified gaps and needs for future studies are listed in Table 10.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABIM = American Board of Internal Medicine; ACC = American College of Cardiology; ACGME = Accreditation Council for Graduate Medical Education; ACHL = Academy for Continued Healthcare Learning; AHA = American Heart Association; FDA = U.S. Food and Drug Administration; HRS = Heart Rhythm Society; ISHNE = International Society for Holter and Noninvasive Electrocardiology; NHLBI = National Heart, Lung, and Blood Institute; NIH = National Institutes of Health; NWO = The Dutch Research Council.

*Research and fellowship support are classed as programmatic support. Sources of programmatic support are disclosed but are not regarded as a relevant relationship with industry for writing committee members.

†Dr Selzman stepped down from the writing committee in September 2022 when she transitioned to a new role in industry, which precluded her from participation in the development of the guideline. Dr Selman was one of the primary authors for Section 3.4 Indications for CPP in Atrial Fibrillation. After her departure, this section was rereviewed by the section lead/authors and the document chairs, and the evidence for this section was rereviewed by the document methodologists.

Appendix 2: Reviewer disclosure of relationships with industry and other entities

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Takanori Ikeda, MD, PhD	Toho University, Tokyo, Japan	1: Pfizer/BMS 2: Bayer Healthcare Pharmaceuticals 2: Daiichi Sankyo	None	None	None	None	None	None	None
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Christopher J. McLeod, MBChB, PhD, FHRS	Mayo Clinic, Jacksonville, Florida	1: BioSig Technologies	None	None	None	None	None	None	None
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ACC = American College of Cardiology; BMS = Bristol Myers Squibb; HRS = Heart Rhythm Society.

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ABBREVIATIONS

AF	atrial fibrillation
AV	atrioventricular
AVJ	atrioventricular junction
BBB	bundle branch block
BiV	biventricular
CABG	coronary artery bypass graft
CCAVB	congenital complete atrioventricular block
CCTGA	congenitally corrected transposition of the great arteries
CHD	congenital heart disease
CHF	congestive heart failure
CIED	cardiovascular implantable electrical device
COR	class of recommendation
CPP	cardiac physiologic pacing
CRT	cardiac resynchronization therapy
CRT-D	cardiac resynchronization therapy–defibrillator

CRT-P	cardiac resynchronization therapy–pacemaker
CS	coronary sinus
CSP	conduction system pacing
ECG	electrocardiogram/electrocardiographic
EF	ejection fraction
FOI	fusion-optimized intervals
GDMT	guideline-directed medical therapy
HBP	His bundle pacing
HF	heart failure
HFH	heart failure hospitalization
HFimpEF	heart failure with improved ejection fraction
HFrEF	heart failure with reduced ejection fraction
HR	hazard ratio
ICD	implantable cardioverter-defibrillator
IVCD	intraventricular conduction delay
LBB	left bundle branch
LBBAP	left bundle branch area pacing
LBBB	left bundle branch block
LOE	level of evidence
LV	left ventricle/ventricular
LVAD	left ventricular assist device
LVEDD	left ventricular end-diastolic diameter
LVEDV	left ventricular enddiastolic volume
LVEF	left ventricular ejection fraction
LVESV	left ventricular end-systolic volume
LVESVI	left ventricular end-systolic volume index
MPP	multipoint pacing
MRI	magnetic resonance imaging
MSP	multisite pacing

NYHA	New York Heart Association
PICM	pacing-induced cardiomyopathy
PVC	premature ventricular contraction
RBBB	right bundle branch block
RCT	randomized controlled trial
RV	right ventricle/ventricular
RVP	right ventricular pacing
RWI	relationships with industry
RWPT	R-wave peak time
TAVI	transcatheter aortic valve implantation
VO_2	oxygen uptake
6MWD	6-minute walk distance

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Top 10 take-home messages

1. Cardiac physiologic pacing (CPP) is defined here as any form of cardiac pacing intended to restore or preserve synchrony of ventricular contraction. CPP can be achieved by engaging the intrinsic conduction system via conduction system pacing (CSP; which includes His bundle pacing or left bundle branch area pacing) or cardiac resynchronization therapy (CRT), the latter most commonly achieved by biventricular (BiV) pacing using a coronary sinus branch or epicardial left ventricular pacing lead.
2. The strength of evidence for CRT in heart failure (HF) is substantially greater than what is available to support CSP. Multiple randomized controlled trials have shown a beneficial effect of CRT in reducing HF symptoms and hospitalization, improving left ventricular function, and increasing survival. The majority of data on CSP are observational, and long-term data on lead survival are lacking. Ongoing and planned studies are likely to provide future guidance on the use of CSP compared to CRT.
3. Response to CRT has a variable definition and includes improvements in mortality and HF hospitalization but may also include improvement in clinical parameters of HF, stabilization of ventricular function, or prevention of progression of HF.
4. Periodic assessment of ventricular function is recommended for patients who require substantial right ventricular (RV) pacing (≥ 20%–40%) or have chronic left bundle branch block (LBBB) to detect pacing- or dyssynchrony-induced cardiomyopathy.
5. Patients undergoing pacemaker implant who are expected to require substantial ventricular pacing (≥ 20%–40%) may be considered for CPP to reduce the risk of pacing-induced cardiomyopathy.
6. Patients with left ventricular ejection fraction (LVEF) of 35%–50% who are expected to require less than substantial (< 20%–40%) ventricular pacing may not have a sizable benefit from CPP; therefore, traditional RV lead placement with minimization of ventricular pacing, CSP, or CRT in the setting of LBBB are all acceptable options.
7. New recommendations for left bundle branch area pacing are made for patients with normal LVEF (class of recommendation [COR] 2b) needing a pacing device.
8. CRT remains recommended for patients with HF, LVEF ≤35%, LBBB, QRS duration ≥150 ms, and New York Heart Association class II–IV symptoms on guideline-directed medical therapy (COR 1). New recommendations are made for CSP when effective CRT cannot be achieved (COR 2a); and for CRT in patients with select characteristics (eg, female sex), as they may derive benefit from CRT at QRS durations of 120–149 ms (COR 1). New recommendations

are also made for patients with HF, LVEF 36%–50%, LBBB, and QRS duration ≥150 ms for CRT or CSP to maintain or improve LVEF (COR 2b).

9. New CPP recommendations are provided for patients with HF, LVEF ≤35%, and non-LBBB pattern for QRS duration both <150 and ≥150 ms (COR 2b).

10. During implantation and follow-up of patients with CPP devices, electrocardiographic demonstration of BiV (for CRT) or conduction system (for CSP) capture is essential.

Other important considerations

1. Shared decision-making is recommended when contemplating implantation of a CPP device and should include considerations of the patient's values, preferences, goals of care, and prognosis, along with the potential benefits, short- and long-term risks (in particular, device-associated infection), effects of these pacing modalities on battery longevity, future lead management issues, evidence base for different types of CPP, and considerations at the end of life.
2. Substantial RV pacing of ≥20%–40% may induce cardiomyopathy in a subset of patients.
3. Remote monitoring and in-person echocardiographic and electrocardiographic evaluations are essential during follow-up after implantation of a CPP device to ensure appropriate capture and optimization of therapy.
4. In patients with HF with improved LVEF or benefit from CRT (including improvement, stabilization, or partial reversal of natural decline), continuation of CRT with BiV pacing is recommended at the time of device replacement.
5. In patients with an unfavorable response to CRT with BiV pacing, optimization of both medical and device therapies is recommended.
6. In selected patients with congenital heart disease or congenital atrioventricular block, CRT or conduction system area pacing may be considered.
7. Long-term data on CSP are emerging, with current data derived from observational studies or small randomized clinical trials without long-term follow-up. Robust data from ongoing, larger randomized trials are expected.

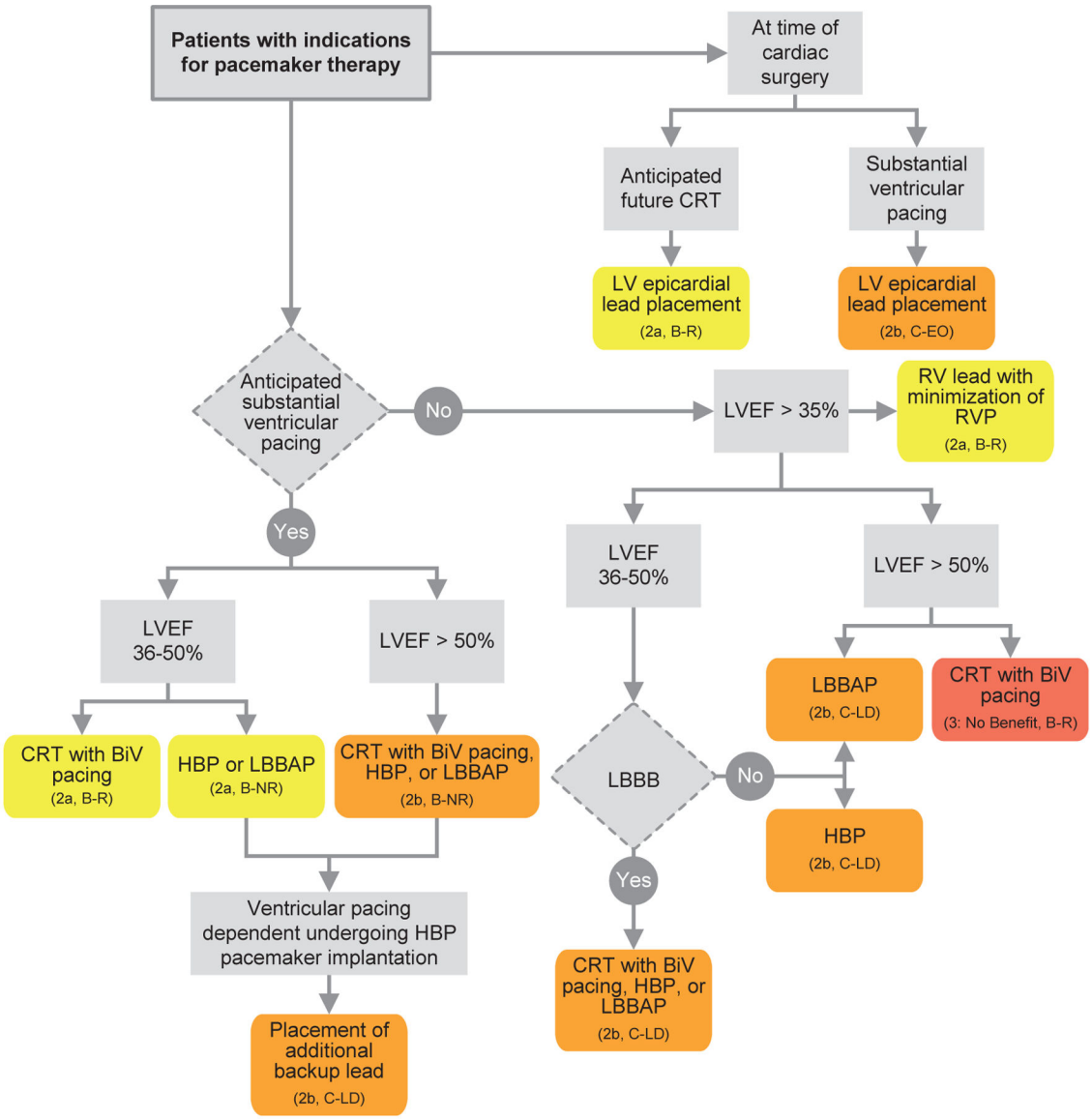

Figure 1.

Algorithm for pacing strategies in patients undergoing pacemaker implantation for bradycardia indications. Colors correspond to the class of recommendation in Table 1. BiV = biventricular; CRT = cardiac resynchronization therapy; HBP = His bundle pacing; LBBAP = left bundle branch area pacing; LBBB = left bundle branch block; LV = left ventricle/ventricular; LVEF = left ventricular ejection fraction; RV = right ventricle/ventricular; RVP = right ventricular pacing.

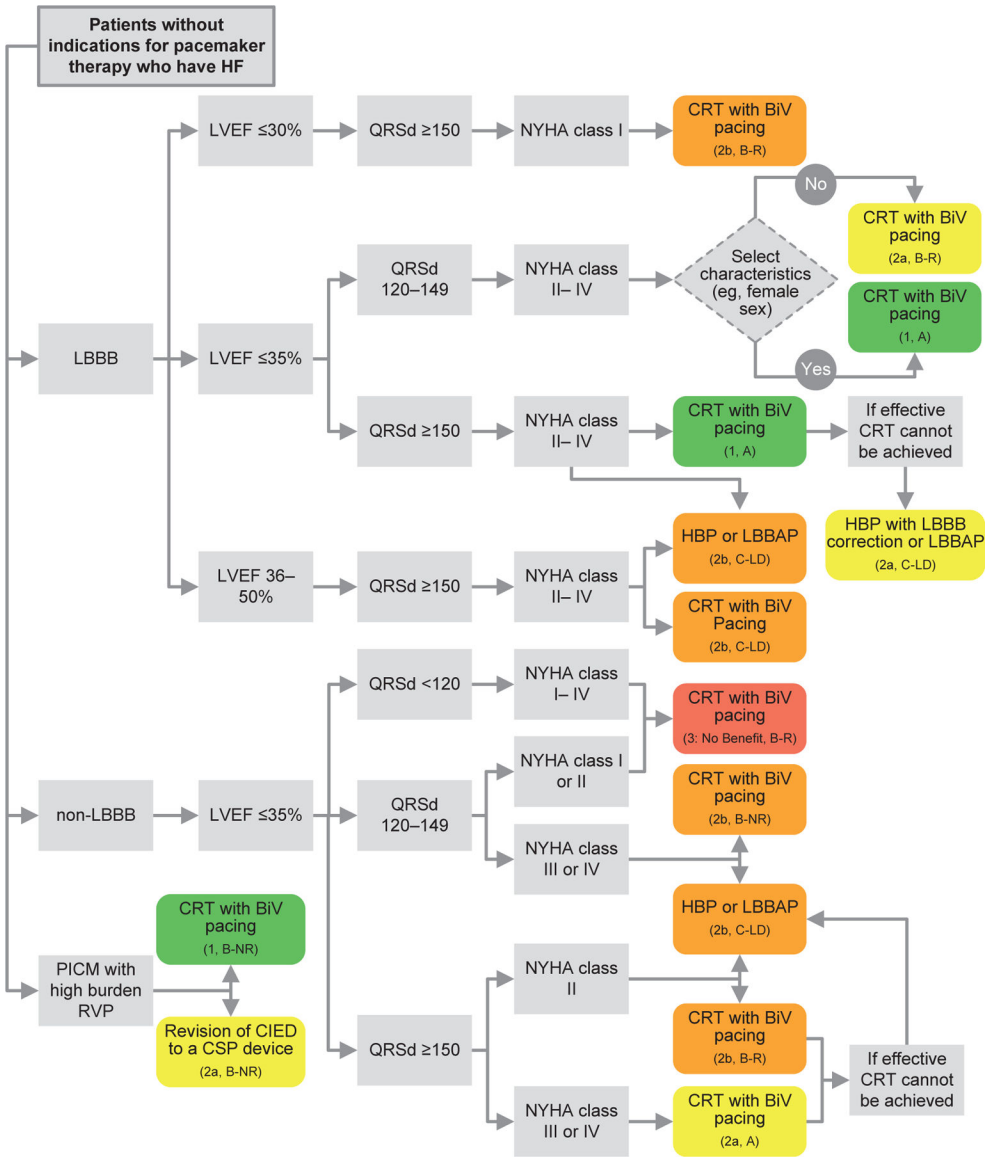

Figure 2.

Algorithm for pacing strategies in patients without bradycardia indications who have HF. Colors correspond to the class of recommendation in Table 1. BiV = biventricular; CIED = cardiovascular implantable electrical device; CRT = cardiac resynchronization therapy; HBP = His bundle pacing; HF = heart failure; LBBAP = left bundle branch area pacing; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PICM = pacing-induced cardiomyopathy; QRSd = QRS duration; RVP = right ventricular pacing.

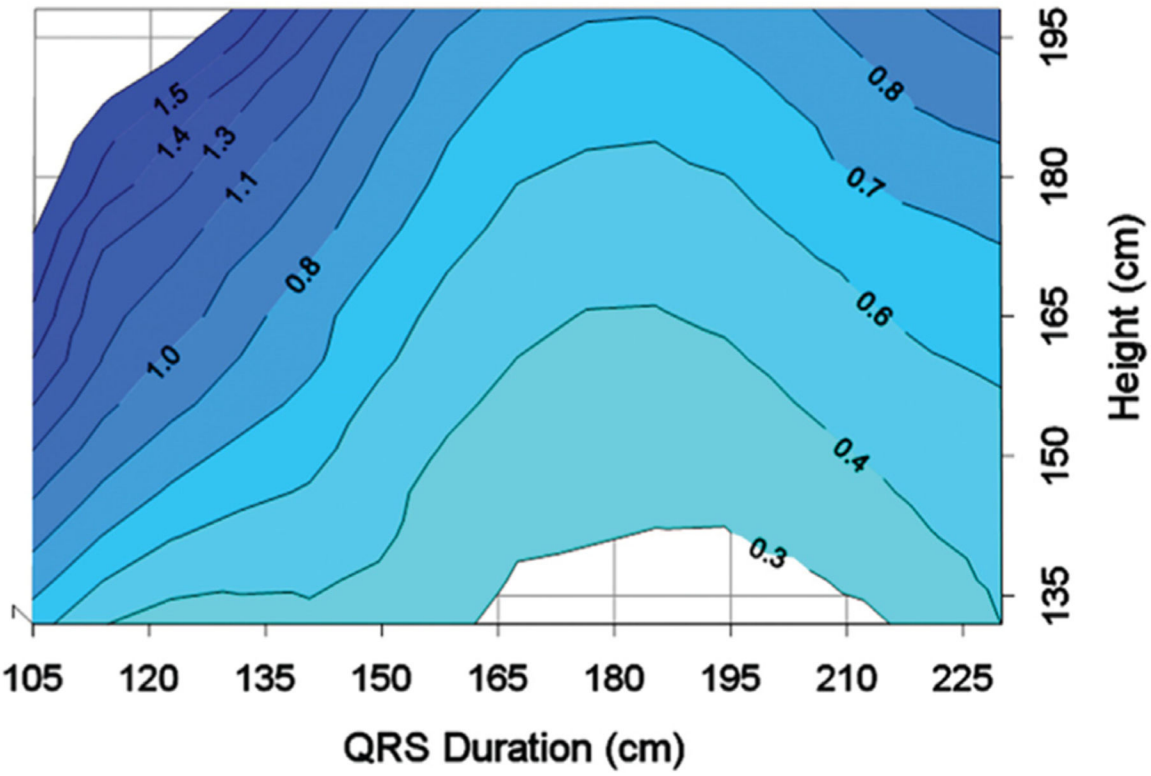

Figure 3.

Cardiac resynchronization therapy hazard ratio by height and QRS duration. Contour lines depict the cardiac resynchronization therapy hazard ratio for different combinations of height (y-axis) and QRS duration (x-axis). The lighter blue color corresponds to greater cardiac resynchronization therapy benefit (ie, lower hazard ratio). Reprinted with permission from Linde et al.[122]

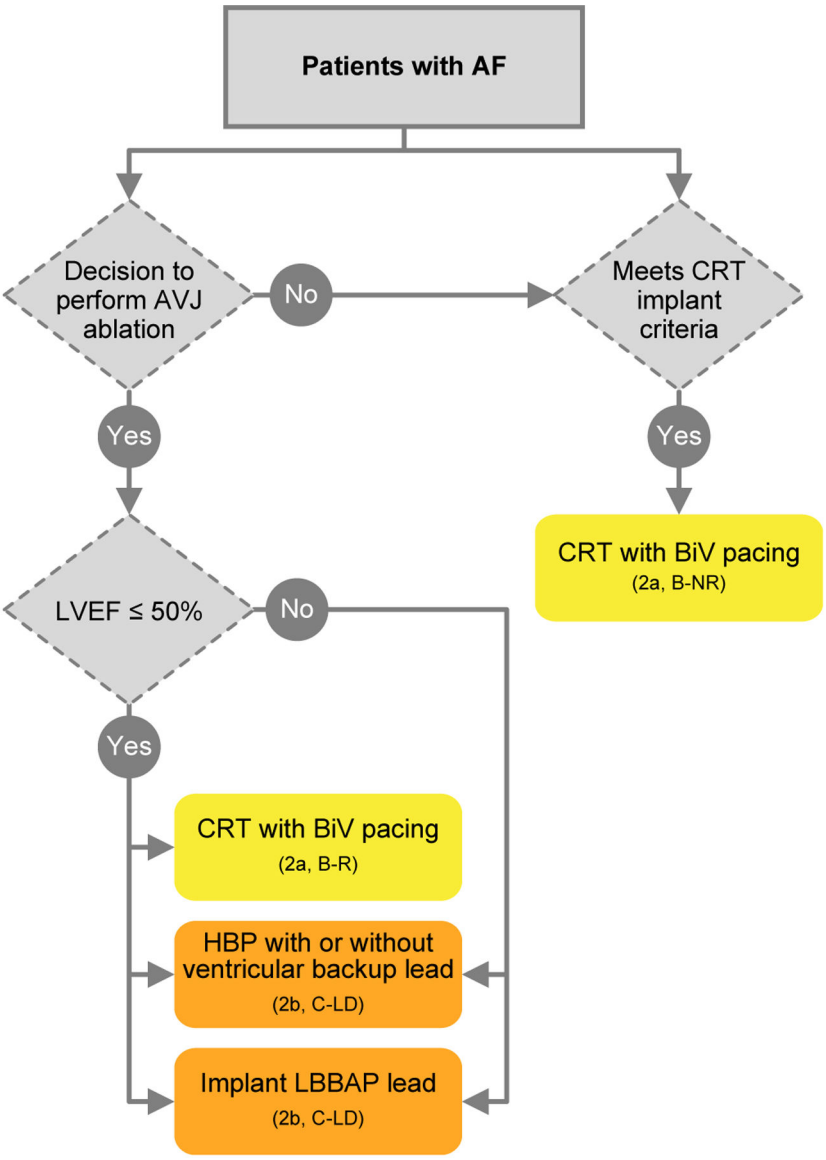

Figure 4.

Algorithm for cardiac physiologic pacing in patients with atrial fibrillation. Colors correspond to the class of recommendation in Table 1. AF = atrial fibrillation; AVJ = atrioventricular junction; BiV = biventricular; CRT = cardiac resynchronization therapy; HBP = His bundle pacing; LBBAP = left bundle branch area pacing; LVEF = left ventricular ejection fraction.

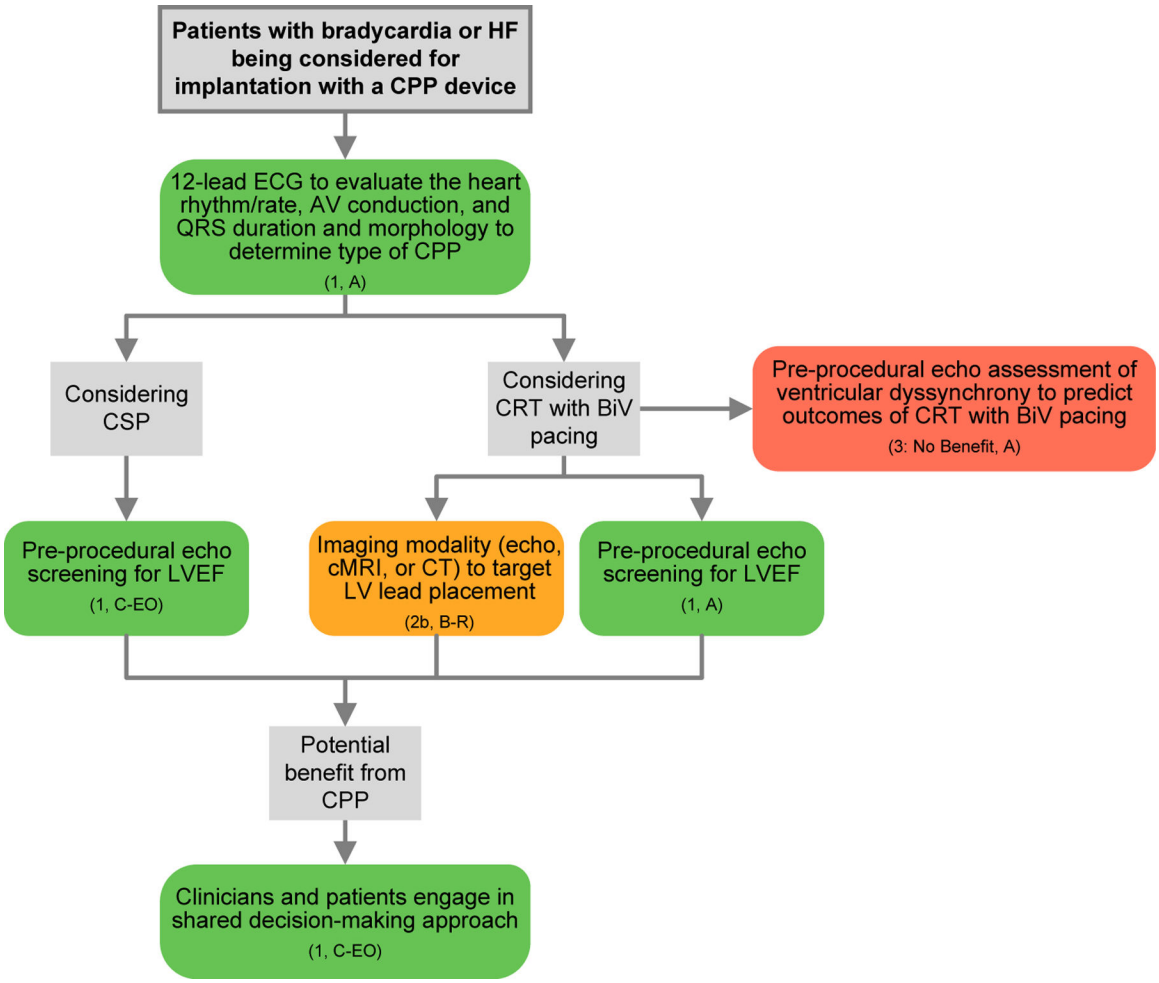

Figure 5.

Preprocedure evaluation and preparation. Colors correspond to the class of recommendation in Table 1. AV = atrioventricular; BiV = biventricular; cMRI = cardiac magnetic resonance imaging; CPP = cardiac physiologic pacing; CRT = cardiac resynchronization therapy; CSP = conduction system pacing; CT = computerized tomography; ECG = electrocardiogram; Echo = echocardiogram; HF = heart failure; LV = left ventricle/ventricular; LVEF = left ventricular ejection fraction.

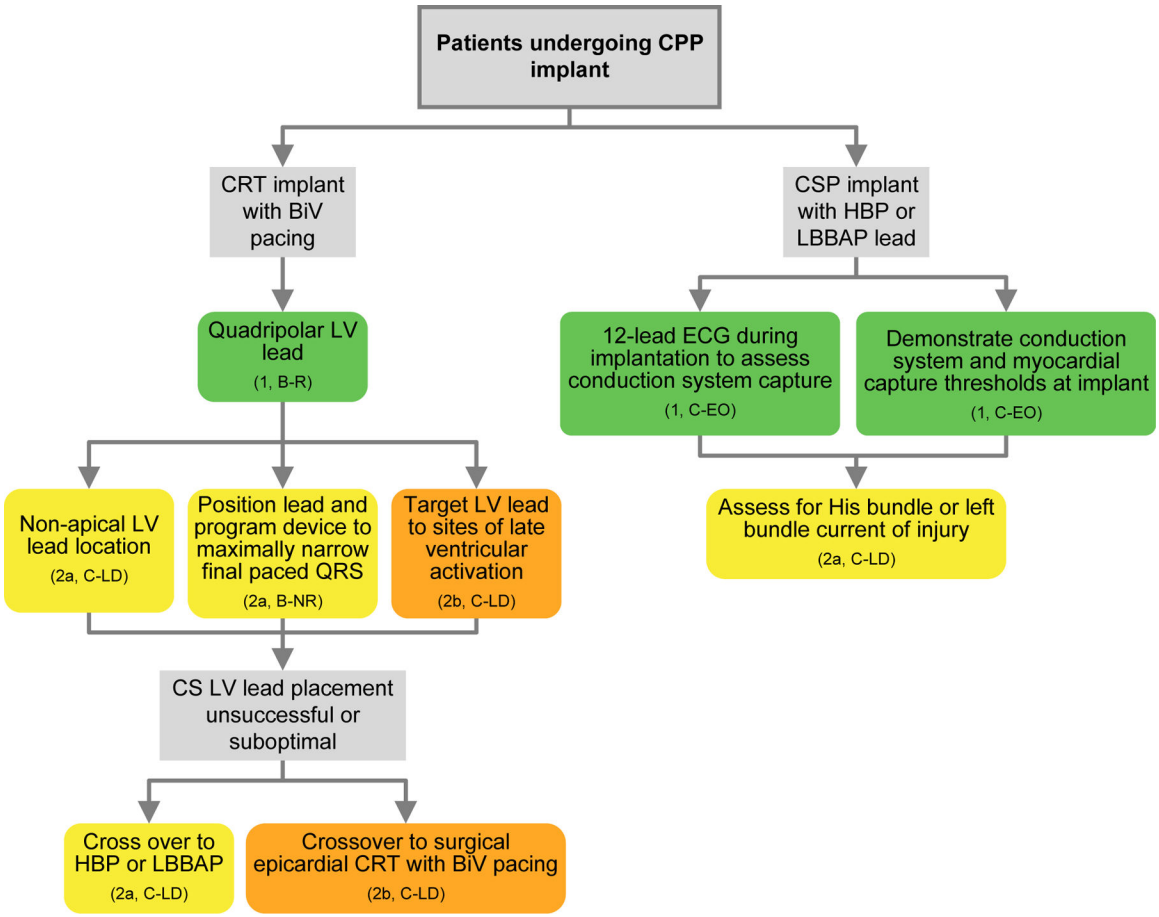

Figure 6.

Implant procedure. Colors correspond to the class of recommendation in Table 1. BiV = biventricular; CPP = cardiac physiologic pacing; CRT = cardiac resynchronization therapy; CS = coronary sinus; CSP = conduction system pacing; ECG = electrocardiogram; HBP = His bundle pacing; LBBAP = left bundle branch area pacing; LV = left ventricle/ventricular.

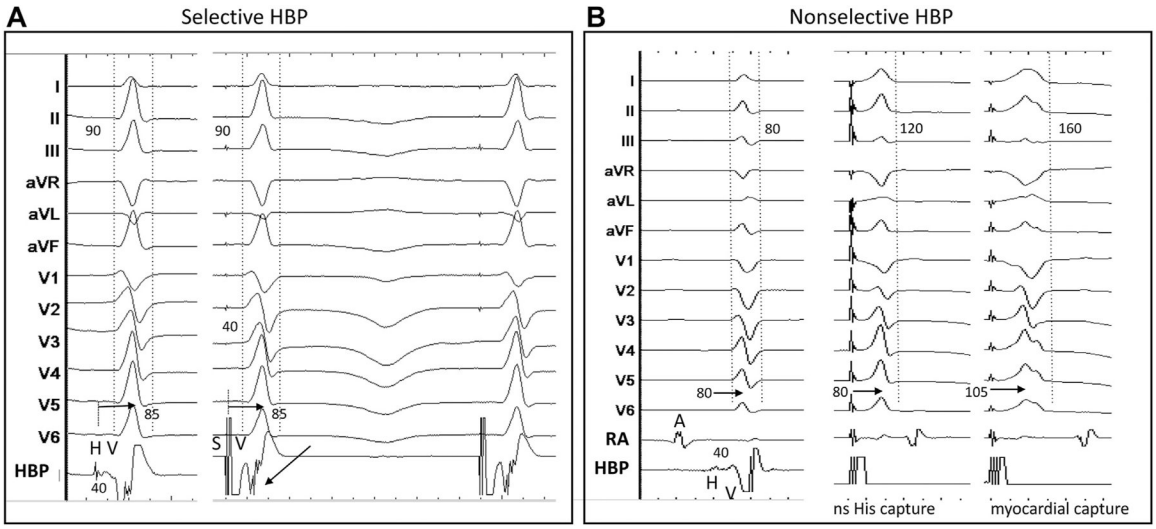

Figure 7.

Selective and nonselective His bundle pacing. **A:** During selective His bundle pacing (HBP), paced QRS duration and morphology are identical to baseline. His-V_6 R-wave peak time (RWPT) is the same as stimulus to V_6 RWPT. **B:** Transition from nonselective (ns) HBP to right ventricular (RV) myocardial pacing is shown. Pseudodelta waves are seen during ns His capture. During RV myocardial–only capture, slur/notch is seen in 1, L, and V_4–V_6; stimulus to V_6 RWPT is 105 ms; and stimulus to V_6 RWPT is 80 ms during ns HBP, which is the same as His-V_6 RWPT. Adapted with permission from Vijayaraman et al.[12] aVF = augmented vector foot; aVL = augmented vector left; aVR = augmented vector right; HBP = His bundle pacing; ns = nonselective.

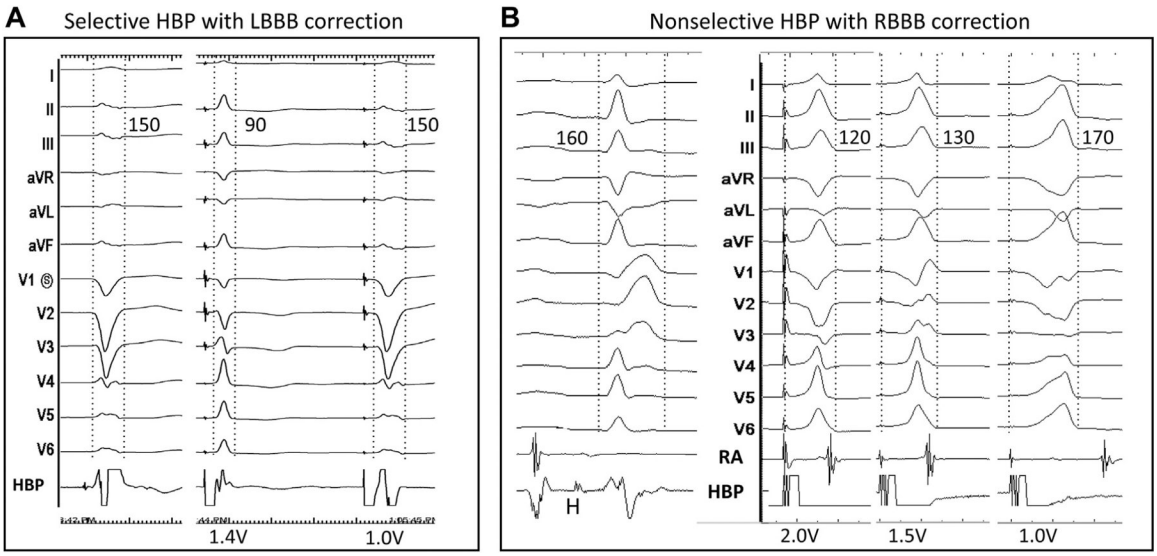

Figure 8.

Bundle branch block correction with His bundle pacing. **A:** Selective His bundle pacing (HBP) with left bundle branch block (LBBB) correction is shown. **B:** Nonselective HBP with right bundle branch block (RBBB) correction is shown. Note the output-dependent transition from nonselective correction of RBBB to nonselective HBP without RBBB correction to right ventricular myocardial–only capture. Adapted with permission from Vijayaraman et al.[12] aVF = augmented vector foot; aVL = augmented vector left; aVR = augmented vector right; HBP = His bundle pacing; LBBB = left bundle branch block; RBBB = right bundle branch block.

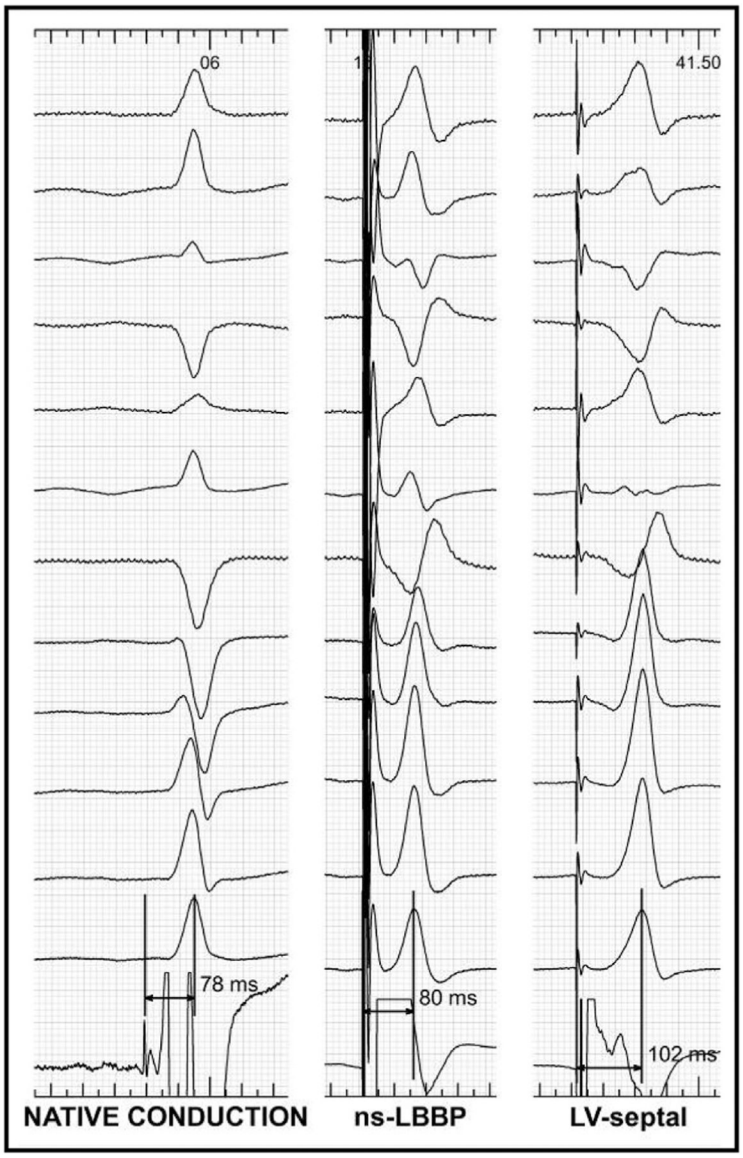

Figure 9.

Left bundle branch pacing (LBBP) in narrow QRS. R-wave peak time in lead V6 (V_6 RWPT) measured from the left bundle branch (LBB) potential at baseline is the same as stimulus to V_6 RWPT during LBB capture, but significantly longer with loss of LBB capture (left ventricular [LV] septal pacing). Adapted with permission from Jastrzebski et al.[311] ns = nonselective.

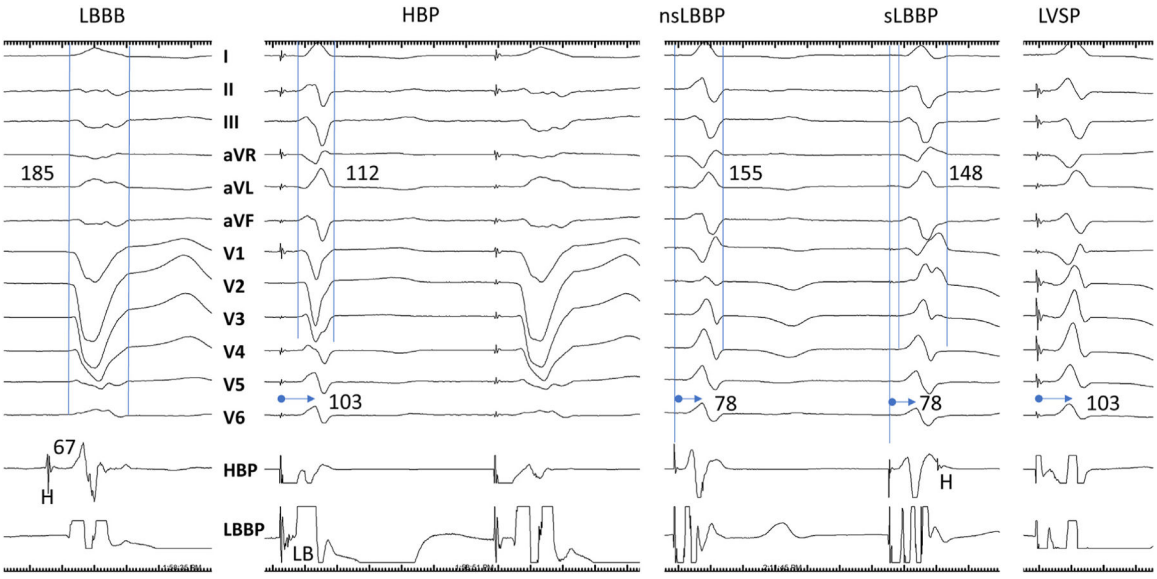

Figure 10.

Left bundle branch pacing in left bundle branch block. Left bundle branch pacing (LBBP) with left bundle branch (LBB) capture and LBB potential during corrective His bundle pacing (HBP) is shown. V_6 R-wave peak time measured from stimulus during LBB capture (selective [s] and nonselective [ns]) is 25 ms shorter than during corrective HBP and left ventricular septal-only pacing (LVSP). Reprinted with permission from Vijayaraman and Jastrzebski.[315] aVF = augmented vector foot; aVL = augmented vector left; aVR = augmented vector right; HBP = His bundle pacing; LBB = left bundle branch; LBBP = left bundle branch pacing; LVSP = left ventricular septal–only pacing; ns = nonselective; s = selective.

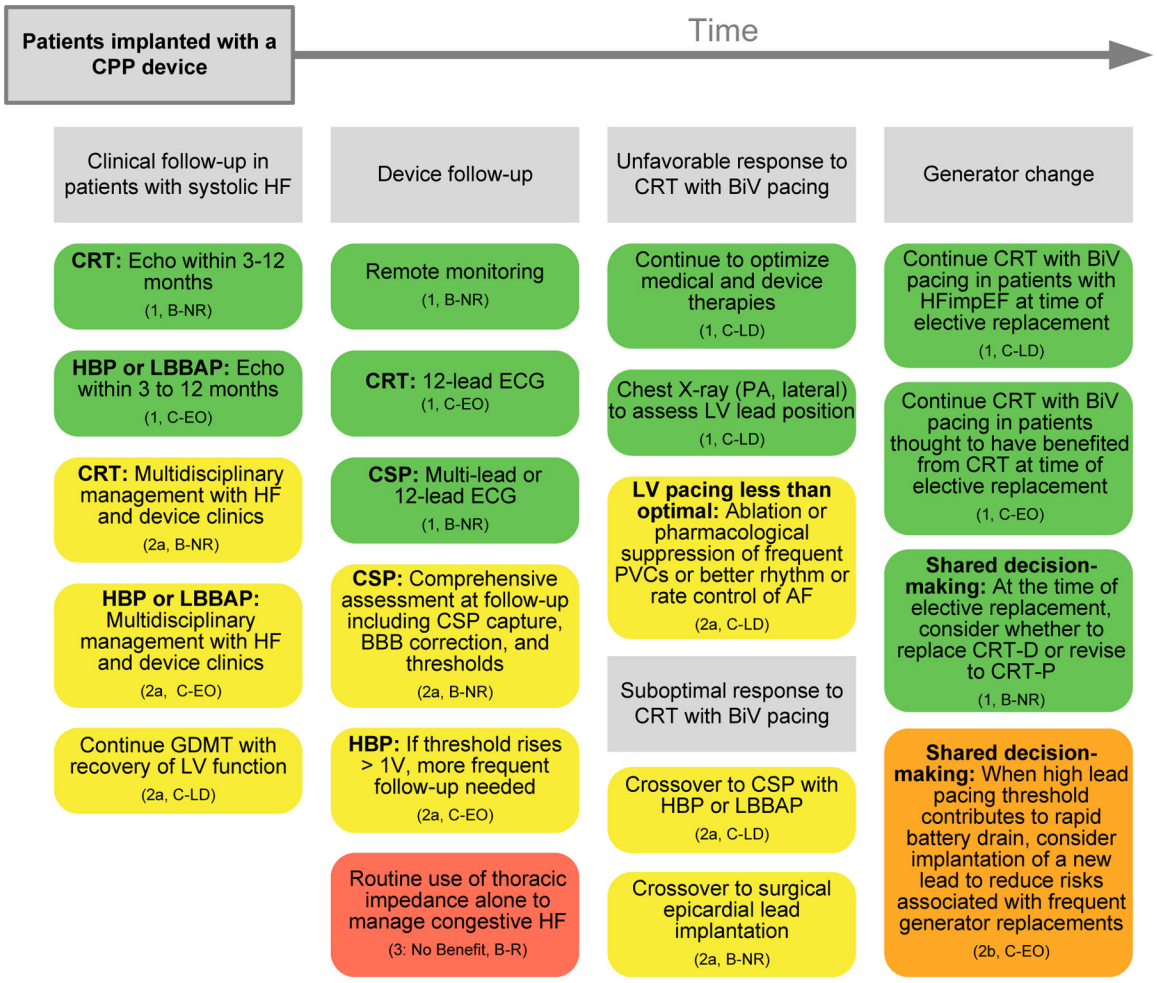

Figure 11.

Patient follow-up and management after implantation with a CPP device. Colors correspond to the class of recommendation in Table 1. AF = atrial fibrillation; BBB = bundle branch block; BiV = biventricular; CPP = cardiac physiologic pacing; CRT = cardiac resynchronization therapy; CRT-D = cardiac resynchronization therapy–defibrillator; CRT-P = cardiac resynchronization therapy–pacemaker; CSP = conduction system pacing; ECG = electrocardiogram; Echo = echocardiogram; GDMT = guideline-directed medical therapy; HBP = His bundle pacing; HF = heart failure; HFimpEF = heart failure with improved ejection fraction; LBBAP = left bundle branch area pacing; LV = left ventricle/ventricular; PA = posterior-anterior; PVC = premature ventricular contraction.

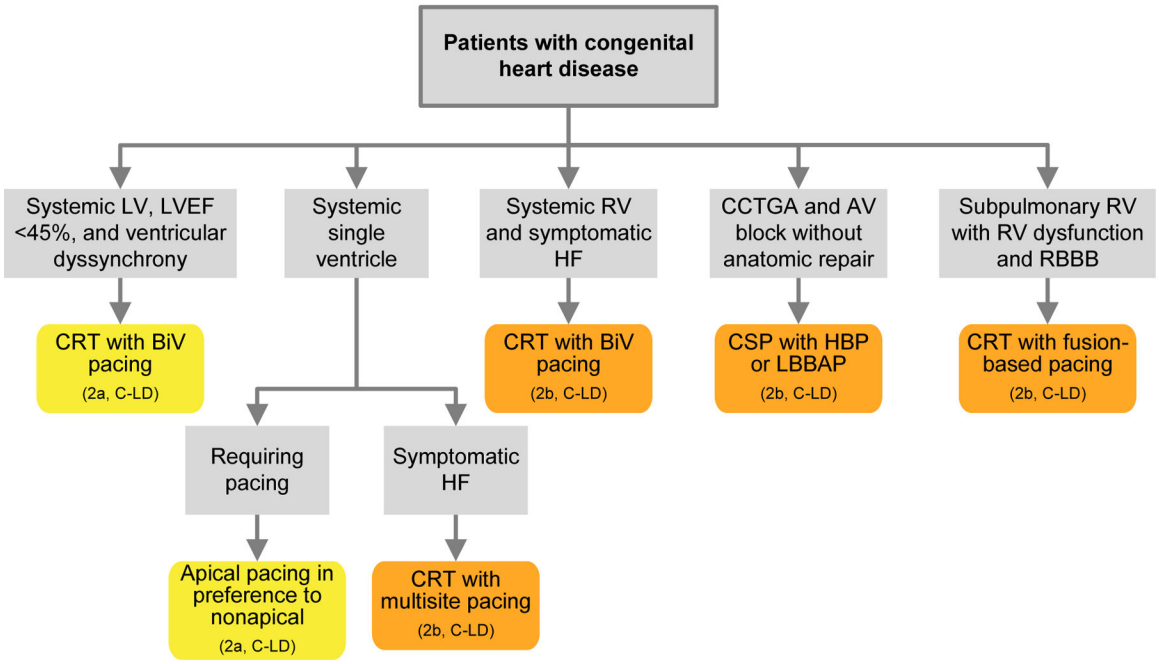

Figure 12.

Patients with congenital heart disease. Colors correspond to the class of recommendation in Table 1. AV = atrioventricular; BiV = biventricular; CCTGA = congenitally corrected transposition of the great arteries; CRT = cardiac resynchronization therapy; CSP = conduction system pacing; HBP = His bundle pacing; HF = heart failure; LBBAP = left bundle branch area pacing; LV = left ventricle/ventricular; LVEF = left ventricular ejection fraction; RBBB = right bundle branch block; RV = right ventricle/ventricular.

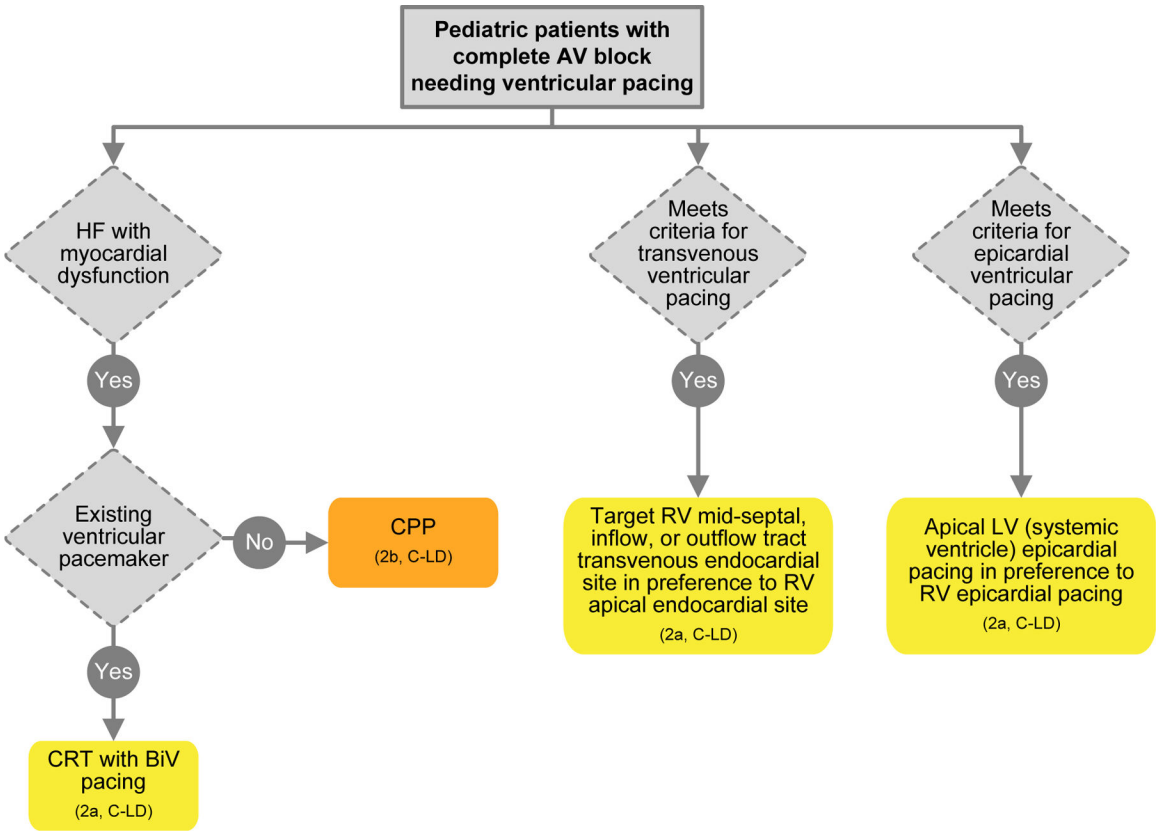

Figure 13.

Cardiac physiologic pacing in pediatric populations. Colors correspond to the class of recommendation in Table 1. AV = atrioventricular; BiV = biventricular; CPP = cardiac physiologic pacing; CRT = cardiac resynchronization therapy; HF = heart failure; LV = left ventricle/ventricular; RV = right ventricle/ventricular.

Table 1

ACC/AHA recommendation system: Applying class of recommendation and level of evidence to clinical strategies, interventions, treatments, and diagnostic testing in patient care (updated May 2019)*

Adapted with permission from the American College of Cardiology (ACC) and the American Heart Association (AHA).

CLASS (STRENGTH) OF RECOMMENDATION	
CLASS 1 (STRONG)	**Benefit >>> Risk**
Suggested phrases for writing recommendations: • Is recommended • Is indicated/useful/effective/beneficial • Should be performed/administered/other • Comparative-Effectiveness Phrases†: – Treatment/strategy A is recommended/indicated in preference to treatment B – Treatment A should be chosen over treatment B	
CLASS 2a (MODERATE)	**Benefit >> Risk**
Suggested phrases for writing recommendations: • Is reasonable • Can be useful/effective/beneficial • Comparative-Effectiveness Phrases†: – Treatment/strategy A is probably recommended/indicated in preference to treatment B – It is reasonable to choose treatment A over treatment B	
CLASS 2b (WEAK)	**Benefit ≥ Risk**
Suggested phrases for writing recommendations: • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	
CLASS 3: No Benefit (MODERATE) **(Generally, LOE A or B use only)**	**Benefit = Risk**
Suggested phrases for writing recommendations: • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	
CLASS 3: Harm (STRONG)	**Risk > Benefit**
Suggested phrases for writing recommendations: • Potentialy harmful • Causes harm • Associated with excess morbidity/mortality • Should not be performed/administered/other	

LEVEL (QUALITY) OF EVIDENCE‡	
LEVEL A	
• High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies	
LEVEL B-R	**(Randomized)**
• Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs	
LEVEL B-NR	**(Nonrandomized)**
• Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies	
LEVEL C-LD	**(Limited Data)**
• Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects	
LEVEL C-EO	**(Expert Opinion)**
• Consensus of expert opinion based on clinical experience	

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*The outcome or result of the intervention should be specified (an Improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

†For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

≠The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR Indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Table 2

Relevant clinical practice documents

Title	Year
2012 ACCF/AHA/HRS Focused Update Incorporated Into the ACCF/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities[6]	2013
2013 ACCF/AHA Guideline for the Management of Heart Failure[7]	2013
2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay[2]	2018
2021 ESC Guidelines on Cardiac Pacing and Cardiac Resynchronization Therapy[8]	2021

Table 3

Relevant systematic reviews

Title	Year
Agency for Healthcare Research and Quality: Use of Cardiac Resynchronization Therapy[9]	2019
Impact of Physiologic Pacing Versus Right Ventricular Pacing Among Patients With Left Ventricular Ejection Fraction Greater Than 35%[10]	2019

Table 4

Definitions

Term	Definition
Left bundle branch block (LBBB)	For the purposes of this guideline, LBBB is defined by the 2009 AHA/ACCF/HRS Scientific Statement on recommendations for the standardization and interpretation of the electrocardiogram[11] as QRS duration ≥120 ms and a broad notched or slurred R-wave in leads I, aVL, V_5, and V_6.
Cardiac physiologic pacing (CPP)	CPP is defined as any form of cardiac pacing intended to restore or preserve ventricular synchrony. CPP can be achieved by engaging the intrinsic conduction system via CSP (eg, HBP or LBBAP) or CRT.
Conduction system pacing (CSP)	CSP involves recruitment of the intrinsic conduction system by either HBP or LBBAP.
His bundle pacing (HBP)	HBP involves the direct stimulation of the His bundle to engage the native conduction system. Based on location and pacing outputs, HBP may be selective (isolated recruitment of the His bundle) or nonselective (recruitment of both the local septal myocardium and the His bundle).[12]
Left bundle branch area pacing (LBBAP)	LBBAP is ventricular pacing that is intended to engage all or any part of the left bundle branch (LBB) fascicular system. Similar to HBP, various responses can be seen based on location and pacing outputs. These include selective LBBP (direct stimulation and isolated recruitment of the LBB fibers), nonselective LBBAP (direct stimulation and recruitment of both the local myocardium and the LBB fibers), or deep septal pacing (no direct recruitment of the LBB fibers).
Cardiac resynchronization therapy (CRT)	CRT aims to restore or preserve ventricular synchrony using left ventricular (LV) stimulation at appropriately timed right ventricular (RV) sensing or stimulation. CRT most commonly refers to BiV pacing, in which a pacing lead is implanted in the RV and another on the epicardial surface of the LV via an epicardial vein. Alternatively, the LV lead may be implanted endocardially or surgically on the epicardium. LV pacing alone in some situations may also deliver CRT. CSP for patients with dyssynchrony may also be considered a form of CRT, but for the purposes of this guideline, CRT refers to use of BiV or LV pacing. These pacing locations refer to standard anatomy but may differ in certain forms of congenital heart disease.
Biventricular (BiV) pacing	BiV pacing is the most common method used to achieve CRT. It most commonly involves the use of 2 ventricular leads, 1 in the RV (apex or septum) and 1 to pace the LV via the coronary sinus or sometimes via direct placement on the epi cardium or endocardium. The LV lead is usually implanted epicardially in the coronary veins, ideally targeting an area of latest activation, which is most often the lateral or posterolateral wall. Alternatively, the LV lead may be implanted endocardially or surgically on the LV epicardium.
Substantial right ventricular pacing (RVP)	Chronic RVP may result in pacing-induced cardiomyopathy in a subset of patients. Substantial RVP may be defined as RVP that is documented to oris anticipated to exceed 40%. However, some observationalstudies have indicated that RVP exceeding 20% can also have detrimental consequences.[13–15] It is acknowledged that the burden of RVP may not be accurately predictable prior to implantation and that these data are based on percentages that have been reported in patients with implanted devices. For the purposes of this document, substantial RVP refers to anticipated or actual pacing ≥ 20%−40% and less than substantial refers to anticipated or actual pacing < 20%−40%. Substantial RVP may occur due to second- or third-degree atrioventricular block or to first-degree atrioventricular block with very prolonged PR intervals.
Response to CRT/CPP	CRT “response” has been variously defined in differentstudies, without an actualconsensus on what constitutes response. Response to CRT may be defined using multiple criteria (see Table 5) in terms of improvement of clinical conditions. The terms CRT “stabilizer” or “nonprogressor” have evolved to include patients who may not derive significant reverse remodeling from CRT but seem to realize a blunting of the natural downhill progression of HF. The terms “favorable responder,” which includes the CRT stabilizer or nonprogressor, and “unfavorable responder” have been proposed to account for this. No specific response criteria have yet been postulated for other types of CPP. However, it is reasonable to apply the criteria above for all forms of CPP.

Table 5

CRT response criteria

Response	Criteria	
Clinical response	**1**	Reduction in mortality
	2	Reduction in HF hospitalization
	3	Improvement in NYHA class
	4	Improvement in quality of life, symptoms, or clinical composite scores
	5	Increase in peak VO_2 (eg, >10%)
	6	Improvement in 6-minute walk distance
	7	Reduction in HF medications, such as diuretic therapy (note: continuation of GDMT is advised)
Echocardiographic response	**1**	Improvement or stability in LVEF (eg, ≥ 5% absolute increase or absence of worsening)
	2	Reduction in LV size (eg, reduction in LV systolic or diastolic dimensions or volume indices)
	3	Increase in LV stroke volume
	4	Reduction in mitral regurgitation

CRT = cardiac resynchronization therapy; GDMT = guideline-directed medical therapy; HF = heart failure; LV = left ventricle/ventricular; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; VO_2 = oxygen uptake.

Table 6

Criteria for His bundle pacing

		His-Purkinje conduction disease	
Baseline	**Normal QRS duration**	**With correction**	**Without correction**
Selective HBP	• S-QRS = H-QRS with isoelectric interval • Discrete local ventricular electrogram in HBP lead with S-V = H-V • Paced QRS = native QRS • Single capture threshold (His bundle)	• S-QRS ≤ H-QRS with isoelectric interval • Discrete local ventricular electrogram in HBP lead • Paced QRS < native QRS • 2 distinct capture thresholds (HBP with BBB correction, HBP without BBB correction)	• S-QRS ≤ or > H-QRS with isoelectric interval • Discrete local ventricular electrogramin HBP lead • Paced QRS = native QRS • Single capture threshold (HBP with • BBB)
Nonselective HBP	• S-QRS < H-QRS (usually 0, S-QRS$_{end}$ = H-QRS$_{end}$) with or without isoelectric interval (pseudodelta wave +/−) • Direct capture of local ventricular electrogram in HBP lead by stimulus artifact (local myocardial capture) • Paced QRS > native QRS with normalization of precordial and limb lead axes with respect to rapid dV/dt components of the QRS • 2 distinct capture thresholds (His bundle capture, RV capture) • No QRS slur/notch in leads I, V_1, or V_4-V_6, and V_6 R-wave peak time ≤100 ms • Change in V_6 RWPT >12 ms between stimulus and His to V_6 RWPT confirms lack of His capture (99.1% sensitivity and 100% specificity)	• S-QRS < H-QRS (usually 0, S-QRS$_{end}$ < H-QRS$_{end}$) with or without isoelectric interval (pseudodelta wave +/−) • Direct capture of local ventricular electrogram in HBP lead by stimulus artifact • Paced QRS ≤ native QRS • 3 distinct capture thresholds (HBP with BBB correction, HBP without BBB correction, RV capture)	• S-QRS < H-QRS (usually 0) with or without isoelectric interval (pseudodelta wave +/−) • Direct capture of local ventricular electrogram in HBP lead by stimulus artifact • Paced QRS > native QRS • 2 distinct capture thresholds (HBP with BBB, RV capture)

Adapted with permission from Vijayaraman et al.[12] BBB = bundle branch block; HBP = His bundle pacing; H-QRS = His-QRS interval; RV = right ventricle/ventricular; S-QRS = stimulus to QRS onset interval; V_6 RWPT = R-wave peak time in lead V_6.

Table 7

Criteria for left bundle branch area pacing *

Pacing type	Criteria	
Left ventricular septal pacing	**1**	Deep septal placement of the pacing lead (confirmed by fulcrum sign, contrast, echocardiogram, or CT) and
	2	Right bundle branch conduction delay pattern in lead V_1 (rare exceptions)
Left bundle branch area pacing	**1**	Evidence for LV septal pacing in addition to any one of the following LBB capture criteria: **LBB capture criteria** • Nonselective to selective LBBP or nonselective to septal capture transition during threshold testing • Abrupt shortening of RWPT † or LVAT in V_6≥10 ms at high output during deep septal position with subsequent short and constant LVAT at low output with further advancement of the lead • V_6 RWPT <74 ms in non-LBBB and <80 ms in LBBB • V_6-V_1 interpeak interval >44 ms • Physiology-based criteria **a.** QRS onset to RWPT ≤ native RWPT (+10 ms) **b.** Stimulus to RWPT ≤ LBB potential to V**6** RWPT (+10 ms) **c.** Stimulus to V_6 RWPT + 10 ms < (intrinsicoid deflection time - transseptal conduction time) in LBBB • Programmed deep septal stimulation demonstrating differential capture • Change in V_6 RWPT between (corrective) HBP and LBBP >8 ms in LBBB • Demonstration of LBB potential with injury current • Demonstration of stimulus to retrograde His <35 ms or anterograde left conduction system potential preceding ventricular electrogram during LBBP

* Left bundle branch area pacing includes both LV septal pacing and left bundle branch pacing.

† RWPT and LVAT here should be assessed starting from the stimulation artifact rather than from the inferred QRS onset. CT = computerized tomography; HBP = His bundle pacing; LBB = left bundle branch; LBBB = left bundle branch block; LBBP = left bundle branch pacing; LBBAP = left bundle branch block area pacing; LV = left ventricle/ventricular; LVAT = left ventricular activation time; RWPT = R-wave peak time; V_6 RWPT = R-wave peak time in lead V_6.

Table 8

Reasons for abandonment and/or crossover to alternative CPP approach during implantation

CPP type	Anatomical/technical considerations	Function considerations	ECG considerations	Major complications
CRT with BiV pacing	• Venous inaccessibility (subclavian, innominate vein, or SVC occlusion) • CS inaccessibility (occlusion, dissection, perforation, Thebesian valve) • Coronary vein inaccessibility (small, angulated, or tortuous vein branches) • Suboptimal vein location (nonlateral vein, anterior interventricular vein) • Persistent SVC • Poor lead stability, prone to dislodgment	• Capture threshold >5 V/1 ms in all available pacing configurations • Diaphragmatic stimulation in all available pacing configurations	• The onset of QRS to LV time <90 ms • Lead I: non-QS or QR • Intrinsic QRS duration <120 ms or narrower than optimized pace QRS duration	• Pericardial effusion/ Tamponade • CS or vascular dissection • Cardiac arrest • Sustained ventricular tachyarrhythmia • Others (PE, stroke, respiratory failure, etc)
HBP	• Unable to identify HB location • Lead instability	• Capture threshold >5 V/1 ms • R sensing <2mV • Atrial oversensing • Potential need for a backup lead	• For baseline wide QRS, unable to have paced QRS duration ≤130 ms or QRS narrowing >20% • Unable to achieve selective or nonselective His capture	• Same as in CRT with BiV pacing • Lead dislodgment • Reduced battery longevity due to elevated pacing capture thresholds • Late rise in thresholds
LBBAP	• Unable to penetrate the septum to reach LBB (LV subendocardium) • Lead instability	• Risk of septal perforation • Inability to correct LBB block	• Unable to achieve the RBBB configuration or to have paced QRS duration ≤130 ms • Unable to achieve LVAT <74–80 ms	• Same as in CRT with BiV pacing • Risk of late septal perforation

BiV = biventricular; CPP = cardiac physiologic pacing; CRT = cardiac resynchronization therapy; CS = coronary sinus; ECG = electrocardiogram; HB = His bundle; HBP = His bundle pacing; LBB = left bundle branch; LBBAP = left bundle branch area pacing; LV = left ventricle/ventricular; LVAT = left ventricular activation time; PE = pulmonary embolism; RBBB = right bundle branch block; SVC = superior vena cava.

Table 9

Pacemaker interrogation and programming approach for CPP

	HBP	LBBAP	CRT
Capture thresholds	Determine His bundle capture relative to RV capture; program output to ensure His bundle capture (at least 1 V above the threshold)	Determine LBB (LV septal) capture and anodal capture	Determine LV (CS lead)-only capture and anodal capture
Capture assessment algorithms	Avoid, unless known that His bundle and RV capture thresholds are similar	Capture assessment algorithms can be utilized successfully	Capture assessment algorithms can be utilized successfully; LV-only pacing may be preferred in some cases
AV delays	Program 30–50 ms shorter than conventional parameters *	Program 20–30 ms shorter than conventional parameters *	Program 10–20 ms shorter than conventional parameters *
Atrial oversensing	Atrial oversensing can occur with proximal lead placement and may need appropriate programming to also avoid ventricular undersensing		
Ventricular unipolar sensing	Avoid if pacing dependent		

* A shorter AV delay than conventional is needed to take account for the time delay from pacing output to QRS onset with conduction system pacing. AV = atrioventricular; CPP = cardiac physiologic pacing; CRT = cardiac resynchronization therapy; CS = coronary sinus; HBP = His bundle pacing; LBB = left bundle branch; LBBAP = left bundle branch area pacing; LV = left ventricle/ventricular; RV = right ventricle/ventricular.

Table 10

Identified gaps and needs for future studies

Knowledge gap	Future needs and directions
Long-term risks and consequences of LBBAP and HBP	Longer-term follow-up of CSP including device-related complications, lead characteristics, lead survival, and extraction outcomes.
Clinical outcome differences between LV septal and LBB pacing	Clinical outcome studies in patients stratified by LV septal or LBB pacing. This includes patients requiring substantial pacing with or without HF.
Normal LVEF anticipated to have substantial RVP	RCT of CSP vs RVP in patients with normal LV function but expected to require substantial RVP.
Infrequent ventricular pacing	RCTs of CSP (LBBAP or HBP) vs RVP in patients undergoing pacemaker implants but with minimal RVP need.
CRT in patients with HF, LBBB, and QRS duration <150 ms	Determination of thresholds for stature and LV size that predict improved outcomes after CRT.
CSP for patients with HF and QRS duration >120 ms or PICM	RCTs of CSP vs CRT with BiV in CRT-indicated patients.
Combination CRT with LV lead + HBP or LBBAP	RCTs of CRT with LV lead vs CRT + HBP or CRT + LBBAP in patients with CRT indications.
Impact of CSP on the prevention of AF	Future randomized studies to evaluate the risk of new-onset AF and progression of AF in patients with CSP.
Standardized criteria for optimal lead placement	Standardization of definitions for failure or success of lead placement for CRT with BiV pacing, HBP, or LBBAP.
Prediction of PICM and HF with LBBB	Identification of factors, imaging, or biomarker features predictive of development of electrical dyssynchrony-induced cardiomyopathy or PICM. This may include novel echocardiography, ECG mapping, vectorcardiography, or cardiac MRI techniques.
Prediction of response to CRT and CSP	Novel echocardiography techniques, ECG mapping, advanced ECG analytics, and vectorcardiography, potentially with the use of artificial intelligence/machine learning methodology, are future directions that may enhance prediction of response to CRT or CSP, aid in patient selection, and guidance of optimization of programming.
Data on follow-up optimization and troubleshooting of CRT and CSP	Studies, tools, and algorithms to achieve optimal CRT and CSP in follow-up clinics.
Replacement or upgrade considerations for CPP	Prospective studies to define outcomes after replacement or upgrade of devices using specified criteria.
Role of CRT in LVAD patients	Randomized studies of CRT inactivation or continued use in patients with LVADs to determine effects on ventricular arrhythmias, ICD shocks, or other clinical outcomes.
CPP for CHD and pediatric populations	Long-term prospective registries in CHD and pediatric patients who receive CPP.
CSP-specific leads, devices, and adapters	Manufacturer development of CSP-specific devices and leads, including devices with features tailored to CSP leads, adaptors to be used with quadripolar lead systems, and CRT-P devices capable of accepting RV coil leads for downgrades.
Role of endocardial LV pacing	Continued development of endocardial LV pacing technologies, including minimization of thromboembolic risks and randomized trials comparing LV endocardial pacing to BiV CRT or CSP pacing.
Cost-effectiveness analyses for CPP	Inclusion of cost-effectiveness analyses in prospective or randomized trials.
Shared decision-making decision aids for CRT and CSP	Development and validation of decision aids for CRT and CSP for shared decision-making discussions with patients.
MRI safety	Safety studies of commercially available leads used for CSP.

AF = atrial fibrillation; BiV = biventricular; CHD = congenital heart disease; CPP = cardiac physiologic pacing; CRT = cardiac resynchronization therapy; CRT-P = cardiac resynchronization therapy–pacemaker; CSP = conduction system pacing; ECG = electrocardiographic; HBP = His bundle pacing; HF = heart failure; ICD = implantable cardioverter-defibrillator; LBB = left bundle branch; LBBAP = left bundle branch area pacing; LBBB = left bundle branch block; LV = left ventricle/ventricular; LVAD = left ventricular assist device; LVEF = left ventricular ejection fraction; MRI = magnetic resonance imaging; PICM = pacing-induced cardiomyopathy; RCT = randomized controlled trial; RV = right ventricle/ventricular; RVP = right ventricular pacing.