PRACTICE GUIDELINE

2012 ACCF/AHA/HRS Focused Update of the 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American Association for Thoracic Surgery, Heart Failure Society of America, and Society of Thoracic Surgeons

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Preamble

Keeping pace with the stream of new data and evolving evidence on which guideline recommendations are based is an ongoing challenge to timely development of clinical practice guidelines. In an effort to respond promptly to new evidence, the American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) Task Force on Practice Guidelines (Task Force) has created a “focused update” process to revise the existing guideline recommendations that are affected by evolving data or opinion. New evidence is reviewed in an ongoing fashion to more efficiently respond to important science and treatment trends that could have a major impact on patient outcomes and quality of care. Evidence is reviewed at least twice a year, and updates are initiated on an as-needed basis and completed as quickly as possible while maintaining the rigorous methodology that the ACCF and AHA have developed during their partnership of >20 years.

These focused updates are prompted following a thorough review of late-breaking clinical trials presented at national and international meetings, in addition to other new published data deemed to have an impact on patient care (Section 1.1, “Methodology and Evidence Review”). Through a broad-based vetting process, the studies included are identified as being important to the relevant patient population. The focused update is not intended to be based on a complete literature review from the date of the previous guideline publication but rather to include pivotal new evidence that may affect changes to current recommendations.

Specific criteria or considerations for inclusion of new data include the following:

- publication in a peer-reviewed journal;
- large, randomized, placebo-controlled trial(s);
- nonrandomized data deemed important on the basis of results affecting current safety and efficacy assumptions, including observational studies and meta-analyses;
- strength/weakness of research methodology and findings;
- likelihood of additional studies influencing current findings;
- impact on current and/or likelihood of need to develop new performance measure(s);
- request(s) and requirement(s) for review and update from the practice community, key stakeholders, and other sources free of industry relationships or other potential bias;
- number of previous trials showing consistent results; and
- need for previous trials showing consistent results to current recommendations.

In analyzing the data and developing recommendations and supporting text, the writing group uses evidence-based methodologies developed by the Task Force (1). The Class of Recommendation (COR) is an estimate of the size of the treatment effect, with consideration given to risks versus benefits, as well as evidence and/or agreement that a given treatment or procedure is or is not useful/effective and in some situations may cause harm. The Level of Evidence (LOE) is an estimate of the certainty or precision of the treatment effect. The writing group reviews and ranks evidence supporting each recommendation, with the weight of evidence ranked as LOE A, B, or C, according to specific definitions that are included in Table 1. Studies are identified as observational, retrospective, prospective, or randomized, as appropriate. For certain conditions for which inadequate data are available, recommendations are based on expert consensus and clinical experience and are ranked as LOE C. When recommendations at LOE C are supported by historical clinical data, appropriate references (including clinical reviews) are cited if available. For issues for which sparse data are available, a survey of current practice among

KEYWORDS ACC Practice Guideline; arrhythmias; cardiac resynchronization therapy; focused update; heart failure; pacemaker (Heart Rhythm 2012;9:1737–1753)
the clinicians on the writing group is the basis for LOE C recommendations, and no references are cited. The schema for COR and LOE is summarized in Table 1, which also provides suggested phrases for writing recommendations within each COR. A new addition to this methodology is separation of the Class III recommendations to delineate whether the recommendation is determined to be of “no benefit” or is associated with “harm” to the patient. In addition, in view of the increasing number of comparative effectiveness studies, comparator verbs and suggested phrases for writing recommendations for the comparative effectiveness of one treatment or strategy versus another have been added for COR I and IIa, LOE A or B only.

In view of the advances in medical therapy across the spectrum of cardiovascular diseases, the Task Force has designated the term guideline-directed medical therapy (GDMT) to represent optimal medical therapy as defined by ACCF/AHA guideline (primarily Class I)–recommended therapies. This new term, GDMT, will be used herein and throughout all future guidelines.

Because the ACCF/AHA practice guidelines address patient populations (and healthcare providers) residing in North America, drugs that are not currently available in North America are discussed in the text without a specific COR. For studies performed in large numbers of subjects outside North America, each writing group reviews the

<table>
<thead>
<tr>
<th>CLASS I</th>
<th>Benefit &gt;&gt; Risk</th>
<th>Procedure/Treatment SHOULD be performed/administered</th>
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</thead>
<tbody>
<tr>
<td>CLASS IIa</td>
<td>Benefit &gt;&gt; Risk</td>
<td>Additional studies with focused objectives needed</td>
</tr>
<tr>
<td>IT IS REASONABLE to perform procedure/administer treatment</td>
<td></td>
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<tr>
<td>CLASS IIb</td>
<td>Benefit ≥ Risk</td>
<td>Additional studies with broad objectives needed, additional registry data would be helpful</td>
</tr>
<tr>
<td>Procedure/Treatment MAY BE CONSIDERED</td>
<td></td>
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<tr>
<td>CLASS III</td>
<td>No Benefit or Class III Harm</td>
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<tr>
<td>Procedure/Test</td>
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<tr>
<td>Treatment</td>
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<tr>
<td>COR IIi: No benefit</td>
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<tr>
<td>COR IIi: Not Helpful</td>
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<td>COR IIi: No Prove Benefit</td>
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<td>COR IIi: Harm</td>
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<td>COR IIi: Excessive Cost w/o Benefit or Harmful</td>
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<td>COR IIi: Harmful to Patients</td>
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### Table 1: Applying Classification of Recommendations and Level of Evidence

**SIZE OF TREATMENT EFFECT**

**LEVEL A**
- Multiple populations evaluated
- Data derived from multiple randomized clinical trials or meta-analyses
  - Recommendation that procedure or treatment is useful/effective
  - Sufficient evidence from multiple randomized trials or meta-analyses

**LEVEL B**
- Limited populations evaluated
- Data derived from a single randomized trial or nonrandomized studies
  - Recommendation that procedure or treatment is useful/effective
  - Evidence from single randomized trial or nonrandomized studies

**LEVEL C**
- Very limited populations evaluated
- Only consensus opinion of experts, case studies, or standard of care
  - Recommendation that procedure or treatment is useful/effective
  - Suggested phrases for writing recommendations

**Comparative effectiveness phrases**
- Treatment/strategy A is recommended/indicated in preference to treatment B
- Treatment/strategy A is probably recommended/indicated in preference to treatment B
- It is reasonable to choose treatment A over treatment B

**Suggested phrases for writing recommendations**
- Should is recommended
- Is indicated
- Is useful/effective/beneficial
- May/might be considered
- May/might be reasonable
- Usualness/effectiveness is unknown/unclear/uncertain or not well established
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

**COR IIi:**
- No Benefit
- Is not indicated
- Not recommended
- Should not be performed/administered/other
- Is not useful/beneficial/effective

**COR IIi:**
- Harm
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

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

*Data available from clinical trials or registries about the usefulness/effectiveness in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.
potential impact of different practice patterns and patient populations on the treatment effect and relevance to the ACCF/AHA target population to determine whether the findings should inform a specific recommendation.

The ACCF/AHA practice guidelines are intended to assist healthcare providers in clinical decision making by describing a range of generally acceptable approaches to the diagnosis, management, and prevention of specific diseases or conditions. The guidelines attempt to define practices that meet the needs of most patients in most circumstances. The ultimate judgment about care of a particular patient must be made by the healthcare provider and patient in light of all the circumstances presented by that patient. As a result, situations may arise in which deviations from these guidelines may be appropriate. Clinical decision making should consider the quality and availability of expertise in the area where care is provided. When these guidelines are used as the basis for regulatory or payer decisions, the goal should be improvement in quality of care. The Task Force recognizes that situations arise in which additional data are needed to inform patient care more effectively; these areas will be identified within each respective guideline when appropriate.

Prescribed courses of treatment in accordance with these recommendations are effective only if they are followed. Because lack of patient understanding and adherence may adversely affect outcomes, physicians and other healthcare providers should make every effort to engage the patient’s active participation in prescribed medical regimens and lifestyles. In addition, patients should be informed of the risks, benefits, and alternatives to a particular treatment and should be involved in shared decision making whenever feasible, particularly for COR IIa and IIb, for which the benefit-to-risk ratio may be lower.

The Task Force makes every effort to avoid actual, potential, or perceived conflicts of interest that may arise as a result of industry relationships or personal interests among the members of the writing group. All writing group members and peer reviewers of the guideline are required to disclose all current healthcare-related relationships, including those existing 12 months before initiation of the writing effort. In December 2009, the ACCF and AHA implemented a new policy for relationships with industry and other entities (RWI) that requires the writing group chair plus a minimum of 50% of the writing group to have no relevant RWI (Appendix 1 includes the ACCF/AHA definition of relevance). These statements are reviewed by the Task Force and all members during each conference call and/or meeting of the writing group and are updated as changes occur. All guideline recommendations require a confident vote by the writing group and must be approved by a consensus of the voting members. Members are not permitted to draft or vote on any text or recommendations pertaining to their RWI. Members who recused themselves from voting are indicated in the list of writing group members, and specific section recusals are noted in Appendix 1. Authors’ and peer reviewers’ RWI pertinent to this guideline are disclosed in Appendices 1 and 2, respectively. Additionally, to ensure complete transparency, writing group members’ comprehensive disclosure information—including RWI not pertinent to this document—is available as an online supplement. Comprehensive disclosure information for the Task Force is also available online at www.cardiosource.org/ACCF/About-ACC/Leadership/Guidelines-and-Documents-Task-Forces.aspx. The work of the writing group is supported exclusively by the ACCF, AHA, and the Heart Rhythm Society (HRS) without commercial support. Writing group members volunteered their time for this activity.

In an effort to maintain relevance at the point of care for practicing physicians, the Task Force continues to oversee an ongoing process improvement initiative. As a result, in response to pilot projects, several changes to these guidelines will be apparent, including limited narrative text, a focus on summary and evidence tables (with references linked to abstracts in PubMed), and more liberal use of summary recommendation tables (with references that support LOE) to serve as a quick reference.

In April 2011, the Institute of Medicine released 2 reports: Finding What Works in Health Care: Standards for Systematic Reviews and Clinical Practice Guidelines We Can Trust (2,3). It is noteworthy that the ACCF/AHA practice guidelines were cited as being compliant with many of the standards that were proposed. A thorough review of these reports and our current methodology is under way, with further enhancements anticipated.

The recommendations in this focused update are considered current until they are superseded in another focused update or the full-text guideline is revised. Guidelines are official policy of both the ACCF and AHA.

Jeffrey L. Anderson, MD, FACC, FAHA
Chair, ACCF/AHA Task Force on Practice Guidelines

1. Introduction

1.1. Methodology and evidence review

Late-breaking clinical trials presented at the annual scientific meetings of the ACC, AHA, HRS, and European Society of Cardiology (2008 through 2010), as well as other selected data reported through January 2012, were reviewed by the guideline writing group along with the Task Force and other experts to identify trials and other key data that might affect guideline recommendations. On the basis of the criteria and considerations noted previously (Preamble), recently published trial data and other clinical information were considered important enough to prompt a focused update of the “ACCF/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities” (4).

To provide clinicians with a comprehensive set of data, the absolute risk difference and number needed to treat or harm, if they were published and their inclusion was deemed appropriate, are provided in the guideline, along with confidence intervals (CIs) and data related to the rel-
ative treatment effects, such as odds ratio, relative risk (RR), hazard ratio (HR), or incidence rate ratio.

Consult the full-text version of the “ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities” for policy on clinical areas not covered by the focused update (4). The individual recommendations in this focused update will be incorporated into future revisions or updates of the full-text guideline.

1.2. Organization of the writing group
For this focused update, selected members of the 2008 Device-Based Therapy (DBT) Writing Committee were invited to participate on the basis of areas of expertise, requirements for committee rotation, and the current RWI policy; those who agreed are referred to as the 2012 Focused Update Writing Group. The HRS was invited to be a partner on this focused update and has provided representation. The writing group also included representatives from the American Association for Thoracic Surgery, Heart Failure Society of America, and Society of Thoracic Surgeons.

1.3. Document review and approval
This document was reviewed by 2 official reviewers each nominated by the ACCF, AHA, and HRS, as well as 1 reviewer each from the American Association for Thoracic Surgery, Heart Failure Society of America, and Society of Thoracic Surgeons, and 21 individual content reviewers. All information on reviewers’ RWI was collected and distributed to the writing group and is published in this document (Appendix 2).

This document was approved for publication by the governing bodies of the ACCF, AHA, and HRS and was endorsed by the American Association for Thoracic Surgery, Heart Failure Society of America, and Society of Thoracic Surgeons.

1.4. Scope of the focused update
Studies relevant to the management of patients treated with DBT for cardiac rhythm abnormalities were identified and reviewed as described previously in Section 1.1, “Methodology and Evidence Review.” On the basis of these data, the writing group determined that updates to the 2008 guideline were necessary for cardiac resynchronization therapy (CRT) and device follow-up.

Many clinical circumstances come into question in daily practice as to the appropriate use of implantable cardioverter-defibrillator (ICD)/CRT devices. Many of these clinical scenarios are both common and of great importance but have not or cannot be addressed by multicenter clinical trials, so many of these will be addressed in the “Appropriate Use Criteria (AUC) for Implantable Cardioverter-Defibrillators and Cardiac Resynchronization Therapy” document that is currently in development. Unlike comprehensive guidelines, AUC documents blend evidence-based information and clinical experience that can help guide allocation of healthcare resources, and they focus on the most common patient scenarios for which procedures may be considered. The AUC document will help define when it is reasonable to perform a procedure and, importantly, when it is not reasonable. Some of the scenarios included in the AUC may be outside guideline indications. As such, AUC are complementary to guidelines and should be used in conjunction with them for determining patient care. Furthermore, the ACCF and AHA are currently undertaking a revision of the guidelines for management of heart failure (HF). The DBT and HF guideline writing committees have worked to maintain concordance on the recommendations with regard to indications for CRT.

The writing group also thoroughly reviewed the following sections from the 2008 DBT guideline (4) and determined that although some new information may be available, the recommendations remain current.

1. Hypertrophic Cardiomyopathy—The management of hypertrophic cardiomyopathy is addressed in the “2011 ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy” (5). In that document, the indications for ICDs have been modified on the basis of reassessment of significance of risk factors. The present writing group did not analyze the source documents that led to these changes and refer the reader to the ACCF/AHA Guideline for full discussion of ICDs in hypertrophic cardiomyopathy.

2. Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy—The writing group reviewed all published evidence since the publication of the 2008 DBT guideline related to arrhythmogenic right ventricular dysplasia/cardio-myopathy and determined that no changes to the current recommendations for ICD indications were warranted.

3. Genetic Arrhythmia Syndromes—The writing group acknowledges that recent guidelines and data suggest that there may be a limited role for primary-prevention ICDs in individuals with a genetically confirmed diagnosis of long QT but without symptoms (6–8). Nevertheless, it is the consensus of this writing group that until more definitive trials or studies are completed, further refinement of criteria for ICD implantation in this patient group would not be appropriate. Therefore, the class of recommendations for ICD implantation in asymptomatic patients with a genetically confirmed mutation will remain unchanged.

4. Congenital Heart Disease—As with other forms of structural heart disease, there has been increased use of ICDs for primary prevention of sudden cardiac death in patients with congenital heart disease (4,9). Although randomized clinical trials have not been performed, multiple observational studies have consistently reported that systemic ventricular dysfunction in patients with congenital heart disease is the risk factor most predictive of subsequent sudden cardiac death or appropriate ICD rescue (10–12). These studies support consideration of an expanded role of ICDs in future revisions of the guideline, provided that consistent benefit with the use of ICDs in patients with congenital heart disease and advanced ventricular dysfunction is demonstrated. Never-
the current recommendations are not changed at this time. There remain insufficient data to make specific recommendations about CRT in patients with congenital heart disease (13).

5. Primary Electrical Disease—The writing group reviewed all published evidence since the publication of the 2008 DBT guideline related to primary electrical disease and determined that no changes were warranted in the current recommendations for ICD indications with regard to idiopathic ventricular fibrillation, short-QT syndrome, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia.

6. Terminal Care—Patients with cardiovascular implantable electronic devices (CIEDs) are living longer, with more surviving to develop comorbid conditions such as dementia or malignancy that may ultimately define their clinical course. This was recognized in the terminal care section of the 2008 DBT guideline. Recommendations on management of CIEDs in patients nearing end of life or requesting withdrawal of therapy were expanded upon in subsequent HRS expert consensus statements in an effort to provide guidance to caregivers dealing with this increasingly prevalent and difficult issue (14,15).

2. Indications for Pacing

2.4. Pacing for Hemodynamic Indications

Although most commonly used to treat or prevent abnormal rhythms, pacing can alter the activation sequence in the paced chambers, influencing regional contractility and hemodynamics. These changes are frequently insignificant clinically but can be beneficial or harmful in some conditions. Pacing to decrease symptoms for patients with obstructive hypertrophic cardiomyopathy is discussed separately in the full-text guideline, Section 2.4.2, “Obstructive Hypertrophic Cardiomyopathy.”

2.4.1. Cardiac Resynchronization Therapy

(See Table 2 and the Online Data Supplement for additional data on the trials that comprise the basis for the recommendations in this focused update.)

The present document proposes several changes in recommendations for CRT, compared with the 2008 document. The most significant changes are 1) limitation of the Class I indication to patients with QRS duration ≥150 ms; 2) limitation of the Class I indication to patients with left bundle-branch block (LBBB) pattern; 3) expansion of Class I indication to New York Heart Association (NYHA) class II (and with LBBB with QRS duration ≥150 ms); and 4) the addition of a Class IIb recommendation for patients who have left ventricular ejection fraction (LVEF) ≤30%, ischemic etiology of HF, sinus rhythm, LBBB with a QRS duration ≥150 ms, and NYHA class I symptoms. These changes may have important implications for patient selection in clinical practice, and the justification for these changes is discussed in the following paragraphs.

Progression of left ventricular (LV) systolic dysfunction to clinical HF is frequently accompanied by impaired electromechanical coupling, which may further diminish effective ventricular contractility. The most common disruptions are prolonged atrioventricular conduction (first-degree atrioventricular block) and prolonged interventricular conduction, most commonly LBBB. Prolonged interventricular and intraventricular conduction causes regional mechanical delay within the left ventricle that can result in reduced ventricular systolic function, altered myocardial metabolism, functional mitral regurgitation, and adverse remodeling with ventricular dilatation (31). Prolongation of the QRS duration occurs in approximately one third of patients with advanced HF (32,33) and has been associated with ventricular electromechanical delay (“dyssynchrony”), as identified by multiple sophisticated echocardiographic indices. QRS duration and dyssynchrony both have been identified as predictors of worsening HF, sudden cardiac death, and total death (34).

Modification of ventricular electromechanical delay with multisite ventricular pacing (commonly called “biventricular pacing” or CRT) can improve ventricular systolic function, reduce metabolic costs, ameliorate functional mitral regurgitation, and, in some patients, induce favorable remodeling with reduction of cardiac chamber dimensions (35–37). Functional improvement has been demonstrated for exercise capacity, with peak oxygen consumption in the range of 1 to 2 mL/kg/min and a 50- to 70-meter increase in 6-minute walking distance, as well as a 10-point or greater reduction of HF symptoms on the 105-point Minnesota Living with Heart Failure scale (16,38,39).

Meta-analyses of initial clinical experiences and larger subsequent trials of CRT confirmed an approximately 30% decrease in hospitalizations and a mortality rate benefit of 24% to 36% (40). In the COMPANION (Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure) trial (NYHA class III/IV HF, QRS duration >120 ms, and LVEF ≤35% on GDMT), GDMT was compared to CRT pacing therapy without backup defibrillation (CRT-Pacemaker) and to CRT therapy with defibrillation backup (CRT-D) (17). Both CRT-Pacemaker and CRT-D reduced the risk of the primary composite endpoint by approximately 20% as compared with GDMT alone. CRT-D reduced the mortality rate by 36% compared with medical therapy, but there was insufficient evidence to conclude that CRT-Pacemaker was inferior to CRT-D. The CARE-HF (Cardiac Resynchronization in Heart Failure) trial (18) limited subjects to a QRS duration >150 ms (89% of patients) or QRS duration 120 to 150 ms with echocardiographic evidence of dyssynchrony (11% of patients). It was the first study to show a significant (36%) reduction in death rate for resynchronization therapy unaccompanied by backup defibrillation compared with GDMT (18).

In the present document, we give a Class I recommendation for CRT in patients with QRS duration ≥150 ms.
The differential classification seen in this document related to QRS duration is based on the results of multiple analyses of CRT benefit. The prevalence of mechanical dyssynchrony has been documented in >40% of patients with dilated cardiomyopathy and QRS duration >120 ms, and as high as 70% among patients with QRS duration >150 ms, and intraventricular mechanical delay, as identified by several echocardiographic techniques (34,41). However, the aggregate clinical experience has consistently demonstrated that a significant clinical benefit from CRT is greatest among patients with QRS duration >150 ms (HR: 0.95; 95% CI: 0.83 to 1.10; p=0.51) (42). In addition, subgroup analyses from several studies have suggested that a QRS duration <150 ms is a risk factor for failure to respond to CRT therapy (43,44). The observed differential benefit of CRT was seen across patients in NYHA classes I through IV. It has not been possible to reliably identify those with shorter QRS durations who may benefit. Patients with shorter QRS durations who otherwise qualify for CRT are afforded Class II recommendations in these guidelines.

An additional difference in the present document compared with the 2008 DBT guideline (4) is the limitation of the recommendation for Class I indication to patients with LBBB pattern as compared to those with non-LBBB patterns, evidence for benefit.
with CRT is less compelling than in the presence of LBBB (45–47). The impact of the specific QRS morphology on clinical event reduction with CRT was evaluated in a meta-analysis of 4 clinical trials including 5,356 patients (43). In those with LBBB, CRT significantly reduced composite adverse clinical events (RR: 0.64; 95% CI: 0.52 to 0.77; p=0.00001). No benefit was observed for patients with non-LBBB conduction abnormalities (RR: 0.97; 95% CI: 0.82 to 1.15; p=0.75). Specifically, there was no benefit in patients with right bundle-branch block (RR: 0.91; 95% CI: 0.69 to 1.20; p=0.49) or nonspecific intraventricular conduction delay (RR: 1.19; 95% CI: 0.87 to 1.63; p=0.28). Overall, the difference in effect of CRT between LBBB versus non-LBBB patients was highly statistically significant (p=0.0001) (43). Nevertheless, other studies have shown that CRT is more likely to be effective in patients with advanced HF and non-LBBB morphologies if they have a markedly prolonged QRS duration (21,30) (see RAFT [Resynchronization-Defibrillation for Ambulatory Heart Failure Trial] (21) discussion below). Furthermore, patients with QRS prolongation due to frequent right ventricular apical pacing may benefit from CRT when other criteria for CRT are met (23,25,48). No large trial has yet demonstrated clinical benefit among patients without QRS prolongation, even when they have been selected with echocardiographic measures of dyssynchrony (49).

The observed heterogeneity of response even among those who would appear to be excellent candidates for CRT also may result from factors such as suboptimal lead location and the location of conduction block from fibrosis in relation to the pacing site. Several recent studies have emphasized the importance of LV lead placement. For example, wider LV–right ventricular lead separation has been shown to provide better results (50). A subanalysis of MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) (20) showed that an apical LV lead position, as compared with a basal or midventricular position, resulted in a significant increased risk for HF or death (51).

Clinical trials of resynchronization included mainly patients in sinus rhythm. However, prospective experience among patients with permanent atrial fibrillation and with decreased LV systolic function suggests that benefit may result from biventricular pacing when the QRS duration is >120 ms, although it may be most evident in patients in whom atrioventricular nodal ablation has been performed, such that right ventricular pacing is obligate (24,26,52). The benefit of CRT in patients with atrial fibrillation is more pronounced in those with depressed ejection fraction (25). Similarly, patients receiving prophylactic ICDs often evolve progressively to dominant ventricular pacing, which may reflect both intrinsic chronotropic incompetence and aggressive up-titration of beta-adrenergic–blocking agents. When device implantation or reimplantation is being considered for patients who require ventricular pacing, it is prudent to recall the results of the DAVID (Dual Chamber and VVI Implantable Defibrillator) trial (53). In this trial, dual-chamber rate-responsive pacing increased HF admissions and mortality rate as compared to sinus rhythm. A cutoff of approximately 40% right ventricular pacing was seen as deleterious (54). Similarly, in a substudy from MADIT-II (Multicenter Automatic Defibrillator Implantation Trial II), patients who were right ventricular paced >50% of the time had a higher rate of new or worsened HF than those right ventricular paced ≥50% of the time (55).

The major experience with resynchronization derives from patients with NYHA class III symptoms of HF and LVEF ≤35%. Patients with NYHA class IV symptoms of HF have accounted for only 10% of all patients in clinical trials of resynchronization therapy. These patients were highly selected ambulatory outpatients who were taking oral medications and had no history of recent hospitalization (56). Although a benefit has occasionally been described in patients with more severe acute decompensation that required brief positive inotropic therapy to aid diuresis, CRT is not generally used as a “rescue therapy” for such patients. Patients with dependence on intravenous inotropic therapy, refractory fluid retention, or advanced chronic kidney disease represent the highest-risk population for complications of any procedure and for early death after hospital discharge, and they are also unlikely to receive a meaningful mortality risk benefit from concomitant defibrillator therapy (19,57).

Patients with NYHA class IV HF symptoms who derive functional benefit from resynchronization therapy may return to a better functional status, in which prevention of sudden death becomes a relevant goal. Even among the selected NYHA class IV patients identified within the COMPANION trial (17), there was no difference in 2-year survival rate between the CRT patients with and without backup defibrillation, although more of the deaths in the CRT-Pacemaker group were classified as sudden deaths (56).

Perhaps the most significant changes in the present document compared to the 2008 DBT Guideline (4) are the expansion of the Class I recommendation for CRT to include patients with LBBB, QRS duration ≥150 ms, and NYHA class II and the addition of a Class IIb recommendation for patients who have LVEF ≤30%, ischemic etiology of HF, sinus rhythm, LBBB with a QRS duration of ≥150 ms, and NYHA class I symptoms. These recommendations are based on 4 studies in which CRT was evaluated in patients with minimal or mild symptoms of HF in the setting of low LVEF. These include MADIT-CRT, RAFT, REVERSE (Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction), and MIRACLE ICD II (Multicenter InSync ICD Randomized Clinical Evaluation II), all of which are discussed in the following paragraphs (20–22,58).

MADIT-CRT (20) randomized patients with NYHA class I or II ischemic and NYHA class II nonischemic cardiomyopathy, LVEF ≤30%, and QRS duration ≥130 ms on GDMT to CRT-D or ICD alone. Of note, only 15% of the total cohort of patients were NYHA class I. The primary
therapy was effective in patients with QRS duration ≥150 ms than in patients with QRS duration <150 ms (HR: 0.48 and 1.06, respectively) (20). Patients with LBBB had a significant reduction in ventricular tachycardia, ventricular fibrillation, and death compared to non-LBBB patients, who derived no benefit (HR: 0.47 and 1.24, respectively) (10).

RAFT (21) reported the use of CRT-D in patients with NYHA class II or class III ischemic or nonischemic cardiomyopathy, LVEF ≤30%, and QRS duration ≥120 ms, as compared to those treated with an ICD alone. The primary outcome of death or hospitalization for HF occurred in 33% of patients receiving CRT-D and in 40% of patients receiving ICD only. RAFT not only showed a significant reduction in hospitalization for HF (HR: 0.68; 95% CI: 0.56 to 0.83; p<0.001) but also was the first study to show a statistically significant reduction in death (HR: 0.75; 95% CI: 0.62 to 0.91; p=0.003) in mildly symptomatic patients with NYHA class II symptoms. However, CRT-D was associated with a higher risk of adverse device- or implantation-related complications at 30 days after implantation (p<0.001) compared with an ICD and no CRT. Patients with LBBB had a better outcome than did non-LBBB patients, but the statistical interaction between benefit and QRS morphology was weak in this trial (p=0.046). CRT-D therapy was effective in patients with QRS duration ≥150 ms but of no benefit in patients with QRS duration <150 ms (HR for QRS duration ≥150 ms: 0.59; 95% CI: 0.48 to 0.73; HR for QRS duration <150 ms: 0.99; 95% CI: 0.77 to 1.27; p=0.002 for interaction). Thus, both MADIT-CRT and RAFT showed benefit in NYHA class II patients treated with CRT-D and demonstrated that the benefit was primarily achieved in patients with QRS duration ≥150 ms and LBBB (20,21).

The REVERSE trial consisted of 610 patients. This study assessed CRT-D therapy in patients with NYHA class I or II HF symptoms on maximum medical therapy, LVEF ≤40%, and QRS duration ≥120 ms followed for 12 months and showed that 16% of patients receiving CRT and 21% without CRT worsened (p=0.10). The time to first HF hospitalization was delayed in patients receiving CRT therapy (HR: 0.47). The primary echocardiographic endpoint of ventricular remodeling assessed by LV end-systolic volume index was significantly improved (reduction in end-systolic volume index) in patients treated with CRT therapy (p<0.0001). REVERSE did not report a mortality rate benefit of CRT-D therapy (22). The lack of reported mortality rate benefit may be related to the higher ejection fraction enrollment criterion (LVEF ≤40%) and the relatively short-term follow-up (12 months) (22).

MIRACLE ICD II included patients with NYHA class II HF on GDMT with LVEF ≤35% and QRS duration ≥130 ms who were undergoing implantation of an otherwise indicated ICD (58). In these patients, CRT did not alter exercise capacity but did result in significant improvement in cardiac structure and function and composite clinical response over 6 months.

Analysis of the multiple clinical trials of CRT is complicated because trials encompass a range of LVEFs in their entry criteria, as well as a range of measured outcomes. For mortality rate, the trials showing benefit in NYHA class III and IV patients typically included those with LVEF ≤35% (22,58). For patients with NYHA class II, trials showing mortality rate benefit included those with LVEF ≤30% (20,21). A mortality rate benefit with CRT has not been shown for patients who are NYHA class I (21). In terms of demonstrating improvement in cardiac function (e.g., significant reduction in LV size and improvement in ejection fraction), trials have included patients with LVEF ≤35% who are NYHA class III and IV (58). Similarly, for patients with LVEF ≤40%, trials demonstrating improvement in function have included those who are NYHA class I and II (22). The congruence of results from the totality of CRT trials with regard to remodeling and HF events provides evidence supporting a common threshold of 35% for benefit from CRT in patients with NYHA class II through IV HF symptoms. Although there is evidence for benefit in both CRT-D and CRT-Pacemaker patients with NYHA class III and IV symptoms, for NYHA class I and II HF, all of the trials tested only CRT-D and not CRT-Pacemaker, and as such, recommendations for these classes of patients can be made only for CRT-D (20–22,58).

Taken together, the evidence from the randomized trials of CRT-D in patients with reduced LVEF and NYHA class I or II shows that CRT can provide functional improvement and decrease the risk of HF events and composite outcomes (20,22,58,59). Still, CRT-D also has been shown to decrease the mortality rate for patients with NYHA class II but not for those who have NYHA class I HF (20,21). As a result, the data support a Class I recommendation for CRT implantation in patients with LBBB and QRS duration ≥150 ms and NYHA class II. Because of the lack of mortality rate benefit and smaller sample size, we believe CRT may be considered for patients who have LVEF <30%, ischemic etiology of HF, sinus rhythm, LBBB with a QRS duration ≥150 ms, and NYHA class I symptoms on GDMT (Class Ib; LOE: B).

For all patients, optimal outcomes with CRT require effective placement of ventricular leads, ongoing HF management with neurohormonal antagonists and diuretic therapy, and in some cases, later optimization of device programming, especially atrioventricular (A-V) and interventricular (V-V) intervals (51,60).

Consistent with entry criteria for studies upon which these recommendations are based, CRT implantation should be performed only when the LVEF meets guideline criteria for patients with nonischemic cardiomyopathy who have received
>3 months of GDMT, or for patients with ischemic cardiomyopathy >40 days after myocardial infarction receiving GDMT when there was no intervening revascularization, or >3 months if revascularization was performed. It is assumed that the final decision to recommend CRT will be based on an assessment of LVEF made after any appropriate waiting period has concluded, during which GDMT has been applied. Finally, the pivotal trials demonstrating the efficacy of CRT took place in centers that provided expertise in device and HF therapy both at implantation and during long-term follow-up.

Two other organizational guidelines by the Heart Failure Society of America (61) and the European Society of Cardiology (62) have recently been published that address indications for CRT. For the patient categories in common between the Heart Failure Society of America document and the present focused update, there was a good deal of concordance. Although there are many areas of agreement, some differences exist between the present guideline and the European Society of Cardiology document. One difference is that in the present guideline, CRT is recommended in NYHA class I patients who have LVEF ≤30%, have ischemic heart disease, are in sinus rhythm, and have a LBBB with a QRS duration ≥150 ms (Class IIb; LOE: C) (20,21). There is no similar recommendation in the European Society of Cardiology document. The European Society of Cardiology recommendations include patients with QRS duration <120 ms. We have not recommended CRT for any functional class or ejection fraction with QRS durations <120 ms. We also have elected to consider the presence of LBBB versus non-LBBB in the class of recommendations, on the basis of perceived differential benefit by functional class, QRS morphology, and QRS duration.

2.8. Pacemaker Follow-Up
2.8.3. Remote Follow-Up and Monitoring

Since the publication of the 2008 DBT guideline, important changes have occurred related to follow-up and remote monitoring of CIEDs (4,15,63). CIEDs include pacemakers, ICDs, CRTs, implantable loop recorders, and implantable cardiovascular monitors. The current technology for follow-up, evidence supporting its use, and clinical practice of CIED monitoring have evolved. Routine in-person office follow-up supplemented by transtelephonic monitoring with limited remote follow-up for pacemakers was the standard approach before 2008 (4,15). Transtelephonic monitoring, with monitors that transmit the patient’s heart rhythm by converting electrocardiographic information to sound and transmitted via telephone lines to a decoding machine that then converts the sound back into a rhythm strip, is now a dated technique (4,15,63) because it allows for limited monitoring of heart rate, rhythm, and battery status of only pacemakers (63).

Contemporary remote monitoring uses bidirectional telemetry with encoded and encrypted radiofrequency signals, allowing transmission and receipt of information from CIEDs (pacemakers, ICDs, CRTs, implantable loop recorders, and implantable hemodynamic monitors) (63). All major CIED manufacturers have developed proprietary systems to allow patients to have their devices interrogated remotely, and many use wireless cellular technology to extend the bidirectional telemetry links into the patient’s location (15,63). The information is analyzed, formatted, and transmitted to a central server, where it can be accessed by clinicians through the Internet. Information provided through remote follow-up includes virtually all of the stored information that would be obtained in an in-office visit, including battery voltage, charge time in ICDs, percent pacing, sensing thresholds, automatically measured pacing thresholds when available, pacing and shock impedance, and stored arrhythmia events with electrograms (15,63).

CIEDs with wireless telemetry capability may be programmed at a face-to-face evaluation to subsequently send automatic alerts for a variety of issues that the clinician deems significant, such as abnormal battery voltage, abnormal lead parameters, or increased duration or frequency of arrhythmia episodes (15). Remote transmissions can be made at predetermined intervals or at unscheduled times for prespecified alerts related to device function or activated by the patient for clinical reasons (63). A detailed description of techniques, indications, personnel, and frequency has been published as a consensus document (15).

Several prospective randomized trials have been conducted evaluating the effect of remote monitoring on clinical outcomes (64–67) since the publication of the 2008 DBT Guideline (4). Collectively, these trials have demonstrated that remote monitoring is a safe alternative to office visits to evaluate CIEDs. Compared with in-person office visits to evaluate CIEDs, remote monitoring leads to early

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<th>Table 3 Minimum Frequency of CIED In-Person or Remote Monitoring*</th>
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<td>Type and Frequency</td>
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<tr>
<td>Pacemaker/ICD/CRT</td>
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<td>Within 72 h of CIED implantation</td>
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<td>2–12 wk postimplantation</td>
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<td>Every 3–12 mo for pacemaker/ CRT-Pacemaker</td>
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<td>Every 3–6 mo for ICD/CRT-D</td>
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<td>Annually until battery depletion</td>
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<td>Every 1–3 mo at signs of battery depletion</td>
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<td>Implantable loop recorder</td>
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<td>Every 1–6 mo depending on patient symptoms and indication</td>
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<td>Implantable hemodynamic monitor</td>
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<td>Every 1–6 mo depending on indication</td>
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<td>More frequent assessment as clinically indicated</td>
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CIED indicates cardiovascular implantable electronic device; CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy defibrillator; CRT-Pacemaker, cardiac resynchronization therapy pacemaker; and ICD, implantable cardioverter-defibrillator.

Modified from Wilkoff et al (15).

*More frequent in-person or remote monitoring may be required for all the above devices as clinically indicated.
discovery of clinically actionable events, decreased time to clinical decision in response to these events, and fewer office visits (64–67). Long-term survival rates of patients monitored remotely with ICDs in a practice setting compare favorably with survival rates of patients in clinical trials (68).

Current suggestions for the minimum frequency of office and remote monitoring of patients with CIEDs are summarized in Table 3 (15). Issues such as lead malfunction, unreliable battery life indicators, and other device or lead recalls influence clinical decisions, which may change the appropriate minimum follow-up.

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**References**


### Appendix 1  Author Relationships With Industry and Other Entities (Relevant)—2012 ACCF/AHA/HRS Focused Update of the 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities

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### Appendix 2  Reviewer Relationships With Industry and Other Entities (Relevant)—2012 ACCF/AHA/HRS Focused Update of the 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities

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AATS indicates American Association for Thoracic Surgery; ACCF, American College of Cardiology Foundation; AHA, American Heart Association; EP, Electrophysiology; HFSA, Heart Failure Society of America; HRS, Heart Rhythm Society; ICD, implantable cardioverter-defibrillator; MADIT-RIT, Multicenter Automatic Defibrillator Implantation Trial—Reduce Inappropriate Therapy; and STS, Society of Thoracic Surgeons.

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Appendix 3  Indications for CRT Therapy—Algorithm

Patient with cardiomyopathy on GDMT for ≥3 mo or on GDMT and ≥40 d after MI, or with implantation of pacing or defibrillation device for special indications

LVEF ≤35%

Evaluate general health status

Comorbidities and/or frailty limit survival with good functional capacity to <1 y

Continue GDMT without implanted device

Acceptable noncardiac health

Evaluate NYHA clinical status

NYHA class I symptoms

NYHA class II, III, and ambulatory class IV symptoms

Class I
LBBB pattern, sinus rhythm, QRS duration ≥150 ms

Class IIa
LBBB pattern, QRS 120-149 ms

Non-LBBB pattern, QRS ≥150 ms

Anticipated to require frequent ventricular pacing (>40%)

Atrial fibrillation; if ventricular pacing is required or QRS criteria above are met and rate control will result in near 100% ventricular pacing with CRT

Class IIb
Non-LBBB pattern, QRS 120-149 ms

NYHA class IV (stage D)
Refractory symptoms or dependence on intravenous inotropes

Device not indicated except in selected patients listed for transplantation or with LV assist devices

If device already in place, consider deactivation of defibrillator

Benefit for NYHA class I and II patients has been shown in CRT-D trials, and while patients may not experience immediate symptomatic benefit, late remodeling may be avoided along with long-term HF consequences. There are no trials that support CRT-pacing (without ICD) in NYHA class I and II patients. Thus, it is anticipated these patients would receive CRT-D unless clinical reasons or personal wishes make CRT-pacing more appropriate. In patients who are NYHA class III and ambulatory class IV, CRT-D may be chosen but clinical reasons and personal wishes may make CRT-pacing appropriate to improve symptoms and quality of life when an ICD is not expected to produce meaningful benefit in survival.

CRT indicates cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy defibrillator; GDMT, guideline-directed medical therapy; ICD, implantable cardioverter-defibrillator; LV, left ventricular; LVEF, left ventricular ejection fraction; LBBB, left bundle-branch block; MI, myocardial infarction; and NYHA, New York Heart Association.