Journal of the American College of Cardiology
© 2013 by the American College of Cardiology Foundation, the American Heart Association, Inc., and the Heart Rhythm Society
Published by Elsevier Inc.

Vol. 61, No. 3, 2013
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.11.007

PRACTICE GUIDELINE

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

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

Developed in Collaboration With the American Association for Thoracic Surgery and Society of Thoracic Surgeons

2008 WRITING COMMITTEE MEMBERS

Andrew E. Epstein, MD, FACC, FAHA, FHRS, *Chair*; John P. DiMarco, MD, PHD, FACC, FHRS; Kenneth A. Ellenbogen. MD, FACC, FAHA, FHRS; N.A. Mark Estes III, MD, FACC, FAHA, FHRS; Roger A. Freedman, MD, FACC, FHRS; Leonard S. Gettes, MD, FACC, FAHA; A. Marc Gillinov, MD, FACC, FAHA; Gabriel Gregoratos, MD, FACC, FAHA; Stephen C. Hammill, MD, FACC, FHRS; David L. Hayes, MD, FACC, FAHA, FHRS; Mark A. Hlatky, MD, FACC, FAHA; L. Kristin Newby, MD, FACC, FAHA; Richard L. Page, MD, FACC, FAHA, FHRS; Mark H. Schoenfeld, MD, FACC, FAHA, FHRS; Michael J. Silka, MD, FACC; Lynne Warner Stevenson, MD, FACC#; Michael O. Sweeney, MD, FACC

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

2012 WRITING GROUP MEMBERS*

Cynthia M. Tracy, MD, FACC, FAHA, Chair; Andrew E. Epstein, MD, FACC, FAHA, FHRS, Vice Chair*; Dawood Darbar, MD, FACC, FHRS†; John P. DiMarco, MD, PHD, FACC, FHRS*‡; Sandra B. Dunbar, RN, DSN, FAAN, FAHA†; N.A. Mark Estes III, MD, FACC, FAHA, FHRS*§; T. Bruce Ferguson, JR, MD, FACC, FAHA*‖¶; Stephen C. Hammill, MD, FACC, FHRS‡; Pamela E. Karasik, MD, FACC, FHRS†; Mark S. Link, MD, FACC, FHRS*†; Joseph E. Marine, MD, FACC, FHRS†; Mark H. Schoenfeld, MD, FACC, FAHA, FHRS*†; Amit J. Shanker, MD, FACC, FHRS‡; Michael J. Silka, MD, FACC†; Lynne Warner Stevenson, MD, FACC*#; William G. Stevenson, MD, FACC, FAHA, FHRS***; Paul D. Varosy, MD, FACC, FHRS†

*The 2012 writing group members were required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply; see Appendix 4 for recusal information. †ACCF/AHA Representative. ‡Heart Rhythm Society Representative. §ACCF/AHA Task Force on Performance Measures Liaison. ‖American Association for Thoracic Surgery Representative. ¶Society of Thoracic Surgeons Representative. #Heart Failure Society of America Representative. **ACCF/AHA Task Force on Practice Guidelines Liaison.

This document was approved by the American College of Cardiology Foundation Board of Trustees, the American Heart Association Science Advisory and Coordinating Committee, and the Heart Rhythm Society Board of Trustees in May 2012.

The American College of Cardiology Foundation requests that this document be cited as follows: Epstein AE, DiMarco JP, Ellenbogen KA, Estes NAM III, Freedman RA, Gettes LS, Gillinov AM, Gregoratos G, Hammill SC, Hayes DL, Hlatky MA, Newby LK, Page RL, Schoenfeld MH, Silka MJ, Stevenson LW, Sweeney MO 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2013;61:e6–75.

This article is copublished in *Circulation*.

Copies: This document is available on the World Wide Web sites of the American College of Cardiology (http://www.cardiosource.org) and the American Heart Association (my.americanheart.org). For copies of this document, please contact Elsevier Inc. Reprint Department, fax (212) 633-3820, e-mail reprints@elsevier.com.

ACCF/AHA TASK FORCE MEMBERS
Jeffrey L. Anderson, MD, FACC, FAHA, Chair; Alice K. Jacobs, MD, FACC, FAHA, Immediate Past Chair; Jonathan L. Halperin, MD, FACC, FAHA, Chair-Elect; Nancy M. Albert, PHD, CCNS, CCRN; Mark A. Creager, MD, FACC, FAHA; David DeMets, PHD; Steven M. Ettinger, MD, FACC; Robert A. Guyton, MD, FACC; Judith S. Hochman, MD, FACC, FAHA; Frederick G. Kushner, MD, FACC, FAHA; E. Magnus Ohman, MD, FACC; William Stevenson, MD, FACC, FAHA; Clyde W. Yancy, MD, FACC, FAHA

TABLE OF CONTENTS

Preamble (UPDATED)

It is important that the medical profession play a significant role in critically evaluating the use of diagnostic procedures and therapies as they are introduced and tested in the detection, management, or prevention of disease states. Rigorous and expert analysis of the available data documenting absolute and relative benefits and risks of those procedures and therapies can produce helpful guidelines that improve the effectiveness of care, optimize patient outcomes, and favorably affect the overall cost of care by focusing resources on the most effective strategies.

The American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) have jointly engaged in the production of such guidelines in the area of cardiovascular disease since 1980. The ACCF/AHA Task Force on Practice Guidelines (Task Force), whose charge is to develop, update, or revise practice guidelines for important cardiovascular diseases and procedures, directs this effort. Writing committees are charged with the task of performing an assessment of the evidence and acting as an independent group of authors to develop, update, or revise written recommendations for clinical practice.

Experts in the subject under consideration have been selected from both organizations to examine subject-specific data and write guidelines. The process includes additional representatives from other medical practitioner and specialty groups when appropriate. Writing committees are specifically charged to perform a literature review, weigh the strength of evidence for or against a particular treatment or procedure, and include estimates of expected health outcomes where data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that may influence the choice of particular tests or therapies are considered, as well as frequency of follow-up and cost-effectiveness. When available, information from studies on cost will be considered; however, review of data on efficacy and clinical outcomes will constitute the primary basis for preparing recommendations in these guidelines.

The guidelines will be reviewed annually by the Task Force. Each guideline is considered current unless it is updated, revised, or a published addendum declares it out of date and no longer official ACCF/AHA policy. 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 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.

The 2012 focused update was 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 1.3, "Methodology and Evidence"). 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. See the 2012 focused update for the complete preamble and evidence review period (1).

In analyzing the data and developing recommendations and supporting text, the focused update writing group uses evidence-based methodologies developed by the Task Force (1a). 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 the clinician members of 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

Table 1. Applying Classification of Recommendations and Level of Evidence

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT: CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* Procedure/Test: COR III: No benefit — Not Helpful; COR III: Harm — Excess Cost w/o Benefit or Harmful Treatment: COR III: No benefit — No Proven Benefit; COR III: Harm — Harmful to Patients
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	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ 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	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ 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 ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit: is not recommended; is not indicated; 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
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

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/efficacy 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.

within each COR. A new addition to this methodology for the 2012 focused update 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. (This version of the COR/LOE table was used for development of the 2012 Focused Update and is included in the current document. (1)) 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, is incorporated into the 2012 focused update and will be used 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 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.

For the 2008 guidelines, all members of the writing committee, as well as peer reviewers of the document, were asked to provide disclosure statements of all such relationships that may be perceived as real or potential conflicts of interest. Writing committee members are also strongly encouraged to declare a previous relationship with industry that may be perceived as relevant to guideline development.

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 4 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 confidential vote by the writing group and must be approved by a consensus of the voting members. Members may not draft or vote on any text or recommendations pertaining to their RWI. The 2012 members who recused themselves from voting are indicated in the list of writing group members, and specific section recusals are noted in Appendix 4. 2008 and 2012 authors' and peer reviewers' RWI pertinent to this guideline are disclosed in Appendixes 1, 2, 4, and 5, 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 http://cardiosource.org/ACC/About-ACC/Who-We-Are/Leadership/Guidelines-and-Documents-Task-Forces.aspx. The work of the 2012 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. Guidelines are official policy of both the ACCF and AHA.

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* (1b,1c). 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 current document is a republication of the "ACCF/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities," (1d) revised to incorporate updated recommendations and text from the 2012 Focused Update (1). For easy reference, this online-only version denotes sections that have been updated.

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

1. Introduction (UPDATED)

1.1. Organization of Committee

This 2008 revision of the ACCF/AHA/HRS Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities (formally named "ACC/AHA/NASPE Guidelines for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices") updates the previous versions published in 1984, 1991, 1998, and 2002. Revision of the statement was deemed necessary for multiple reasons: 1) Major studies have been reported that have advanced our knowledge of the natural history of bradyarrhythmias and tachyarrhythmias, which may be treated optimally with device therapy; 2) there have been tremendous changes in the management of heart failure that involve both drug and device therapy; and 3) major advances in the technology of devices to treat, delay, and even prevent morbidity and mortality from bradyarrhythmias, tachyarrhythmias, and heart failure have occurred. The writing committee was composed of physicians who are experts in the areas of device therapy and follow-up and senior clinicians skilled in cardiovascular care, internal medicine, cardiovascular surgery, ethics, and socioeconomics. The committee included representatives of the American Association for Thoracic Surgery, Heart Failure Society of America, and Society of Thoracic Surgeons.

For the 2012 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.

1.2. Document Review and Approval

The 2008 Guideline document was reviewed by 2 official reviewers nominated by each of the ACC, AHA, and HRS and by 11 additional peer reviewers. Of the total 17 peer reviewers, 10 had no significant relevant relationships with industry. In addition, this document has been reviewed and approved by the governing bodies of the ACC, AHA, and HRS, which include 19 ACC Board of Trustees members (none of whom had any significant relevant relationships with industry), 15 AHA Science Advisory Coordinating Committee members (none of whom had any significant relevant relationships with industry), and 14 HRS Board of Trustees members (6 of whom had no significant relevant relationships with industry). All guideline recommendations underwent a formal, blinded writing committee vote. Writing committee members were required to recuse themselves if they had a significant relevant relationship with industry. The guideline recommendations were unanimously approved by all members of the writing committee who were eligible to vote. The section "Pacing in Children and Adolescents" was reviewed by additional reviewers with special expertise in pediatric electrophysiology. The committee thanks all the reviewers for their comments. Many of their suggestions were incorporated into the final document.

The 2012 focused update 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 5). The 2012 focused update 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.

1.3. Methodology and Evidence

The recommendations listed in this document are, whenever possible, evidence based. An extensive literature survey was conducted that led to the incorporation of 595 references. Searches were limited to studies, reviews, and other evidence conducted in human subjects and published in English. Key search words included but were not limited to antiarrhythmic, antibradycardia, atrial fibrillation, bradyarrhythmia, cardiac, CRT, defibrillator, device therapy, devices, dual chamber, heart, heart failure, ICD, implantable defibrillator, device implantation, long-QT syndrome, medical therapy, pacemaker, pacing, quality-of-life, resynchronization, rhythm, sinus node dysfunction, sleep apnea, sudden cardiac death, syncope, tachyarrhythmia, terminal care, and transplantation. Additionally, the committee reviewed documents related to the subject matter previously published by the ACC, AHA, and HRS. References selected and published in this document are representative and not all-inclusive.

The focus of the 2008 guidelines is the appropriate use of heart pacing devices (e.g., pacemakers for bradyarrhythmias and heart failure management, cardiac resynchronization, and implantable cardioverter-defibrillators [ICDs]), not the treatment of cardiac arrhythmias. The fact that the use of a device for treatment of a particular condition is listed as a Class I indication (beneficial, useful, and effective) does not preclude the use of other therapeutic modalities that may be equally effective. As with all clinical practice guidelines, the recommendations in this document focus on treatment of an average patient with a specific disorder and may be modified by patient comorbidities, limitation of life expectancy because of coexisting diseases, and other situations that only the primary treating physician may evaluate appropriately.

These guidelines include sections on selection of pacemakers and ICDs, optimization of technology, cost, and follow-up of implanted devices. Although the section on follow-up is relatively brief, its importance cannot be overemphasized: First, optimal results from an implanted device can be obtained only if the device is adjusted to changing clinical conditions; second, recent advisories and recalls serve as warnings that devices are not infallible, and failure of electronics, batteries, and leads can occur (2,3).

The committee considered including a section on extraction of failed/unused leads, a topic of current interest, but elected not to do so in the absence of convincing evidence to support specific criteria for timing and methods of lead extraction. A policy statement on lead extraction from the North American Society of Pacing and Electrophysiology (now the HRS) provides information on this topic (4). Similarly, the issue of when to discontinue long-term cardiac pacing or defibrillator therapy has not been studied sufficiently to allow formulation of appropriate guidelines (5); however, the question is of such importance that this topic is addressed to emphasize the importance of patient-family-physician discussion and ethical principles.

The text that accompanies the listed indications should be read carefully, because it includes the rationale and supporting evidence for many of the indications, and in several instances, it includes a discussion of alternative acceptable therapies. Many of the indications are modified by the term "potentially reversible." This term is used to indicate abnormal pathophysiology (e.g., complete heart block) that may be the result of reversible factors. Examples include complete heart block due to drug toxicity (digitalis), electrolyte abnormalities, diseases with periatrioventricular node inflammation (Lyme disease), and transient injury to the conduction system at the time of open heart surgery. When faced with a potentially reversible situation, the treating physician must decide how long of a waiting period is justified before device therapy is begun. The committee recognizes that this statement does not address the issue of length of hospital stay vis-à-vis managed-care regulations. It is emphasized that these guidelines are not intended to address this issue, which falls strictly within the purview of the treating physician.

The term "symptomatic bradycardia" is used in this document. Symptomatic bradycardia is defined as a documented bradyarrhythmia that is directly responsible for development of the clinical manifestations of syncope or near syncope, transient dizziness or lightheadedness, or confusional states resulting from cerebral hypoperfusion attributable to slow heart rate. Fatigue, exercise intolerance, and congestive heart failure may also result from bradycardia. These symptoms may occur at rest or with exertion. Definite correlation of symptoms with a bradyarrhythmia is required to fulfill the criteria that define symptomatic bradycardia. Caution should be exercised not to confuse physiological sinus bradycardia (as occurs in highly trained athletes) with pathological bradyarrhythmias. Occasionally, symptoms may become apparent only in retrospect after antibradycardia pacing. Nevertheless, the universal application of pacing therapy to treat a specific heart rate cannot be recommended except in specific circumstances, as detailed subsequently.

In these guidelines, the terms "persistent," "transient," and "not expected to resolve" are used but not specifically defined because the time element varies in different clinical conditions. The treating physician must use appropriate clinical judgment and available data in deciding when a condition is persistent or when it can be expected to be transient. Section 2.1.4, "Pacing for Atrioventricular Block Associated With Acute Myocardial Infarction," overlaps with the "ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction" (6) and includes expanded indications and stylistic changes. The statement "incidental finding at electrophysiological study" is used several times in this document and does not mean that such a study is indicated. Appropriate indications for electrophysiological studies have been published (7).

The section on indications for ICDs has been updated to reflect the numerous new developments in this field and the voluminous literature related to the efficacy of these devices in the treatment and prophylaxis of sudden cardiac death (SCD) and malignant ventricular arrhythmias. As previously noted, indications for ICDs, cardiac resynchronization therapy (CRT) devices, and combined ICDs and CRT devices (hereafter called CRT-Ds) are continuously changing and can be expected to change further as new trials are reported. Indeed, it is inevitable that the indications for device therapy will be refined with respect to both expanded use and the identification of patients expected to benefit the most from these therapies. Furthermore, it is emphasized that when a patient has an indication for both a pacemaker (whether it be single-chamber, dual-chamber, or biventricular) and an ICD, a combined device with appropriate programming is indicated.

In this document, the term "mortality" is used to indicate all-cause mortality unless otherwise specified. The committee elected to use all-cause mortality because of the variable definition of sudden death and the developing consensus to use all-cause mortality as the most appropriate end point of clinical trials (8,9).

These guidelines are not designed to specify training or credentials required for physicians to use device therapy. Nevertheless, in view of the complexity of both the cognitive and technical aspects of device therapy, only appropriately trained physicians should use device therapy. Appropriate training guidelines for physicians have been published previously (10–13).

The 2008 revision reflects what the committee believes are the most relevant and significant advances in pacemaker/ICD therapy since the publication of these guidelines in the *Journal of the American College of Cardiology* and *Circulation* in 2002 (14,15).

All recommendations assume that patients are treated with optimal medical therapy according to published guidelines, as had been required in all the randomized controlled clinical trials on which these guidelines are based, and that human issues related to individual patients are addressed. The committee believes that comorbidities, life expectancy, and quality-of-life (QOL) issues must be addressed forthrightly with patients and their families. We have repeatedly used the phrase "reasonable expectation of survival with a good functional status for more than 1 year" to emphasize this integration of factors in decision-making. Even when physicians believe that the anticipated benefits warrant device implantation, patients have the option to decline intervention after having been provided with a full explanation of the potential risks and benefits of device therapy. Finally, the committee is aware that other guideline/expert groups have interpreted the same data differently (16–19).

In preparing this revision, the committee was guided by the following principles:

1. Changes in recommendations and levels of evidence were made either because of new randomized trials or because of the accumulation of new clinical evidence and the development of clinical consensus.
2. The committee was cognizant of the health care, logistic, and financial implications of recent trials and factored in these considerations to arrive at the classification of certain recommendations.
3. For recommendations taken from other guidelines, wording changes were made to render some of the original recommendations more precise.
4. The committee would like to reemphasize that the recommendations in this guideline apply to most patients but may require modification because of existing situations that only the primary treating physician can evaluate properly.
5. All of the listed recommendations for implantation of a device presume the absence of inciting causes that may be eliminated without detriment to the patient (e.g., nonessential drug therapy).
6. The committee endeavored to maintain consistency of recommendations in this and other previously published guidelines. In the section on atrioventricular (AV) block associated with acute myocardial infarction (AMI), the recommendations follow closely those in the "ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction" (6). However, because of the rapid evolution of pacemaker/ICD science, it has not always been possible to maintain consistency with other published guidelines.

For the 2012 focused update, 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 February 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. Studies relevant to the management of patients treated with DBT for cardiac rhythm abnormalities were identified and reviewed. 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. The writing group also thoroughly reviewed other sections from the 2008 DBT guideline on hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia/cardiomyopathy, genetic arrhythmia syndromes, congenital heart disease, primary electrical disease, and terminal care; and determined that although some new information may be available, the recommendations remain current. See the 2012 focused update for a complete review of the scope (1).

2. Indications for Pacing

2.1. Pacing for Bradycardia Due to Sinus and Atrioventricular Node Dysfunction

In some patients, bradycardia is the consequence of essential long-term drug therapy of a type and dose for which there is no acceptable alternative. In these patients, pacing therapy is necessary to allow maintenance of ongoing medical treatment.

2.1.1. Sinus Node Dysfunction

Sinus node dysfunction (SND) was first described as a clinical entity in 1968 (20), although Wenckebach reported the electrocardiographic (ECG) manifestation of SND in 1923. SND refers to a broad array of abnormalities in sinus node and atrial impulse formation and propagation. These include persistent sinus bradycardia and chronotropic incompetence without identifiable causes, paroxysmal or persistent sinus arrest with replacement by subsidiary escape rhythms in the atrium, AV junction, or ventricular myocardium. The frequent association of paroxysmal atrial fibrillation (AF) and sinus bradycardia or sinus bradyarrhythmias, which may oscillate suddenly from one to the other, usually accompanied by symptoms, is termed "tachy-brady syndrome."

SND is primarily a disease of the elderly and is presumed to be due to senescence of the sinus node and atrial muscle. Collected data from 28 different studies on atrial pacing for SND showed a median annual incidence of complete AV block of 0.6% (range 0% to 4.5%) with a total prevalence of 2.1% (range 0% to 11.9%) (21). This suggests that the degenerative process also affects the specialized conduction system, although the rate of progression is slow and does not dominate the clinical course of disease (21). SND is typically diagnosed in the seventh and eighth decades of life, which is also the average age at enrollment in clinical trials of pacemaker therapy for SND (22,23). Identical clinical manifestations may occur at any age as a secondary phenomenon of any condition that results in destruction of sinus node cells, such as ischemia or infarction, infiltrative disease, collagen vascular disease, surgical trauma, endocrinologic abnormalities, autonomic insufficiency, and others (24).

The clinical manifestations of SND are diverse, reflecting the range of typical sinoatrial rhythm disturbances. The most dramatic presentation is syncope. The mechanism of syncope is a sudden pause in sinus impulse formation or sinus exit block, either spontaneously or after the termination of an atrial tachyarrhythmia, that causes cerebral hypoperfusion. The pause in sinus node activity is frequently accompanied by an inadequate, delayed, or absent response of subsidiary escape pacemakers in the AV junction or ventricular myocardium, which aggravates the hemodynamic consequences.

However, in many patients, the clinical manifestations of SND are more insidious and relate to an inadequate heart rate response to activities of daily living that can be difficult to diagnose (25). The term "chronotropic incompetence" is used to denote an inadequate heart rate response to physical activity. Although many experienced clinicians claim to recognize chronotropic incompetence in individual patients, no single metric has been established as a diagnostic standard upon which therapeutic decisions can be based. The most obvious example of chronotropic incompetence is a monotonic daily heart rate profile in an ambulatory patient. Various protocols have been proposed to quantify subphysiological heart rate responses to exercise (26,27), and many clinicians would consider failure to achieve 80% of the maximum predicted heart rate (220 minus age) at peak exercise as evidence of a blunted heart rate response (28,29). However, none of these approaches have been validated clinically, and it is likely that the appropriate heart rate response to exercise in individual patients is too idiosyncratic for standardized testing.

The natural history of untreated SND may be highly variable. The majority of patients who have experienced syncope because of a sinus pause or marked sinus bradycardia will have recurrent syncope (30). Not uncommonly, the natural history of SND is interrupted by other necessary medical therapies that aggravate the underlying tendency to bradycardia (24). MOST (Mode Selection Trial) included symptomatic pauses greater than or equal to 3 seconds or sinus bradycardia with rates greater than 50 bpm, which restricted the use of indicated long-term medical therapy. Supraventricular tachycardia (SVT) including AF was present in 47% and 53% of patients, respectively, enrolled in a large randomized clinical trial of pacing mode selection in SND (22,31). The incidence of sudden death is extremely low, and SND does not appear to affect survival whether untreated (30) or treated with pacemaker therapy (32,33).

The only effective treatment for symptomatic bradycardia is permanent cardiac pacing. The decision to implant a pacemaker for SND is often accompanied by uncertainty that arises from incomplete linkage between sporadic symptoms and ECG evidence of coexisting bradycardia. It is crucial to distinguish between physiological bradycardia due to autonomic conditions or training effects and circumstantially inappropriate bradycardia that requires permanent cardiac pacing. For example, sinus bradycardia is accepted as a physiological finding that does not require cardiac pacing in

trained athletes. Such individuals may have heart rates of 40 to 50 bpm while at rest and awake and may have a sleeping rate as slow as 30 bpm, with sinus pauses or progressive sinus slowing accompanied by AV conduction delay (PR prolongation), sometimes culminating in type I second-degree AV block (34,35). The basis of the distinction between physiological and pathological bradycardia, which may overlap in ECG presentation, therefore pivots on correlation of episodic bradycardia with symptoms compatible with cerebral hypoperfusion. Intermittent ECG monitoring with Holter monitors and event recorders may be helpful (36,37), although the duration of monitoring required to capture such evidence may be very long (38). The use of insertable loop recorders offers the advantages of compliance and convenience during very long-term monitoring efforts (39).

The optimal pacing system for prevention of symptomatic bradycardia in SND is unknown. Recent evidence suggests that ventricular desynchronization due to right ventricular apical (RVA) pacing may have adverse effects on left ventricular (LV) and left atrial structure and function (40–47). These adverse effects likely explain the association of RVA pacing, independent of AV synchrony, with increased risks of AF and heart failure in randomized clinical trials of pacemaker therapy (45,48,49) and, additionally, ventricular arrhythmias and death during ICD therapy (50,51). Likewise, although simulation of the normal sinus node response to exercise in bradycardia patients with pacemaker sensors seems logical, a clinical benefit on a population scale has not been demonstrated in large randomized controlled trials of pacemaker therapy (52). These rapidly evolving areas of clinical investigation should inform the choice of pacing system in SND (see Section 2.6, "Selection of Pacemaker Device").

Recommendations for Permanent Pacing in Sinus Node Dysfunction

CLASS I

1. **Permanent pacemaker implantation is indicated for SND with documented symptomatic bradycardia, including frequent sinus pauses that produce symptoms. (*Level of Evidence: C*) (53–55)**
2. **Permanent pacemaker implantation is indicated for symptomatic chronotropic incompetence. (*Level of Evidence: C*) (53–57)**
3. **Permanent pacemaker implantation is indicated for symptomatic sinus bradycardia that results from required drug therapy for medical conditions. (*Level of Evidence: C*)**

CLASS IIa

1. **Permanent pacemaker implantation is reasonable for SND with heart rate less than 40 bpm when a clear association between significant symptoms consistent with bradycardia and the actual presence of bradycardia has not been documented. (*Level of Evidence: C*) (53–55,58–60)**
2. **Permanent pacemaker implantation is reasonable for syncope of unexplained origin when clinically significant abnormalities of sinus node function are discovered or provoked in electrophysiological studies. (*Level of Evidence: C*) (61,62)**

CLASS IIb

1. **Permanent pacemaker implantation may be considered in minimally symptomatic patients with chronic heart rate less than 40 bpm while awake. (*Level of Evidence: C*) (53,55,56, 58–60)**

CLASS III

1. **Permanent pacemaker implantation is not indicated for SND in asymptomatic patients. (*Level of Evidence: C*)**
2. **Permanent pacemaker implantation is not indicated for SND in patients for whom the symptoms suggestive of bradycardia have been clearly documented to occur in the absence of bradycardia. (*Level of Evidence: C*)**
3. **Permanent pacemaker implantation is not indicated for SND with symptomatic bradycardia due to nonessential drug therapy. (*Level of Evidence: C*)**

2.1.2. Acquired Atrioventricular Block in Adults

AV block is classified as first-, second-, or third-degree (complete) block; anatomically, it is defined as supra-, intra-, or infra-His. First-degree AV block is defined as abnormal prolongation of the PR interval (greater than 0.20 seconds). Second-degree AV block is subclassified as type I and type II. Type I second-degree AV block is characterized by progressive prolongation of the interval between the onset of atrial (P wave) and ventricular (R wave) conduction (PR) before a nonconducted beat and is usually seen in conjunction with QRS. Type I second-degree AV block is characterized by progressive prolongation of the PR interval before a nonconducted beat and a shorter PR interval after the blocked beat. Type II second-degree AV block is characterized by fixed PR intervals before and after blocked beats and is usually associated with a wide QRS complex. When AV conduction occurs in a 2:1 pattern, block cannot be classified unequivocally as type I or type II, although the width of the QRS can be suggestive, as just described. Advanced second-degree AV block refers to the blocking of 2 or more consecutive P waves with some conducted beats, which indicates some preservation of AV conduction. In the setting of AF, a prolonged pause (e.g., greater than 5 seconds) should be considered to be due to advanced second-degree AV block. Third-degree AV block (complete heart block) is defined as absence of AV conduction.

Patients with abnormalities of AV conduction may be asymptomatic or may experience serious symptoms related to bradycardia, ventricular arrhythmias, or both. Decisions regarding the need for a pacemaker are importantly influenced by the presence or absence of symptoms directly attributable to bradycardia. Furthermore, many of the indications for pacing have evolved over the past 40 years on the basis of experience without the benefit of comparative randomized clinical trials, in part because no acceptable alternative options exist to treat most bradycardias.

Nonrandomized studies strongly suggest that permanent pacing does improve survival in patients with third-degree AV block, especially if syncope has occurred (63–68). Although there is little evidence to suggest that pacemakers improve survival in patients with isolated first-degree AV block (69), it is now recognized that marked (PR more than

300 milliseconds) first-degree AV block can lead to symptoms even in the absence of higher degrees of AV block (70). When marked first-degree AV block for any reason causes atrial systole in close proximity to the preceding ventricular systole and produces hemodynamic consequences usually associated with retrograde (ventriculoatrial) conduction, signs and symptoms similar to the pacemaker syndrome may occur (71). With marked first-degree AV block, atrial contraction occurs before complete atrial filling, ventricular filling is compromised, and an increase in pulmonary capillary wedge pressure and a decrease in cardiac output follow. Small uncontrolled trials have suggested some symptomatic and functional improvement by pacing of patients with PR intervals more than 0.30 seconds by decreasing the time for AV conduction (70). Finally, a long PR interval may identify a subgroup of patients with LV dysfunction, some of whom may benefit from dual-chamber pacing with a short(er) AV delay (72). These same principles also may be applied to patients with type I second-degree AV block who experience hemodynamic compromise due to loss of AV synchrony, even without bradycardia. Although echocardiographic or invasive techniques may be used to assess hemodynamic improvement before permanent pacemaker implantation, such studies are not required.

Type I second-degree AV block is usually due to delay in the AV node irrespective of QRS width. Because progression to advanced AV block in this situation is uncommon (73–75), pacing is usually not indicated unless the patient is symptomatic. Although controversy exists, pacemaker implantation is supported for this finding (76–78). Type II second-degree AV block is usually infranodal (either intra- or infra-His), especially when the QRS is wide. In these patients, symptoms are frequent, prognosis is compromised, and progression to third-degree AV block is common and sudden (73,75,79). Thus, type II second-degree AV block with a wide QRS typically indicates diffuse conduction system disease and constitutes an indication for pacing even in the absence of symptoms. However, it is not always possible to determine the site of AV block without electrophysiological evaluation, because type I second-degree AV block can be infranodal even when the QRS is narrow (80). If type I second-degree AV block with a narrow or wide QRS is found to be intra- or infra-Hisian at electrophysiological study, pacing should be considered.

Because it may be difficult for both patients and their physicians to attribute ambiguous symptoms such as fatigue to bradycardia, special vigilance must be exercised to acknowledge the patient's concerns about symptoms that may be caused by a slow heart rate. In a patient with third-degree AV block, permanent pacing should be strongly considered even when the ventricular rate is more than 40 bpm, because the choice of a 40 bpm cutoff in these guidelines was not determined from clinical trial data. Indeed, it is not the escape rate that is necessarily critical for safety but rather the site of origin of the escape rhythm (i.e., in the AV node, the His bundle, or infra-His).

AV block can sometimes be provoked by exercise. If not secondary to myocardial ischemia, AV block in this circumstance usually is due to disease in the His-Purkinje system and is associated with a poor prognosis; thus, pacing is indicated (81,82). Long sinus pauses and AV block can also occur during sleep apnea. In the absence of symptoms, these abnormalities are reversible and do not require pacing (83). If symptoms are present, pacing is indicated as in other conditions.

Recommendations for permanent pacemaker implantation in patients with AV block in AMI, congenital AV block, and AV block associated with enhanced vagal tone are discussed in separate sections. Neurocardiogenic causes in young patients with AV block should be assessed before proceeding with permanent pacing. Physiological AV block in the presence of supraventricular tachyarrhythmias does not constitute an indication for pacemaker implantation except as specifically defined in the recommendations that follow.

In general, the decision regarding implantation of a pacemaker must be considered with respect to whether AV block will be permanent. Reversible causes of AV block, such as electrolyte abnormalities, should be corrected first. Some diseases may follow a natural history to resolution (e.g., Lyme disease), and some AV block can be expected to reverse (e.g., hypervagotonia due to recognizable and avoidable physiological factors, perioperative AV block due to hypothermia, or inflammation near the AV conduction system after surgery in this region). Conversely, some conditions may warrant pacemaker implantation because of the possibility of disease progression even if the AV block reverses transiently (e.g., sarcoidosis, amyloidosis, and neuromuscular diseases). Finally, permanent pacing for AV block after valve surgery follows a variable natural history; therefore, the decision for permanent pacing is at the physician's discretion (84).

Recommendations for Acquired Atrioventricular Block in Adults

CLASS I

1. **Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level associated with bradycardia with symptoms (including heart failure) or ventricular arrhythmias presumed to be due to AV block. (*Level of Evidence: C*) (59,63,76,85)**
2. **Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level associated with arrhythmias and other medical conditions that require drug therapy that results in symptomatic bradycardia. (*Level of Evidence: C*) (59,63,76,85)**
3. **Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level in awake, symptom-free patients in sinus rhythm, with documented periods of asystole greater than or equal to 3.0 seconds (86) or any escape rate less than 40 bpm, or with an escape rhythm that is below the AV node. (*Level of Evidence: C*) (53,58)**
4. **Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level in awake, symptom-free patients with AF and bradycardia with 1 or more pauses of at least 5 seconds or longer. (*Level of Evidence: C*)**

5. **Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level after catheter ablation of the AV junction. (*Level of Evidence: C*) (87,88)**
6. **Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level associated with postoperative AV block that is not expected to resolve after cardiac surgery. (*Level of Evidence: C*) (84,85,89,90)**
7. **Permanent pacemaker implantation is indicated for third-degree and advanced second-degree AV block at any anatomic level associated with neuromuscular diseases with AV block, such as myotonic muscular dystrophy, Kearns-Sayre syndrome, Erb dystrophy (limb-girdle muscular dystrophy), and peroneal muscular atrophy, with or without symptoms. (*Level of Evidence: B*) (91–97)**
8. **Permanent pacemaker implantation is indicated for second-degree AV block with associated symptomatic bradycardia regardless of type or site of block. (*Level of Evidence: B*) (74)**
9. **Permanent pacemaker implantation is indicated for asymptomatic persistent third-degree AV block at any anatomic site with average awake ventricular rates of 40 bpm or faster if cardiomegaly or LV dysfunction is present or if the site of block is below the AV node. (*Level of Evidence: B*) (76,78)**
10. **Permanent pacemaker implantation is indicated for second- or third-degree AV block during exercise in the absence of myocardial ischemia. (*Level of Evidence: C*) (81,82)**

CLASS IIa

1. **Permanent pacemaker implantation is reasonable for persistent third-degree AV block with an escape rate greater than 40 bpm in asymptomatic adult patients without cardiomegaly. (*Level of Evidence: C*) (59,63,64,76,82,85)**
2. **Permanent pacemaker implantation is reasonable for asymptomatic second-degree AV block at intra- or infra-His levels found at electrophysiological study. (*Level of Evidence: B*) (74,76,78)**
3. **Permanent pacemaker implantation is reasonable for first- or second-degree AV block with symptoms similar to those of pacemaker syndrome or hemodynamic compromise. (*Level of Evidence: B*) (70,71)**
4. **Permanent pacemaker implantation is reasonable for asymptomatic type II second-degree AV block with a narrow QRS. When type II second-degree AV block occurs with a wide QRS, including isolated right bundle-branch block, pacing becomes a Class I recommendation. (See Section 2.1.3, "Chronic Bifascicular Block.") (*Level of Evidence: B*) (70,76,80,85)**

CLASS IIb

1. **Permanent pacemaker implantation may be considered for neuromuscular diseases such as myotonic muscular dystrophy, Erb dystrophy (limb-girdle muscular dystrophy), and peroneal muscular atrophy with any degree of AV block (including first-degree AV block), with or without symptoms, because there may be unpredictable progression of AV conduction disease. (*Level of Evidence: B*) (91–97)**
2. **Permanent pacemaker implantation may be considered for AV block in the setting of drug use and/or drug toxicity when the block is expected to recur even after the drug is withdrawn. (*Level of Evidence: B*) (98,99)**

CLASS III

1. **Permanent pacemaker implantation is not indicated for asymptomatic first-degree AV block. (*Level of Evidence: B*) (69) (See Section 2.1.3, "Chronic Bifascicular Block.")**
2. **Permanent pacemaker implantation is not indicated for asymptomatic type I second-degree AV block at the supra-His (AV node) level or that which is not known to be intra- or infra-Hisian. (*Level of Evidence: C*) (74)**
3. **Permanent pacemaker implantation is not indicated for AV block that is expected to resolve and is unlikely to recur (100) (e.g., drug toxicity, Lyme disease, or transient increases in vagal tone or during hypoxia in sleep apnea syndrome in the absence of symptoms). (*Level of Evidence: B*) (99,100)**

2.1.3. Chronic Bifascicular Block

Bifascicular block refers to ECG evidence of impaired conduction below the AV node in the right and left bundles. Alternating bundle-branch block (also known as bilateral bundle-branch block) refers to situations in which clear ECG evidence for block in all 3 fascicles is manifested on successive ECGs. Examples are right bundle-branch block and left bundle-branch block on successive ECGs or right bundle-branch block with associated left anterior fascicular block on 1 ECG and associated left posterior fascicular block on another ECG. Patients with first-degree AV block in association with bifascicular block and symptomatic, advanced AV block have a high mortality rate and a substantial incidence of sudden death (64,101). Although third-degree AV block is most often preceded by bifascicular block, there is evidence that the rate of progression of bifascicular block to third-degree AV block is slow (102). Furthermore, no single clinical or laboratory variable, including bifascicular block, identifies patients at high risk of death due to a future bradyarrhythmia caused by bundle-branch block (103).

Syncope is common in patients with bifascicular block. Although syncope may be recurrent, it is not associated with an increased incidence of sudden death (73,102–112). Even though pacing relieves the neurological symptoms, it does not reduce the occurrence of sudden death (108). An electrophysiological study may be helpful to evaluate and direct the treatment of inducible ventricular arrhythmias (113,114) that are common in patients with bifascicular block. There is convincing evidence that in the presence of permanent or transient third-degree AV block, syncope is associated with an increased incidence of sudden death regardless of the results of the electrophysiological study (64,114,115). Finally, if the cause of syncope in the presence of bifascicular block cannot be determined with certainty, or if treatments used (such as drugs) may exacerbate AV block, prophylactic permanent pacing is indicated, especially if syncope may have been due to transient third-degree AV block (102–112,116).

Of the many laboratory variables, the PR and HV intervals have been identified as possible predictors of third-degree AV block and sudden death. Although PR-interval prolongation is common in patients with bifascicular block, the delay is often at the level of the AV node. There is no correlation between the PR and HV intervals or between the length of the PR interval, progression to third-degree AV block, and sudden

death (107,109,116). Although most patients with chronic or intermittent third-degree AV block demonstrate prolongation of the HV interval during anterograde conduction, some investigators (110,111) have suggested that asymptomatic patients with bifascicular block and a prolonged HV interval should be considered for permanent pacing, especially if the HV interval is greater than or equal to 100 milliseconds (109). Although the prevalence of HV-interval prolongation is high, the incidence of progression to third-degree AV block is low. Because HV prolongation accompanies advanced cardiac disease and is associated with increased mortality, death is often not sudden or due to AV block but rather is due to the underlying heart disease itself and nonarrhythmic cardiac causes (102,103,108,109,111,114–117).

Atrial pacing at electrophysiological study in asymptomatic patients as a means of identifying patients at increased risk of future high- or third-degree AV block is controversial. The probability of inducing block distal to the AV node (i.e., intra- or infra-His) with rapid atrial pacing is low (102,110,111,118–121). Failure to induce distal block cannot be taken as evidence that the patient will not develop third-degree AV block in the future. However, if atrial pacing induces nonphysiological infra-His block, some consider this an indication for pacing (118). Nevertheless, infra-His block that occurs during either rapid atrial pacing or programmed stimulation at short coupling intervals may be physiological and not pathological, simply reflecting disparity between refractoriness of the AV node and His-Purkinje systems (122).

Recommendations for Permanent Pacing in Chronic Bifascicular Block

CLASS I

1. **Permanent pacemaker implantation is indicated for advanced second-degree AV block or intermittent third-degree AV block. (*Level of Evidence: B*) (63–68,101)**
2. **Permanent pacemaker implantation is indicated for type II second-degree AV block. (*Level of Evidence: B*) (73,75,79,123)**
3. **Permanent pacemaker implantation is indicated for alternating bundle-branch block. (*Level of Evidence: C*) (124)**

CLASS IIa

1. **Permanent pacemaker implantation is reasonable for syncope not demonstrated to be due to AV block when other likely causes have been excluded, specifically ventricular tachycardia (VT). (*Level of Evidence: B*) (102–111,113–119,123,125)**
2. **Permanent pacemaker implantation is reasonable for an incidental finding at electrophysiological study of a markedly prolonged HV interval (greater than or equal to 100 milliseconds) in asymptomatic patients. (*Level of Evidence: B*) (109)**
3. **Permanent pacemaker implantation is reasonable for an incidental finding at electrophysiological study of pacing-induced infra-His block that is not physiological. (*Level of Evidence: B*) (118)**

CLASS IIb

1. **Permanent pacemaker implantation may be considered in the setting of neuromuscular diseases such as myotonic muscular dystrophy, Erb dystrophy (limb-girdle muscular dystrophy), and peroneal muscular atrophy with bifascicular block or any fascicular block, with or without symptoms. (*Level of Evidence: C*) (91–97)**

CLASS III

1. **Permanent pacemaker implantation is not indicated for fascicular block without AV block or symptoms. (*Level of Evidence: B*) (103,107,109,116)**
2. **Permanent pacemaker implantation is not indicated for fascicular block with first-degree AV block without symptoms. (*Level of Evidence: B*) (103,107,109,116)**

2.1.4. Pacing for Atrioventricular Block Associated With Acute Myocardial Infarction

Indications for permanent pacing after myocardial infarction (MI) in patients experiencing AV block are related in large measure to the presence of intraventricular conduction defects. The criteria for patients with MI and AV block do not necessarily depend on the presence of symptoms. Furthermore, the requirement for temporary pacing in AMI does not by itself constitute an indication for permanent pacing (see "ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction" (6)). The long-term prognosis for survivors of AMI who have had AV block is related primarily to the extent of myocardial injury and the character of intraventricular conduction disturbances rather than the AV block itself (66,126–130). Patients with AMI who have intraventricular conduction defects, with the exception of isolated left anterior fascicular block, have an unfavorable short- and long-term prognosis and an increased risk of sudden death (66,79,126,128,130). This unfavorable prognosis is not necessarily due to development of high-grade AV block, although the incidence of such block is higher in postinfarction patients with abnormal intraventricular conduction (126,131,132).

When AV or intraventricular conduction block complicates AMI, the type of conduction disturbance, location of infarction, and relation of electrical disturbance to infarction must be considered if permanent pacing is contemplated. Even with data available, the decision is not always straightforward, because the reported incidence and significance of various conduction disturbances vary widely (133). Despite the use of thrombolytic therapy and primary angioplasty, which have decreased the incidence of AV block in AMI, mortality remains high if AV block occurs (130,134–137).

Although more severe disturbances in conduction have generally been associated with greater arrhythmic and nonarrhythmic mortality, (126–129,131,133) the impact of preexisting bundle-branch block on mortality after AMI is controversial (112,133). A particularly ominous prognosis is associated with left bundle-branch block combined with advanced second- or third-degree AV block and with right bundle-branch block combined with left anterior or left posterior fascicular block (105,112,127,129). Regardless of whether the infarction is anterior or inferior, the development of an intraventricular conduction delay reflects extensive myocardial damage rather than an electrical problem in isolation (129). Although AV block that occurs during inferior MI can be associated with a favorable long-term

clinical outcome, in-hospital survival is impaired irrespective of temporary or permanent pacing in this situation (134,135,138,139). Pacemakers generally should not be implanted with inferior MI if the peri-infarctional AV block is expected to resolve or is not expected to negatively affect long-term prognosis (136). When symptomatic high-degree or third-degree heart block complicates inferior MI, even when the QRS is narrow, permanent pacing may be considered if the block does not resolve. For the patient with recent MI with a left ventricular ejection fraction (LVEF) less than or equal to 35% and an indication for permanent pacing, consideration may be given to use of an ICD, a CRT device that provides pacing but not defibrillation capability (CRT-P), or a CRT device that incorporates both pacing and defibrillation capabilities (CRT-D) when improvement in LVEF is not anticipated.

Recommendations for Permanent Pacing After the Acute Phase of Myocardial Infarction*

CLASS I

1. **Permanent ventricular pacing is indicated for persistent second-degree AV block in the His-Purkinje system with alternating bundle-branch block or third-degree AV block within or below the His-Purkinje system after ST-segment elevation MI. (*Level of Evidence: B*) (79,126–129,131)**
2. **Permanent ventricular pacing is indicated for transient advanced second- or third-degree infranodal AV block and associated bundle-branch block. If the site of block is uncertain, an electrophysiological study may be necessary. (*Level of Evidence: B*) (126,127)**
3. **Permanent ventricular pacing is indicated for persistent and symptomatic second- or third-degree AV block. (*Level of Evidence: C*)**

CLASS IIb

1. **Permanent ventricular pacing may be considered for persistent second- or third-degree AV block at the AV node level, even in the absence of symptoms. (*Level of Evidence: B*) (58)**

CLASS III

1. **Permanent ventricular pacing is not indicated for transient AV block in the absence of intraventricular conduction defects. (*Level of Evidence: B*) (126)**
2. **Permanent ventricular pacing is not indicated for transient AV block in the presence of isolated left anterior fascicular block. (*Level of Evidence: B*) (128)**
3. **Permanent ventricular pacing is not indicated for new bundle-branch block or fascicular block in the absence of AV block. (*Level of Evidence: B*) (66,126)**
4. **Permanent ventricular pacing is not indicated for persistent asymptomatic first-degree AV block in the presence of bundle-branch or fascicular block. (*Level of Evidence: B*) (126)**

2.1.5. Hypersensitive Carotid Sinus Syndrome and Neurocardiogenic Syncope

The hypersensitive carotid sinus syndrome is defined as syncope or presyncope resulting from an extreme reflex response to carotid sinus stimulation. There are 2 components of the reflex:

Cardioinhibitory, which results from increased parasympathetic tone and is manifested by slowing of the sinus rate or prolongation of the PR interval and advanced AV block, alone or in combination.

Vasodepressor, which is secondary to a reduction in sympathetic activity that results in loss of vascular tone and hypotension. This effect is independent of heart rate changes.

Before concluding that permanent pacing is clinically indicated, the physician should determine the relative contribution of the 2 components of carotid sinus stimulation to the individual patient's symptom complex. Hyperactive response to carotid sinus stimulation is defined as asystole due to either sinus arrest or AV block of more than 3 seconds, a substantial symptomatic decrease in systolic blood pressure, or both (140). Pauses up to 3 seconds during carotid sinus massage are considered to be within normal limits. Such heart rate and hemodynamic responses may occur in normal subjects and patients with coronary artery disease. The cause-and-effect relation between the hypersensitive carotid sinus and the patient's symptoms must be drawn with great caution (141). Spontaneous syncope reproduced by carotid sinus stimulation should alert the physician to the presence of this syndrome. Minimal pressure on the carotid sinus in elderly patients may result in marked changes in heart rate and blood pressure yet may not be of clinical significance. Permanent pacing for patients with an excessive cardioinhibitory response to carotid stimulation is effective in relieving symptoms (142,143). Because 10% to 20% of patients with this syndrome may have an important vasodepressive component of their reflex response, it is desirable that this component be defined before one concludes that all symptoms are related to asystole alone. Among patients whose reflex response includes both cardioinhibitory and vasodepressive components, attention to the latter is essential for effective therapy in patients undergoing pacing.

Carotid sinus hypersensitivity should be considered in elderly patients who have had otherwise unexplained falls. In 1 study, 175 elderly patients who had fallen without loss of consciousness and who had pauses of more than 3 seconds during carotid sinus massage (thus fulfilling the diagnosis of carotid sinus hypersensitivity) were randomized to pacing or nonpacing therapy. The paced group had a significantly lower likelihood of subsequent falling episodes during follow-up (144).

Neurocardiogenic syncope and neurocardiogenic syndromes refer to a variety of clinical scenarios in which triggering of a neural reflex results in a usually self-limited episode of systemic hypotension characterized by both bradycardia and peripheral vasodilation (145,146). Neurocardiogenic syncope accounts for an estimated 10% to 40% of syncope episodes. Vasovagal syncope is a term used to denote one of the most common clinical scenarios within the category of neurocardiogenic syncopal syndromes. Patients classically have a prodrome of nausea and diaphoresis (often absent in the elderly), and there may be a positive family history of the condition. Spells may be considered situational (e.g., they may be triggered by pain, anxiety, stress, specific

*These recommendations are consistent with the "ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction" (6).

bodily functions, or crowded conditions). Typically, no evidence of structural heart disease is present. Other causes of syncope such as LV outflow obstruction, bradyarrhythmias, and tachyarrhythmias should be excluded. Head-up tilt-table testing may be diagnostic.

The role of permanent pacing in refractory neurocardiogenic syncope associated with significant bradycardia or asystole remains controversial. Approximately 25% of patients have a predominant vasodepressor reaction without significant bradycardia. Many patients will have a mixed vasodepressive/cardioinhibitory cause of their symptoms. It has been estimated that approximately one third of patients will have substantial bradycardia or asystole during head-up tilt testing or during observed and recorded spontaneous episodes of syncope. Outcomes from clinical trials have not been consistent. Results from a randomized controlled trial (147) in highly symptomatic patients with bradycardia demonstrated that permanent pacing increased the time to the first syncopal event. Another study demonstrated that DDD (a dual-chamber pacemaker that senses/paces in the atrium/ventricle and is inhibited/triggered by intrinsic rhythm) pacing with a sudden bradycardia response function was more effective than beta blockade in preventing recurrent syncope in highly symptomatic patients with vasovagal syncope and relative bradycardia during tilt-table testing (148). In VPS (Vasovagal Pacemaker Study) (149), the actuarial rate of recurrent syncope at 1 year was 18.5% for pacemaker patients and 59.7% for control patients. However, in VPS-II (Vasovagal Pacemaker Study II) (150), a double-blind randomized trial, pacing therapy did not reduce the risk of recurrent syncopal events. In VPS-II, all patients received a permanent pacemaker and were randomized to therapy versus no therapy in contrast to VPS, in which patients were randomized to pacemaker implantation versus no pacemaker. On the basis of VPS-II and prevailing expert opinion (145), pacing therapy is not considered first-line therapy for most patients with neurocardiogenic syncope. However, pacing therapy does have a role for some patients, specifically those with little or no prodrome before their syncopal event, those with profound bradycardia or asystole during a documented event, and those in whom other therapies have failed. Dual-chamber pacing, carefully prescribed on the basis of tilt-table test results with consideration of alternative medical therapy, may be effective in reducing symptoms if the patient has a significant cardioinhibitory component to the cause of their symptoms. Although spontaneous or provoked prolonged pauses are a concern in this population, the prognosis without pacing is excellent (151).

The evaluation of patients with syncope of undetermined origin should take into account clinical status and should not overlook other, more serious causes of syncope, such as ventricular tachyarrhythmias.

Recommendations for Permanent Pacing in Hypersensitive Carotid Sinus Syndrome and Neurocardiogenic Syncope

CLASS I

1. **Permanent pacing is indicated for recurrent syncope caused by spontaneously occurring carotid sinus stimulation and carotid sinus pressure that induces ventricular asystole of more than 3 seconds. (*Level of Evidence: C*) (142,152)**

CLASS IIa

1. **Permanent pacing is reasonable for syncope without clear, provocative events and with a hypersensitive cardioinhibitory response of 3 seconds or longer. (*Level of Evidence: C*) (142)**

CLASS IIb

1. **Permanent pacing may be considered for significantly symptomatic neurocardiogenic syncope associated with bradycardia documented spontaneously or at the time of tilt-table testing. (*Level of Evidence: B*) (147,148,150,153)**

CLASS III

1. **Permanent pacing is not indicated for a hypersensitive cardioinhibitory response to carotid sinus stimulation without symptoms or with vague symptoms. (*Level of Evidence: C*)**
2. **Permanent pacing is not indicated for situational vasovagal syncope in which avoidance behavior is effective and preferred. (*Level of Evidence: C*)**

2.2. Pacing for Specific Conditions

The following sections on cardiac transplantation, neuromuscular diseases, sleep apnea syndromes, and infiltrative and inflammatory diseases are provided to recognize developments in these specific areas and new information that has been obtained since publication of prior guidelines. Some of the information has been addressed in prior sections but herein is explored in more detail.

2.2.1. Cardiac Transplantation

The incidence of bradyarrhythmias after cardiac transplantation varies from 8% to 23% (154–156). Most bradyarrhythmias are associated with SND and are more ominous after transplantation, when the basal heart rate should be high. Significant bradyarrhythmias and asystole have been associated with reported cases of sudden death (157). Attempts to treat the bradycardia temporarily with measures such as theophylline(158) may minimize the need for pacing. To accelerate rehabilitation, some transplant programs recommend more liberal use of cardiac pacing for persistent postoperative bradycardia, although approximately 50% of patients show resolution of the bradyarrhythmia within 6 to 12 months (159–161). The role of prophylactic pacemaker implantation is unknown for patients who develop bradycardia and syncope in the setting of rejection, which may be associated with localized inflammation of the conduction system. Posttransplant patients who have irreversible SND or AV block with previously stated Class I indications should have permanent pacemaker implantation, as the benefits of the atrial rate contribution to cardiac output and to chronotropic competence may optimize the patient's functional status. When recurrent syncope develops late after transplantation, pacemaker implantation may be considered despite repeated negative evaluations, as sudden episodes of bradycardia are often eventually documented and may be a sign of transplant vasculopathy.

Recommendations for Pacing After Cardiac Transplantation

CLASS I

1. **Permanent pacing is indicated for persistent inappropriate or symptomatic bradycardia not expected to resolve and for other Class I indications for permanent pacing. (*Level of Evidence: C*)**

CLASS IIb

1. **Permanent pacing may be considered when relative bradycardia is prolonged or recurrent, which limits rehabilitation or discharge after postoperative recovery from cardiac transplantation. (*Level of Evidence: C*)**
2. **Permanent pacing may be considered for syncope after cardiac transplantation even when bradyarrhythmia has not been documented. (*Level of Evidence: C*)**

2.2.2. Neuromuscular Diseases

Conduction system disease with progression to complete AV block is a well-recognized complication of several neuromuscular disorders, including myotonic dystrophy and Emery-Dreifuss muscular dystrophy. Supraventricular and ventricular arrhythmias may also be observed. Implantation of a permanent pacemaker has been found useful even in asymptomatic patients with an abnormal resting ECG or with HV interval prolongation during electrophysiological study (162). Indications for pacing have been addressed in previous sections on AV block.

2.2.3. Sleep Apnea Syndrome

A variety of heart rhythm disturbances may occur in obstructive sleep apnea. Most commonly, these include sinus bradycardia or pauses during hypopneic episodes. Atrial tachyarrhythmias may also be observed, particularly during the arousal phase that follows the offset of apnea. A small retrospective trial of atrial overdrive pacing in the treatment of sleep apnea demonstrated a decrease "in episodes of central or obstructive sleep apnea without reducing the total sleep time" (163). Subsequent randomized clinical trials have not validated a role for atrial overdrive pacing in obstructive sleep apnea (164,165). Furthermore, nasal continuous positive airway pressure therapy has been shown to be highly effective for obstructive sleep apnea, whereas atrial overdrive pacing has not (166,167). Whether cardiac pacing is indicated among patients with obstructive sleep apnea and persistent episodes of bradycardia despite nasal continuous positive airway pressure has not been established.

Central sleep apnea and Cheyne-Stokes sleep-disordered breathing frequently accompany systolic heart failure and are associated with increased mortality (168). CRT has been shown to reduce central sleep apnea and increase sleep quality in heart failure patients with ventricular conduction delay (169). This improvement in sleep-disordered breathing may be due to the beneficial effects of CRT on LV function and central hemodynamics, which favorably modifies the neuroendocrine reflex cascade in central sleep apnea.

2.2.4. Cardiac Sarcoidosis

Cardiac sarcoidosis usually affects individuals aged 20 to 40 years and is associated with noncaseating granulomas with an affinity for involvement of the AV conduction system, which results in various degrees of AV conduction block. Myocardial involvement occurs in 25% of patients with sarcoidosis, as many as 30% of whom develop complete heart block. Owing to the possibility of disease progression, pacemaker implantation is recommended even if high-grade or complete AV conduction block reverses transiently (170–172).

Cardiac sarcoidosis can also be a cause of life-threatening ventricular arrhythmias with sustained monomorphic VT due to myocardial involvement (173–175). Sudden cardiac arrest may be the initial manifestation of the condition, and patients may have few if any manifestations of dysfunction in organ systems other than the heart (173,174). Although there are no large randomized trials or prospective registries of patients with cardiac sarcoidosis, the available literature indicates that cardiac sarcoidosis with heart block, ventricular arrhythmias, or LV dysfunction is associated with a poor prognosis. Therapy with steroids or other immunosuppressant agents may prevent progression of the cardiac involvement. Bradyarrhythmias warrant pacemaker therapy, but they are not effective in preventing or treating life-threatening ventricular arrhythmias. Sufficient clinical data are not available to stratify risk of SCD among patients with cardiac sarcoidosis. Accordingly, clinicians must use the available literature along with their own clinical experience and judgment in making management decisions regarding ICD therapy. Consideration should be given to symptoms such as syncope, heart failure status, LV function, and spontaneous or induced ventricular arrhythmias at electrophysiological study to make individualized decisions regarding use of the ICD for primary prevention of SCD.

2.3. Prevention and Termination of Arrhythmias by Pacing

Under certain circumstances, an implanted pacemaker may be useful to treat or prevent recurrent ventricular and SVTs (176–185). Re-entrant rhythms including atrial flutter, paroxysmal re-entrant SVT, and VT may be terminated by a variety of pacing techniques, including programmed stimulation and short bursts of rapid pacing (186,187). Although rarely used in contemporary practice after tachycardia detection, these antitachyarrhythmia devices may automatically activate a pacing sequence or respond to an external instruction (e.g., application of a magnet).

Prevention of arrhythmias by pacing has been demonstrated in certain situations. In some patients with long-QT syndrome, recurrent pause-dependent VT may be prevented by continuous pacing (188). A combination of pacing and beta blockade has been reported to shorten the QT interval and help prevent SCD (189,190). ICD therapy in combination with overdrive suppression pacing should be considered in high-risk patients.

Although this technique is rarely used today given the availability of catheter ablation and antiarrhythmic drugs, atrial synchronous ventricular pacing may prevent recurrences of reentrant SVT (191). Furthermore, although ventricular ectopic activity may be suppressed by pacing in other conditions, serious or symptomatic arrhythmias are rarely prevented (192).

Potential recipients of antitachyarrhythmia devices that interrupt arrhythmias should undergo extensive testing before implantation to ensure that the devices safely and reliably terminate the tachyarrhythmias without accelerating the tachycardia or causing proarrhythmia. Patients for whom an antitachycardia pacemaker has been prescribed have usually been unresponsive to antiarrhythmic drugs or were receiving agents that could not control their cardiac arrhythmias. When permanent antitachycardia pacemakers detect and interrupt SVT, all pacing should be done in the atrium because of the risk of ventricular pacing–induced proarrhythmia (176,193). Permanent antitachycardia pacing (ATP) as monotherapy for VT is not appropriate given that ATP algorithms are available in tiered-therapy ICDs that have the capability for cardioversion and defibrillation in cases when ATP is ineffective or causes acceleration of the treated tachycardia.

Recommendations for Permanent Pacemakers That Automatically Detect and Pace to Terminate Tachycardias

CLASS IIa

1. **Permanent pacing is reasonable for symptomatic recurrent SVT that is reproducibly terminated by pacing when catheter ablation and/or drugs fail to control the arrhythmia or produce intolerable side effects. (*Level of Evidence: C*) (177–179,181,182)**

CLASS III

1. **Permanent pacing is not indicated in the presence of an accessory pathway that has the capacity for rapid anterograde conduction. (*Level of Evidence: C*)**

2.3.1. Pacing to Prevent Atrial Arrhythmias

Many patients with indications for pacemaker or ICD therapy have atrial tachyarrhythmias that are recognized before or after device implantation (194). Re-entrant atrial tachyarrhythmias are susceptible to termination with ATP. Additionally, some atrial tachyarrhythmias that are due to focal automaticity may respond to overdrive suppression. Accordingly, some dual-chamber pacemakers and ICDs incorporate suites of atrial therapies that are automatically applied upon detection of atrial tachyarrhythmias.

The efficacy of atrial ATP is difficult to measure, primarily because atrial tachyarrhythmias tend to initiate and terminate spontaneously with a very high frequency. With device-classified efficacy criteria, approximately 30% to 60% of atrial tachyarrhythmias may be terminated with atrial ATP in patients who receive pacemakers for symptomatic bradycardia (195–197). Although this has been associated with a reduction in atrial tachyarrhythmia burden over time in selected patients (195,196), the success of this approach has not been duplicated reliably in randomized clinical trials (197). Similar efficacy has been demonstrated in ICD patients (194,198,199) without compromising detection of VT, ventricular fibrillation (VF), or ventricular proarrhythmia (200). In either situation, automatic atrial therapies should not be activated until the atrial lead is chronically stable, because dislodgement into the ventricle could result in the induction of VT/VF.

2.3.2. Long-QT Syndrome

The use of cardiac pacing with beta blockade for prevention of symptoms in patients with the congenital long-QT syndrome is supported by observational studies (189,201,202). The primary benefit of pacemaker therapy may be in patients with pause-dependent initiation of ventricular tachyarrhythmias (203) or those with sinus bradycardia or advanced AV block in association with the congenital long-QT syndrome (204,205), which is most commonly associated with a sodium channelopathy. Benson et al (206) discuss sinus bradycardia due to a (sodium) channelopathy. Although pacemaker implantation may reduce the incidence of symptoms in these patients, the long-term survival benefit remains to be determined (189,201,204).

Recommendations for Pacing to Prevent Tachycardia

CLASS I

1. **Permanent pacing is indicated for sustained pause-dependent VT, with or without QT prolongation. (*Level of Evidence: C*) (188,189)**

CLASS IIa

1. **Permanent pacing is reasonable for high-risk patients with congenital long-QT syndrome. (*Level of Evidence: C*) (188,189)**

CLASS IIb

1. **Permanent pacing may be considered for prevention of symptomatic, drug-refractory, recurrent AF in patients with coexisting SND. (*Level of Evidence: B*) (31,184,207)**

CLASS III

1. **Permanent pacing is not indicated for frequent or complex ventricular ectopic activity without sustained VT in the absence of the long-QT syndrome. (*Level of Evidence: C*) (192)**
2. **Permanent pacing is not indicated for torsade de pointes VT due to reversible causes. (*Level of Evidence: A*) (190,203)**

2.3.3. Atrial Fibrillation (Dual-Site, Dual-Chamber, Alternative Pacing Sites)

In some patients with bradycardia-dependent AF, atrial pacing may be effective in reducing the frequency of recurrences (208). In MOST, 2,010 patients with SND were randomized between DDDR and VVIR pacing. After a mean follow-up of 33 months, there was a 21% lower risk of AF ($p=0.008$) in the DDDR group than in the VVIR group (209). Other trials are under way to assess the efficacy of atrial overdrive pacing algorithms and algorithms that react to premature atrial complexes in preventing AF, but data to date are sparse and inconsistent (197,210). Dual-site right atrial pacing or alternate single-site atrial pacing from unconventional sites (e.g., atrial septum or Bachmann's bundle) may offer additional benefits to single-site right atrial pacing from the appendage in patients with symptomatic drug-refractory AF and concomitant bradyarrhythmias; however, results from these studies are also contradictory and inconclusive (211,212). Additionally, analysis of the efficacy of pacing prevention algorithms and alternative pacing sites is limited by short-term follow-up (213). In patients with sick sinus syndrome

and intra-atrial block (P wave more than 180 milliseconds), biatrial pacing may lower recurrence rates of AF (214).

Recommendation for Pacing to Prevent Atrial Fibrillation

CLASS III

1. **Permanent pacing is not indicated for the prevention of AF in patients without any other indication for pacemaker implantation. (*Level of Evidence: B*) (215)**

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 central 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 (HCM) is discussed separately in Section 2.4.2, "Obstructive Hypertrophic Cardiomyopathy."

2.4.1. Cardiac Resynchronization Therapy (UPDATED)

(See *Online Data Supplement* for additional data on the trials that comprise the basis for the recommendations from this section.)

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 LVEF ≤30%, ischemic etiology of heart failure (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 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 (558). Prolongation of the QRS duration occurs in approximately one third of patients with advanced HF (559,560) 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 (561).

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 (562,563,564). 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 (542,565,566).

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% (567). 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) (543). 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 (544) 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 (544).

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 is as high as 70% among patients with QRS duration >150 ms and intraventricular mechanical delay, as identified by several echocardiographic techniques (561,568). However, the aggregate clinical experience has consistently demonstrated that a significant clinical benefit from CRT is greatest among patients with QRS duration >150 ms (569,570). In a meta-analysis of 5 trials involving 6501 patients, CRT significantly decreased the primary endpoint of death or hospitalization for HF in patients with QRS duration ≥150 ms (HR: 0.58; 95% CI: 0.50 to 0.68; $p<0.00001$) but not in patients with QRS duration <150 ms (HR: 0.95; 95% CI: 0.83 to 1.10; $p=0.51$) (569). 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 (570,571). 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 (1d) is the limitation of the recommendation for Class I indication to patients with LBBB pattern as compared to those with non-LBBB. For patients with QRS duration ≥120 ms who do not have a complete LBBB (non-LBBB patterns), evidence for benefit with CRT is less compelling than in the presence of LBBB (572,573,574). 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 (571a). 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) (571a). 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 (547,557) (see RAFT [Resynchronization-Defibrillation for Ambulatory Heart Failure Trial] (547) 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 (549,551,575). No large trial has yet demonstrated clinical benefit among patients without QRS prolongation, even when they have been selected with echocardiographic measures of dyssynchrony (576).

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 (577). A subanalysis of MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) (546) 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 (578).

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 (550,552,579). The benefit of CRT in patients with atrial fibrillation is more pronounced in those with depressed ejection fraction (551). 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 (580). 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 (581). 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 (582).

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 (583). Although a benefit has occasionally been described in patients with more severe acute decompensation that required brief positive intravenous 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 (545,584).

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 (543), 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 (583).

Perhaps the most significant changes in the present document compared to the 2008 DBT Guideline 1d 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 (547,548,585), 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 endpoint, a composite of death or

HF event, was reduced by 34% by CRT-D (HR: 0.66), with comparable benefit for both ischemic and nonischemic etiology of HF. HF events were reduced by 41%, without significant reduction in mortality rate. CRT-D therapy was demonstrated to be of more benefit in women than in men (HR: 0.37 and 0.76, respectively) and in patients with QRS duration ≥150 ms than in patients with QRS duration <150 ms (HR: 0.48 and 1.06, respectively) (546). 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) (540).

RAFT (547) 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 (546,547).

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 (548). 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) (548).

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 (585). 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% (548,585). For patients with NYHA class II, trials showing mortality rate benefit included those with LVEF ≤30% (546,547). A mortality rate benefit with CRT has not been shown for patients who are NYHA class I (547). 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 (585). Similarly, for patients with LVEF ≤40%, trials demonstrating improvement in function have included those who are NYHA class I and II (548). 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 (546,547,548,585).

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 (546,548,585,586). 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 (546,547). 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 IIb; 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 (578,587).

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 (588) and the European Society of Cardiology (589) 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*) (546,547). 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.

Recommendations for Cardiac Resynchronization Therapy

See Appendix 6, "Indications for CRT Therapy–Algorithm."

CLASS I

1. **CRT is indicated for patients who have LVEF less than or equal to 35%, sinus rhythm, LBBB with a QRS duration greater than or equal to 150 ms, and NYHA class II, (546,547) III, or ambulatory IV (542–545); symptoms on GDMT. *(Level of Evidence: A for NYHA class III/IV; Level of Evidence: B for NYHA class II)***

CLASS IIa

1. **CRT can be useful for patients who have LVEF less than or equal to 35%, sinus rhythm, LBBB with a QRS duration 120 to 149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT (542–544,546–548). (*Level of Evidence: B*)**
2. **CRT can be useful for patients who have LVEF less than or equal to 35%, sinus rhythm, a non-LBBB pattern with a QRS duration greater than or equal to 150 ms, and NYHA class III/ambulatory class IV symptoms on GDMT (542–544,547). (*Level of Evidence: A*)**
3. **CRT can be useful in patients with atrial fibrillation and LVEF less than or equal to 35% on GDMT if a) the patient requires ventricular pacing or otherwise meets CRT criteria and b) AV nodal ablation or pharmacologic rate control will allow near 100% ventricular pacing with CRT (549–553,575). (*Level of Evidence: B*)**
4. **CRT can be useful for patients on GDMT who have LVEF less than or equal to 35% and are undergoing new or replacement device placement with anticipated requirement for significant (>40%) ventricular pacing (551,554,555,556). (*Level of Evidence: C*)**

CLASS IIb

1. **CRT may be considered for patients who have LVEF less than or equal to 30%, ischemic etiology of heart failure, sinus rhythm, LBBB with a QRS duration of greater than or equal to 150 ms, and NYHA class I symptoms on GDMT (546,547). (*Level of Evidence: C*)**
2. **CRT may be considered for patients who have LVEF less than or equal to 35%, sinus rhythm, a non-LBBB pattern with QRS duration 120 to 149 ms, and NYHA class III/ambulatory class IV on GDMT (547,557). (*Level of Evidence: B*)**
3. **CRT may be considered for patients who have LVEF less than or equal to 35%, sinus rhythm, a non-LBBB pattern with a QRS duration greater than or equal to 150 ms, and NYHA class II symptoms on GDMT (546,547). (*Level of Evidence: B*)**

CLASS III: NO BENEFIT

1. **CRT is not recommended for patients with NYHA class I or II symptoms and non-LBBB pattern with QRS duration less than 150 ms (546,547,557). (*Level of Evidence: B*)**
2. **CRT is not indicated for patients whose comorbidities and/or frailty limit survival with good functional capacity to less than 1 year (545). (*Level of Evidence: C*)**

2.4.2. Obstructive Hypertrophic Cardiomyopathy

Early nonrandomized studies demonstrated a fall in the LV outflow gradient with dual-chamber pacing and a short AV delay and symptomatic improvement in some patients with obstructive HCM (232–235). One long-term study (236) in 8 patients supported the long-term benefit of dual-chamber pacing in this group of patients. The outflow gradient was reduced even after cessation of pacing, which suggests that some ventricular remodeling had occurred as a consequence of pacing. Two randomized trials (235,237) demonstrated subjective improvement in approximately 50% of study participants, but there was no correlation with gradient reduction, and a significant placebo effect was present. A third randomized, double-blinded trial (238) failed to demonstrate any overall improvement in QOL with pacing, although there was a suggestion that elderly patients (more than 65 years of age) may derive more benefit from pacing.

In a small group of patients with symptomatic, hypertensive cardiac hypertrophy with cavity obliteration, VDD pacing with premature excitation statistically improved exercise capacity, cardiac reserve, and clinical symptoms (239). Dual-chamber pacing may improve symptoms and LV outflow gradient in pediatric patients. However, rapid atrial rates, rapid AV conduction, and congenital mitral valve abnormalities may preclude effective pacing in some patients (240).

There are currently no data available to support the contention that pacing alters the clinical course of the disease or improves survival or long-term QOL in HCM. Therefore, routine implantation of dual-chamber pacemakers should not be advocated in all patients with symptomatic obstructive HCM. Patients who may benefit the most are those with significant gradients (more than 30 mm Hg at rest or more than 50 mm Hg provoked). (235,241–243). Complete heart block can develop after transcoronary alcohol ablation of

septal hypertrophy in patients with HCM and should be treated with permanent pacing (244).

For the patient with obstructive HCM who is at high risk for sudden death and who has an indication for pacemaker implantation, consideration should be given to completion of risk stratification of the patient for SCD and to implantation of an ICD for primary prevention of sudden death. A single risk marker of high risk for sudden cardiac arrest may be sufficient to justify consideration for prophylactic ICD implantation in selected patients with HCM (245).

Recommendations for Pacing in Patients With Hypertrophic Cardiomyopathy

CLASS I

1. **Permanent pacing is indicated for SND or AV block in patients with HCM as described previously (see Section 2.1.1, "Sinus Node Dysfunction," and Section 2.1.2, "Acquired Atrioventricular Block in Adults"). (*Level of Evidence: C*)**

CLASS IIa

1. **Permanent pacing may be considered in medically refractory symptomatic patients with HCM and significant resting or provoked LV outflow tract obstruction. (*Level of Evidence: A*) As for Class I indications, when risk factors for SCD are present, consider a DDD ICD (see Section 3, "Indications for Implantable Cardioverter-Defibrillator Therapy") (233,235,237,238,246,247).**

CLASS III

1. **Permanent pacemaker implantation is not indicated for patients who are asymptomatic or whose symptoms are medically controlled. (*Level of Evidence: C*)**
2. **Permanent pacemaker implantation is not indicated for symptomatic patients without evidence of LV outflow tract obstruction. (*Level of Evidence: C*)**

2.5. Pacing in Children, Adolescents, and Patients With Congenital Heart Disease

The most common indications for permanent pacemaker implantation in children, adolescents, and patients with congenital heart disease may be classified as 1) symptomatic sinus bradycardia, 2) the bradycardia-tachycardia syndromes, and 3) advanced second- or third-degree AV block, either congenital or postsurgical. Although the general indications for pacemaker implantation in children and adolescents (defined as less than 19 years of age) (248) are similar to those in adults, there are several important considerations in young patients. First, an increasing number of young patients are long-term survivors of complex surgical procedures for congenital heart defects that result in palliation rather than correction of circulatory physiology. The residua of impaired ventricular function and abnormal physiology may result in symptoms due to sinus bradycardia or loss of AV synchrony at heart rates that do not produce symptoms in individuals with normal cardiovascular physiology (249,250). Hence, the indications for pacemaker implantation in these patients need to be based on the correlation of symptoms with relative bradycardia rather than absolute heart rate criteria. Second, the clinical significance of bradycardia is age dependent; whereas a heart rate of 45 bpm may be a normal finding in an adolescent, the same rate in a newborn or infant indicates profound bradycardia. Third, significant technical challenges may complicate device and transvenous lead implantation in very small patients or those with abnormalities of venous or intracardiac anatomy. Epicardial pacemaker lead implantation represents an alternative technique for these patients; however, the risks associated with sternotomy or thoracotomy and the somewhat higher incidence of lead failure must be considered when epicardial pacing systems are required (251). Fourth, because there are no randomized clinical trials of cardiac pacing in pediatric or congenital heart disease patients, the level of evidence for most recommendations is consensus based (*Level of Evidence: C*). Diagnoses that require pacing in both children and adults, such as long-QT syndrome or neuromuscular diseases, are discussed in specific sections on these topics in this document.

Bradycardia and associated symptoms in children are often transient (e.g., sinus arrest or paroxysmal AV block) and difficult to document (252). Although SND (sick sinus syndrome) is recognized in pediatric patients and may be associated with specific genetic channelopathies (206), it is not itself an indication for pacemaker implantation. In the young patient with sinus bradycardia, the primary criterion for pacemaker implantation is the concurrent observation of a symptom (e.g., syncope) with bradycardia (e.g., heart rate less than 40 bpm or asystole more than 3 seconds) (53,86,253). In general, correlation of symptoms with bradycardia is determined by ambulatory ECG or an implantable loop recorder (254). Symptomatic bradycardia is an indication for pacemaker implantation provided that other causes have been excluded. Alternative causes to be considered include apnea, seizures, medication effects, and neurocardiogenic mechanisms (255,256). In carefully selected cases, cardiac pacing has been effective in the prevention of recurrent seizures and syncope in infants with recurrent pallid breath-holding spells associated with profound bradycardia or asystole (257).

A variant of the bradycardia-tachycardia syndrome, sinus bradycardia that alternates with intra-atrial re-entrant tachycardia, is a significant problem after surgery for congenital heart disease. Substantial morbidity and mortality have been observed in patients with recurrent or chronic intra-atrial re-entrant tachycardia, with the loss of sinus rhythm an independent risk factor for the subsequent development of this arrhythmia (258,259). Thus, both long-term atrial pacing at physiological rates and atrial ATP have been reported as potential treatments for sinus bradycardia and the prevention or termination of recurrent episodes of intra-atrial re-entrant tachycardia (260,261). The results of either mode of pacing for this arrhythmia have been equivocal and remain a topic of considerable controversy (262,263). In other patients, pharmacological therapy (e.g., sotalol or amiodarone) may be effective in the control of intra-atrial re-entrant tachycardia but also result in symptomatic bradycardia (264). In these patients, radiofrequency catheter ablation of the intra-atrial re-entrant tachycardia circuit should be considered as an alternative to combined pharmacological and pacemaker therapies (265). Surgical resection of atrial tissue with con-

comitant atrial pacing has also been advocated for congenital heart disease patients with intra-atrial re-entrant tachycardia refractory to other therapies (266).

The indications for permanent pacing in patients with congenital complete AV block continue to evolve on the basis of improved definition of the natural history of the disease and advances in pacemaker technology and diagnostic methods. Pacemaker implantation is a Class I indication in the symptomatic individual with congenital complete AV block or the infant with a resting heart rate less than 55 bpm, or less than 70 bpm when associated with structural heart disease (267,268). In the asymptomatic child or adolescent with congenital complete AV block, several criteria (average heart rate, pauses in the intrinsic rate, associated structural heart disease, QT interval, and exercise tolerance) must be considered (208,269). Several studies have demonstrated that pacemaker implantation is associated with both improved long-term survival and prevention of syncopal episodes in asymptomatic patients with congenital complete AV block (270,271). However, periodic evaluation of ventricular function is required in patients with congenital AV block after pacemaker implantation, because ventricular dysfunction may occur as a consequence of myocardial autoimmune disease at a young age or pacemaker-associated dyssynchrony years or decades after pacemaker implantation (272,273). The actual incidence of ventricular dysfunction due to pacemaker-related chronic ventricular dyssynchrony remains undefined.

A very poor prognosis has been established for congenital heart disease patients with permanent postsurgical AV block who do not receive permanent pacemakers (209). Therefore, advanced second- or third-degree AV block that persists for at least 7 days and that is not expected to resolve after cardiac surgery is considered a Class I indication for pacemaker implantation (274). Conversely, patients in whom AV conduction returns to normal generally have a favorable prognosis (275). Recent reports have emphasized that there is a small but definite risk of late-onset complete AV block years or decades after surgery for congenital heart disease in patients with transient postoperative AV block (276,277). Limited data suggest that residual bifascicular conduction block and progressive PR prolongation may predict late-onset AV block (278). Because of the possibility of intermittent complete AV block, unexplained syncope is a Class IIa indication for pacing in individuals with a history of temporary postoperative complete AV block and residual bifascicular conduction block after a careful evaluation for both cardiac and noncardiac causes.

Additional details that need to be considered in pacemaker implantation in young patients include risk of paradoxical embolism due to thrombus formation on an endocardial lead system in the presence of residual intracardiac defects and the lifelong need for permanent cardiac pacing (279). Decisions about pacemaker implantation must also take into account the implantation technique (transvenous versus epicardial), with preservation of vascular access at a young age a primary objective (280).

Recommendations for Permanent Pacing in Children, Adolescents, and Patients With Congenital Heart Disease

CLASS I

1. **Permanent pacemaker implantation is indicated for advanced second- or third-degree AV block associated with symptomatic bradycardia, ventricular dysfunction, or low cardiac output. (*Level of Evidence: C*)**
2. **Permanent pacemaker implantation is indicated for SND with correlation of symptoms during age-inappropriate bradycardia. The definition of bradycardia varies with the patient's age and expected heart rate. (*Level of Evidence: B*) (53,86,253,257)**
3. **Permanent pacemaker implantation is indicated for postoperative advanced second- or third-degree AV block that is not expected to resolve or that persists at least 7 days after cardiac surgery. (*Level of Evidence: B*) (74,209)**
4. **Permanent pacemaker implantation is indicated for congenital third-degree AV block with a wide QRS escape rhythm, complex ventricular ectopy, or ventricular dysfunction. (*Level of Evidence: B*) (271–273)**
5. **Permanent pacemaker implantation is indicated for congenital third-degree AV block in the infant with a ventricular rate less than 55 bpm or with congenital heart disease and a ventricular rate less than 70 bpm. (*Level of Evidence: C*) (267,268)**

CLASS IIa

1. **Permanent pacemaker implantation is reasonable for patients with congenital heart disease and sinus bradycardia for the prevention of recurrent episodes of intra-atrial reentrant tachycardia; SND may be intrinsic or secondary to antiarrhythmic treatment. (*Level of Evidence: C*) (260,261,264)**
2. **Permanent pacemaker implantation is reasonable for congenital third-degree AV block beyond the first year of life with an average heart rate less than 50 bpm, abrupt pauses in ventricular rate that are 2 or 3 times the basic cycle length, or associated with symptoms due to chronotropic incompetence. (*Level of Evidence: B*) (208,270)**
3. **Permanent pacemaker implantation is reasonable for sinus bradycardia with complex congenital heart disease with a resting heart rate less than 40 bpm or pauses in ventricular rate longer than 3 seconds. (*Level of Evidence: C*)**
4. **Permanent pacemaker implantation is reasonable for patients with congenital heart disease and impaired hemodynamics due to sinus bradycardia or loss of AV synchrony. (*Level of Evidence: C*) (250)**
5. **Permanent pacemaker implantation is reasonable for unexplained syncope in the patient with prior congenital heart surgery complicated by transient complete heart block with residual fascicular block after a careful evaluation to exclude other causes of syncope. (*Level of Evidence: B*) (273,276–278)**

CLASS IIb

1. **Permanent pacemaker implantation may be considered for transient postoperative third-degree AV block that reverts to sinus rhythm with residual bifascicular block. (*Level of Evidence: C*) (275)**
2. **Permanent pacemaker implantation may be considered for congenital third-degree AV block in asymptomatic children or adolescents with an acceptable rate, a narrow QRS complex,**

Table 2. Choice of Pacemaker Generator in Selected Indications for Pacing

Pacemaker Generator	Sinus Node Dysfunction	Atrioventricular Block	Neurally Mediated Syncope or Carotid Sinus Hypersensitivity
Single-chamber atrial pacemaker	No suspected abnormality of atrioventricular conduction and not at increased risk for future atrioventricular block	Not appropriate	Not appropriate
	Maintenance of atrioventricular synchrony during pacing desired		
Single-chamber ventricular pacemaker	Maintenance of atrioventricular synchrony during pacing not necessary	Chronic atrial fibrillation or other atrial tachyarrhythmia or maintenance of atrioventricular synchrony during pacing not necessary	Chronic atrial fibrillation or other atrial tachyarrhythmia
	Rate response available if desired	Rate response available if desired	Rate response available if desired
Dual-chamber pacemaker	Atrioventricular synchrony during pacing desired	Rate response available if desired	Sinus mechanism present
	Suspected abnormality of atrioventricular conduction or increased risk for future atrioventricular block	Atrioventricular synchrony during pacing desired	Rate response available if desired
	Rate response available if desired	Atrial pacing desired	
		Rate response available if desired	
Single-lead, atrial-sensing ventricular pacemaker	Not appropriate	Desire to limit the number of pacemaker leads	Not appropriate

and normal ventricular function. (*Level of Evidence: B*) (270,271)

3. Permanent pacemaker implantation may be considered for asymptomatic sinus bradycardia after biventricular repair of congenital heart disease with a resting heart rate less than 40 bpm or pauses in ventricular rate longer than 3 seconds. (*Level of Evidence: C*)

CLASS III

1. Permanent pacemaker implantation is not indicated for transient postoperative AV block with return of normal AV conduction in the otherwise asymptomatic patient. (*Level of Evidence: B*) (274,275)

2. Permanent pacemaker implantation is not indicated for asymptomatic bifascicular block with or without first-degree AV block after surgery for congenital heart disease in the absence of prior transient complete AV block. (*Level of Evidence: C*)

3. Permanent pacemaker implantation is not indicated for asymptomatic type I second-degree AV block. (*Level of Evidence: C*)

4. Permanent pacemaker implantation is not indicated for asymptomatic sinus bradycardia with the longest relative risk interval less than 3 seconds and a minimum heart rate more than 40 bpm. (*Level of Evidence: C*)

2.6. Selection of Pacemaker Device

Once the decision has been made to implant a pacemaker in a given patient, the clinician must decide among a large number of available pacemaker generators and leads. Generator choices include single- versus dual-chamber versus biventricular devices, unipolar versus bipolar pacing/sensing configuration, presence and type of sensor for rate response, advanced features such as automatic capture verification, atrial therapies, size, and battery capacity. Lead choices include diameter, polarity, type of insulation material, and fixation mechanism (active versus passive). Other factors that importantly influence the choice of pacemaker system components include the capabilities of the pacemaker programmer, local availability of technical support, and remote monitoring capabilities.

Even after selecting and implanting the pacing system, the physician has a number of options for programming the device. In modern single-chamber pacemakers, programmable features include pacing mode, lower rate, pulse width and amplitude, sensitivity, and refractory period. Dual-chamber pacemakers have the same programmable features, as well as maximum tracking rate, AV delay, mode-switching algorithms for atrial arrhythmias, and others. Rate-responsive pacemakers require programmable features to regulate the relation between sensor output and pacing rate and to limit the maximum sensor-driven pacing rate. Biventricular pacemakers require the LV pacing output to be programmed, and often the delay between LV and RV pacing must also be programmed. With the advent of more sophisticated pacemaker generators, optimal programming of pacemakers has become increasingly complex and device-specific and requires specialized knowledge on the part of the physician.

Many of these considerations are beyond the scope of this document. Later discussion focuses primarily on the choice regarding the pacemaker prescription that has the greatest impact on procedural time and complexity, follow-up, patient outcome, and cost: the choice among single-chamber ventricular pacing, single-chamber atrial pacing, and dual-chamber pacing.

Table 2 summarizes the appropriateness of different pacemakers for the most commonly encountered indications for pacing. Figure 1 is a decision tree for selecting a pacing system for patients with AV block. Figure 2 is a decision tree for selecting a pacing system for patients with SND.

An important challenge for the physician in selecting a pacemaker system for a given patient is to anticipate progression of abnormalities of that patient's cardiac automaticity and conduction and then to select a system that will best

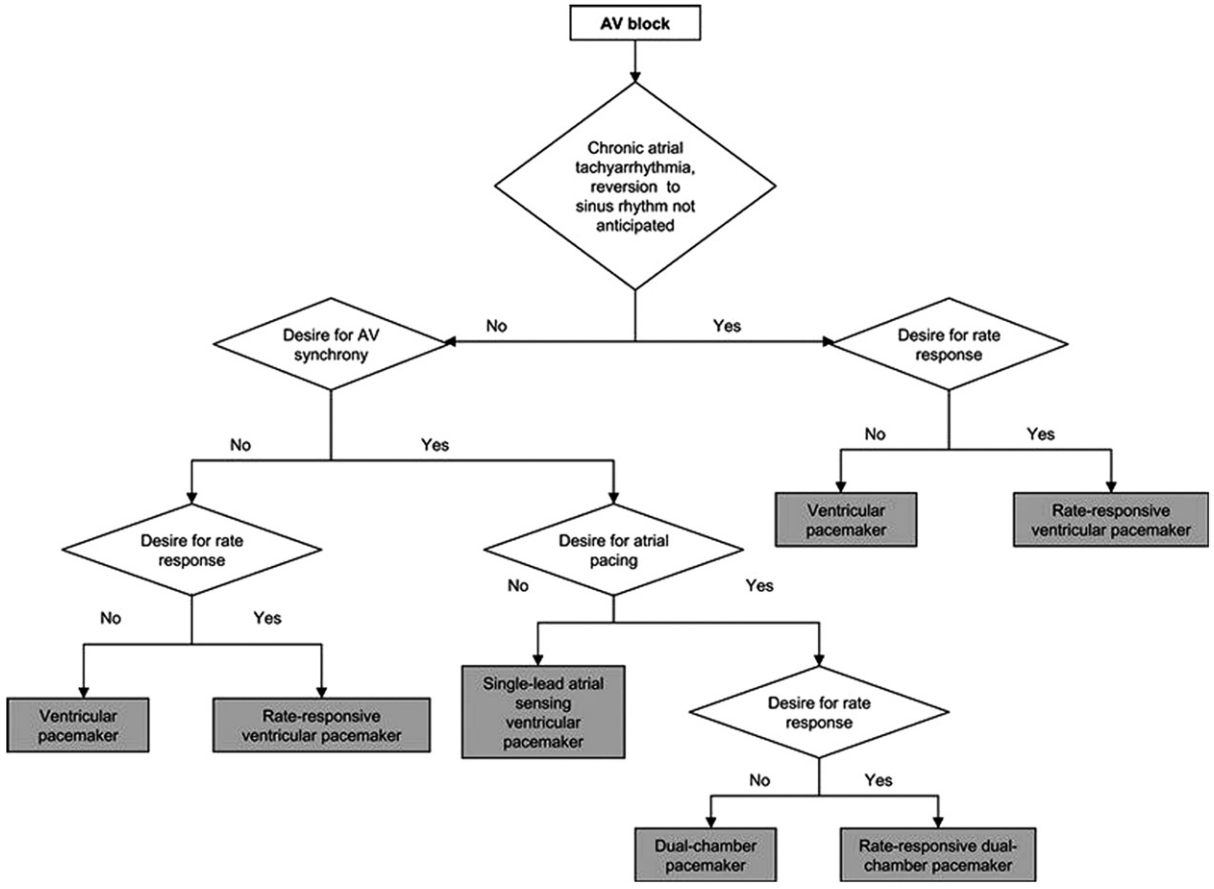


Figure 1. Selection of pacemaker systems for patients with atrioventricular block. Decisions are illustrated by diamonds. Shaded boxes indicate type of pacemaker. AV indicates atrioventricular.

accommodate these developments. Thus, it is reasonable to select a pacemaker with more extensive capabilities than needed at the time of implantation but that may prove useful in the future. Some patients with SND and paroxysmal AF, for example, may develop AV block in the future (as a result of natural progression of disease, drug therapy, or catheter ablation) and may ultimately benefit from a dual-chamber pacemaker with mode-switching capability.

Similarly, when pacemaker implantation is indicated, consideration should be given to implantation of a more capable device (CRT, CRT-P, or CRT-D) if it is thought likely that the patient will qualify for the latter within a short time period. For example, a patient who requires a pacemaker for heart block that occurs in the setting of MI who also has an extremely low LVEF may be best served by initial implantation of an ICD rather than a pacemaker. In such cases, the advantage of avoiding a second upgrade procedure should be balanced against the uncertainty regarding the ultimate need for the more capable device.

2.6.1. Major Trials Comparing Atrial or Dual-Chamber Pacing With Ventricular Pacing

Over the past decade, the principal debate with respect to choice of pacemaker systems has concerned the relative merits of dual-chamber pacing, single-chamber ventricular pacing, and single-chamber atrial pacing. The physiological rationale for atrial and dual-chamber pacing is preservation of AV synchrony; therefore, trials comparing these modes have often combined patients with atrial or dual-chamber pacemakers in a single treatment arm. There have been 5 major randomized trials comparing atrial or dual-chamber pacing with ventricular pacing; they are summarized in Table 3. Of the 5 studies, 2 were limited to patients paced for SND, 1 was limited to patients paced for AV block, and 2 included patients paced for either indication. Only the Danish study (281) included a true atrial pacing arm; among patients in the AAI/DDD arm in CTOPP (Canadian Trial of Physiologic Pacing), only 5.2% had an atrial pacemaker (282). A significant limitation of all of these studies is the percentage of patients (up to 37.6%) who crossed over from 1 treatment arm to another or otherwise dropped out of their assigned pacing mode.

An important consideration in the assessment of trials that compare pacing modes is the percent of pacing among the study patients. For example, a patient who is paced only for very infrequent sinus pauses or infrequent AV block will probably have a similar outcome with ventricular pacing as with dual-chamber pacing, regardless of any differential effects between the 2 pacing configurations. With the exception of the MOST study (31) and limited data in the UK-PACE trial (United Kingdom Pacing and Cardiovascular Events) (283), the trials included in Table 3 do not include information about the percent of atrial or ventricular pacing in the study patients.

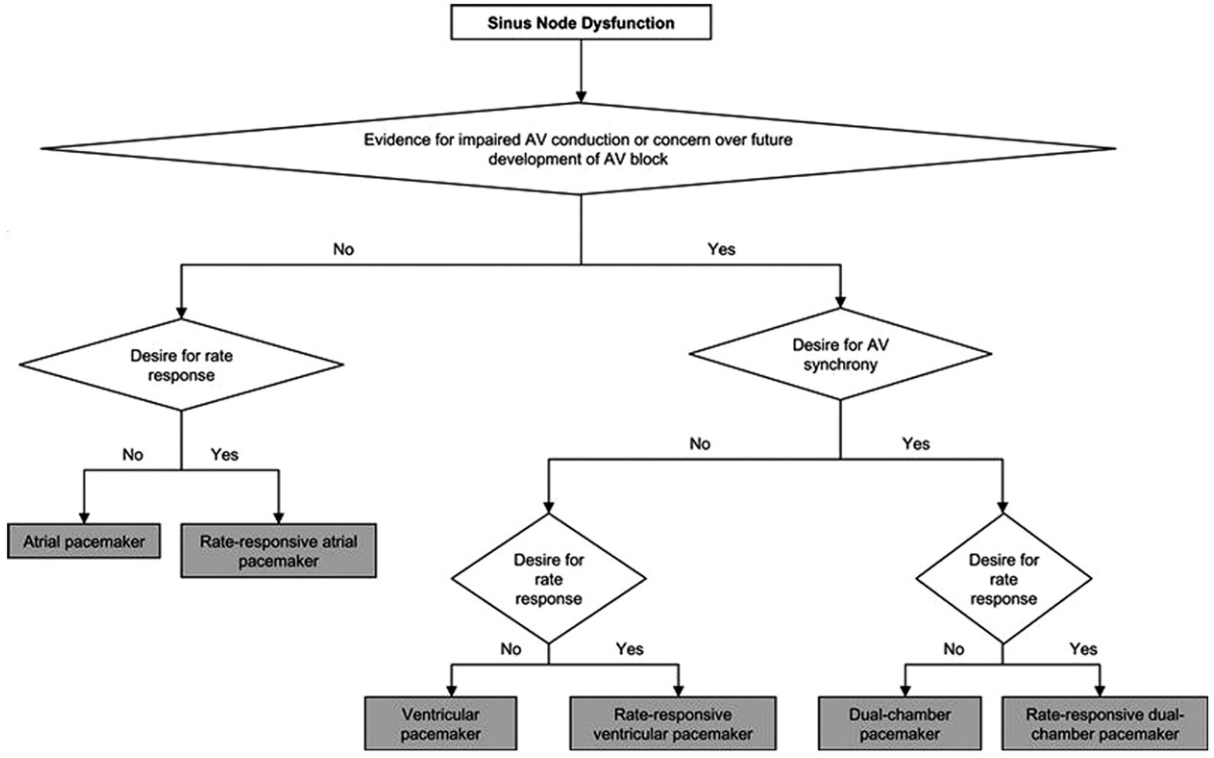


Figure 2. Selection of pacemaker systems for patients with sinus node dysfunction. Decisions are illustrated by diamonds. Shaded boxes indicate type of pacemaker. AV indicates atrioventricular.

2.6.2. Quality of Life and Functional Status End Points

Numerous studies have shown significant improvement in reported QOL and functional status after pacemaker implantation, (22,23,285,286) but there is also a well-documented placebo effect after device implantation (222). This section will focus on differences between pacing modes with respect to these outcomes.

In the subset of patients in the PASE (Pacemaker Selection in the Elderly) study who received implants for SND, dual-chamber pacing was associated with greater improvement than was ventricular pacing with regard to a minority of

Table 3. Randomized Trials Comparing Atrium-Based Pacing With Ventricular Pacing

Characteristics	Danish Study (281)	PASE (23)	CTOPP (282,284,285)	MOST (22,31,48,49,286,287)	UK-PACE (283)
Pacing indication	SND	SND and AVB	SND and AVB	SND	AVB
No. of patients randomized	225	407	2,568	2,010	2,021
Mean follow-up (years)	5.5	1.5	6.4	2.8	3
Pacing modes	AAI vs VVI	DDDR* vs VVIR*	DDD/AAI vs VVI(R)	DDDR vs VVIR*	DDD(R) vs VVI(R)
Atrium-based pacing superior with respect to:					
Quality of life or functional status	NA	• SND patients: yes • AVB patients: no	No	Yes	NA
Heart failure	Yes	No	No	Marginal	No
Atrial fibrillation	Yes	No	Yes	Yes	No
Stroke or thromboembolism	Yes	No	No	No	No
Mortality	Yes	No	No	No	No
Cross-over or pacing dropout	• VVI to AAI/DDD: 4% • AAI to DDD: 5% • AAI to VVI: 10%	VVIR* to DDDR*: 26%	• VVI(R) dropout: 7% • DDD/AAI dropout: 25%	VVIR* to DDDR*: 37.6%	• VVI(R) to DDD(R): 3.1% • DDD(R) dropout: 8.3%

R* added to pacing mode designation indicates rate-responsive pacemakers implanted in all patients. (R) added to pacing mode designation indicates rate-responsive pacemakers implanted in some patients.

AAI indicates atrial demand; AVB, atrioventricular block; CTOPP, Canadian Trial of Physiologic Pacing; DDD, fully automatic; MOST, Mode Selection Trial; PASE, Pacemaker Selection in the Elderly; SND, sinus node dysfunction; UK-PACE, United Kingdom Pacing and Cardiovascular Events; and VVI, ventricular demand.

QOL and functional status measures, but there were no such differences among patients paced for AV block (23). In the MOST patients, all of whom received implants for SND, dual-chamber–paced patients had superior outcomes in some but not all QOL and functional status measures (22,286). CTOPP, which included patients who received implants for both SND and AV block, failed to detect any difference between pacing modes with respect to QOL or functional status in a subset of 269 patients who underwent this evaluation; a breakdown by pacing indication was not reported (284).

Older cross-over studies of dual-chamber versus ventricular pacing, which allowed for intrapatient comparisons between the 2 modes, indicate improved functional status and patient preference for dual-chamber pacing. For instance, Sulke et al (288) studied 22 patients who received dual-chamber rate-responsive pacemakers for high-grade AV block and found improved exercise time, functional status, and symptoms with DDDR compared with VVIR pacing, as well as vastly greater patient preference for DDDR pacing.

2.6.3. Heart Failure End Points

A Danish study showed an improvement in heart failure status among atrially paced patients compared with ventricularly paced patients, as measured by NYHA functional class and diuretic use (281). MOST showed a marginal improvement in a similar heart failure score with dual-chamber versus ventricular pacing, as well as a weak association between dual-chamber pacing and fewer heart failure hospitalizations (22). None of the other studies listed in Table 3 detected a difference between pacing modes with respect to new-onset heart failure, worsening of heart failure, or heart failure hospitalization. A meta-analysis of the 5 studies listed in Table 3 did not show a significant difference between atrially paced- or dual-chamber–paced patients compared with ventricularly paced patients with respect to heart failure hospitalization (289).

2.6.4. Atrial Fibrillation End Points

The Danish study, MOST, and CTOPP showed significantly less AF among the atrially paced or dual-chamber–paced patients than the ventricularly paced patients (22,281,282). In MOST, the divergence in AF incidence became apparent at 6 months, whereas in CTOPP, the divergence was apparent only at 2 years. PASE, a much smaller study, did not detect any difference in AF between its 2 groups (23). The UK-PACE trial did not demonstrate a significant difference in AF between its 2 treatment arms; however, a trend toward less AF with dual-chamber pacing began to appear at the end of the scheduled 3-year follow-up period (28). The meta-analysis of the 5 studies listed in Table 3 showed a significant decrease in AF with atrial or dual-chamber pacing compared with ventricular pacing, with a hazard ratio (HR) of 0.80 (289).

2.6.5. Stroke or Thromboembolism End Points

Of the 5 studies listed in Table 3, only the Danish study detected a difference between pacing modes with respect to stroke or thromboembolism (281). However, the meta-analysis of the 5 studies in Table 3 showed a decrease of borderline statistical significance in stroke with atrial or dual-chamber pacing compared with ventricular pacing, with an HR of 0.81 (289).

2.6.6. Mortality End Points

The Danish study showed significant improvement in both overall mortality and cardiovascular mortality among the atrially paced patients compared with the ventricularly paced patients (281). None of the other studies showed a significant difference between pacing modes in either overall or cardiovascular mortality. The meta-analysis of the 5 studies in Table 3 did not show a significant difference between atrially paced or dual-chamber–paced patients compared with ventricularly paced patients with respect to overall mortality (289).

Taken together, the evidence from the 5 studies most strongly supports the conclusion that dual-chamber or atrial pacing reduces the incidence of AF compared with ventricular pacing in patients paced for either SND or AV block. There may also be a benefit of dual-chamber or atrial pacing with respect to stroke. The evidence also supports a modest improvement in QOL and functional status with dual-chamber pacing compared with ventricular pacing in patients with SND. The preponderance of evidence from these trials regarding heart failure and mortality argues against any advantage of atrial or dual-chamber pacing for these 2 end points.

2.6.7. Importance of Minimizing Unnecessary Ventricular Pacing

In the past 5 years, there has been increasing recognition of the deleterious clinical effects of RVA pacing, both in patients with pacemakers (48,49,215) and in those with ICDs (50,51,290). Among the patients in MOST with a normal native QRS duration, the percent of ventricular pacing was correlated with heart failure hospitalization and new onset of AF (48). It has been speculated that the more frequent ventricular pacing in patients randomized to DDDR pacing (90%) compared with patients randomized to VVIR pacing (58%) may have negated whatever positive effects may have accrued from the AV synchrony afforded by dual-chamber pacing in this study. A possible explanation for the striking benefits of AAI pacing found in the Danish study (281) described above is the obvious absence of ventricular pacing in patients with single-chamber atrial pacemakers (281).

In a subsequent Danish study, patients with SND were randomized between AAIR pacing, DDDR pacing with a long AV delay (300 milliseconds), and DDDR pacing with a short AV delay (less than or equal to 150 milliseconds) (45). The prevalence of ventricular pacing was 17% in the DDDR–long-AV-delay patients and 90% in the DDDR–short-AV-delay patients. At 2.9 years of follow-up, the incidence of AF was 7.4% in the AAIR group, 17.5% in the DDDR–long-AV-delay group, and 23.3% in the DDDR–short-AV-delay group. There were also increases in left atrial and LV dimensions seen in both DDDR groups but not the AAIR group. This study supports the superiority of atrial over dual-chamber pacing and indicates that there may be deleterious effects from even the modest amount of ventricular pacing that typically occurs with maximally programmed AV delays in the DDD mode.

Patients included in studies showing deleterious effects of RV pacing were either specified as having their RV lead positioned at the RV apex (40,43,280) or can be presumed in most cases to have had the lead positioned there based on prevailing practices of pacemaker and defibrillator implantation (45,46,277). Therefore, conclusions about deleterious effects of RV pacing at this time should be limited to patients with RVA pacing. Studies are currently under way that compare the effects of pacing at alternative RV sites (septum, outflow tract) with RVA pacing.

Despite the appeal of atrium-only pacing, there remains concern about implanting single-chamber atrial pacemakers in patients with SND because of the risk of subsequent AV block. Also, in the subsequent Danish study comparing atrial with dual-chamber pacing, the incidence of progression to symptomatic AV block, including syncope, was 1.9% per year, even with rigorous screening for risk of AV block at the time of implantation (45). Programming a dual-chamber device to the conventional DDD mode with a maximally programmable AV delay or with AV search hysteresis does not eliminate frequent ventricular pacing in a significant fraction of patients (291,292). Accordingly, several pacing algorithms that avoid ventricular pacing except during periods of high-grade AV block have been introduced recently (293). These new modes dramatically decrease the prevalence of ventricular pacing in both pacemaker and defibrillator patients (294–296). A recent trial showed the frequency of RV pacing was 9% with one of these new algorithms compared with 99% with conventional dual-chamber pacing, and this decrease in RV pacing was associated with a 40% relative reduction in the incidence of persistent AF (296). Additional trials are under way to assess the clinical benefits of these new pacing modes (297).

2.6.8. Role of Biventricular Pacemakers

As discussed in Section 2.4.1, "Cardiac Resynchronization Therapy," multiple controlled trials have shown biventricular pacing to improve both functional capacity and QOL and decrease hospitalizations and mortality for selected patients with Class III to IV symptoms of heart failure. Although patients with a conventional indication for pacemaker implantation were excluded from these trials, it is reasonable to assume that patients who otherwise meet their inclusion criteria but have QRS prolongation due to ventricular pacing might also benefit from biventricular pacing.

Regardless of the duration of the native QRS complex, patients with LV dysfunction who have a conventional indication for pacing and in whom ventricular pacing is expected to predominate may benefit from biventricular pacing. A prospective randomized trial published in 2006 concerning patients with LV enlargement, LVEF less than or equal to 40%, and conventional indications for pacing showed that biventricular pacing was associated with improved functional class, exercise capacity, LVEF, and serum brain natriuretic peptide levels compared with RV pacing (298). It has also been demonstrated that LV dysfunction in the setting of chronic RV pacing, and possibly as a result of RV pacing, can be improved with an upgrade to biventricular pacing (299).

Among patients undergoing AV junction ablation for chronic AF, the PAVE (Left Ventricular-Based Cardiac Stimulation Post AV Nodal Ablation Evaluation) trial prospectively randomized patients between RVA pacing and biventricular pacing (300). The patients with RVA pacing had deterioration in LVEF that was avoided by the patients with biventricular pacing. The group with biventricular pacing also had improved exercise capacity compared with the group with right apical pacing. The advantages of biventricular pacing were seen predominantly among patients with reduced LVEF or heart failure at baseline. Other studies have shown that among AF patients who experience heart failure after AV junction ablation and RV pacing, an upgrade to biventricular pacing results in improved symptomatology and improved LV function (301,302).

These findings raise the question of whether patients with preserved LV function requiring ventricular pacing would benefit from initial implantation with a biventricular device (or one with RV pacing at a site with more synchronous ventricular activation than at the RV apex, such as pacing at the RV septum, the RV outflow tract (303,304), or the area of the His bundle) (305). Some patients with normal baseline LV function experience deterioration in LVEF after chronic RV pacing (47,306). The concern over the effects of long-term RV pacing is naturally greatest among younger patients who could be exposed to ventricular pacing for many decades. Studies have suggested that chronic RVA pacing in young patients, primarily those with congenital complete heart block, can lead to adverse histological changes, LV dilation, and LV dysfunction (41,306,307).

There is a role for CRT-P in some patients, especially those who wish to enhance their QOL without defibrillation backup. Elderly patients with important comorbidities are such individuals. Notably, there is an important survival benefit from CRT-P alone (224,225).

2.7. Optimizing Pacemaker Technology and Cost

The cost of a pacemaker system increases with its degree of complexity and sophistication. For example, the cost of a dual-chamber pacemaker system exceeds that of a single-chamber system with respect to the cost of the generator and the second lead (increased by approximately $2,500 [287]), additional implantation time and supplies (approximately $160 [287]), and additional follow-up costs (approximately $550 per year [287]). A biventricular pacemaker entails even greater costs, with the hardware alone adding $5,000 to $10,000 to the system cost. With respect to battery life, that of a dual-chamber generator is shorter than that of a single-chamber generator (287,308) and that of a biventricular device is shorter still. There are also QOL concerns associated with the more complex systems, including increased device size and increased frequency of follow-up. Against these additional costs are the potential benefits of the more sophisticated systems with respect to QOL, morbidity, and mortality. Furthermore, when a single-chamber system requires upgrading to a dual-chamber system, the costs are significant; one study estimated the cost of such an upgrade to be $14,451 (287).

An analysis of MOST found that the cost-effectiveness of dual-chamber pacemaker implantation compared with ventricular pacemaker implantation (287) was approximately $53,000 per quality-adjusted year of life gained over 4 years of follow-up. Extended over the expected lifetime of a typical patient, the calculated cost-effectiveness of dual-chamber pacing improved to $6,800 per quality-adjusted year of life gained.

It has been estimated that 16% to 24% of pacemaker implantations are for replacement of generators; of those, 76% are replaced because their batteries have reached their elective replacement time (309,310). Hardware and software (i.e., programming) features of pacemaker systems that prolong useful battery longevity may improve the cost-effectiveness of pacing. Leads with steroid elution and/or high pacing impedance allow for less current drain. Optimal programming of output voltages, pulse widths, and AV delays can markedly decrease battery drain; one study showed that expert programming of pacemaker generators can have a major impact on longevity, prolonging it by an average of 4.2 years compared with nominal settings (311). Generators that automatically determine whether a pacing impulse results in capture allow for pacing outputs closer to threshold values than conventional generators. Although these and other features arguably should prolong generator life, there are other constraints on the useful life of a pacemaker generator, including battery drain not directly related to pulse generation and the limited life expectancy of many pacemaker recipients; rigorous studies supporting the overall cost-effectiveness of these advanced pacing features are lacking.

2.8. Pacemaker Follow-Up

After implantation of a pacemaker, careful follow-up and continuity of care are required. The writing committee considered the advisability of extending the scope of these guidelines to include recommendations for follow-up and device replacement but deferred this decision given other published statements and guidelines on this topic. These are addressed below as a matter of information; however, no endorsement is implied. The HRS has published a series of reports on antibradycardia pacemaker follow-up (312,313). The Canadian Working Group in Cardiac Pacing has also published a consensus statement on pacemaker follow-up (314). In addition, the Centers for Medicare and Medicaid Services has established guidelines for monitoring of patients covered by Medicare who have antibradycardia pacemakers, although these have not been updated for some time (315).

Many of the same considerations are relevant to follow-up of pacemakers, ICDs, and CRT systems. Programming undertaken at implantation should be reviewed before discharge and changed accordingly at subsequent follow-up visits as indicated by interrogation, testing, and patient needs. With careful attention to programming pacing amplitude, pulse width, and diagnostic functions, battery life can be enhanced significantly without compromising patient safety. Taking advantage of programmable options also allows optimization of pacemaker function for the individual patient.

The frequency and method of follow-up are dictated by multiple factors, including other cardiovascular or medical problems managed by the physician involved, the age of the pacemaker, and geographic accessibility of the patient to medical care. Some centers may prefer to use remote monitoring with intermittent clinic evaluations, whereas others may prefer to do the majority or all of the patient follow-up in a clinic.

For many years, the only "remote" follow-up was transtelephonic monitoring (TTM). Available for many years, TTM provides information regarding capture of the chamber(s) being paced and battery status. TTM may also provide the caregiver with information regarding appropriate sensing. However, in recent years, the term "remote monitoring" has evolved to indicate a technology that is capable of providing a great deal of additional information. Automatic features, such as automatic threshold assessment, have been incorporated increasingly into newer devices and facilitate follow-up for patients who live far from follow-up clinics (316). However, these automatic functions are not universal and need not and cannot supplant the benefits of direct patient contact, particularly with regard to history taking and physical examination.

A more extensive clinic follow-up usually includes assessment of the clinical status of the patient, battery status, pacing threshold and pulse width, sensing function, and lead integrity, as well as optimization of sensor-driven rate response and evaluation of recorded events, such as mode switching for AF detection and surveillance and ventricular tachyarrhythmia events. The schedule for clinic follow-up should be at the discretion of the caregivers who are providing pacemaker follow-up. As a guideline, the 1984 Health Care Financing Administration document suggests the following: for single-chamber pacemakers, twice in the first 6 months after implantation and then once every 12 months; for dual-chamber pacemakers, twice in the first 6 months, then once every 6 months (315).

Regulations regarding TTM have not been revised since 1984 (315). Guidelines that truly encompass remote monitoring of devices have not yet been endorsed by any of the major professional societies. The Centers for Medicare and Medicaid Services have not provided regulations regarding the use of this technology, but have provided limited direction regarding reimbursement. The Centers for Medicare and Medicaid Services have published a statement that physicians should use the existing current procedural terminology codes for in-office pacemaker and ICD interrogation codes for remote monitoring of cardiac devices (317). Clearly stated guidelines from professional societies are necessary and should be written in such a way as to permit remote monitoring that achieves specific clinical goals. Guidelines are currently in development given the rapid advancement in remote monitoring technology.

Appropriate clinical goals of remote monitoring should be identified and guidelines developed to give caregivers the ability to optimize the amount of clinical information that can be derived from this technology. Appropriate clinical goals of TTM should be divided into those pieces of information obtainable during nonmagnet (i.e., free-running) ECG assessment and assessment of the ECG tracing obtained during magnet application. The same goals should be achieved

whether the service is being provided by a commercial or noncommercial monitoring service.

Goals of TTM nonmagnet ECG assessment are as follows:

- Determine whether the patient displays intrinsic rhythm or is being intermittently or continuously paced at the programmed settings.
- Characterize the patient's underlying atrial mechanism, for example, sinus versus AF, atrial tachycardia, etc.
- If intrinsic rhythm is displayed, determine that normal (appropriate) sensing is present for 1 or both chambers depending on whether it is a single- or dual-chamber pacemaker and programmed pacing mode.

Goals of TTM ECG assessment during magnet application are as follows:

- Verify effective capture of the appropriate chamber(s) depending on whether it is a single- or dual-chamber pacemaker and verify the programmed pacing mode.
- Assess magnet rate. Once magnet rate is determined, the value should be compared with values obtained on previous transmissions to determine whether any change has occurred. The person assessing the TTM should also be aware of the magnet rate that represents elective replacement indicators for that pacemaker.
- If the pacemaker is one in which pulse width is 1 of the elective replacement indicators, the pulse width should also be assessed and compared with previous values.
- If the pacemaker has some mechanism to allow transtelephonic assessment of threshold (i.e., Threshold Margin Test [TMT™]) and that function is programmed "on," the results of this test should be demonstrated and analyzed.
- If a dual-chamber pacemaker is being assessed and magnet application results in a change in AV interval during magnet application, that change should be demonstrated and verified.

2.8.1. Length of Electrocardiographic Samples for Storage

It is important that the caregiver(s) providing TTM assessment be able to refer to a paper copy or computer-archived copy of the transtelephonic assessment for subsequent care. The length of the ECG sample saved should be based on the clinical information that is required (e.g., the points listed above). It is the experience of personnel trained in TTM that a carefully selected ECG sample of 6 to 9 seconds can demonstrate all of the points for each of the categories listed above (i.e., a 6- to 9-second strip of nonmagnet and 6- to 9-second strip of magnet-applied ECG tracing).

2.8.2. Frequency of Transtelephonic Monitoring

The follow-up schedule for TTM varies among centers, and there is no absolute schedule that needs be mandated. Regardless of the schedule to which the center may adhere, TTM may be necessary at unscheduled times if, for example, the patient experiences symptoms that potentially reflect an alteration in rhythm or device function.

The majority of centers with TTM services follow the schedule established by the Health Care Financing Administration (now the Centers for Medicare and Medicaid Services). In the 1984 Health Care Financing Administration guidelines, there are 2 broad categories for follow-up (as shown in Table 4): Guideline I, which was thought to apply to the majority of pacemakers in use at that time, and Guideline II, which would apply to pacemaker systems for which sufficient long-term clinical information exists to ensure that they meet the standards of the Inter-Society Commission for Heart Disease Resources for longevity and end-of-life decay. The standards to which they referred are 90% cumulative survival at 5 years after implantation and an end-of-life decay of less than a 50% drop in output voltage and less than a 20% deviation in magnet rate, or a drop of 5 bpm or less, over a period of 3 months or more. As of 2000, it appears that most pacemakers would meet the specifications in Guideline II.

Table 4. Device Monitoring Times Postimplantation: Health Care Financing Administration 1984 Guidelines for Transtelephonic Monitoring

Postimplantation Milestone	Monitoring Time
Guideline I	
Single chamber	
1st month	Every 2 weeks
2nd to 36th month	Every 8 weeks
37th month to failure	Every 4 weeks
Dual chamber	
1st month	Every 2 weeks
2nd to 6th month	Every 4 weeks
7th to 36th month	Every 8 weeks
37th month to failure	Every 4 weeks
Guideline II	
Single chamber	
1st month	Every 2 weeks
2nd to 48th month	Every 12 weeks
49th month to failure	Every 4 weeks
Dual chamber	
1st month	Every 2 weeks
2nd to 30th month	Every 12 weeks
31st to 48th month	Every 8 weeks
49th month to failure	Every 4 weeks

Modified from the US Department of Health and Human Services (315). In the public domain.

Note that there is no federal or clinical mandate that these TTM guidelines be followed. The ACC, AHA, and HRS have not officially endorsed the Health Care Financing Administration guidelines. Nevertheless, they may be useful as a framework for TTM. An experienced center may choose to do less frequent TTM and supplement it with in-clinic evaluations as stated previously.

Goals of contemporary remote monitoring are as follows:

- Review all programmed parameters
- Review stored events (e.g., counters, histograms, and electrograms)
- If review of programmed parameters or stored events suggests a need for reprogramming or a change in therapy, arrange a focused in-clinic appointment.

2.8.3. Remote Follow-Up and Monitoring (NEW SECTION)

Since the publication of the 2008 DBT guideline, important changes have occurred related to follow-up and remote monitoring of cardiovascular implantable electronic devices (CIEDs). (1d,541,590). 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 (1d,541). Transtelephonic monitoring, with monitors that transmit the patient's heart rhythm by converting electrocardiographic information to sound and transmitting it via telephone lines to a decoding machine that then converts the sound back into a rhythm strip, is now a dated technique (1d,541,590). because it allows for limited monitoring of heart rate, rhythm, and battery status of only pacemakers (590).

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) (590). 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 (541,590). 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 (541,590). 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 (541). 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 (590). A detailed description of techniques, indications, personnel, and frequency has been published as a consensus document (541).

Several prospective randomized trials have been conducted evaluating the effect of remote monitoring on clinical outcomes (591–594) since the publication of the 2008 DBT Guideline (1d). 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 discovery of clinically actionable events, decreased time to clinical decision in response to these events, and fewer office visits (591–594). Long-term survival rates of patients monitored remotely with ICDs in a practice setting compare favorably with survival rates of patients in clinical trials (595).

Table 4a. Minimum Frequency of CIED In-Person or Remote Monitoring*

Type and Frequency	Method
Pacemaker/ICD/CRT	
Within 72 h of CIED implantation	In person
2–12 wk postimplantation	In person
Every 3–12 mo for pacemaker/CRT-Pacemaker	In person or remote
Every 3–6 mo for ICD/CRT-D	In person or remote
Annually until battery depletion	In person
Every 1–3 mo at signs of battery depletion	In person or remote
Implantable loop recorder	
Every 1–6 mo depending on patient symptoms and indication	In person or remote
Implantable hemodynamic monitor	
Every 1–6 mo depending on indication	In person or remote
More frequent assessment as clinically indicated	In person or remote

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.

*More frequent in-person or remote monitoring may be required for all the above devices as clinically indicated.

Modified from Wilkoff et al (541).

Current suggestions for the minimum frequency of in-office and remote monitoring of patients with CIEDs are summarized in Table 4a (541). 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.

3. Indications for Implantable Cardioverter-Defibrillator Therapy

Indications for ICDs have evolved considerably from initial implantation exclusively in patients who had survived 1 or more cardiac arrests and failed pharmacological therapy (318). Multiple clinical trials have established that ICD use results in improved survival compared with antiarrhythmic agents for secondary prevention of SCD (16,319–326). Large prospective, randomized, multicenter studies have also established that ICD therapy is effective for primary prevention of sudden death and improves total survival in selected patient populations who have not previously had a cardiac arrest or sustained VT (16–19,327–331).

We acknowledge that the "ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death" (16) used an LVEF of less than 40% as a critical point to justify ICD implantation for primary prevention of SCD. The LVEF used in clinical trials assessing the ICD for primary prevention of SCD ranged from less than or equal to 40% in MUSTT (Multicenter Unsustained Ventricular Tachycardia Trial) to less than or equal to 30% in MADIT II (Multicenter Automatic Defibrillator Implantation Trial II) (329,332). Two trials, MADIT I (Multicenter Automatic Defibrillator Implan-

tation Trial I) (327) and SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial) (333), used LVEFs of less than or equal to 35% as entry criteria. The present writing committee reached the consensus that it would be best to have ICDs offered to patients with clinical profiles as similar to those included in the trials as possible. Having given careful consideration to the issues related to LVEF for these updated ICD guidelines, we have written these indications for ICDs based on the specific inclusion criteria for LVEF in the trials. Because of this, there may be some variation from previously published guidelines (16).

We also acknowledge that the determination of LVEF lacks a "gold standard" and that there may be variation among the commonly used clinical techniques of LVEF determination. All clinical methods of LVEF determination lack precision, and the accuracy of techniques varies amongst laboratories and institutions. Given these considerations, the present writing committee recommends that the clinician use the LVEF determination that they believe is the most clinically accurate and appropriate in their institution.

Patient selection, device and lead implantation, follow-up, and replacement are parts of a complex process that requires familiarity with device capabilities, adequate case volume, continuing education, and skill in the management of ventricular arrhythmias, thus mandating appropriate training and credentialing. Training program requirements for certification programs in clinical cardiac electrophysiology that include ICD implantation have been established by the American Board of Internal Medicine and the American Osteopathic Board of Internal Medicine. Individuals with basic certification in pediatric cardiology and cardiac surgery may receive similar training in ICD implantation. In 2004, requirements for an "alternate training pathway" for those with substantial prior experience in pacemaker implantation were proposed by the HRS with a scheduled expiration for this alternate pathway in 2008 (11,12). Fifteen percent of physicians who implanted ICDs in 2006 reported in the national ICD registry that they had no formal training (electrophysiology fellowship, cardiac surgical training, or completion of the alternate pathway recommendation) (11,12,334).

The options for management of patients with ventricular arrhythmias include antiarrhythmic agents, catheter ablation, and surgery. The "ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death" have been published with a comprehensive review of management options, including antiarrhythmic agents, catheter ablation, surgery, and ICD therapy (16).

3.1. Secondary Prevention of Sudden Cardiac Death

3.1.1. Implantable Cardioverter-Defibrillator Therapy for Secondary Prevention of Cardiac Arrest and Sustained Ventricular Tachycardia

Secondary prevention refers to prevention of SCD in those patients who have survived a prior sudden cardiac arrest or sustained VT (16). Evidence from multiple randomized controlled trials supports the use of ICDs for secondary prevention of sudden cardiac arrest regardless of the type of underlying structural heart disease. In patients resuscitated from cardiac arrest, the ICD is associated with clinically and statistically significant reductions in sudden death and total mortality compared with antiarrhythmic drug therapy in prospective randomized controlled trials (16,319–326).

Trials of the ICD in patients who have been resuscitated from cardiac arrest demonstrate survival benefits with ICD therapy compared with electrophysiologically guided drug therapy with Class I agents, sotalol, and empirical amiodarone therapy (320,323). A large prospective, randomized secondary prevention trial comparing ICD therapy with Class III antiarrhythmic drug therapy (predominantly empirical amiodarone) demonstrated improved survival with ICD therapy (319). Unadjusted survival estimates for the ICD group and the antiarrhythmic drug group, respectively, were 89.3% versus 82.3% at 1 year, 81.6% versus 74.7% at 2 years, and 75.4% versus 64.1% at 3 years ($p=0.02$). Estimated relative risk reduction with ICD therapy was 39% (95% CI 19% to 59%) at 1 year, 27% (95% CI 6% to 48%) at 2 years, and 31% (95% CI 10% to 52%) at 3 years. Two other reports of large prospective trials in similar patient groups have shown similar results (322,323).

The effectiveness of ICDs on outcomes in the recent large, prospective secondary prevention trials—AVID (Antiarrhythmics Versus Implantable Defibrillators) (319), CASH (Cardiac Arrest Study Hamburg) (321), and CIDS (Canadian Implantable Defibrillator Study) (322)—were consistent with prior investigations (320). Specifically, the ICD was associated with a 50% relative risk reduction for arrhythmic death and a 25% relative risk reduction for all-cause mortality (324). Thus, the secondary prevention trials have been robust and have shown a consistent effect of improved survival with ICD therapy compared with antiarrhythmic drug therapy across studies (324).

Some individuals are resuscitated from cardiac arrest due to possible transient reversible causes. In such patients, myocardial revascularization may be performed when appropriate to reduce the risk of recurrent sudden death, with individualized decisions made with regard to the need for ICD therapy (16). Sustained monomorphic VT with prior MI is unlikely to be affected by revascularization (16). Myocardial revascularization may be sufficient therapy in patients surviving VF in association with myocardial ischemia when ventricular function is normal and there is no history of an MI (16).

Unless electrolyte abnormalities are proven to be the sole cause of cardiac arrest, survivors of cardiac arrest in whom electrolyte abnormalities are discovered in general should be treated in a manner similar to that of cardiac arrest survivors without electrolyte abnormalities (16). Patients who experience sustained monomorphic VT in the presence of antiarrhythmic drugs or electrolyte abnormalities should also be evaluated and treated in a manner similar to patients with VT or VF without electrolyte abnormalities or antiarrhythmic drugs (16).

3.1.2. Specific Disease States and Secondary Prevention of Cardiac Arrest or Sustained Ventricular Tachycardia

The majority of patients included in prior prospective randomized trials of patients resuscitated from cardiac arrest have had coronary artery disease with impaired ventricular function (320,322,323,325,326). Patients with other types of structural heart disease constitute a minority of patients in the secondary prevention trials. However, supplemental observational and registry data support the ICD as the preferred strategy over antiarrhythmic drug therapy for secondary prevention for patients resuscitated from cardiac arrest due to VT or fibrillation with coronary artery disease and other underlying structural heart disease.

3.1.3. Coronary Artery Disease

Patients with coronary artery disease represent the majority of patients receiving devices in prior reports of patients surviving cardiac arrest. Evidence strongly supports a survival benefit in such patients with an ICD compared with other therapy options (319,322,323). Between 73% and 83% of patients enrolled in the AVID, CASH, and CIDS trials had underlying coronary artery disease (319,321,322). The mean LVEF ranged from 32% to 45% in these trials, which indicates prior MI in the majority of patients (319,322,323). Multiple analyses have supported the notion that patients with reduced LV function may experience greater benefit with ICD therapy than with drug therapy (320,335–338). All patients undergoing evaluation for ICD therapy should be given optimum medical treatment for their underlying cardiovascular condition (16).

Patients experiencing cardiac arrest due to VF that occurs more than 48 hours after an MI may be at risk for recurrent cardiac arrest (16). It is recommended that such patients be evaluated and optimally treated for ischemia (16). If there is evidence that directly and clearly implicates ischemia immediately preceding the onset of VF without evidence of a prior MI, the primary therapy should be complete coronary revascularization (16). If coronary revascularization is not possible and there is evidence of significant LV dysfunction, the primary therapy for patients resuscitated from VF should be the ICD (16).

Patients with coronary artery disease who present with sustained monomorphic VT or VF and low-level elevations of cardiac biomarkers of myocyte injury/necrosis should be treated similarly to patients who have sustained VT and no documented rise in biomarkers (16). Prolonged episodes of sustained monomorphic VT or VF may be associated with a rise in cardiac troponin and creatine phosphokinase levels due to myocardial metabolic demands that exceed supply in patients with coronary artery disease. Evaluation for ischemia should be undertaken in such patients (16). However, when sustained VT or VF is accompanied by modest elevations of cardiac enzymes, it should not be assumed that a new MI was the cause of the sustained VT (16). Without other clinical data to support the occurrence of a new MI, it is reasonable to consider that such patients are at risk for recurrent sustained VT or VF (16). With these considerations in mind, these patients should be treated for this arrhythmia in the same manner as patients without biomarker release accompanying VT (16).

3.1.4. Nonischemic Dilated Cardiomyopathy

Patients with nonischemic DCM and prior episodes of VF or sustained VT are at high risk for recurrent cardiac arrest. Empirical antiarrhythmic therapy or drug therapy guided by electrophysiological testing has not been demonstrated to improve survival in these patients. The ICD has been shown to be superior to amiodarone for secondary prevention of VT and VF in studies in which the majority of patients had coronary artery disease (322,323,336), but the subgroups with nonischemic DCM in these studies benefited similarly (319,322,323) or more than the group with ischemic heart failure (324). On the basis of these data, the ICD is the preferred treatment for patients with nonischemic DCM resuscitated from prior cardiac arrest from VF or VT.

3.1.5. Hypertrophic Cardiomyopathy

HCM is an inherited heart muscle disease that affects approximately 1 of every 500 persons in the general population and is the most common cause of cardiac arrest in individuals younger than 40 years of age (339). HCM should be suspected as the cause of cardiac arrest in young individuals during exertion, because exercise increases the risk of life-threatening ventricular arrhythmias with this condition (339). Sudden death may also be the first manifestation of the disease in a previously asymptomatic individual. A history of prior cardiac arrest indicates a substantial risk of future VT or VF with this condition (339). Prospective randomized trials of ICD versus pharmacological therapy for patients with prior cardiac arrest and HCM have not been performed; however, registry data and observational trials are available (339,340).

In those patients with HCM resuscitated from prior cardiac arrest, there is a high frequency of subsequent ICD therapy for life-threatening ventricular arrhythmias (339). On the basis of these data, the ICD is the preferred therapy for such patients with HCM resuscitated from prior cardiac arrest (339,340).

3.1.6. Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy

Arrhythmogenic RV dysplasia/cardiomyopathy (ARVD/C) is a genetic condition characterized by fibrofatty infiltration of the RV and less commonly the LV. It usually manifests clinically with sustained monomorphic VT with left bundle morphology in young individuals during exercise. There are no prospective randomized trials of pharmacological therapy versus ICD therapy in patients with ARVD/C for secondary prevention of SCD; however, observational reports from multiple centers consistently demonstrate a high frequency of appropriate ICD use for life-threatening ventricular arrhythmias and a very low rate of arrhythmic death in patients with ARVD/C treated with an ICD (341–348).

3.1.7. Genetic Arrhythmia Syndromes

Genetic syndromes that predispose to sustained VT or VF include the long- and short-QT syndromes, Brugada syndrome, idiopathic VF, and catecholaminergic polymorphic VT (338,349–356). These primary electrical conditions typ-

ically exist in the absence of any underlying structural heart disease and predispose to cardiac arrest. Although controversy still exists with regard to risk factors for sudden death with these conditions, there is consensus that those with prior cardiac arrest or syncope are at very high risk for recurrent arrhythmic events. On the basis of the absence of any clear or consistent survival benefit of pharmacological therapy for those individuals with these genetic arrhythmia syndromes, the ICD is the preferred therapy for those with prior episodes of sustained VT or VF and may also be considered for primary prevention for some patients with a very strong family history of early mortality (see Section 3.2.4, "Hypertrophic Cardiomyopathy," and Section 3.2.7, "Primary Electrical Disease").

3.1.8. Syncope With Inducible Sustained Ventricular Tachycardia

Patients with syncope of undetermined origin in whom clinically relevant VT/VF is induced at electrophysiological study should be considered candidates for ICD therapy. In these patients, the induced arrhythmia is presumed to be the cause of syncope (341,357–366). In patients with hemodynamically significant and symptomatic inducible sustained VT, ICD therapy can be a primary treatment option. Appropriate ICD therapy of VT and VF documented by stored electrograms lends support to ICD therapy as a primary treatment for DCM patients with syncope (341,367).

3.2. Primary Prevention of Sudden Cardiac Death

Primary prevention of SCD refers to the use of ICDs in individuals who are at risk for but have not yet had an episode of sustained VT, VF, or resuscitated cardiac arrest. Clinical trials have evaluated the risks and benefits of the ICD in prevention of sudden death and have improved survival in multiple patient populations, including those with prior MI and heart failure due to either coronary artery disease or nonischemic DCM. Prospective registry data are less robust but still useful for risk stratification and recommendations for ICD implantation in selected other patient populations, such as those with HCM, ARVD/C, and the long-QT syndrome. In less common conditions (e.g., Brugada syndrome, catecholaminergic polymorphic VT, cardiac sarcoidosis, and LV noncompaction), clinical reports and retrospectively analyzed series provide less rigorous evidence in support of current recommendations for ICD use, but this constitutes the best available evidence for these conditions.

3.2.1. Coronary Artery Disease

There now exists a substantial body of clinical trial data that support the use of ICDs in patients with chronic ischemic heart disease. A variety of risk factors have been used to identify a high-risk population for these studies. MADIT I (327) and MUSTT (329) required a history of MI, spontaneous nonsustained VT, inducible VT at electrophysiological study, and a depressed LVEF (less than or equal to 35% or less than or equal to 40%, respectively) to enter the study. MADIT I showed a major relative risk reduction of 54% with the ICD. MUSTT was not specifically a trial of ICD therapy, because it compared no therapy with electrophysiologically guided therapy, but in the group randomized to electrophysiologically guided therapy, benefit was seen only among those who received an ICD.

MADIT II (332) enrolled 1,232 patients with ischemic cardiomyopathy and an LVEF less than or equal to 30%. No spontaneous or induced arrhythmia was required for enrollment. All-cause mortality was 20% in the control group and 14.2% in the ICD group (relative risk 31%; p=0.016). SCD-HeFT included patients with both ischemic and nonischemic cardiomyopathies, an LVEF less than or equal to 35%, and NYHA Class II or III congestive heart failure (333). Among the 1,486 patients with ischemic heart disease randomized to either placebo or ICD therapy, the 5-year event rates were 0.432 and 0.359, respectively (HR 0.79; p=0.05). Two recent meta-analyses of these trials have supported the overall conclusion that ICD therapy in high-risk individuals with coronary artery disease results in a net risk reduction for total mortality of between 20% and 30% (325,368).

Two trials, however, have failed to show improved survival with ICD therapy in patients either at the time of surgical revascularization or within 40 days of an acute MI. In the CABG-Patch (Coronary Artery Bypass Graft-Patch) trial (328), routine ICD insertion did not improve survival in patients with coronary artery disease undergoing bypass surgery who were believed to be at high risk of sudden death on the basis of an abnormal signal-averaged ECG and severe LV dysfunction (LVEF less than or equal to 35%). Similar data about the effects of percutaneous revascularization are not available. In DINAMIT (Defibrillator in Acute Myocardial Infarction Trial) (331), 674 patients with a recent MI (within 6 to 40 days), reduced LV function (LVEF less than or equal to 35%), and impaired cardiac autonomic function (depressed heart rate variability or elevated average heart rate) were randomized to either ICD therapy or no ICD therapy. Although arrhythmic death was reduced in the ICD group, there was no difference in total mortality (18.7% versus 17.0%; HR for death in the ICD group 1.08; p=0.66). See Table 5 for further information.

3.2.2. Nonischemic Dilated Cardiomyopathy

Multiple randomized prospective trials now supplement the available observational studies that have reported on the role of the ICD in primary prevention of SCD in patients with nonischemic DCM (16,224,333,369–379) Observational studies suggest that up to 30% of deaths in patients with DCM are sudden (380). Mortality in medically treated patients with DCM and a prior history of syncope may exceed 30% at 2 years, whereas those treated with an ICD experience a high frequency of appropriate ICD therapy (16,372,373).

CAT (Cardiomyopathy Trial) enrolled patients with recently diagnosed DCM with randomization to medical therapy versus medical therapy with an ICD (377). The study was terminated before the primary end point was reached because of a lower-than-expected incidence of all-cause mortality (377). There was no statistical probability of finding a significant survival advantage with either strategy. With 50 patients in the ICD arm and 54 in the control group, the study was underpowered to find a difference in survival with ICD

Table 5. Major Implantable Cardioverter-Defibrillator Trials for Prevention of Sudden Cardiac Death

Trial	Year	Patients (n)	Inclusion Criterion: LVEF % Less Than or Equal to	Other Inclusion Criteria	Hazard Ratio*	95% Confidence Interval	p
MADIT I (327)	1996	196	35	NSVT and positive EP	0.46	0.26 to 0.82	0.009
MADIT II (332)	2002	1,232	30	Prior MI	0.69	0.51 to 0.93	0.016
CABG-Patch (328)	1997	900	36	Positive SAECG and CABG	1.07	0.81 to 1.42	0.64
DEFINITE (369)	2004	485	35	NICM, PVCs, or NSVT	0.65	0.40 to 1.06	0.08
DINAMIT (331)	2004	674	35	6 to 40 days after MI and impaired HRV	1.08	0.76 to 1.55	0.66
SCD-HeFT (333)	2005	1,676	35	Prior MI or NICM	0.77	0.62 to 0.96	0.007
AVID (319)	1997	1,016	40	Prior cardiac arrest	0.62	0.43 to 0.82	<0.02
CASH† (323)	2000	191	M: 45±18 at baseline	Prior cardiac arrest	0.77	1.112‡	0.081§
CIDS (322)	2000	659	35	Prior cardiac arrest, syncope	0.82	0.60 to 1.10	NS

AVID indicates Antiarrhythmics Versus Implantable Defibrillators; CABG, coronary artery bypass graft surgery; CASH, Cardiac Arrest Study Hamburg; CIDS, Canadian Implantable Defibrillator Study; DEFINITE, Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation; DINAMIT, Defibrillator in Acute Myocardial Infarction Trial; EP, electrophysiological study; HRV, heart rate variability; LVD, left ventricular dysfunction; LVEF, left ventricular ejection fraction; MADIT I, Multicenter Automatic Defibrillator Implantation Trial I; MADIT II, Multicenter Automatic Defibrillator Implantation Trial II; MI, myocardial infarction; NA, not applicable; NICM, nonischemic cardiomyopathy; NS, not statistically significant; NSVT, nonsustained ventricular tachycardia; PVCs, premature ventricular complexes; SAECG, signal-averaged electrocardiogram; and SCD-HeFT, Sudden Cardiac Death in Heart Failure Trial.

*Hazard ratios for death due to any cause in the implantable cardioverter-defibrillator group compared with the non-implantable cardioverter-defibrillator group.

†Includes only implantable cardioverter-defibrillator and amiodarone patients from CASH.

‡Upper bound of 97.5% confidence interval.

§One-tailed.

therapy. At the time of 5-year follow-up, there were fewer deaths in the ICD group than in the control group (13 versus 17, respectively) (377).

Another inconclusive trial was the AMIOVIRT (Amiodarone Versus Implantable Defibrillator in Patients with Nonischemic Cardiomyopathy and Asymptomatic Nonsustained Ventricular Tachycardia) study (378). The trial randomized 103 patients with DCM, LVEF less than or equal to 35%, and nonsustained VT to amiodarone or ICD. The study was stopped prematurely due to statistical futility in reaching the primary end point of reduced total mortality (378). The DEFINITE (Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation) trial randomized 458 patients with nonischemic cardiomyopathy, NYHA Class I to III heart failure, LVEF less than or equal to 35%, and more than 10 premature ventricular complexes per hour or nonsustained VT to optimal medical therapy with or without an ICD (369). With a primary end point of all-cause mortality, statistical significance was not reached, but there was a strong trend toward reduction of mortality with ICD therapy (p=0.08). After 2 years, mortality was 14.1% in the standard therapy group versus 7.9% among those receiving an ICD, which resulted in a 6.2% absolute reduction and a 35% relative risk reduction with ICD implantation (369). The results were consistent and comparable to those of other similar trials (16,333,379).

SCD-HeFT compared amiodarone, ICD, and optimal medical therapy in 2,521 patients with coronary artery disease or nonischemic cardiomyopathy with NYHA functional Class II or III heart failure and LVEF less than or equal to 35% (333). The amiodarone treatment group received the drug by way of a double-blinded, placebo-controlled design (333). The median follow-up was 45.5 months. The absolute mortality decrease in the medical group was 7.2% after 5 years in the overall population. The ICD group experienced a decreased risk of death of 23% compared with the placebo group (HR 0.77, 97.5% CI 0.62 to 0.96), and total mortality in the medical group was 7.2% per year, with a risk reduction of 23% in the ICD group versus placebo (95% CI 0.62 to 0.96; p=0.007). Relative risk reduction was comparable for the group with LV dysfunction due to prior MI and the nonischemic group, but absolute mortality was lower in the nonischemic group. This resulted in a greater number needed to treat per life saved among ischemic patients. There was no mortality difference between the amiodarone and placebo groups. Further risk stratification may decrease the number of individuals needed to undergo ICD implantation to save a life in this population.

With the exception of DEFINITE (25% in the ICD arm), trials assessing ICD therapy in primary prophylaxis of DCM have not generally included asymptomatic patients in NYHA functional Class I; therefore, the efficacy of ICDs in this population is not fully known. Because mortality may be low in this subgroup, the benefit of ICD therapy is moderate at best (369).

The COMPANION trial randomized patients with Class III or IV heart failure, ischemic or nonischemic DCM, and QRS duration greater than 120 milliseconds in a 1:2:2 ratio to receive optimal pharmacological therapy alone or in combination with CRT with either a pacemaker or a pacemaker-defibrillator (224). Of the 1,520 patients randomized in the trial, 903 were allocated to either the medical therapy or defibrillator arms; of this subset, 397 (44%) had DCM. Cardiac resynchronization with an ICD significantly reduced all-cause mortality compared with pharmacological therapy alone in patients with DCM (HR for all-cause death 0.50, 95% CI 0.29 to 0.88; p=0.015) (224).

Two studies have evaluated the time dependence of risk for sudden death relative to the time of diagnosis of nonischemic DCM (369,381). An analysis of the DEFINITE study demonstrated that those who have a recent cardiomyopathy diagnosis do not benefit less from use of an ICD than those with a remote diagnosis (369). On the basis of these data, ICD therapy should be considered in such patients provided that a reversible cause of transient LV function has been excluded and their response to optimal medical therapy has been assessed. The optimal time required for this assessment is uncertain; however, another analysis determined that patients with nonischemic DCM experienced equivalent occurrences of treated and potentially lethal arrhythmias irrespective of diagnosis duration (381). These findings suggest that use of a time qualifier relative to the time since diagnosis of a nonischemic DCM may not reliably discriminate patients at high risk for SCD in this selected population (381). Given these considerations, physicians should consider the timing of defibrillator implantation carefully.

3.2.3. Long-QT Syndrome

The long-QT syndromes represent a complex spectrum of electrophysiological disorders characterized by a propensity for development of malignant ventricular arrhythmias, especially polymorphic VT (382,383). Because this is a primary electrical disorder, with most patients having no evidence of structural heart disease or LV dysfunction, the long-term prognosis is excellent if arrhythmia is controlled. Long-term treatment with beta blockers, permanent pacing, or left cervicothoracic sympathectomy may be helpful (384–386). ICD implantation is recommended for selected patients with recurrent syncope despite drug therapy, sustained ventricular arrhythmias, or sudden cardiac arrest (349,351,352,387,388). Furthermore, use of the ICD for primary prevention of SCD may be considered when there is a strong family history of SCD or when compliance or intolerance to drugs is a concern (349,351,352,387,388).

The clinical manifestations of a long-QT mutation may be influenced by the specific gene involved and the functional consequences of the mutation in that gene. Risk stratification of patients with long-QT syndrome continues to evolve, with data from genetic analysis becoming increasingly useful for clinical decision making (389–394).

3.2.4. Hypertrophic Cardiomyopathy

Most individuals with HCM are asymptomatic, and the first manifestation of the condition may be SCD (245,395–400). SCD in patients with HCM is generally related to ventricular arrhythmia thought to be triggered by factors such as ischemia, outflow obstruction, or AF (339). SCD is less frequently due to bradycardia (16,339). Among selected high-risk patients, the annual mortality from HCM has been estimated to be as high as 6% in reports from tertiary centers (245,395–398). However, community-based studies suggest a more benign disease in the majority of individuals, with an annual mortality rate in the range of 1% or less (16,401–403).

Risk factors for SCD have been derived from multiple observational studies and registries (339,404–408). A consensus document on HCM from the ACC and the European Society of Cardiology categorized known risk factors for SCD as "major" and "possible" in individual patients (395). The major risk factors include prior cardiac arrest, spontaneous sustained VT, spontaneous nonsustained VT, family history of SCD, syncope, LV thickness greater than or equal to 30 mm, and an abnormal blood pressure response to exercise (395). This consensus document also noted possible risk factors, which included AF, myocardial ischemia, LV outflow obstruction, high-risk mutations, and intense (competitive) physical exertion (395). The severity of other symptoms, such as dyspnea, chest pain, and effort intolerance, has not been correlated with increased risk of SCD (16,395). A flat or hypotensive response to upright or supine exercise testing in patients younger than 40 years old has been shown to be a risk factor for SCD, although the positive predictive value of this finding is low (395). A normal blood pressure response identifies a low-risk group (16,395). The presence of nonsustained VT on Holter monitoring has been associated with a higher risk of SCD, although the positive predictive accuracy is relatively low (395). Recent analyses indicate that in a high-risk HCM cohort, ICD interventions were frequent and were highly effective in restoring normal sinus rhythm (245). However, an important proportion of ICD discharges occur in primary prevention patients who undergo implantation of the ICD for a single risk factor. Therefore, a single risk marker of high risk for sudden cardiac arrest may be sufficient to justify consideration for prophylactic ICD implantation in selected patients (245).

Although no randomized studies are available, the ICD has been used in patients with cardiac arrest, sustained VT, or VF, with a high percentage of patients receiving appropriate ICD discharge during follow-up at a rate of 11% per year (245,339). In a nonrandomized study of ICD implantation in HCM, ICD implantation in a subgroup of patients for primary prophylaxis on the basis of perceived high risk for SCD (syncope, family history of SCD, nonsustained VT, inducible VT, or septal thickness greater than or equal to 30 mm) resulted in a lower rate of appropriate discharge of 5% per year (245,339). The ICD is not indicated in the majority of asymptomatic patients with HCM, who will have a relatively benign course. Its role is individualized in the patient considered to be at high risk for SCD (245,339,395). Although precise risk stratification has not been validated, patients with multiple risk factors (especially severe septal hypertrophy, greater than or equal to 30 mm) and those with SCD (especially multiple SCDs) in close relatives appear to be at sufficiently high risk to merit consideration of ICD therapy (16,245).

3.2.5. Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy

Selected patients with ARVD/C may be at risk for SCD. Because clinical series have reported favorable outcomes with this therapy for primary prevention of SCD in ARVD/C, the ICD has assumed a larger role in therapy (16,341,342,345–348,409,410). On the basis of the available clinical data from observational studies, it is reasonable to conclude that the ICD is a reasonable therapy for secondary prevention of sudden cardiac arrest in patients with ARVD/C (16,341,342,345–348,409,410).

When the ICD is being considered for primary prevention, it should be kept in mind that predictive markers of SCD in patients with ARVD/C have not yet been defined in large prospective studies focusing on survival (16,341,342,345–348,409,410). Risk factors that have clinical utility in identifying patients with ARVD/C who are at risk for life-threatening ventricular arrhythmias include induction of VT during electrophysiological testing, detection of nonsustained VT on noninvasive monitoring, male gender, severe RV dilation, and extensive RV involvement (16,341,342,345–348,409,410). Young age at presentation (less than 5 years), LV involvement, prior cardiac arrest, and unexplained syncope serve as markers of risk (341,342,346–348,411,412). Patients with genotypes of ARVD/C associated with a high risk for SCD should be considered for ICD therapy (345).

Although the role of ICD therapy for primary prevention of sudden death in patients with ischemic heart disease and dilated, nonischemic cardiomyopathy is well established on the basis of multiple clinical trials with a consistent finding of benefit, the data supporting ICD use in patients with ARVD/C are less extensive (16,341,342,345–348,409,410). Some authorities have proposed that an ICD should be implanted in patients with ARVD/C and an increased risk for SCD based on the presence of a previous cardiac arrest, syncope due to VT, evidence of extensive RV disease, LV involvement, or presentation with polymorphic VT and RVA aneurysm, which is associated with a genetic locus on chromosome 1q42–43 (16,341,342,345–348,409,410).

It is evident that there is not yet clear consensus on the specific risk factors that identify those patients with ARVD/C in whom the probability of SCD is sufficiently high to warrant an ICD for primary prevention. In the future, the results of large prospective registries with rigorous enrollment criteria for patients with ARVD/C in whom ICDs have been placed for primary prevention will give insights into the optimal risk stratification techniques for primary prevention. In the meantime, individualized decisions for primary prevention of SCD must be based on experience, judgment, and the available data. In considering this decision, the clinician should be mindful that in patients with ARVD/C, the ICD has proved safe and reliable in sensing and terminating sustained ventricular arrhythmias. Sudden death is rare in the available clinical series, whereas appropriate ICD shocks are common (16,341,342,345–348,409,410).

3.2.6. Noncompaction of the Left Ventricle

Noncompaction of the LV is a rare congenital cardiomyopathy characterized anatomically by excessive prominent trabeculae and deep intertrabecular recesses in the LV without other major congenital cardiac malfunction (410,413–421). The origin of the anatomic abnormalities is likely due to an arrest of normal embryogenesis of the endocardium and epicardium of the ventricle during development. This leads to suspension of the normal compaction process of the loose myocardial meshwork. Diagnosis is difficult and is frequently missed or delayed owing to lack of knowledge about this uncommon disease. Echocardiography is considered by many to be the diagnostic procedure of choice, but some cases are detected by computed tomography or magnetic resonance imaging. Abnormalities in the resting ECG, including bundle-branch block or ST-segment depression, are found in most patients, but the findings do not have a high degree of sensitivity or specificity (410,413–421).

Ventricular arrhythmias and sudden death are among the major complications of this disorder. Sudden death can occur at any age, and there are currently no techniques clinically useful for risk stratification for life-threatening ventricular arrhythmias with noncompaction. Although there is no impairment of systolic function, ventricular arrhythmias are frequent in noncompaction. Approximately 40% of children with noncompaction demonstrate complex ventricular arrhythmias. Available clinical data indicate that sudden death is the most common cause of mortality. Although there are no prospective trials or registry data, there are sufficient observational data to indicate that placement of an ICD as a strategy to reduce the risk of sudden death is a reasonable clinical strategy (410,413–421).

3.2.7. Primary Electrical Disease (Idiopathic Ventricular Fibrillation, Short-QT Syndrome, Brugada Syndrome, and Catecholaminergic Polymorphic Ventricular Tachycardia)

The Brugada syndrome is characterized by ST-segment elevation across the right precordial leads in association with a high risk of SCD (16,422–425). Although the Brugada-pattern ECG most commonly shows J-point segment elevation in leads V_1 to V_3 and right bundle-branch block, the ECG pattern can be intermittent (16). Less commonly, the J-point elevation occurs in the inferior leads (16). Patients with the Brugada syndrome have a structurally normal heart with a primary channelopathy (16,426). This is transmitted with an autosomal dominant pattern of inheritance, and more than 90% of those affected are male. The genetic basis for the Brugada syndrome involves the cardiac sodium channel gene (SCN5A) (16,426).

Cardiac events such as syncope or cardiac arrest occur predominantly in the third and fourth decades of life, although presentation with cardiac arrest in neonates or children has been reported (16,422,424). Fever can acutely predispose to cardiac arrest in the Brugada syndrome (16,422–424.)

Risk stratification for SCD in patients with the Brugada syndrome is of clinical importance, because implantation of an ICD is the only prophylactic measure able to prevent SCD (16,422–424). As with long-QT syndrome, there are no data showing that family history predicts cardiac events among family members with the Brugada syndrome (16). Accordingly, asymptomatic individuals with the characteristic ECG but with no family history are not necessarily at low risk (16). Additionally, family members of an individual with SCD due to Brugada syndrome should not be assumed to be at increased risk of SCD (16). Patients with a spontaneous Brugada pattern have a worse prognosis than individuals in whom the typical ECG is observed only after pharmacological drug challenge (16,422–424). Patients with syncope and the ECG pattern of spontaneous ST-segment elevation have a 6-fold higher risk of cardiac arrest than patients without syncope and the spontaneous ECG pattern (16,422,424).

The role of electrophysiological testing remains controversial in the Brugada syndrome. Although some investigators suggest that electrophysiological testing has a useful role in risk stratification, others have not confirmed this observation. Electrophysiological testing had a low positive predictive value (23%), but over a 3-year follow-up, it had a very high negative predictive value (93%) (16,422,424). By contrast, Priori et al. reported that electrophysiological testing has a low accuracy in predicting individuals who will experience cardiac arrest (16,410). Priori et al. have proposed that noninvasive risk stratification based on the ECG and symptoms provides an accurate alternative for risk stratification (16,410).

Because only a single gene has been linked to the Brugada syndrome, there is still insufficient information about the contribution of genetic defects in predicting clinical outcome (16,410,426). Specific mutations in the SCN5A gene do not identify a subset of patients at higher risk of cardiac events (16,410,426). SCD is caused by rapid polymorphic VT or VF that frequently occurs at rest or during sleep (16). Patients with Brugada syndrome usually do not have ventricular extrasystoles or nonsustained runs of VT at Holter recording. Therefore, the therapeutic approach for these patients is centered on the prevention of cardiac arrest.

Catecholaminergic polymorphic VT is characterized by ventricular tachyarrhythmias that develop in relation to physical or emotional stress in the presence of a resting ECG that shows no diagnostic abnormalities at rest (16,428–431). The initial symptoms often manifest during childhood, although late-onset cases have been described (16,385,410,427–431). Catecholaminergic polymorphic VT is transmitted by either an autosomal dominant or recessive inheritance pattern. Approximately one-half of the autosomal dominant cases are caused by mutations in the gene encoding the cardiac ryanodine receptor (RyR2) (16). This receptor is responsible for calcium release from the stores of the sarcoplasmic reticulum (16). Mutations in the gene that encodes calsequestrin (CASQ2), a calcium buffering protein in the sarcoplasmic reticulum, have been associated with the recessive form of catecholaminergic polymorphic VT (16).

Risk stratification for SCD in catecholaminergic polymorphic VT is not possible given the relatively small number of patients reported. Most clinical reports indicate that beta blockers appear to be an effective treatment. Patients who have had an episode of VF are considered at higher risk and are usually treated with an ICD in addition to beta-blocker therapy (16,385,410,431). The recurrence of sustained VT, hemodynamically untolerated VT, or syncope for which causes other than VT are excluded while the patient is receiving a beta blocker are similarly considered markers of higher risk (16). In such patients, an ICD is a commonly used and reasonable approach (16). Furthermore, electrophysiological testing is not useful in the management of patients with catecholaminergic polymorphic VT since the arrhythmia is usually not inducible with programmed ventricular stimulation (16,385,410,431). Both supraventricular and ventricular arrhythmias are usually reproducibly induced by exercise stress test (16,385,410,431). Isolated premature ventricular complexes generally precede runs of nonsustained VT (16). With continued exercise, the runs of VT typically increase in duration, and VT may become sustained (16). A beat-to-beat alternating QRS axis that changes by 180° ("bidirectional VT") is a typical pattern of catecholaminergic polymorphic VT-related arrhythmias (16). Catecholaminergic polymorphic VT patients can also present with irregular polymorphic VT or VF (16). Beta blockers are generally effective in preventing recurrences of syncope even when arrhythmias can still be elicited during an exercise stress test (16). If syncope occurs in a patient taking a beta blocker, implantation of an ICD is recommended (16).

VF has been reported in patients with abnormal repolarization due to ion channel mutations that result in a markedly shortened QT interval (432). Only a few small series of such patients have been described, and at present, evidence-based recommendations about management of asymptomatic individuals with a short QT interval cannot be made. Some patients who survive a clinical episode of VF have no identifiable structural heart disease, no documented transient cause for arrhythmia, and no known ion channel defect. In such patients, VF is termed "idiopathic." ICD therapy is appropriate for secondary prevention in patients with the short-QT syndrome and idiopathic VF.

3.2.8. Idiopathic Ventricular Tachycardias

Monomorphic VT may be seen in individuals with structurally normal hearts who have no known ion channelopathies. The most common sites of origin are the RV outflow tract, the fascicular region of the LV, structures in the LV outflow tract, and the mitral annular region. The risk for sudden death related to these arrhythmias is low (433).

3.2.9. Advanced Heart Failure and Cardiac Transplantation

Patients with moderate to severe heart failure face the twin risks of terminal heart failure decompensation and death due to unanticipated ventricular tachyarrhythmias. When ICD or CRT-D implantation is discussed with these patients, the likelihood of both life-saving and inappropriate shocks should be placed in the context of the overall anticipated mortality with heart failure, the expected duration of life prolongation after effective therapies, and the likely evolution to limiting symptoms and ultimately death due to pump failure (434). The relative contribution of preventable sudden death to mortality decreases with repeated hospitalizations and multiple comorbidities, particularly in the setting of kidney dysfunction or advanced age. These factors, whether cardiac or noncardiac, also influence the value that patients place on quality versus length of life remaining. However, individual preferences cannot be assumed and should be explored with each patient.

Candidates for transplantation constitute a special case of severe heart failure because of the likelihood of prolonged survival after transplantation, with 50% of patients currently surviving at 10 years after transplantation. The high rate of sudden death on the transplant waiting list merits ICD implantation in most candidates with heart failure who are awaiting transplantation out of the hospital. The ICD has been highly effective as a bridge to transplan-

tation for these individuals both with and without a prior history of life-threatening arrhythmias.

Class IV status itself is a heterogenous and dynamic state (435) in which the absolute incidence of sudden death increases but the proportion of sudden deaths prevented by ICDs declines, and heart failure deaths account for a greater proportion of overall mortality. Once patients have persistent or frequently recurrent Class IV symptoms despite optimal management, life expectancy is less than 12 months, and ICD implantation is not indicated, regardless of patient and family preferences. Occasionally, patients cannot be weaned from intravenous inotropic infusions and are discharged with chronic inotropic infusion therapy for symptom palliation, with the expectation that death due to heart failure will likely occur within the next 6 months. Despite the proarrhythmic potential of inotropic agents, these patients receiving chronic infusions should not be given an ICD (unless awaiting transplantation or other definitive therapy).

Often, patients hospitalized with Class IV symptoms will undergo substantial improvement and can be discharged on oral therapy with minimal or no symptoms at rest. For these patients who can remain stable at 1 month after discharge, without evidence of recurrent congestion or worsening renal function, survival is similar to that of other Class III patients who have not been recently hospitalized. In this situation, ICD implantation can be discussed and may be expected to improve survival.

Patients with Class IV symptoms of heart failure with prolonged QRS duration and optimal lead placement may return to Class III status or better for both function and survival, at which point prevention of sudden death again becomes a relevant goal. Information on this group is limited because only 10% of the almost 4,000 patients in resynchronization trials have had Class IV symptoms. In the COMPANION trial (224), there were Class IV patients for whom resynchronization improved QOL and reduced rehospitalization and mortality; however, these patients had been stable at home before study entry and may not represent typical Class IV patients. Even in this selected group, there was no difference in 2-year survival between CRT patients with and without the defibrillator feature (230). In patients with Class IV symptoms in whom resynchronization is inadequate to restore clinical stability, the presence of a defibrillator often complicates the impending transition to end-of-life care.

Recommendations for Implantable Cardioverter Defibrillators

Secondary prevention refers to the prevention of SCD in those patients who have survived a prior cardiac arrest or sustained VT. Primary prevention refers to the prevention of SCD in individuals without a history of cardiac arrest or sustained VT. Patients with cardiac conditions associated with a high risk of sudden death who have unexplained syncope that is likely to be due to ventricular arrhythmias are considered to have a secondary indication.

Recommendations for consideration of ICD therapy, particularly those for primary prevention, apply only to patients who are receiving optimal medical therapy and have a reasonable expectation of survival with a good functional status for more than 1 year. It is difficult to estimate survival with heart failure in the general population, for whom comorbidities and age differ from those in trial populations from which the predictive models have been derived. Patients with repeated heart failure hospitalizations, particularly in the presence of reduced renal function, are at high risk for early death due to heart failure (436–438). See above for discussion regarding the use of LVEFs based on trial inclusion criteria.

We acknowledge that the "ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death" (16) used the LVEF of less than 40% as a critical point to justify ICD implantation for primary prevention of SCD. The LVEF used in clinical trials assessing the ICD for primary prevention of SCD ranged from less than or equal to 40% in MUSTT to less than or equal to 30% in MADIT II (329,332). Two trials, MADIT I (18) and SCD-HeFT (19) used LVEFs of less than or equal to 35% as entry criteria for the trial. This writing committee reached consensus that it would be best to have ICDs offered to patients with clinical profiles as similar to those included in the trials as possible. Having given careful consideration to the issues related to LVEF for these updated ICD guidelines, we have written these indications for ICDs on the basis of the specific inclusion criteria for LVEF in the trials. Because of this, there may be some variation from previously published guidelines (16).

We also acknowledge that the determination of LVEF lacks a "gold standard" and that there may be variation among the commonly used clinical techniques of LVEF determination. All clinical methods of LVEF determination lack precision and the accuracy of techniques varies amongst laboratories and institutions. Based on these considerations, this writing committee recommends that the clinician use the LVEF determination that they feel is the most clinically accurate and appropriate in their institution.

CLASS I

1. **ICD therapy is indicated in patients who are survivors of cardiac arrest due to VF or hemodynamically unstable sustained VT after evaluation to define the cause of the event and to exclude any completely reversible causes. (*Level of Evidence: A*) (16,319–324)**
2. **ICD therapy is indicated in patients with structural heart disease and spontaneous sustained VT, whether hemodynamically stable or unstable. (*Level of Evidence: B*) (16,319–324)**
3. **ICD therapy is indicated in patients with syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiological study. (*Level of Evidence: B*) (16,322)**
4. **ICD therapy is indicated in patients with LVEF less than or equal to 35% due to prior MI who are at least 40 days post-MI and are in NYHA functional Class II or III. (*Level of Evidence: A*) (16,333)**
5. **ICD therapy is indicated in patients with nonischemic DCM who have an LVEF less than or equal to 35% and who are in NYHA functional Class II or III. (*Level of Evidence: B*) (16,333,369,379)**
6. **ICD therapy is indicated in patients with LV dysfunction due to prior MI who are at least 40 days post-MI, have an LVEF less**

than or equal to 30%, and are in NYHA functional Class I. (*Level of Evidence: A*) (16,332)

7. ICD therapy is indicated in patients with nonsustained VT due to prior MI, LVEF less than or equal to 40%, and inducible VF or sustained VT at electrophysiological study. (*Level of Evidence: B*) (16,327,329)

CLASS IIa

1. ICD implantation is reasonable for patients with unexplained syncope, significant LV dysfunction, and nonischemic DCM. (*Level of Evidence: C*)
2. ICD implantation is reasonable for patients with sustained VT and normal or near-normal ventricular function. (*Level of Evidence: C*)
3. ICD implantation is reasonable for patients with HCM who have 1 or more major† risk factors for SCD. (*Level of Evidence: C*)
4. ICD implantation is reasonable for the prevention of SCD in patients with ARVD/C who have 1 or more risk factors for SCD. (*Level of Evidence: C*)
5. ICD implantation is reasonable to reduce SCD in patients with long-QT syndrome who are experiencing syncope and/or VT while receiving beta blockers. (*Level of Evidence: B*) (349–354)
6. ICD implantation is reasonable for nonhospitalized patients awaiting transplantation. (*Level of Evidence: C*)
7. ICD implantation is reasonable for patients with Brugada syndrome who have had syncope. (*Level of Evidence: C*)
8. ICD implantation is reasonable for patients with Brugada syndrome who have documented VT that has not resulted in cardiac arrest. (*Level of Evidence: C*)
9. ICD implantation is reasonable for patients with catecholaminergic polymorphic VT who have syncope and/or documented sustained VT while receiving beta blockers. (*Level of Evidence: C*)
10. ICD implantation is reasonable for patients with cardiac sarcoidosis, giant cell myocarditis, or Chagas disease. (*Level of Evidence: C*)

CLASS IIb

1. ICD therapy may be considered in patients with nonischemic heart disease who have an LVEF of less than or equal to 35% and who are in NYHA functional Class I. (*Level of Evidence: C*)
2. ICD therapy may be considered for patients with long-QT syndrome and risk factors for SCD. (*Level of Evidence: B*) (16,349–354)
3. ICD therapy may be considered in patients with syncope and advanced structural heart disease in whom thorough invasive and noninvasive investigations have failed to define a cause. (*Level of Evidence: C*)
4. ICD therapy may be considered in patients with a familial cardiomyopathy associated with sudden death. (*Level of Evidence: C*)
5. ICD therapy may be considered in patients with LV noncompaction. (*Level of Evidence: C*)

CLASS III

1. ICD therapy is not indicated for patients who do not have a reasonable expectation of survival with an acceptable functional status for at least 1 year, even if they meet ICD implantation criteria specified in the Class I, IIa, and IIb recommendations above. (*Level of Evidence: C*)
2. ICD therapy is not indicated for patients with incessant VT or VF. (*Level of Evidence: C*)
3. ICD therapy is not indicated in patients with significant psychiatric illnesses that may be aggravated by device implantation or that may preclude systematic follow-up. (*Level of Evidence: C*)
4. ICD therapy is not indicated for NYHA Class IV patients with drug-refractory congestive heart failure who are not candidates for cardiac transplantation or CRT-D. (*Level of Evidence: C*)
5. ICD therapy is not indicated for syncope of undetermined cause in a patient without inducible ventricular tachyarrhythmias and without structural heart disease. (*Level of Evidence: C*)
6. ICD therapy is not indicated when VF or VT is amenable to surgical or catheter ablation (e.g., atrial arrhythmias associated with the Wolff-Parkinson-White syndrome, RV or LV outflow tract VT, idiopathic VT, or fascicular VT in the absence of structural heart disease). (*Level of Evidence: C*)
7. ICD therapy is not indicated for patients with ventricular tachyarrhythmias due to a completely reversible disorder in the absence of structural heart disease (e.g., electrolyte imbalance, drugs, or trauma). (*Level of Evidence: B*) (16)

3.3. Implantable Cardioverter-Defibrillators in Children, Adolescents, and Patients With Congenital Heart Disease

The indications for ICD implantation in young patients and those with congenital heart disease have evolved over the past 15 years based on data derived primarily from adult randomized clinical trials. Similar to adults, ICD indications have evolved from the secondary prevention of SCD to the treatment of patients with sustained ventricular arrhythmias to the current use of ICDs for primary prevention in patients with an increased risk of SCD. However, in contrast to adults, there are minimal prospective data regarding ICD survival benefit, because fewer than 1% of all ICDs are implanted in pediatric or congenital heart disease patients (439). Considerations such as the cumulative lifetime risk of SCD in high-risk patients and the need for decades of antiarrhythmic therapy make the ICD an important treatment option for young patients.

SCD in childhood and adolescence is associated with 3 principal forms of cardiovascular disease: 1) congenital heart disease, 2) cardiomyopathies, and 3) genetic arrhythmia syndromes (440,441). Prospective identification and treatment of young patients at risk for sudden death is crucial because compared with adults, a very low percentage of children undergoing resuscitation survive to hospital discharge (442).

The indications for ICD therapy in pediatric patients who have been resuscitated or who are at high risk for SCD are similar to those for adults. Data from nonrandomized studies provide support for the Class I recommendation that young patients who have been resuscitated from SCD should undergo ICD implantation after a careful evaluation to exclude any potentially reversible causes (440,443–445). Spontaneous sustained VT or unexplained syncope with inducible sustained hypotensive VT in patients with congenital heart disease are also considered Class I ICD indications when other remediable causes (hemodynamic or arrhythmic) have been excluded (446). Catheter ablation or surgical therapies may provide an alternative to use of an ICD in patients with congenital heart disease and recurrent VT (447).

Recommendations regarding ICD implantation for primary prevention of SCD in young patients are based on limited clinical experience and extrapolation of data from adult studies. No randomized clinical trials have been performed to date, and given the relative infrequency of SCD in young patients, they are unlikely to be completed in the near future. Because the risk of unexpected sudden death is greater in young patients than in adults with genetic diseases such as HCM or the long-QT syndrome, a family history of sudden death, possibly with genetic confirmation, may influence the decision to implant an ICD for primary prevention. Additional risk factors to be considered in these diseases are discussed in specific sections in this document (354,382,448).

With regard to primary prevention of SCD in patients with congenital heart disease, the marked heterogeneity of defects precludes generalization of risk stratification. Unexpected sudden death is reported in 1.2% to 3.0% of patients per decade after surgical treatment of tetralogy of Fallot, with risk factors including ventricular dysfunction, QRS duration, and atrial and ventricular arrhythmias (249). A significantly greater risk of SCD has been identified for patients with transposition of the great arteries or aortic stenosis, with most cases presumed to be due to a malignant ventricular arrhythmia associated with ischemia, ventricular dysfunction, or a rapid ventricular response to atrial flutter or fibrillation (449–451).

The risk of SCD associated with systemic ventricular dysfunction in congenital heart disease patients remains controversial (452,453). The ability to define the risk associated with impaired function is complicated by the fact that right (pulmonary) ventricular dysfunction is more common than left (systemic) ventricular dysfunction and that a variety of atrial arrhythmias and conduction blocks may independently predispose these patients to arrhythmias or syncope. The lack of prospective and randomized clinical trials precludes exact recommendations regarding risk stratification and indications for ICD implantation for primary prevention of SCD in patients with postoperative congenital heart disease and ventricular dysfunction. One other potential ICD indication in young patients, which is similar to adults, is the patient with congenital coronary anomalies or coronary aneurysms or stenoses after Kawasaki disease, in which an ischemic substrate for malignant arrhythmias may be present (441).

Because of concern about drug-induced proarrhythmia and myocardial depression, an ICD (with or without CRT) may be preferable to antiarrhythmic drugs in young patients with DCM or other causes of impaired ventricular function who experience syncope or sustained ventricular arrhythmias. ICDs may also be considered as a bridge to orthotopic heart transplantation in pediatric patients, particularly given the longer times to donor procurement in younger patients (454,455).

Recommendations for Implantable Cardioverter-Defibrillators in Pediatric Patients and Patients With Congenital Heart Disease

CLASS I

1. **ICD implantation is indicated in the survivor of cardiac arrest after evaluation to define the cause of the event and to exclude any reversible causes. (*Level of Evidence: B*) (440,443–445)**
2. **ICD implantation is indicated for patients with symptomatic sustained VT in association with congenital heart disease who have undergone hemodynamic and electrophysiological evaluation. Catheter ablation or surgical repair may offer possible alternatives in carefully selected patients. (*Level of Evidence: C*) (447)**

CLASS IIa

1. **ICD implantation is reasonable for patients with congenital heart disease with recurrent syncope of undetermined origin in the presence of either ventricular dysfunction or inducible ventricular arrhythmias at electrophysiological study. (*Level of Evidence: B*) (18,446)**

CLASS IIb

1. **ICD implantation may be considered for patients with recurrent syncope associated with complex congenital heart disease and advanced systemic ventricular dysfunction when thorough invasive and noninvasive investigations have failed to define a cause. (*Level of Evidence: C*) (451,454)**

CLASS III

1. **All Class III recommendations found in Section 3, "Indications for Implantable Cardioverter-Defibrillator Therapy," apply to pediatric patients and patients with congenital heart disease, and ICD implantation is not indicated in these patient populations. (*Level of Evidence: C*)**

3.3.1. Hypertrophic Cardiomyopathy

Prior studies of ICD therapy for primary and secondary prevention of SCD in HCM are discussed in Section 3.1.5 and Section 3.2.4; most of these studies have included both pediatric and adult patients. The indications for ICDs in pediatric patients with HCM for primary and secondary prevention of sudden cardiac arrest are the same as those for adults. Clinical decisions should be based on risks and benefits that may be unique to pediatric patients. In the pediatric population, recommendations for ICD therapy should be made with careful consideration of the risks of device implantation, which may be increased on the basis of body size. Additionally, consideration should be given to the additional years of benefit that could potentially result from prevention of SCD in this population.

3.4. Limitations and Other Considerations

3.4.1. Impact on Quality of Life (Inappropriate Shocks)

Despite its life-saving potential, the use of ICD therapy carries a risk for psychological consequences and may lead to a decrement in QOL, particularly among patients who have experienced shocks (456). Reports of significant behavioral disorders, including anxiety, device dependence, or social withdrawal, have been described with ICD implantation (457–459). However, QOL substudies from large, randomized clinical trials of ICD therapy demonstrated that overall, QOL was no different or was somewhat better among patients randomized to ICD therapy than among those in the control groups, with decreases in physical, emotional, and psychological measures of health-related QOL concentrated among

patients who experienced ICD shocks (328,367,460). Given the broader indication for and marked increase in implantation of ICDs for primary prevention that is being driven by the results of the SCD-HeFT and MADIT II trials (332,333), understanding the frequency and causes of inappropriate shocks and devising management strategies to mitigate both inappropriate therapies and their psychological and QOL consequences will be important for an increasingly large segment of the population.

A systematic review summarized the frequency of inappropriate ICD therapies reported in randomized clinical trials of primary and secondary prevention (461). In these trials, during follow-up that ranged from 20 to 45 months, inappropriate ICD therapy was delivered in 10% to 24% of patients. In the PainFREE Rx II (Pacing Fast VT Reduces Shock Therapies II) trial, in which patients were randomized to either ATP or shocks as first therapy for fast VT, at least 1 inappropriate detection occurred in 15% of patients during approximately 11 months of follow-up (294). The proportion of detections that were inappropriate was modestly but not significantly higher among primary prevention patients than among secondary prevention patients (46% versus 34%; $p=0.09$). Both older and more recent registry reports suggest similar rates of inappropriate therapy in unselected populations (462,463).

By far, the leading cause of inappropriate therapy is the misclassification of SVT, most commonly AF (294,358,462,463). But ICD lead malfunction and other causes, such as oversensing of T waves, double counting of prolonged QRS, and electromagnetic interference, may account for 4% to 30% of inappropriate therapy (305,367,462,464). Patients with multiple ICD shocks should be evaluated immediately to determine the cause of the shocks and to direct urgent management. Short-term therapy with anxiolytic drugs may be instituted early for patients after recurrent device firings to minimize acute and delayed anxiety reactions.

A variety of approaches to reduce the occurrence of inappropriate shocks are currently available, and selection depends on the cause of the shocks and the type of device implanted. Although there has been debate as to the utility of dual-chamber versus single-chamber devices in reducing rates of inappropriate ICD therapy, a recently published randomized trial suggests that optimal programming of dual-chamber devices can reduce the rate of inappropriate detections and therapies due to SVTs (465). In the multicenter Detect Supraventricular Tachycardia Study, 400 patients with a clinical indication for an ICD received dual-chamber devices and were randomized in a single-blind fashion to optimal single- or dual-chamber detection programming. SVT occurred in 34% of subjects (31% in the single-chamber arm and 37% in the dual-chamber arm). Rates of inappropriate detection of SVT were substantial in both arms (39.5% in the single-chamber arm and 30.9% in the dual-chamber arm), but the adjusted odds ratio of inappropriate detection of SVT in the dual-chamber arm compared with the single-chamber arm was 0.53 (95% CI 0.30 to 0.94; $p=0.03$). This reduction in inappropriate detection translated to a similar reduction in inappropriate therapy, with no compromise of VT detection, which makes this trial the first to show superiority of dual-chamber devices when optimally programmed. Other areas of active research include the development of enhanced mathematically modeled detection protocols for evaluation of internal electrograms to improve discrimination of SVT from VT and to increase the ability to detect lead failures (466–468). Regardless of the cause of or solution for inappropriate ICD therapy (particularly shocks), careful attention to a team-based approach that includes the patient and family in emotional and psychological support is also recommended (456,469).

3.4.2. Surgical Needs

Surgically placed epicardial pacing leads are indicated in selected instances when standard transvenous lead placement is either not feasible or contraindicated. Examples of such circumstances include: 1) inability or failure to place an adequate LV lead in patients requiring biventricular pacing, 2) indications for permanent pacing in certain pediatric patients and in pediatric or adult patients with tricuspid valve prostheses or recurrent or prolonged bacteremia, and 3) congenital acquired venous anomalies that preclude transvenous access to the heart.

The reported success rate of coronary venous lead implantation for biventricular pacing ranges from 81% to 99% (470,471). Causes of failed percutaneous lead placement may be anatomic (superior vena cava or coronary sinus obstruction or inadequate coronary venous anatomy) or technical (failure to cannulate the coronary sinus, coronary sinus dissection, inadequately high pacing thresholds with intermittent capture, diaphragmatic pacing due to proximity of the phrenic nerve to the target coronary sinus branch, or lead dislodgement) (470,472,473). When coronary sinus lead implantation fails, several nonrandomized studies have demonstrated that surgical LV lead placement is almost always successful (470–473). In this setting, the key advantage of surgical lead placement is access to the entire posterior and lateral walls of the LV, which enables the choice of the best pacing site (471,474). The combination of echocardiography with tissue Doppler imaging and electrophysiological measurements may facilitate the choice of a transthoracically directed LV epicardial pacing site (473). Implantation of 2 epicardial leads may be considered to provide backup capability if 1 lead should fail or become dislodged (475). Steroid-eluting epicardial leads may be preferable to screw-on leads (473).

The choice of surgical procedure appears to influence hospital morbidity. Surgical approaches for placement of LV epicardial leads include left thoracotomy, left thoracoscopy, and robotically assisted port-based placement. Thoracotomy in fragile patients with heart failure has been associated with bleeding, stroke, hypotension, and arrhythmias (470,476). In contrast, thoracoscopic and robotic approaches have been reported to be associated with minimal morbidity and may be preferred (472,473,475). These less invasive procedures generally require 60 to 90 minutes of operative time and a mean hospital stay of 4 to 5 days (472). However, not all patients are candidates for minimally invasive or robotic procedures. Subjects who have undergone prior thoracotomy or

sternotomy operations may have limited pericardial/epicardial accessibility.

In certain instances, it may be advisable to place an LV epicardial lead at the time of concomitant cardiac surgery. In patients who are currently or in the future may be candidates for CRT who require coronary artery bypass grafting or mitral valve surgery and have medically refractory, symptomatic heart failure, ischemic cardiomyopathy or DCM, prolonged QRS interval, LV end-diastolic diameter greater than or equal to 55 mm, and LVEF less than or equal to 35%, the surgeon may elect to place an LV epicardial lead (477). The lead is tunneled to a prepectoral pocket for intraoperative or postoperative attachment to an appropriate pacing generator. This approach is probably not indicated for the patient who is expected to have substantial improvement in LVEF after cardiac surgery (e.g., the patient with extensive viable myocardium who is undergoing revascularization). There are limited data documenting outcomes of this "preemptive" strategy.

Epicardial leads may be necessary in some pediatric patients. The most common indications for permanent pacemaker implantation in the pediatric population are SND or AV block after surgery for congenital heart disease and congenital AV block (478). In most instances, such pacing systems can be placed by standard transvenous techniques (479). However, epicardial leads may be needed in children as a result of their small size, the presence of congenital heart defects with a right-to-left shunt, or an inability to pace the chamber desired because of anatomic barriers (e.g., after a Fontan procedure) (478–480). In such instances, steroid-eluting leads provide excellent durability (479).

Epicardial leads are suggested in some pediatric or adult patients who need pacing and who have recurrent or prolonged bacteremia (481). For a single episode of device-related bacteremia, extraction of all hardware followed by reimplantation by the transvenous route at a later date is appropriate.

Implantation of permanent epicardial pacing leads is indicated in the pacemaker-dependent patient undergoing mechanical tricuspid valve replacement. A prosthetic mechanical tricuspid valve represents an absolute contraindication to placement of transvenous RV leads, because such leads will cross the valve and may interfere with valve function. This scenario occurs commonly in patients with tricuspid valve endocarditis and a transvenous pacemaker. At surgery, all hardware should be removed. If the tricuspid valve is repairable, standard transvenous pacing leads can be placed postoperatively. However, if tricuspid valve replacement is necessary, epicardial ventricular leads should be implanted at the time of surgery.

3.4.3. Patient Longevity and Comorbidities

Physicians, patients, and their families increasingly will be faced with decisions about device-based therapies (ICD and CRT) in elderly patients who meet conventional criteria for implantation. These decisions require not only evidence of clinical benefit demonstrated in randomized clinical trials but also estimates of life expectancy, consideration of comorbidities and procedural risk, and patient preferences. Although these factors are important when device implantation is considered in any age group, they assume greater weight in clinical decision-making among the elderly.

Unfortunately, few clinical trials of device-based therapy have enrolled enough elderly patients (age greater than 75 years) to reliably estimate the benefits of device-based therapy in this group. Indeed, patients in device trials have generally had an average age less than 65 years and little comorbidity. In contrast, the average patient hospitalized with heart failure and low LVEF is 75 years old with 2 comorbidities. The 1-year mortality rate for this population is in the range of 30% to 50%, with a 2-fold higher risk of death in patients with estimated creatinine clearance less than 60 ml per minute (326,482). The presence of chronic pulmonary disease and dementia further increases the risk for death. Fewer than 10% of deaths in this population could be attributed to presumed SCD in patients living independently (482). After 3 hospitalizations for heart failure in a community population, median survival declines to 1 year and would be prolonged by only 0.3 years even if all presumed SCDs were prevented (5). For all patients, the likelihood of meaningful prolongation of life by prevention of SCD must be assessed against the background of other factors that limit patient function and survival.

Among 204 elderly patients with prior MI and LVEF less than or equal to 30% enrolled in MADIT II (total n=1,223), a trial of primary prevention of SCD with ICD therapy, the HR for mortality with ICD therapy was 0.56 (95% CI 0.29 to 1.08; p=0.08), which was similar to that for younger patients (HR 0.63, 95% CI 0.45 to 0.88; p=0.01) (482a). Furthermore, QOL scores were similar among older and younger patients. Subgroup analyses by age (less than or equal to 65 versus greater than 65 years) from COMPANION and SCD-HeFT showed some erosion of benefit among the older group, but there were no significant treatment interactions with age (224,333).

In a study of 107 consecutive patients greater than 80 years old (82% with ischemic cardiomyopathy) and 241 consecutive patients 60 to 70 years of age (80% with ischemic cardiomyopathy), life expectancy after device implantation (predominantly ICD alone) among the octogenarians was 4.2 years compared with 7 years among those 60 to 70 years old (483). Thus, although survival after implantation is shorter among the elderly than among younger groups, survival is substantial, and age itself should not be the predominant consideration in the use of device-based therapy among the elderly.

The presence and number of noncardiac comorbidities are another important consideration in the decision to proceed with device-based therapy in the elderly. In one registry, although age greater than 75 years and heart failure were important predictors of death at 1 and 2 years of follow-up, after adjustment for age, heart failure, and patient sex, the number of noncardiac comorbidities was statistically significantly associated with survival among 2,467 patients who received ICD therapy (484). The presence of 3 or more noncardiac comorbidities was associated with a nearly 3-fold increase in the hazard for mortality (HR 2.98, 95% CI 1.74 to 5.10). Therefore, as much as age, the presence and number of

noncardiac comorbidities are critical considerations in the decision to use device-based therapy.

A meta-analysis of secondary prevention trials (AVID, CASH, and CIDS) revealed that although ICD therapy reduced all-cause and arrhythmic death among patients less than 75 years old, among 252 patients older than 75 years, the HR for all-cause mortality (predominantly due to progressive heart failure) was 1.06 (95% CI 0.69 to 1.64; p=0.79), and for arrhythmic death, it was 0.90 (95% CI 0.42 to 1.95; p=0.79) (485). The interaction p value was 0.09, which suggests that the elderly may derive less benefit from ICD therapy in secondary prevention than younger patients.

In summary, these data suggest that although age is an important predictor of outcome after ICD therapy, mean survival of more than 4 years may be expected even among octogenarians, and age alone should not be used as a sole criterion to withhold device-based therapy. However, important considerations in the decision to use device-based therapy should include the indication for device implantation (for ICDs, primary versus secondary prevention), the number of comorbidities, and patient preferences.

Considerations specific to elderly patients are also relevant to pacing, CRT, and ICD therapies. Similar to enrollment in ICD trials, few patients older than 75 years have been enrolled in trials of CRT. However, subgroup analyses from CARE-HF (age less than 66.4 versus greater than or equal to 66.4 years) and COMPANION (age less than or equal to 65 versus greater than 65 years) suggest that older patients derive similar benefit from CRT as younger patients (224,225).

The "ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death" addressed ICD implantation in the elderly (16). Many of those considerations are relevant to other types of device implantation. Because of underrepresentation of the elderly in clinical trials, much of the rationale for implanting devices in these patients rests on subgroup analyses that were not prespecified and is therefore relatively weak. Furthermore, not only relative efficacy but also procedural complication rates in older versus younger patients are largely unexplored. These unknowns must be balanced against the fact that many elderly patients remain functional until shortly before death and reasonably deserve similar treatment options as younger patients in many cases. The ethical principles of autonomy, beneficence ("do good and avoid evil"), and nonmaleficence ("do no harm") must always prevail.

3.4.4. Terminal Care

In the United States, the withholding and withdrawal of life-sustaining treatments (e.g., cardiopulmonary resuscitation, mechanical ventilation, or hemodialysis) from terminally ill patients who do not want the treatments is ethical and legal (486). Honoring these requests is an integral aspect of patient-centered care and should not be regarded as physician-assisted suicide or euthanasia.

When terminally ill patients (or their surrogates) request pacemaker, ICD, or CRT deactivation, questions related to the ethics of device deactivation may arise. Questions commonly asked include: Are implantable devices life-sustaining treatments? Is deactivation the same as physician-assisted suicide or euthanasia? Is deactivation ethical? Is it legal? Under what conditions (e.g., code status) should deactivation be performed? Who should carry out deactivation? What documentation should exist?

The prevalence of implantable devices in patients dying of noncardiac diseases makes this an increasingly encountered clinical issue. Patients and families fear that devices will prolong the dying process, and some dying patients with ICDs fear uncomfortable defibrillations. In fact, investigators have found that some patients with ICDs experience uncomfortable defibrillations throughout the dying process, including moments before death. Cardiologists who implant devices do not commonly have discussions with patients about end-of-life issues and device deactivation. Furthermore, published experience with deactivation of devices is limited (487).

There is general consensus regarding the ethical and legal permissibility of deactivating ICDs in dying patients who request deactivation (488). However, caregivers involved in device management generally make a distinction between deactivating a pacemaker and deactivating an ICD or CRT device. Given the clinical context, all 3 can be considered life-sustaining treatments. Notably, all of these devices may be refused by patients, and to impose them on patients who do not want them is unethical and illegal (battery). Furthermore, ethics and law make no distinction between withholding and withdrawing treatments.

An approach to dying patients who request pacemaker, ICD, or CRT deactivation should include the following:

- A dying patient (or, if the patient lacks decision-making capacity, the patient's surrogate decision maker) who requests device deactivation should be fully informed of the consequences and alternatives to device deactivation, and a summary of the conversation should be recorded in the medical record.
- An order for device deactivation should be accompanied by a do-not-resuscitate (DNR) order; these orders should be recorded in the patient's medical record.
- Psychiatric consultation should be sought in any situation in which a dying patient who requests device deactivation is thought to have impaired decision-making capacity.
- Ethics consultation should be sought in any situation in which the clinician or clinicians disagree, based on their clinical judgment, with a request for device deactivation.
- If the clinician asked to deactivate a device has personal beliefs that prohibit him or her from carrying out device deactivation (conscientious objection), then the patient should be referred to another clinician.
- If the patient is remote from the implanting medical center, the clinician who is responsible for the patient's care at the local site should document the information noted above in the medical record, and someone capable of programming the device to "inactive" status should be recruited to reprogram the device under the direction of the local physician.

Clinicians involved in device education at the time of implantation may need to provide more comprehensive information with regard to end-of-life issues. For example, clinicians should encourage patients undergoing device implantation to complete advanced directives and specifically address the matter of device management and deactivation if the patient is terminally ill.

3.5. Cost-Effectiveness of Implantable Cardioverter-Defibrillator Therapy

Long-term follow-up studies have consistently demonstrated that cumulative medical costs are increased substantially among patients receiving an ICD (17–19,489–491). Several studies have attempted to weigh whether these added costs are worthwhile in light of the potential for improved survival among patients receiving ICD therapy (492). These studies calculate a cost-effectiveness ratio that is defined as the difference in the total cost of patients receiving an ICD and patients receiving alternative therapy, divided by the additional life-years of survival provided by an ICD compared with alternative therapy. A benchmark for comparison is provided by renal dialysis, which costs approximately $50,000 to add 1 life-year of survival. Cost-effectiveness, like other outcome measures in clinical research studies, must be interpreted in light of the characteristics of the study populations and the length of follow-up available.

The early studies of ICD cost-effectiveness were based on mathematical models and relied on nonrandomized studies to estimate clinical efficacy and cost. These studies found cost-effectiveness ratios of $17,000 (493), $18,100 (494), and $29,200 per year of life saved (495). Another model incorporated costs of nonthoracotomy ICDs and efficacy estimates based on randomized trials and found ICD cost-effectiveness was between $27,300 and $54,000 per life-year gained, which corresponded to risk reductions of 40% and 20%, respectively (496).

Several randomized clinical trials have measured both cost and clinical outcomes and thus can directly estimate ICD cost-effectiveness. MADIT found a 54% reduction in total mortality and a cost-effectiveness ratio of $27,000 per life-year added (18). In contrast, CIDS found a 20% reduction in total mortality and a cost-effectiveness ratio of $139,000 per life-year added (322,490). The cost-effectiveness ratio from the AVID trial was $66,677 per life-year added (491). MADIT II found a 32% reduction in total mortality and $39,200 higher costs among ICD-assigned patients than among those treated with conventional therapy (17). The cost-effectiveness ratio in MADIT II was measured as $235,000 per year of life added at 2 years of follow-up but was projected to be between $78,600 and $114,000 per year of life added by 12 years of follow-up. SCD-HeFT reported that total mortality was reduced by 23% and costs increased by $19,000 over 5 years of follow-up in patients assigned to ICDs compared with patients assigned to placebo (19). SCD-HeFT estimated the lifetime cost-effectiveness ratio of the ICD strategy was $38,400 per year of life added. This range of results from randomized studies is primarily due to different estimates of the effectiveness of the ICD in reducing mortality, because all showed similar increases in the cost of care among ICD recipients. When the results of all clinical trials were used in a model that used a consistent framework to project the full gain in life expectancy and lifetime costs in each trial (497), the cost-effectiveness of the ICD ranged from $25,300 to $50,700 per life-year added in the randomized trials in which the ICD reduced mortality. In the CABG-Patch trial and DINAMIT, however, patients assigned to an ICD had lower survival and higher costs than patients assigned to conventional therapy, and the ICD strategy was not cost-effective. The evidence suggests that proper patient selection is necessary for ICD implantation to be cost-effective; when ICD implantation is restricted to appropriately selected patients, it has a cost-effectiveness ratio similar to other accepted cardiovascular therapies and compares well to the standard benchmark of renal dialysis ($30,000 to $50,000 per year of life saved). In principle, ICD implantation will be more cost-effective when used for patients at high risk of arrhythmic death and at low risk of other causes of death. Additional risk stratification of patients with a reduced LVEF may improve patient selection for the ICD and thereby enhance its cost-effectiveness (498). Cost-effectiveness of the ICD would also be improved by lowering the cost of the device itself and further improving its reliability and longevity.

The cost-effectiveness of CRT has not been evaluated extensively. A CRT-P device reduces hospitalization for heart failure patients, and these cost savings partially offset the initial cost of device implantation. CRT-P devices are also effective in improving QOL and may improve survival. The cost-effectiveness of CRT-P devices versus medical therapy appears to be favorable. There are few data on the cost-effectiveness of CRT-D compared with CRT-P devices.

3.6. Selection of Implantable Cardioverter-Defibrillator Generators

A single RV lead for sensing and defibrillation is mandatory for all currently available ICD systems. Single-chamber ICD systems are capable of bradycardia support in the ventricle and ATP. Dual-chamber ICD systems (right atrial and RV leads) are additionally capable of AV sequential pacing. Triple-chamber ICD systems (right atrial, RV, and LV leads) are capable of CRT (CRT-D). Despite these increasing complexities, the optimal hardware system for ICD indications derived from mortality studies has not been fully evaluated. There is increasing evidence that choice of hardware may affect important outcomes in ICD patients. This relates primarily to 2 considerations: 1) management of ventricular pacing and 2) pain associated with high-voltage shocks. Conventional ICD therapy in any form may be associated with worsening heart failure, VT, VF, and noncardiac death that can be related to the adverse effects of RVA pacing (50,51). This is consistent with the increased risks of AF and heart failure attributable to RVA pacing in pacemaker trials (45,48). The issue of QOL in the ICD patient population has been evaluated extensively (460,499–502). Although ICD therapy is generally well tolerated by most patients, approximately 30% to 50% experience some degree of psychological distress after implantation (503). One of the principal limitations of ICD therapy is the discomfort asso-

ciated with high-voltage shocks. Several studies have noted a direct correlation between poor QOL scores and the experience of ICD shocks (460,499–501).

Any hardware system that increases unnecessary ventricular pacing from any site may increase the risk of heart failure, particularly in patients with poor cardiac ventricular systolic function (293). The risk of heart failure is increased even in hearts with initially normal ventricular systolic function and with part-time ventricular pacing. RVA pacing creates abnormal contraction, reduced ventricular systolic function, hypertrophy, and ultrastructural abnormalities. The magnitude of the effect relates to the frequency of ventricular pacing and the degree of pacing-induced mechanical dyssynchrony rather than the hardware system (49). Although these effects have been demonstrated most clearly during RVA pacing, biventricular or LV pacing may also induce dyssynchrony in hearts with normal ventricular conduction (504) and can reduce LV systolic function in patients with no baseline dyssynchrony (505).

In patients with no AV block and no intraventricular conduction abnormalities, ventricular pacing should be avoided as much as possible. For many ICD patients who do not have an indication for bradycardia support, this can be achieved by programming a very low backup ventricular pacing rate (i.e., 30 to 40 bpm). The optimal management of cardiac pacing in ICD patients in whom bradycardia support is required, desired, or emerges is unknown. For ICD patients with SND in whom bradycardia support is required or desired, ventricular pacing may be minimized by use of newer techniques specifically designed to promote intrinsic conduction (292,506). In patients with AV block, alternate single-site RV or LV pacing or biventricular pacing (CRT-P/CRT-D) may be superior to RVA pacing. Efforts to optimize pacing mode or site should be greater in patients with longer expected duration of pacing, poorer cardiac function, and larger mechanical asynchrony. Awareness of the problem of dyssynchrony should also lead to more regular monitoring of cardiac ventricular systolic function and mechanical asynchrony in any patient with ventricular pacing.

ATP refers to the use of pacing stimulation techniques for termination of tachyarrhythmias. Tachycardias that require reentry to persist are susceptible to termination with pacing. The most common mechanism of VT in ICD patients is scar-related reentry. The sine qua non of a re-entrant arrhythmia is the ability to reproducibly initiate and terminate the tachycardia by critically timed extrastimuli (124). Therefore, the possibility of successful termination of tachycardias with pacing can be anticipated on the basis of the mechanism. Such techniques can be applied automatically with ICDs and offer the potential for painless termination of VT.

Adjudicated analysis of stored electrograms has revealed that the majority (approximately 85% to 90%) of spontaneous ventricular tachyarrhythmias in ICD patients are due to VT and fast VT, whereas only approximately 10% are due to VF (507,508). Numerous older studies have consistently demonstrated that ATP can reliably terminate approximately 85% to 90% of slow VTs (cycle lengths less than 300 milliseconds to 320 milliseconds) with a low risk of acceleration (1% to 5%) (509–511). More recently, similarly high rates of success and low acceleration and syncope rates for fast VTs (average cycle length 240 milliseconds to 320 milliseconds) have been demonstrated (507,508). These observations have repositioned the ICD as primarily an ATP device with defibrillation backup only as needed. Reduction in painful shocks may improve patient QOL (508) and extend ICD pulse-generator longevity. It is not yet clear whether important differences in optimal application of ATP exist in different ICD patient populations. In general, secondary prevention patients have a greater frequency of spontaneous ventricular arrhythmia than primary prevention patients. However, differences in the incidence of specific ventricular rhythms (VT, fast VT, and VF), response to therapy (ATP or shocks), and susceptibility to spurious therapies due to SVT are incompletely characterized (294,512). Differences in substrate may be important as well. Monomorphic VT associated with chronic ischemic heart disease is most commonly due to classic reentry and is therefore susceptible to termination by ATP. Monomorphic VT is less commonly due to reentry and occurs with lower frequency in nonischemic DCM.

3.7. Implantable Cardioverter-Defibrillator Follow-Up

All patients with ICDs require periodic and meticulous follow-up to ensure safety and optimal device performance, as well as to monitor a patient's clinical status (513). The goals of ICD follow-up include monitoring of device system function; optimization of performance for maximal clinical effectiveness and system longevity; minimization of complications; anticipation of replacement of system components and tracking devices under advisory; ensuring timely intervention for clinical problems; patient tracking, education, and support; and maintenance of ICD system records. The importance of device surveillance and management should be discussed with patients before ICD implantation. Compliance with device follow-up is an important element in the evaluation of appropriate candidates for device therapy and to obtain the best long-term result.

ICD follow-up is best achieved in an organized program analogous to pacemaker follow-up at outpatient clinics (312). Physicians and institutions performing implantation of these devices should maintain follow-up facilities for inpatient and outpatient use. Such facilities should obtain and maintain implantation and follow-up support devices for all ICDs used at that facility. The facility should be staffed or supported by a cardiologist and/or electrophysiologist, who may work in conjunction with trained associated professionals (312,514,515). Continuous access to these services should be available as much as feasible on both a regularly scheduled and more emergent basis. The implantation and/or follow-up facility should be able to locate and track patients who have received ICDs or who have entered the follow-up program.

3.7.1. Elements of Implantable Cardioverter-Defibrillator Follow-Up

The follow-up of an ICD patient must be individualized in accordance with the patient's clinical status and conducted by a physician fully trained in ICD follow-up(12); if this is

not a physician fully trained in all aspects of ICD implantation and follow-up, then such an individual should be available for any problems that may develop. Direct patient contact is ideal, allowing for interval history taking, physical examination of the implantation site, and device programming changes that may be warranted. Six-month intervals for device follow-up appear to be safe (516), but more frequent evaluations may be required depending on the device characteristics and the patient's clinical status. Manufacturers' guidelines for device follow-up may vary with individual models and should be available. Device automaticity has facilitated follow-up (316), as has the implementation of remote monitoring techniques (513,517). Depending on the manufacturer, remote device interrogation is achieved through Internet-based systems or via radiofrequency transmissions from the ICD via a phone device to a central monitoring center; remote reprogramming of devices is not available currently. Remote monitoring may lessen the dependence on clinic visits, particularly in patients who live at a considerable distance from the follow-up clinic, and may allow for the earlier detection of real or potential problems associated with the device. Guidelines for remote monitoring have yet to be established. It should be recognized, furthermore, that remote monitoring is an adjunct to follow-up and cannot entirely supplant clinic visits (518,519).

In general, device programming is initiated at implantation and may be reviewed periodically. It is often necessary to reprogram the initially selected parameters either in the outpatient clinic or during electrophysiological testing. When device function or concomitant antiarrhythmic therapy is modified, electrophysiological testing may be warranted to evaluate sensing, pacing, or defibrillation functions of the device. Particular attention should be given to review of sensing parameters, programmed defibrillation and pacing therapies, device activation, and event logs. Technical elements that require review include battery status, lead system parameters, and elective replacement indicators. Intervening evaluation of device function is often necessary. In general, when ICD therapy is delivered, the device should be interrogated.

After implantation of a device, its performance should be reviewed, limitations on the patient's specific physical activities established, and registration accomplished. Current policies on driving advise patients with an ICD implanted for secondary prevention to avoid operating a motor vehicle for 6 months after the last arrhythmic event if it was associated with loss or near loss of consciousness to determine the pattern of recurrent VT/VF (520,521). For patients with ICDs implanted for primary prevention, avoidance of driving for at least 7 days to allow healing has been recommended (522). Interactions with electromagnetic interference sources potentially affect employment. Sports involvement(523) and recommendations regarding safeguards for future surgical procedures (524) should be discussed. There are currently not enough data to make recommendations regarding antibiotic prophylaxis for procedures or operations required in the first 6 months after ICD implantation; physicians must weigh the risks and benefits of antibiotic prophylaxis and use their judgment in each case. ICD recipients should be encouraged to carry proper identification and information about their device at all times. Patients receiving these devices can experience transient or sustained device-related anxiety. Education and psychological support before, during, and after ICD insertion are highly desirable and can improve the patient's QOL (457,458).

Increasing attention has been paid to the safety and efficacy of implantable devices. It is incumbent upon the follow-up physician to be aware of advisories issued in relation to potential device malfunction (2). Specific recommendations for clinicians managing such advisories are to consider lead/device replacement if death is a likely result of device malfunction; the mechanism of device/lead failure is known, potentially recurrent, and possibly life-threatening; the patient is pacemaker-dependent; the risk of replacement is substantially lower than the risk of device malfunction; or the device is approaching its elective replacement indicator (3). Complications related to replacement of ICD generators under advisory have been well documented, including infection, the need for reoperation, and death (525). The estimated device failure rate and the likelihood of mortality resulting from device failure must be weighed against the risk of procedural morbidity and mortality associated with device replacement. In general, for pacemaker-dependent patients, advisory device failure rates in excess of 0.3% warrant consideration of device replacement; in patients with ICD generators under advisory, an estimated failure rate of 3% favors replacement in the majority of cases, decreasing to 1% when procedural mortality rates are 0.1% or less and/or risk of fatal arrhythmias increases to 20% per year (526). It is anticipated that the above general recommendations and estimates will vary as a function of the specific nature of the advisory, how the malfunction presents, whether early detection and/or reprogramming may be employed in addressing the potential device failure, and whether the lead (versus the generator) is affected. This has been demonstrated, for example, in the case of a recent lead advisory associated with spurious shocks attributable to lead fracture, oversensing, and high impedance; reprogramming to minimize overdetection of noise, enabling of alert features to detect changes in impedance, and increasing utilization of remote monitoring to follow such leads may have an effect on future rates of invasive lead replacement and/or extraction (527).

3.7.2. Focus on Heart Failure After First Appropriate Implantable Cardioverter-Defibrillator Therapy

In patients with heart failure who have not previously had a life-threatening arrhythmia, the first event identifies them as being at higher risk than before for both sudden death and death due to heart failure, with the majority of patients surviving less than 2 years (17,19). It is not known to what extent these herald events serve as markers or as contributors to progression of disease. They should trigger reevaluation of treatable causes of heart failure and of the medical regimen. In addition, the treatment regimen should be evaluated for interventions that may decrease the risk of arrhythmia recurrence. Particular care should be paid to the titration of beta-adrenergic blockers. These agents have been shown to decrease disease progression and improve outcomes, but

uptitration can lead to heart failure exacerbation and must be attempted gradually in small dose increments. Many patients with symptomatic heart failure cannot tolerate "target doses" of beta-adrenergic blockers, whether used primarily for the indication of heart failure or to prevent recurrent arrhythmias. Although patients with heart failure who have had device therapy would ideally be followed up by specialists in both arrhythmia management and heart failure management, most patients do not have routine access to such settings. To maximize the benefit after a sudden death has been prevented, it is crucial that the management team evaluate the heart failure profile, review the medical regimen, and plan for ongoing care.

4. Areas in Need of Further Research

The ACC/AHA Task Force on Practice Guidelines has charged writing committees to suggest areas in need of further research. To this end, the present writing committee offers the following suggestions. They are presented in tabular form for ease of readability. Their order does not imply any order of priority.

1. Optimal access to device therapy should be provided to all eligible populations irrespective of sex and ethnicity.
2. Risk stratification of patients meeting current clinical indications for primary prevention ICD implantation should be improved to better target therapy to those most likely to benefit from it.
3. Identification of patients most likely to benefit from/respond to CRT must be improved.
4. Identify patients without current pacemaker or ICD indications among those who may benefit from such therapies.
5. Indicators should be identified that provide direction about when it is safe to not replace an ICD that has reached the end of its effective battery life.
6. The cost-effectiveness of device therapy should be explored further
7. Guidelines for remote monitoring should be developed
8. Ways to improve reliability and longevity of leads and generators must be found, as well as methods to ensure discovery of performance issues when they arise.
9. Representation of the elderly in clinical trials should be increased
10. The influence of age on procedural complication rates and the risk/benefit ratio for device implantation should be defined.
11. The effect (positive, negative, or neutral) of biventricular or LV stimulation in patients with normal ventricular function should be determined.
12. The need for pacing after MI in the current era should be determined
13. Long-term outcomes and risk factors for patients receiving ICDs in general practice compared with trial populations and at academic centers should be identified and described.
14. Guidelines for device management in patients with terminal illness or other requests to terminate device therapy should be developed.
15. The role of ICDs in primary prevention for children with genetic channelopathies, cardiomyopathies, and congenital heart defects should be defined more precisely.
16. The efficacy of biventricular pacing in children with congenital heart disease and dilated cardiomyopathy should be determined. Appendix 3

2012 Presidents and Staff

References

1. Tracy CM, Epstein AE, Darbar D, et al. 2012 ACCF/AHA/HRS focused update of the 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2012;60:1297–313.

1a. ACCF/AHA Task Force on Practice Guidelines. Methodology Manual and Policies From the ACCF/AHA Task Force on Practice Guidelines. American College of Cardiology Foundation and American Heart Association, Inc. 2010. Available at: http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf and http://my.americanheart.org/idc/groups/ahamah-public/@wcm/@sop/documents/downloadable/ucm_319826.pdf. Accessed May 16, 2012.

1b. Committee on Standards for Systematic Reviews of Comparative Effectiveness Research, Institute of Medicine. Finding What Works in Health Care: Standards for Systematic Reviews. Washington, DC: The National Academies Press; 2011.

1c. Committee on Standards for Developing Trustworthy Clinical Practice Guidelines, Institute of Medicine. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press; 2011.

1d. Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices). J Am Coll Cardiol. 2008;51:e1–62.

2. Maisel WH, Moynahan M, Zuckerman BD, et al. Pacemaker and ICD generator malfunctions: analysis of Food and Drug Administration annual reports. JAMA. 2006;295:1901–6.

3. Carlson MD, Wilkoff BL, Maisel WH, et al. Recommendations from the Heart Rhythm Society Task Force on Device Performance Policies and

Guidelines. Endorsed by the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) and the International Coalition of Pacing and Electrophysiology Organizations (COPE). Heart Rhythm. 2006;3:1250–73.

4. Love CJ, Wilkoff BL, Byrd CL, et al. Recommendations for extraction of chronically implanted transvenous pacing and defibrillator leads: indications, facilities, training. North American Society of Pacing and Electrophysiology Lead Extraction Conference Faculty. Pacing Clin Electrophysiol. 2000;23:544–51.
5. Goldstein NE, Lampert R, Bradley E, Lynn J, Krumholz HM. Management of implantable cardioverter defibrillators in end-of-life care. Ann Intern Med. 2004;141:835–8.
8. Kim SG, Fogoros RN, Furman S, Connolly SJ, Kuck KH, Moss AJ. Standardized reporting of ICD patient outcome: the report of a North American Society of Pacing and Electrophysiology Policy Conference, February 9–10, 1993. Pacing Clin Electrophysiol. 1993;16:1358–62.
9. Epstein AE, Carlson MD, Fogoros RN, Higgins SL, Venditti FJ Jr. Classification of death in antiarrhythmia trials. J Am Coll Cardiol. 1996;27:433–42.
10. Hayes DL, Naccarelli GV, Furman S, Parsonnet V. Report of the NASPE Policy Conference training requirements for permanent pacemaker selection, implantation, and follow-up. North American Society of Pacing and Electrophysiology. Pacing Clin Electrophysiol. 1994;17:6–12.
11. Day JD, Curtis AB, Epstein AE, et al. Addendum to the clinical competency statement: training pathways for implantation of cardioverter defibrillators and cardiac resynchronization devices. Heart Rhythm. 2005;2:1161–3.
12. Curtis AB, Ellenbogen KA, Hammill SC, et al. Clinical competency statement: training pathways for implantation of cardioverter defibrillators and cardiac resynchronization devices. Heart Rhythm. 2004;1:371–5.
13. Beller GA, Bonow RO, Fuster V. ACCF 2008 Recommendations for Training in Adult Cardiovascular Medicine Core Cardiology Training (COCATS 3) (Revision of the 2002 COCATS Training Statement): a report of the American College of Cardiology Foundation/American Heart Association/American College of Physicians Task Force on Clinical Competence and Training. J Am Coll Cardiol. 2008;51:333–8.
14. Gregoratos G, Abrams J, Epstein AE, et al. ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee to Update the 1998 Pacemaker Guidelines). J Am Coll Cardiol. 2002;40:1703–19.
15. Gregoratos G, Abrams J, Epstein AE, et al. ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee to Update the 1998 Pacemaker Guidelines). Circulation. 2002;106:2145–61.
16. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death. J Am Coll Cardiol. 2006;48:e247–346.
17. Zwanziger J, Hall WJ, Dick AW, et al. The cost effectiveness of implantable cardioverter-defibrillators: results from the Multicenter Automatic Defibrillator Implantation Trial (MADIT)-II. J Am Coll Cardiol. 2006;47:2310–8.
18. Mushlin AI, Hall WJ, Zwanziger J, et al. The cost-effectiveness of automatic implantable cardiac defibrillators: results from MADIT. Multicenter Automatic Defibrillator Implantation Trial. Circulation. 1998;97:2129–35.
19. Mark DB, Nelson CL, Anstrom KJ, et al. Cost-effectiveness of defibrillator therapy or amiodarone in chronic stable heart failure: results from the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). Circulation. 2006;114:135–42.
20. Ferrer MI. The sick sinus syndrome in atrial disease. JAMA. 1968;206:645–6.
21. Rosenqvist M, Obel IW. Atrial pacing and the risk for AV block: is there a time for change in attitude? Pacing Clin Electrophysiol. 1989;12:97–101.
22. Lamas GA, Lee KL, Sweeney MO, et al. Ventricular pacing or dual-chamber pacing for sinus-node dysfunction. N Engl J Med. 2002;346:1854–62.
23. Lamas GA, Orav EJ, Stambler BS, et al. Quality of life and clinical outcomes in elderly patients treated with ventricular pacing as compared with dual-chamber pacing. Pacemaker Selection in the Elderly Investigators. N Engl J Med. 1998;338:1097–104.
24. Mangrum JM, DiMarco JP. The evaluation and management of bradycardia. N Engl J Med. 2000;342:703–9.
25. Sweeney MO, Hellkamp AS, Ellenbogen KA, et al. Prospective randomized study of mode switching in a clinical trial of pacemaker therapy for sinus node dysfunction. J Cardiovasc Electrophysiol. 2004;15:153–60.
26. Ballas SL, Rashidi R, McAlister H, et al. The use of beep-o-grams in the assessment of automatic implantable cardioverter defibrillator sensing function. Pacing Clin Electrophysiol. 1989;12:1737–45.
27. Kay GN. Quantitation of chronotropic response: comparison of methods for rate-modulating permanent pacemakers. J Am Coll Cardiol. 1992;20:1533–41.
28. Wilkoff B, Corey J, Blackburn G. A mathematical model of the cardiac chronotropic response to exercise. J Electrophysiol. 1989;3:176–80.
29. Katritsis D, Camm AJ. Chronotropic incompetence: a proposal for definition and diagnosis. Br Heart J. 1993;70:400–2.
30. Menozzi C, Brignole M, Alboni P, et al. The natural course of untreated sick sinus syndrome and identification of the variables predictive of unfavorable outcome. Am J Cardiol. 1998;82:1205–9.
31. Lamas GA, Lee K, Sweeney M, et al. The mode selection trial (MOST) in sinus node dysfunction: design, rationale, and baseline characteristics of the first 1000 patients. Am Heart J. 2000;140:541–51.
32. Alt E, Volker R, Wirtzfeld A, Ulm K. Survival and follow-up after pacemaker implantation: a comparison of patients with sick sinus syndrome, complete heart block, and atrial fibrillation. Pacing Clin Electrophysiol. 1985;8:849–55.
33. Simon AB, Janz N. Symptomatic bradyarrhythmias in the adult: natural history following ventricular pacemaker implantation. Pacing Clin Electrophysiol. 1982;5:372–83.
34. Meytes I, Kaplinsky E, Yahini JH, Hanne-Paparo N, Neufeld HN. Wenckebach A-V block: a frequent feature following heavy physical training. Am Heart J. 1975;90:426–30.
35. Talan DA, Bauernfeind RA, Ashley WW, Kanakis C Jr, Rosen KM. Twenty-four hour continuous ECG recordings in long-distance runners. Chest. 1982;82:19–24.
36. Zimetbaum P, Kim KY, Ho KK, Zebede J, Josephson ME, Goldberger AL. Utility of patient-activated cardiac event recorders in general clinical practice. Am J Cardiol. 1997;79:371–2.
37. Zimetbaum PJ, Josephson ME. The evolving role of ambulatory arrhythmia monitoring in general clinical practice. Ann Intern Med. 1999;130:848–56.
38. Assar MD, Krahn AD, Klein GJ, Yee R, Skanes AC. Optimal duration of monitoring in patients with unexplained syncope. Am J Cardiol. 2003;92:1231–3.
39. Krahn AD, Klein GJ, Skanes AC, Yee R. Use of the implantable loop recorder in evaluation of patients with unexplained syncope. J Cardiovasc Electrophysiol. 2003;14:S70–S73.
40. Prinzen FW, Augustijn CH, Arts T, Allessie MA, Reneman RS. Redistribution of myocardial fiber strain and blood flow by asynchronous activation. Am J Physiol. 1990;259:H300–8.
41. Thambo JB, Bordachar P, Garrigue S, et al. Detrimental ventricular remodeling in patients with congenital complete heart block and chronic right ventricular apical pacing. Circulation. 2004;110:3766–72.
42. Kanzaki H, Bazaz R, Schwartzman D, Dohi K, Sade LE, Gorcsan J III. A mechanism for immediate reduction in mitral regurgitation after cardiac resynchronization therapy: insights from mechanical activation strain mapping. J Am Coll Cardiol. 2004;44:1619–25.
43. Maurer G, Torres MA, Corday E, Haendchen RV, Meerbaum S. Two-dimensional echocardiographic contrast assessment of pacing-induced mitral regurgitation: relation to altered regional left ventricular function. J Am Coll Cardiol. 1984;3:986–91.
44. Vanderheyden M, Goethals M, Anguera I, et al. Hemodynamic deterioration following radiofrequency ablation of the atrioventricular conduction system. Pacing Clin Electrophysiol. 1997;20:2422–8.
45. Nielsen JC, Kristensen L, Andersen HR, Mortensen PT, Pedersen OL, Pedersen AK. A randomized comparison of atrial and dual-chamber pacing in 177 consecutive patients with sick sinus syndrome: echocardiographic and clinical outcome. J Am Coll Cardiol. 2003;42:614–23.

46. Nielsen JC, Andersen HR, Thomsen PE, et al. Heart failure and echocardiographic changes during long-term follow-up of patients with sick sinus syndrome randomized to single-chamber atrial or ventricular pacing. Circulation. 1998;97:987–95.
47. Nahlawi M, Waligora M, Spies SM, Bonow RO, Kadish AH, Goldberger JJ. Left ventricular function during and after right ventricular pacing. J Am Coll Cardiol. 2004;44:1883–8.
48. Sweeney MO, Hellkamp AS, Ellenbogen KA, et al. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. Circulation. 2003;107:2932–7.
49. Sweeney MO, Hellkamp AS. Heart failure during cardiac pacing. Circulation. 2006;113:2082–8.
50. Steinberg JS, Fischer A, Wang P, et al. The clinical implications of cumulative right ventricular pacing in the multicenter automatic defibrillator trial II. J Cardiovasc Electrophysiol. 2005;16:359–65.
51. Wilkoff BL, Cook JR, Epstein AE, et al. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. JAMA. 2002;288:3115–23.
52. Lamas GA, Knight JD, Sweeney MO, et al. Impact of rate-modulated pacing on quality of life and exercise capacity: evidence from the Advanced Elements of Pacing Randomized Controlled Trial (ADEPT). Heart Rhythm. 2007;4:1125–32.
53. Kay R, Estioko M, Wiener I. Primary sick sinus syndrome as an indication for chronic pacemaker therapy in young adults: incidence, clinical features, and long-term evaluation. Am Heart J. 1982;103:338–42.
54. Kusumoto FM, Goldschlager N. Cardiac pacing. N Engl J Med. 1996;334:89–97.
55. Rasmussen K. Chronic sinus node disease: natural course and indications for pacing. Eur Heart J. 1981;2:455–9.
56. Linde-Edelstam C, Nordlander R, Pehrsson SK, Ryden L. A double-blind study of submaximal exercise tolerance and variation in paced rate in atrial synchronous compared to activity sensor modulated ventricular pacing. Pacing Clin Electrophysiol. 1992;15:905–15.
57. Gammage M, Schofield S, Rankin I, Bennett M, Coles P, Pentecost B. Benefit of single setting rate responsive ventricular pacing compared with fixed rate demand pacing in elderly patients. Pacing Clin Electrophysiol. 1991;14:174–80.
58. Shaw DB, Holman RR, Gowers JI. Survival in sinoatrial disorder (sick-sinus syndrome). Br Med J. 1980;280:139–41.
59. Dreifus LS, Michelson EL, Kaplinsky E. Bradyarrhythmias: clinical significance and management. J Am Coll Cardiol. 1983;1:327–38.
60. Rubenstein JJ, Schulman CL, Yurchak PM, DeSanctis RW. Clinical spectrum of the sick sinus syndrome. Circulation. 1972;46:5–13.
61. Fisher JD. Role of electrophysiologic testing in the diagnosis and treatment of patients with known and suspected bradycardias and tachycardias. Prog Cardiovasc Dis. 1981;24:25–90.
62. Reiffel JA, Kuehnert MJ. Electrophysiological testing of sinus node function: diagnostic and prognostic application-including updated information from sinus node electrograms. Pacing Clin Electrophysiol. 1994;17:349–65.
63. Friedberg CK, Donoso E, Stein WG. Nonsurgical acquired heart block. Ann NY Acad Sci. 1964;111:835–47.
64. Gadboys HL, Wisoff G, Litwak RS. Surgical treatment of complete heart block. An analysis of 36 cases. JAMA. 1964;189:97–102.
65. Johansson BW. Complete heart block. A clinical, hemodynamic and pharmacological study in patients with and without an artificial pacemaker. Acta Med Scand Suppl. 1966;451:1–127.
66. Hindman MC, Wagner GS, JaRo M, et al. The clinical significance of bundle branch block complicating acute myocardial infarction. 2. Indications for temporary and permanent pacemaker insertion. Circulation. 1978;58:689–99.
67. Donmoyer TL, DeSanctis RW, Austen WG. Experience with implantable pacemakers using myocardial electrodes in the management of heart block. Ann Thorac Surg. 1967;3:218–27.
68. Edhag O, Swahn A. Prognosis of patients with complete heart block or arrhythmic syncope who were not treated with artificial pacemakers. A long-term follow-up study of 101 patients. Acta Med Scand. 1976;200:457–63.
69. Mymin D, Mathewson FA, Tate RB, Manfreda J. The natural history of primary first-degree atrioventricular heart block. N Engl J Med. 1986;315:1183–7.
70. Barold SS. Indications for permanent cardiac pacing in first-degree AV block: class I, II, or III? Pacing Clin Electrophysiol. 1996;19:747–51.
71. Kim YH, O'Nunain S, Trouton T, et al. Pseudo-pacemaker syndrome following inadvertent fast pathway ablation for atrioventricular nodal reentrant tachycardia. J Cardiovasc Electrophysiol. 1993;4:178–82.
72. Brecker SJ, Xiao HB, Sparrow J, Gibson DG. Effects of dual-chamber pacing with short atrioventricular delay in dilated cardiomyopathy. Lancet 1992;340:1308–12.
73. Dhingra RC, Denes P, Wu D, Chuquimia R, Rosen KM. The significance of second degree atrioventricular block and bundle branch block. Observations regarding site and type of block. Circulation. 1974;49:638–46.
74. Strasberg B, Amat-Y-Leon F, Dhingra RC, et al. Natural history of chronic second-degree atrioventricular nodal block. Circulation. 1981;63:1043–9.
75. Donoso E, Adler LN, Friedberg CK. Unusual forms of second-degree atrioventricular block, including mobitz type-II block, associated with the Morgagni-Adams-Stokes Syndrome. Am Heart J. 1964;67:150–7.
76. Recommendations for pacemaker prescription for symptomatic bradycardia. Report of a working party of the British Pacing and Electrophysiology Group. Br Heart J. 1991;66:185–91.
77. Connelly DT, Steinhaus DM. Mobitz type I atrioventricular block: an indication for permanent pacing? Pacing Clin Electrophysiol. 1996;19:261–4.
78. Shaw DB, Kekwick CA, Veale D, Gowers J, Whistance T. Survival in second degree atrioventricular block. Br Heart J. 1985;53:587–93.
79. Ranganathan N, Dhurandhar R, Phillips JH, Wigle ED. His Bundle electrogram in bundle-branch block. Circulation. 1972;45:282–94.
80. Zipes DP. Second-degree atrioventricular block. Circulation. 1979;60:465–72.
81. Chokshi SK, Sarmiento J, Nazari J, Mattioni T, Zheutlin T, Kehoe R. Exercise-provoked distal atrioventricular block. Am J Cardiol. 1990;66:114–6.
82. Barold SS, Mugica J. New Perspectives in Cardiac Pacing. Mount Kisco, NY: Futura Publishing Co., 1991:23.
83. Grimm W, Koehler U, Fus E, et al. Outcome of patients with sleep apnea-associated severe bradyarrhythmias after continuous positive airway pressure therapy. Am J Cardiol. 2000;86:688–92.
84. Kim MH, Deeb GM, Eagle KA, et al. Complete atrioventricular block after valvular heart surgery and the timing of pacemaker implantation. Am J Cardiol. 2001;87:649–51, A10.
85. Kastor JA. Atrioventricular block (first of two parts). N Engl J Med. 1975;292:462–5.
86. Ector H, Rolies L, De Geest H. Dynamic electrocardiography and ventricular pauses of 3 seconds and more: etiology and therapeutic implications. Pacing Clin Electrophysiol. 1983;6:548–51.
87. Gallagher JJ, Svenson RH, Kasell JH, et al. Catheter technique for closed-chest ablation of the atrioventricular conduction system. N Engl J Med. 1982;306:194–200.
88. Langberg JJ, Chin MC, Rosenqvist M, et al. Catheter ablation of the atrioventricular junction with radiofrequency energy. Circulation. 1989;80:1527–35.
89. Glikson M, Dearani JA, Hyberger LK, Schaff HV, Hammill SC, Hayes DL. Indications, effectiveness, and long-term dependency in permanent pacing after cardiac surgery. Am J Cardiol. 1997;80:1309–13.
90. Koplan BA, Stevenson WG, Epstein LM, Aranki SF, Maisel WH. Development and validation of a simple risk score to predict the need for permanent pacing after cardiac valve surgery. J Am Coll Cardiol. 2003;41:795–801.
91. Perloff JK, Stevenson WG, Roberts NK, Cabeen W, Weiss J. Cardiac involvement in myotonic muscular dystrophy (Steinert's disease): a prospective study of 25 patients. Am J Cardiol. 1984;54:1074–81.
92. Hiromasa S, Ikeda T, Kubota K, et al. Myotonic dystrophy: ambulatory electrocardiogram, electrophysiologic study, and echocardiographic evaluation. Am Heart J. 1987;113:1482–8.
93. Stevenson WG, Perloff JK, Weiss JN, Anderson TL. Facioscapulohumeral muscular dystrophy: evidence for selective, genetic electrophysiologic cardiac involvement. J Am Coll Cardiol. 1990;15:292–9.
94. James TN, Fisch C. Observations on the cardiovascular involvement in Friedreich's ataxia. Am Heart J. 1963;66:164–75.
95. Roberts NK, Perloff JK, Kark RA. Cardiac conduction in the Kearns-Sayre syndrome (a neuromuscular disorder associated with progressive external ophthalmoplegia and pigmentary retinopathy). Report of 2 cases and review of 17 published cases. Am J Cardiol. 1979;44:1396–400.

96. Charles R, Holt S, Kay JM, Epstein EJ, Rees JR. Myocardial ultrastructure and the development of atrioventricular block in Kearns-Sayre syndrome. Circulation. 1981;63:214–9.
97. James TN. Observations on the cardiovascular involvement, including the cardiac conduction system, in progressive muscular dystrophy. Am Heart J. 1962;63:48–56.
98. Zeltser D, Justo D, Halkin A, et al. Drug-induced atrioventricular block: prognosis after discontinuation of the culprit drug. J Am Coll Cardiol. 2004;44:105–8.
99. Shohat-Zabarski R, Iakobishvili Z, Kusniec J, Mazur A, Strasberg B. Paroxysmal atrioventricular block: clinical experience with 20 patients. Int J Cardiol. 2004;97:399–405.
100. McAlister HF, Klementowicz PT, Andrews C, Fisher JD, Feld M, Furman S. Lyme carditis: an important cause of reversible heart block. Ann Intern Med. 1989;110:339–45.
101. Levine SA, Millier H, Penton GB. Some clinical features of complete heart block. Circulation. 1956;13:801–24.
102. Fisch GR, Zipes DP, Fisch C. Bundle branch block and sudden death. Prog Cardiovasc Dis. 1980;23:187–224.
103. McAnulty JH, Rahimtoola SH, Murphy E, et al. Natural history of "high-risk" bundle-branch block: final report of a prospective study. N Engl J Med. 1982;307:137–43.
104. Kulbertus H, Collignon P. Association of right bundle-branch block with left superior or inferior intraventricular block. Its relation to complete heart block and Adams-Stokes syndrome. Br Heart J. 1969;31:435–40.
105. DePasquale NP, Bruno MS. Natural history of combined right bundle branch block and left anterior hemiblock (bilateral bundle branch block). Am J Med. 1973;54:297–303.
106. Denes P, Dhingra RC, Wu D, Wyndham CR, Leon F, Rosen KM. Sudden death in patients with chronic bifascicular block. Arch Intern Med. 1977;137:1005–10.
107. McAnulty JH, Kauffman S, Murphy E, Kassebaum DG, Rahimtoola SH. Survival in patients with intraventricular conduction defects. Arch Intern Med. 1978;138:30–5.
108. Peters RW, Scheinman MM, Modin C, O'Young J, Somelofski CA, Mies C. Prophylactic permanent pacemakers for patients with chronic bundle branch block. Am J Med. 1979;66:978–85.
109. Scheinman MM, Peters RW, Suave MJ, et al. Value of the H-Q interval in patients with bundle branch block and the role of prophylactic permanent pacing. Am J Cardiol. 1982;50:1316–22.
110. Morady F, Higgins J, Peters RW, et al. Electrophysiologic testing in bundle branch block and unexplained syncope. Am J Cardiol. 1984;54:587–91.
111. Click RL, Gersh BJ, Sugrue DD, et al. Role of invasive electrophysiologic testing in patients with symptomatic bundle branch block. Am J Cardiol. 1987;59:817–23.
112. Lie K, Wellens HJ, Schuilenburg R. Bundle branch block and acute myocardial infarction. In: Wellens HJ, Lie K, Janse M, editors. The Conduction System of the Heart: Structure, Function and Clinical Implications. Philadelphia, PA: Lea & Febiger, 1976:662–72.
113. Ezri M, Lerman BB, Marchlinski FE, Buxton AE, Josephson ME. Electrophysiologic evaluation of syncope in patients with bifascicular block. Am Heart J. 1983;106:693–7.
114. Twidale N, Heddle WF, Ayres BF, Tonkin AM. Clinical implications of electrophysiology study findings in patients with chronic bifascicular block and syncope. Aust N Z J Med. 1988;18:841–7.
115. Englund A, Bergfeldt L, Rehnqvist N, Astrom H, Rosenqvist M. Diagnostic value of programmed ventricular stimulation in patients with bifascicular block: a prospective study of patients with and without syncope. J Am Coll Cardiol. 1995;26:1508–15.
116. Scheinman MM, Peters RW, Modin G, Brennan M, Mies C, O'Young J. Prognostic value of infranodal conduction time in patients with chronic bundle branch block. Circulation. 1977;56:240–4.
117. Probst P, Pachinger O, Akbar MA, Leisch F, Kaindl F. The HQ time in congestive cardiomyopathies. Am Heart J. 1979;97:436–41.
118. Dhingra RC, Wyndham C, Bauernfeind R, et al. Significance of block distal to the His bundle induced by atrial pacing in patients with chronic bifascicular block. Circulation. 1979;60:1455–64.
119. Cheng TO. Atrial pacing: its diagnostic and therapeutic applications. Prog Cardiovasc Dis. 1971;14:230–47.
120. Gupta PK, Lichstein E, Chadda KD. Intraventricular conduction time (H-V interval) during antegrade conduction in patients with heart block. Am J Cardiol. 1973;32:27–31.
121. Altschuler H, Fisher JD, Furman S. Significance of isolated H-V interval prolongation in symptomatic patients without documented heart block. Am Heart J. 1979;97:19–26.
122. Josephson ME. Clinical cardiac electrophysiology: techniques and interpretations. 3rd edition. Philadelphia, PA: Lippincott Williams & Wilkins, 2002:102–5.
123. Dhingra RC, Denes P, Wu D, et al. Syncope in patients with chronic bifascicular block. Significance, causative mechanisms, and clinical implications. Ann Intern Med 1974;81:302–6.
124. Josephson M. Clinical Cardiac Electrophysiology: Techniques and Interpretations. 2nd edition. Philadelphia, PA: Lea & Febiger, 1993:145.
125. Brignole M, Menozzi C, Moya A, et al. Mechanism of syncope in patients with bundle branch block and negative electrophysiological test. Circulation. 2001;104:2045–50.
126. Col JJ, Weinberg SL. The incidence and mortality of intraventricular conduction defects in acute myocardial infarction. Am J Cardiol. 1972;29:344–50.
127. Ritter WS, Atkins JM, Blomqvist CG, Mullins CB. Permanent pacing in patients with transient trifascicular block during acute myocardial infarction. Am J Cardiol. 1976;38:205–8.
128. Ginks WR, Sutton R, Oh W, Leatham A. Long-term prognosis after acute anterior infarction with atrioventricular block. Br Heart J. 1977;39:186–9.
129. Domenighetti G, Perret C. Intraventricular conduction disturbances in acute myocardial infarction: short- and long-term prognosis. Eur J Cardiol. 1980;11:51–9.
130. Petrina M, Goodman SG, Eagle KA. The 12–lead electrocardiogram as a predictive tool of mortality after acute myocardial infarction: current status in an era of revascularization and reperfusion. Am Heart J. 2006;152:11–8.
131. Lamas GA, Muller JE, Turi ZG, et al. A simplified method to predict occurrence of complete heart block during acute myocardial infarction. Am J Cardiol. 1986;57:1213–9.
132. Harthorne J. Atherosclerosis and Coronary Artery Disease. Philadelphia, PA: Lippincott-Raven Publishers, 1996:1013.
133. Juma Z, Castellanos A, Myerburg RJ. Prognostic significance of the electrocardiogram in patients with coronary heart disease. In: What's New in Electrocardiography. The Hague: Martinus Nijhoff Publishers, 1981:5–22.
134. Clemmensen P, Bates ER, Califf RM, et al. Complete atrioventricular block complicating inferior wall acute myocardial infarction treated with reperfusion therapy. TAMI Study Group. Am J Cardiol. 1991;67:225–30.
135. Goldberg RJ, Zevallos JC, Yarzebski J, et al. Prognosis of acute myocardial infarction complicated by complete heart block (the Worcester Heart Attack Study). Am J Cardiol. 1992;69:1135–41.
136. Behar S, Zissman E, Zion M, et al. Prognostic significance of second-degree atrioventricular block in inferior wall acute myocardial infarction. SPRINT Study Group. Am J Cardiol. 1993;72:831–4.
137. Berger PB, Ruocco NA Jr, Ryan TJ, Frederick MM, Jacobs AK, Faxon DP. Incidence and prognostic implications of heart block complicating inferior myocardial infarction treated with thrombolytic therapy: results from TIMI II. J Am Coll Cardiol. 1992;20:533–40.
138. Nicod P, Gilpin E, Dittrich H, Polikar R, Henning H, Ross J Jr. Long-term outcome in patients with inferior myocardial infarction and complete atrioventricular block. J Am Coll Cardiol. 1988;12:589–94.
139. Dubois C, Pierard LA, Smeets JP, Carlier J, Kulbertus HE. Long-term prognostic significance of atrioventricular block in inferior acute myocardial infarction. Eur Heart J. 1989;10:816–20.
140. Sra JS, Jazayeri MR, Avitall B, et al. Comparison of cardiac pacing with drug therapy in the treatment of neurocardiogenic (vasovagal) syncope with bradycardia or asystole. N Engl J Med. 1993;328:1085–90.
141. Sugrue DD, Gersh BJ, Holmes DR Jr, Wood DL, Osborn MJ, Hammill SC. Symptomatic "isolated" carotid sinus hypersensitivity: natural history and results of treatment with anticholinergic drugs or pacemaker. J Am Coll Cardiol. 1986;7:158–62.
142. Brignole M, Menozzi C, Lolli G, Bottoni N, Gaggioli G. Long-term outcome of paced and nonpaced patients with severe carotid sinus syndrome. Am J Cardiol. 1992;69:1039–43.
143. Brignole M. Randomized clinical trials of neurally mediated syncope. J Cardiovasc Electrophysiol. 2003;14:S64–S69.
144. Kenny RA, Richardson DA, Steen N, Bexton RS, Shaw FE, Bond J. Carotid sinus syndrome: a modifiable risk factor for nonaccidental falls in older adults (SAFE PACE). J Am Coll Cardiol. 2001;38:1491–6.
145. Grubb BP. Neurocardiogenic syncope and related disorders of orthostatic intolerance. Circulation. 2005;111:2997–3006.

146. Benditt DG, Ferguson DW, Grubb BP, et al. Tilt table testing for assessing syncope. American College of Cardiology. J Am Coll Cardiol. 1996;28:263–75.
147. Sutton R, Brignole M, Menozzi C, et al. Dual-chamber pacing in the treatment of neurally mediated tilt-positive cardioinhibitory syncope: pacemaker versus no therapy: a multicenter randomized study. The Vasovagal Syncope International Study (VASIS) Investigators. Circulation. 2000;102:294–9.
148. Ammirati F, Colivicchi F, Santini M. Permanent cardiac pacing versus medical treatment for the prevention of recurrent vasovagal syncope: a multicenter, randomized, controlled trial. Circulation. 2001;104:52–7.
149. Connolly SJ, Sheldon R, Roberts RS, Gent M. The North American Vasovagal Pacemaker Study (VPS). A randomized trial of permanent cardiac pacing for the prevention of vasovagal syncope. J Am Coll Cardiol. 1999;33:16–20.
150. Connolly SJ, Sheldon R, Thorpe KE, et al. Pacemaker therapy for prevention of syncope in patients with recurrent severe vasovagal syncope: Second Vasovagal Pacemaker Study (VPS II): a randomized trial. JAMA. 2003;289:2224–9.
151. Grubb BP, Gerard G, Roush K, et al. Differentiation of convulsive syncope and epilepsy with head-up tilt testing. Ann Intern Med. 1991;115:871–6.
152. Brignole M, Menozzi C, Gianfranchi L, Oddone D, Lolli G, Bertulla A. Neurally mediated syncope detected by carotid sinus massage and head-up tilt test in sick sinus syndrome. Am J Cardiol. 1991;68:1032–6.
153. Sheldon R, Koshman ML, Wilson W, Kieser T, Rose S. Effect of dual-chamber pacing with automatic rate-drop sensing on recurrent neurally mediated syncope. Am J Cardiol. 1998;81:158–62.
154. DiBiase A, Tse TM, Schnittger I, Wexler L, Stinson EB, Valantine HA. Frequency and mechanism of bradycardia in cardiac transplant recipients and need for pacemakers. Am J Cardiol. 1991;67:1385–9.
155. Heinz G, Hirschl M, Buxbaum P, Laufer G, Gasic S, Laczkovics A. Sinus node dysfunction after orthotopic cardiac transplantation: postoperative incidence and long-term implications. Pacing Clin Electrophysiol. 1992;15:731–7.
156. Scott CD, Dark JH, McComb JM. Sinus node function after cardiac transplantation. J Am Coll Cardiol. 1994;24:1334–41.
157. Grinstead WC, Smart FW, Pratt CM, et al. Sudden death caused by bradycardia and asystole in a heart transplant patient with coronary arteriopathy. J Heart Lung Transplant. 1991;10:931–6.
158. Bertolet BD, Eagle DA, Conti JB, Mills RM, Belardinelli L. Bradycardia after heart transplantation: reversal with theophylline. J Am Coll Cardiol. 1996;28:396–9.
159. Scott CD, Omar I, McComb JM, Dark JH, Bexton RS. Long-term pacing in heart transplant recipients is usually unnecessary. Pacing Clin Electrophysiol. 1991;14:1792–6.
160. Montero JA, Anguita M, Concha M, et al. Pacing requirements after orthotopic heart transplantation: incidence and related factors. J Heart Lung Transplant. 1992;11:799–802.
161. Payne ME, Murray KD, Watson KM, et al. Permanent pacing in heart transplant recipients: underlying causes and long-term results. J Heart Lung Transplant. 1991;10:738–42.
162. Lazarus A, Varin J, Babuty D, Anselme F, Coste J, Duboc D. Long-term follow-up of arrhythmias in patients with myotonic dystrophy treated by pacing: a multicenter diagnostic pacemaker study. J Am Coll Cardiol. 2002;40:1645–52.
163. Garrigue S, Bordier P, Jais P, et al. Benefit of atrial pacing in sleep apnea syndrome. N Engl J Med. 2002;346:404–12.
164. Krahn AD, Yee R, Erickson MK, et al. Physiologic pacing in patients with obstructive sleep apnea: a prospective, randomized crossover trial. J Am Coll Cardiol. 2006;47:379–83.
165. Shalaby AA, Atwood CW, Hansen C, et al. Analysis of interaction of acute atrial overdrive pacing with sleep-related breathing disorder. Am J Cardiol. 2007;99:573–8.
166. Simantirakis EN, Schiza SE, Chrysostomakis SI, et al. Atrial overdrive pacing for the obstructive sleep apnea-hypopnea syndrome. N Engl J Med. 2005;353:2568–77.
167. Unterberg C, Luthje L, Szych J, Vollmann D, Hasenfuss G, Andreas S. Atrial overdrive pacing compared to CPAP in patients with obstructive sleep apnoea syndrome. Eur Heart J. 2005;26:2568–75.
168. Bradley TD. The ups and downs of periodic breathing: implications for mortality in heart failure. J Am Coll Cardiol. 2003;41:2182–4.
169. Sinha AM, Skobel EC, Breithardt OA, et al. Cardiac resynchronization therapy improves central sleep apnea and Cheyne-Stokes respiration in patients with chronic heart failure. J Am Coll Cardiol. 2004;44:68–71.
170. Sharma OP. Diagnosis of cardiac sarcoidosis: an imperfect science, a hesitant art. Chest. 2003;123:18–9.
171. Doughan AR, Williams BR. Cardiac sarcoidosis. Heart. 2006;92:282–8.
172. Thomas KW, Hunninghake GW. Sarcoidosis. JAMA. 2003;289:3300–3.
173. Syed J, Myers R. Sarcoid heart disease. Can J Cardiol. 2004;20:89–93.
174. Roberts WC, McAllister HA Jr, Ferrans VJ. Sarcoidosis of the heart. A clinicopathologic study of 35 necropsy patients (group 1) and review of 78 previously described necropsy patients (group 11). Am J Med. 1977;63:86–108.
175. Duke C, Rosenthal E. Sudden death caused by cardiac sarcoidosis in childhood. J Cardiovasc Electrophysiol. 2002;13:939–42.
176. Spurrell RA, Nathan AW, Camm AJ. Clinical experience with implantable scanning tachycardia reversion pacemakers. Pacing Clin Electrophysiol. 1984;7:1296–300.
177. Peters RW, Scheinman MM, Morady F, Jacobson L. Long-term management of recurrent paroxysmal tachycardia by cardiac burst pacing. Pacing Clin Electrophysiol. 1985;8:35–44.
178. Fisher JD, Johnston DR, Furman S, Mercando AD, Kim SG. Long-term efficacy of antitachycardia pacing for supraventricular and ventricular tachycardias. Am J Cardiol. 1987;60:1311–6.
179. Den DK, Bertholet M, Brugada P, et al. Clinical experience with implantable devices for control of tachyarrhythmias. Pacing Clin Electrophysiol. 1984;7:548–56.
180. Herre JM, Griffin JC, Nielsen AP, et al. Permanent triggered antitachycardia pacemakers in the management of recurrent sustained ventricular tachycardia. J Am Coll Cardiol. 1985;6:206–14.
181. Saksena S, Pantopoulos D, Parsonnet V, Rothbart ST, Hussain SM, Gielchinsky I. Usefulness of an implantable antitachycardia pacemaker system for supraventricular or ventricular tachycardia. Am J Cardiol. 1986;58:70–4.
182. Barold SS, Wyndham CR, Kappenberger LL, Abinader EG, Griffin JC, Falkoff MD. Implanted atrial pacemakers for paroxysmal atrial flutter. Long-term efficacy. Ann Intern Med. 1987;107:144–9.
183. Attuel P, Pellerin D, Mugica J, Coumel P. DDD pacing: an effective treatment modality for recurrent atrial arrhythmias. Pacing Clin Electrophysiol. 1988;11:1647–54.
184. Saksena S, Prakash A, Hill M, et al. Prevention of recurrent atrial fibrillation with chronic dual-site right atrial pacing. J Am Coll Cardiol. 1996;28:687–94.
185. Daubert C, Mabo P, Druelles P, Foulgoc JL, de Place C, Paillard F. Benefits and limits of selective right ventricular cineangiography in arrhythmogenic right ventricular dysplasia. Eur Heart J. 1989;10 Suppl D:46–8.
186. Ward DE, Camm AJ, Spurrell RA. The response of regular re-entrant supraventricular tachycardia to right heart stimulation. Pacing Clin Electrophysiol. 1979;2:586–95.
187. Naccarelli GV, Zipes DP, Rahilly GT, Heger JJ, Prystowsky EN. Influence of tachycardia cycle length and antiarrhythmic drugs on pacing termination and acceleration of ventricular tachycardia. Am Heart J. 1983;105:1–5.
188. Eldar M, Griffin JC, Abbott JA, et al. Permanent cardiac pacing in patients with the long QT syndrome. J Am Coll Cardiol. 1987;10:600–7.
189. Eldar M, Griffin JC, Van Hare GF, et al. Combined use of beta-adrenergic blocking agents and long-term cardiac pacing for patients with the long QT syndrome. J Am Coll Cardiol. 1992;20:830–7.
190. Moss AJ, Robinson J. Clinical features of the idiopathic long QT syndrome. Circulation. 1992;85:I140–4.
191. Naccarelli GV, Dorian P, Hohnloser SH, Coumel P. Prospective comparison of flecainide versus quinidine for the treatment of paroxysmal atrial fibrillation/flutter. The Flecainide Multicenter Atrial Fibrillation Study Group. Am J Cardiol. 1996;77:53A–9A.
192. Fisher JD, Teichman SL, Ferrick A, Kim SG, Waspe LE, Martinez MR. Antiarrhythmic effects of VVI pacing at physiologic rates: a crossover controlled evaluation. Pacing Clin Electrophysiol. 1987;10:822–30.
193. Lau CP, Cornu E, Camm AJ. Fatal and nonfatal cardiac arrest in patients with an implanted antitachycardia device for the treatment of supraventricular tachycardia. Am J Cardiol. 1988;61:919–21.
194. Gillis AM, Morck M. Atrial fibrillation after DDDR pacemaker implantation. J Cardiovasc Electrophysiol. 2002;13:542–7.
195. Gillis AM, Koehler J, Morck M, Mehra R, Hettrick DA. High atrial antitachycardia pacing therapy efficacy is associated with a reduction in atrial tachyarrhythmia burden in a subset of patients with sinus node dysfunction and paroxysmal atrial fibrillation. Heart Rhythm. 2005;2:791–6.

196. Israel CW, Hugl B, Unterberg C, et al. Pace-termination and pacing for prevention of atrial tachyarrhythmias: results from a multicenter study with an implantable device for atrial therapy. J Cardiovasc Electrophysiol. 2001;12:1121–8.
197. Lee MA, Weachter R, Pollak S, et al. The effect of atrial pacing therapies on atrial tachyarrhythmia burden and frequency: results of a randomized trial in patients with bradycardia and atrial tachyarrhythmias. J Am Coll Cardiol. 2003;41:1926–32.
198. Friedman PA, Dijkman B, Warman EN, et al. Atrial therapies reduce atrial arrhythmia burden in defibrillator patients. Circulation. 2001;104:1023–8.
199. Gold MR, Sulke N, Schwartzman DS, Mehra R, Euler DE. Clinical experience with a dual-chamber implantable cardioverter defibrillator to treat atrial tachyarrhythmias. J Cardiovasc Electrophysiol. 2001;12:1247–53.
200. Swerdlow CD, Schsls W, Dijkman B, et al, Worldwide Jewel AF Investigators. Detection of atrial fibrillation and flutter by a dual-chamber implantable cardioverter-defibrillator. Circulation. 2000;101:878–85.
201. Moss AJ, Liu JE, Gottlieb S, Locati EH, Schwartz PJ, Robinson JL. Efficacy of permanent pacing in the management of high-risk patients with long QT syndrome. Circulation. 1991;84:1524–9.
202. Dorostkar PC, Eldar M, Belhassen B, Scheinman MM. Long-term follow-up of patients with long-QT syndrome treated with beta-blockers and continuous pacing. Circulation. 1999;100:2431–6.
203. Viskin S, Alla SR, Barron HV, et al. Mode of onset of torsade de pointes in congenital long QT syndrome. J Am Coll Cardiol. 1996;28:1262–8.
204. Trippel DL, Parsons MK, Gillette PC. Infants with long-QT syndrome and 2:1 atrioventricular block. Am Heart J. 1995;130:1130–4.
205. Solti F, Szatmary L, Vecsey T, Renyi-Vamos F Jr, Bodor E. Congenital complete heart block associated with QT prolongation. Eur Heart J. 1992;13:1080–3.
206. Benson DW, Wang DW, Dyment M, et al. Congenital sick sinus syndrome caused by recessive mutations in the cardiac sodium channel gene (SCN5A). J Clin Invest. 2003;112:1019–28.
207. Saksena S, Delfaut P, Prakash A, Kaushik RR, Krol RB. Multisite electrode pacing for prevention of atrial fibrillation. J Cardiovasc Electrophysiol. 1998;9:S155–62.
208. Dewey RC, Capeless MA, Levy AM. Use of ambulatory electrocardiographic monitoring to identify high-risk patients with congenital complete heart block. N Engl J Med. 1987;316:835–9.
209. Lillehei CW, Sellers RD, Bonnabeau RC, Eliot RS. Chronic postsurgical complete heart block with particular reference to prognosis, management, and a new P-wave pacemaker. J Thorac Cardiovasc Surg. 1963;46:436–56.
210. Carlson MD, Ip J, Messenger J, et al. A new pacemaker algorithm for the treatment of atrial fibrillation: results of the Atrial Dynamic Overdrive Pacing Trial (ADOPT). J Am Coll Cardiol. 2003;42:627–33.
211. Madan N, Saksena S. Long-term rhythm control of drug-refractory atrial fibrillation with "hybrid therapy" incorporating dual-site right atrial pacing, antiarrhythmic drugs, and right atrial ablation. Am J Cardiol. 2004;93:569–75.
212. Hermida JS, Kubala M, Lescure FX, et al. Atrial septal pacing to prevent atrial fibrillation in patients with sinus node dysfunction: results of a randomized controlled study. Am Heart J. 2004;148:312–7.
213. Ellenbogen K. Pacing therapy for prevention of atrial fibrillation. Heart Rhythm 2007;4 Suppl 1:S84–7.
214. Daubert JC, Mabo P, Berder V, et al. Atrial tachyarrhythmias associated with high degree interatrial conduction block: prevention by permanent atrial resynchronization. Eur J Card Pacing Electrophysiol. 1994;4:35.
215. Knight BP, Gersh BJ, Carlson MD, et al. Role of permanent pacing to prevent atrial fibrillation: science advisory from the American Heart Association Council on Clinical Cardiology (Subcommittee on Electrocardiography and Arrhythmias) and the Quality of Care and Outcomes Research Interdisciplinary Working Group, in collaboration with the Heart Rhythm Society. Circulation. 2005;111:240–3.
216. Doval HC, Nul DR, Grancelli HO, Perrone SV, Bortman GR, Curiel R. Randomised trial of low-dose amiodarone in severe congestive heart failure. Grupo de Estudio de la Sobrevida en la Insuficiencia Cardiaca en Argentina (GESICA). Lancet. 1994;344:493–8.
217. Naccarelli GV, Luck JC, Wolbrette DL, et al. Pacing therapy for congestive heart failure: is it ready for prime time?. Curr Opin Cardiol. 1999;14:1–3.
218. Blanc JJ, Etienne Y, Gilard M, et al. Evaluation of different ventricular pacing sites in patients with severe heart failure: results of an acute hemodynamic study. Circulation. 1997;96:3273–7.
219. Leclercq JF, Chouty F, Cauchemez B, Leenhardt A, Coumel P, Slama R. Results of electrical fulguration in arrhythmogenic right ventricular disease. Am J Cardiol. 1988;62:220–4.
220. Cazeau S, Leclercq C, Lavergne T, et al. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. N Engl J Med. 2001;344:873–80.
221. Stellbrink C, Breithardt OA, Franke A, et al. Impact of cardiac resynchronization therapy using hemodynamically optimized pacing on left ventricular remodeling in patients with congestive heart failure and ventricular conduction disturbances. J Am Coll Cardiol. 2001;38:1957–65.
222. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med. 2002;346:1845–53.
223. Bradley DJ, Bradley EA, Baughman KL, et al. Cardiac resynchronization and death from progressive heart failure: a meta-analysis of randomized controlled trials. JAMA. 2003;289:730–40.
224. Bristow MR, Saxon LA, Boehmer J, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. 2004;350:2140–50.
225. Cleland JG, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med. 2005;352:1539–49.
226. Beshai JF, Grimm RA, Nagueh SF, et al. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. N Engl J Med. 2007;357:2461–71.
227. Gasparini M, Auricchio A, Regoli F, et al. Four-year efficacy of cardiac resynchronization therapy on exercise tolerance and disease progression: the importance of performing atrioventricular junction ablation in patients with atrial fibrillation. J Am Coll Cardiol. 2006;48:734–43.
228. Linde C, Leclercq C, Rex S, et al. Long-term benefits of biventricular pacing in congestive heart failure: results from the MUltisite STimulation in cardiomyopathy (MUSTIC) study. J Am Coll Cardiol. 2002;40:111–8.
229. Shaddy RE, Boucek MM, Hsu DT, et al. Carvedilol for children and adolescents with heart failure: a randomized controlled trial. JAMA. 2007;298:1171–9.
230. Lindenfeld J, Feldman AM, Saxon L, et al. Effects of cardiac resynchronization therapy with or without a defibrillator on survival and hospitalizations in patients with New York Heart Association class IV heart failure. Circulation. 2007;115:204–12.
231. Goldstein NE, Lampert R, Bradley E, Lynn J, Krumholz HM. Management of implantable cardioverter defibrillators in end-of-life care. Ann Intern Med. 2004;141:835–8.
232. McDonald K, McWilliams E, O'Keeffe B, Maurer B. Functional assessment of patients treated with permanent dual chamber pacing as a primary treatment for hypertrophic cardiomyopathy. Eur Heart J. 1988;9:893–8.
233. Fananapazir L, Epstein ND, Curiel RV, Panza JA, Tripodi D, McAreavey D. Long-term results of dual-chamber (DDD) pacing in obstructive hypertrophic cardiomyopathy. Evidence for progressive symptomatic and hemodynamic improvement and reduction of left ventricular hypertrophy. Circulation. 1994;90:2731–42.
234. Fananapazir L, Cannon RO III, Tripodi D, Panza JA. Impact of dual-chamber permanent pacing in patients with obstructive hypertrophic cardiomyopathy with symptoms refractory to verapamil and beta-adrenergic blocker therapy. Circulation. 1992;85:2149–61.
235. Nishimura RA, Trusty JM, Hayes DL, et al. Dual-chamber pacing for hypertrophic cardiomyopathy: a randomized, double-blind, crossover trial. J Am Coll Cardiol. 1997;29:435–41.
236. Jeanrenaud X, Goy JJ, Kappenberger L. Effects of dual-chamber pacing in hypertrophic obstructive cardiomyopathy. Lancet. 1992;339:1318–23.
237. Kappenberger L, Linde C, Daubert C, et al. PIC Study Group. Pacing in hypertrophic obstructive cardiomyopathy. A randomized crossover study. Eur Heart J. 1997;18:1249–56.
238. Maron BJ, Nishimura RA, McKenna WJ, Rakowski H, Josephson ME, Kieval RS. Assessment of permanent dual-chamber pacing as a treatment for drug-refractory symptomatic patients with obstructive hypertrophic cardiomyopathy. A randomized, double-blind, crossover study (M-PATHY). Circulation. 1999;99:2927–33.

239. Kass DA, Chen CH, Curry C, et al. Improved left ventricular mechanics from acute VDD pacing in patients with dilated cardiomyopathy and ventricular conduction delay. Circulation. 1999;99:1567–73.
240. Rishi F, Hulse JE, Auld DO, et al. Effects of dual-chamber pacing for pediatric patients with hypertrophic obstructive cardiomyopathy. J Am Coll Cardiol. 1997;29:734–40.
241. Symanski JD, Nishimura RA. The use of pacemakers in the treatment of cardiomyopathies. Curr Probl Cardiol. 1996;21:385–443.
242. Hayes DL, Barold SS, Camm AJ, Goldschlager NF. Evolving indications for permanent cardiac pacing: an appraisal of the 1998 American College of Cardiology/American Heart Association Guidelines. Am J Cardiol. 1998;82:1082–6.
243. Erwin JP III, Nishimura RA, Lloyd MA, Tajik AJ. Dual chamber pacing for patients with hypertrophic obstructive cardiomyopathy: a clinical perspective in 2000. Mayo Clin Proc. 2000;75:173–80.
244. Lawrenz T, Lieder F, Bartelsmeier M, et al. Predictors of complete heart block after transcoronary ablation of septal hypertrophy: results of a prospective electrophysiological investigation in 172 patients with hypertrophic obstructive cardiomyopathy. J Am Coll Cardiol. 2007;49:2356–63.
245. Maron BJ, Spirito P, Shen WK, et al. Implantable cardioverter-defibrillators and prevention of sudden cardiac death in hypertrophic cardiomyopathy. JAMA. 2007;298:405–12.
246. Nishimura RA, Hayes DL, Ilstrup DM, Holmes DR Jr, Tajik AJ. Effect of dual-chamber pacing on systolic and diastolic function in patients with hypertrophic cardiomyopathy. Acute Doppler echocardiographic and catheterization hemodynamic study. J Am Coll Cardiol. 1996;27:421–30.
247. Nishimura RA, Symanski JD, Hurrell DG, Trusty JM, Hayes DL, Tajik AJ. Dual-chamber pacing for cardiomyopathies: a 1996 clinical perspective. Mayo Clin Proc. 1996;71:1077–87.
248. Low Cost Health Insurance for Families & Children. Overview. Available at: http://www.cms.hhs.gov/LowCostHealthInsFamChild/. Accessed February 22, 2007
249. Walsh EP, Cecchin F. Arrhythmias in adult patients with congenital heart disease. Circulation. 2007;115:534–45.
250. Cohen MI, Rhodes LA, Wernovsky G, Gaynor JW, Spray TL, Rychik J. Atrial pacing: an alternative treatment for protein-losing enteropathy after the Fontan operation. J Thorac Cardiovasc Surg. 2001;121:582–3.
251. Cohen MI, Bush DM, Vetter VL, et al. Permanent epicardial pacing in pediatric patients: seventeen years of experience and 1200 outpatient visits. Circulation. 2001;103:2585–90.
252. Silvetti MS, Grutter G, Di Ciommo V, Drago F. Paroxysmal atrioventricular block in young patients. Pediatr Cardiol. 2004;25:506–12.
253. Beder SD, Gillette PC, Garson A Jr, Porter CB, McNamara DG. Symptomatic sick sinus syndrome in children and adolescents as the only manifestation of cardiac abnormality or associated with unoperated congenital heart disease. Am J Cardiol. 1983;51:1133–6.
254. Kothari DS, Riddell F, Smith W, Voss J, Skinner JR. Digital implantable loop recorders in the investigation of syncope in children: benefits and limitations. Heart Rhythm. 2006;3:1306–12.
255. Dorostkar PC, Arko MK, Baird TM, Rodriguez S, Martin RJ. Asystole and severe bradycardia in preterm infants. Biol Neonate. 2005;88:299–305.
256. Akikusa JD, Feldman BM, Gross GJ, Silverman ED, Schneider R. Sinus bradycardia after intravenous pulse methylprednisolone. Pediatrics. 2007;119:e778–e782.
257. Kelly AM, Porter CJ, McGoon MD, Espinosa RE, Osborn MJ, Hayes DL. Breath-holding spells associated with significant bradycardia: successful treatment with permanent pacemaker implantation. Pediatrics. 2001;108:698–702.
258. Garson A Jr, Bink-Boelkens M, Hesslein PS, et al. Atrial flutter in the young: a collaborative study of 380 cases. J Am Coll Cardiol. 1985;6:871–8.
259. Gelatt M, Hamilton RM, McCrindle BW, et al. Arrhythmia and mortality after the Mustard procedure: a 30–year single-center experience. J Am Coll Cardiol. 1997;29:194–201.
260. Silka MJ, Manwill JR, Kron J, McAnulty JH. Bradycardia-mediated tachyarrhythmias in congenital heart disease and responses to chronic pacing at physiologic rates. Am J Cardiol. 1990;65:488–93.
261. Stephenson EA, Casavant D, Tuzi J, et al. Efficacy of atrial antitachycardia pacing using the Medtronic AT500 pacemaker in patients with congenital heart disease. Am J Cardiol. 2003;92:871–6.
262. Rhodes LA, Walsh EP, Gamble WJ, Triedman JK, Saul JP. Benefits and potential risks of atrial antitachycardia pacing after repair of congenital heart disease. Pacing Clin Electrophysiol. 1995;18:1005–16.
263. Anand N, McCrindle BW, Chiu CC, et al. Chronotropic incompetence in young patients with late postoperative atrial flutter: a case-control study. Eur Heart J. 2006;27:2069–73.
264. Pfammatter JP, Paul T, Lehmann C, Kallfelz HC. Efficacy and proarrhythmia of oral sotalol in pediatric patients. J Am Coll Cardiol. 1995;26:1002–7.
265. Triedman JK, Alexander ME, Love BA, et al. Influence of patient factors and ablative technologies on outcomes of radiofrequency ablation of intra-atrial re-entrant tachycardia in patients with congenital heart disease. J Am Coll Cardiol. 2002;39:1827–35.
266. Mavroudis C, Backer CL, Deal BJ, Johnsrude C, Strasburger J. Total cavopulmonary conversion and maze procedure for patients with failure of the Fontan operation. J Thorac Cardiovasc Surg. 2001;122:863–71.
267. Pinsky WW, Gillette PC, Garson A Jr, McNamara DG. Diagnosis, management, and long-term results of patients with congenital complete atrioventricular block. Pediatrics. 1982;69:728–33.
268. Jaeggi ET, Hamilton RM, Silverman ED, Zamora SA, Hornberger LK. Outcome of children with fetal, neonatal or childhood diagnosis of isolated congenital atrioventricular block. A single institution's experience of 30 years. J Am Coll Cardiol. 2002;39:130–7.
269. Michaelsson M, Engle MA. Congenital complete heart block: an international study of the natural history. Cardiovasc Clin. 1972;4:85–101.
270. Sholler GF, Walsh EP. Congenital complete heart block in patients without anatomic cardiac defects. Am Heart J. 1989;118:1193–8.
271. Michaelsson M, Jonzon A, Riesenfeld T. Isolated congenital complete atrioventricular block in adult life. A prospective study. Circulation. 1995;92:442–9.
272. Moak JP, Barron KS, Hougen TJ, et al. Congenital heart block: development of late-onset cardiomyopathy, a previously underappreciated sequela. J Am Coll Cardiol. 2001;37:238–42.
273. Villain E, Coastedoat-Chalumeau N, Marijon E, Boudjemline Y, Piette JC, Bonnet D. Presentation and prognosis of complete atrioventricular block in childhood, according to maternal antibody status. J Am Coll Cardiol. 2006;48:1682–7.
274. Weindling SN, Saul JP, Gamble WJ, Mayer JE, Wessel D, Walsh EP. Duration of complete atrioventricular block after congenital heart disease surgery. Am J Cardiol. 1998;82:525–7.
275. Krongrad E. Prognosis for patients with congenital heart disease and postoperative intraventricular conduction defects. Circulation. 1978;57:867–70.
276. Banks MA, Jenson J, Kugler JD. Late development of atrioventricular block after congenital heart surgery in Down syndrome. Am J Cardiol. 2001;88:86–9.
277. Gross GJ, Chiu CC, Hamilton RM, Kirsh JA, Stephenson EA. Natural history of postoperative heart block in congenital heart disease: implications for pacing intervention. Heart Rhythm. 2006;3:601–4.
278. Villain E, Ouarda F, Beyler C, Sidi D, Abid F. [Predictive factors for late complete atrio-ventricular block after surgical treatment for congenital cardiopathy]. Arch Mal Coeur Vaiss. 2003;96:495–8.
279. Khairy P, Landzberg MJ, Gatzoulis MA, et al. Transvenous pacing leads and systemic thromboemboli in patients with intracardiac shunts: a multicenter study. Circulation. 2006;113:2391–7.
280. Bar-Cohen Y, Berul CI, Alexander ME, et al. Age, size, and lead factors alone do not predict venous obstruction in children and young adults with transvenous lead systems. J Cardiovasc Electrophysiol. 2006;17:754–9.
281. Andersen HR, Nielsen JC, Thomsen PE, et al. Long-term follow-up of patients from a randomised trial of atrial versus ventricular pacing for sick-sinus syndrome. Lancet. 1997;350:1210–6.
282. Kerr CR, Connolly SJ, Abdollah H, et al. Canadian Trial of Physiological Pacing: effects of physiological pacing during long-term follow-up. Circulation. 2004;109:357–62.
283. Toff WD, Camm AJ, Skehan JD. Single-chamber versus dual-chamber pacing for high-grade atrioventricular block. N Engl J Med. 2005;353:145–55.
284. Connolly SJ, Kerr CR, Gent M, et al. Effects of physiologic pacing versus ventricular pacing on the risk of stroke and death due to cardiovascular causes. Canadian Trial of Physiologic Pacing Investigators. N Engl J Med. 2000;342:1385–91.

285. Newman D, Lau C, Tang AS, et al. Effect of pacing mode on health-related quality of life in the Canadian Trial of Physiologic Pacing. Am Heart J. 2003;145:430–7.
286. Fleischmann KE, Orav EJ, Lamas GA, et al. Pacemaker implantation and quality of life in the Mode Selection Trial (MOST). Heart Rhythm. 2006;3:653–9.
287. Rinfret S, Cohen DJ, Lamas GA, et al. Cost-effectiveness of dual-chamber pacing compared with ventricular pacing for sinus node dysfunction. Circulation. 2005;111:165–72.
288. Sulke N, Chambers J, Dritsas A, Sowton E. A randomized double-blind crossover comparison of four rate-responsive pacing modes. J Am Coll Cardiol. 1991;17:696–706.
289. Healey JS, Toff WD, Lamas GA, et al. Cardiovascular outcomes with atrial-based pacing compared with ventricular pacing: meta-analysis of randomized trials, using individual patient data. Circulation. 2006;114:11–7.
290. Saad EB, Marrouche NF, Martin DO, et al. Frequency and associations of symptomatic deterioration after dual-chamber defibrillator implantation in patients with ischemic or idiopathic dilated cardiomyopathy. Am J Cardiol. 2002;90:79–82.
291. Nielsen JC, Pedersen AK, Mortensen PT, Andersen HR. Programming a fixed long atrioventricular delay is not effective in preventing ventricular pacing in patients with sick sinus syndrome. Europace. 1999;1:113–20.
292. Olshansky B, Day JD, Moore S, et al. Is dual-chamber programming inferior to single-chamber programming in an implantable cardioverter-defibrillator? Results of the INTRINSIC RV (Inhibition of Unnecessary RV Pacing With AVSH in ICDs) study. Circulation. 2007;115:9–16.
293. Sweeney MO, Prinzen FW. A new paradigm for physiologic ventricular pacing. J Am Coll Cardiol. 2006;47:282–8.
294. Sweeney MO, Wathen MS, Volosin K, et al. Appropriate and inappropriate ventricular therapies, quality of life, and mortality among primary and secondary prevention implantable cardioverter defibrillator patients: results from the Pacing Fast VT REduces Shock ThErapies (PainFREE Rx II) trial. Circulation. 2005;111:2898–905.
295. Gillis AM, Purerfellner H, Israel CW, et al. Reducing unnecessary right ventricular pacing with the managed ventricular pacing mode in patients with sinus node disease and AV block. Pacing Clin Electrophysiol. 2006;29:697–705.
296. Sweeney MO, Bank AJ, Nsah E, et al. Minimizing ventricular pacing to reduce atrial fibrillation in sinus-node disease. N Engl J Med. 2007;357:1000–8.
297. Sweeney MO, Ellenbogen KA, Miller EH, Sherfesee L, Sheldon T, Whellan D. The Managed Ventricular pacing versus VVI 40 Pacing (MVP) Trial: clinical background, rationale, design, and implementation. J Cardiovasc Electrophysiol. 2006;17:1295–8.
298. Kindermann M, Hennen B, Jung J, Geisel J, Bohm M, Frohlig G. Biventricular versus conventional right ventricular stimulation for patients with standard pacing indication and left ventricular dysfunction: the Homburg Biventricular Pacing Evaluation (HOBIPACE). J Am Coll Cardiol. 2006;47:1927–37.
299. Baker CM, Christopher TJ, Smith PF, Langberg JJ, Delurgio DB, Leon AR. Addition of a left ventricular lead to conventional pacing systems in patients with congestive heart failure: feasibility, safety, and early results in 60 consecutive patients. Pacing Clin Electrophysiol. 2002;25:1166–71.
300. Doshi RN, Daoud EG, Fellows C, et al. Left ventricular-based cardiac stimulation post AV nodal ablation evaluation (the PAVE study). J Cardiovasc Electrophysiol. 2005;16:1160–5.
301. Leon AR, Greenberg JM, Kanuru N, et al. Cardiac resynchronization in patients with congestive heart failure and chronic atrial fibrillation: effect of upgrading to biventricular pacing after chronic right ventricular pacing. J Am Coll Cardiol. 2002;39:1258–63.
302. Valls-Bertault V, Fatemi M, Gilard M, Pennec PY, Etienne Y, Blanc JJ. Assessment of upgrading to biventricular pacing in patients with right ventricular pacing and congestive heart failure after atrioventricular junctional ablation for chronic atrial fibrillation. Europace. 2004;6:438–43.
303. de Cock CC, Meyer A, Kamp O, Visser CA. Hemodynamic benefits of right ventricular outflow tract pacing: comparison with right ventricular apex pacing. Pacing Clin Electrophysiol. 1998;21:536–41.
304. Tse HF, Yu C, Wong KK, et al. Functional abnormalities in patients with permanent right ventricular pacing: the effect of sites of electrical stimulation. J Am Coll Cardiol. 2002;40:1451–8.
305. Occhetta E, Bortnik M, Magnani A, et al. Prevention of ventricular desynchronization by permanent para-Hisian pacing after atrioventricular node ablation in chronic atrial fibrillation: a crossover, blinded, randomized study versus apical right ventricular pacing. J Am Coll Cardiol. 2006;47:1938–45.
306. Tantengco MV, Thomas RL, Karpawich PP. Left ventricular dysfunction after long-term right ventricular apical pacing in the young. J Am Coll Cardiol. 2001;37:2093–100.
307. Karpawich PP, Rabah R, Haas JE. Altered cardiac histology following apical right ventricular pacing in patients with congenital atrioventricular block. Pacing Clin Electrophysiol. 1999;22:1372–7.
308. Hauser RG, Hayes DL, Kallinen LM, et al. Clinical experience with pacemaker pulse generators and transvenous leads: an 8–year prospective multicenter study. Heart Rhythm. 2007;4:154–60.
309. Bernstein AD, Parsonnet V. Survey of cardiac pacing and defibrillation in the United States in 1993. Am J Cardiol. 1996;78:187–96.
310. A Review of Pacemaker and ICD Implantation Practice in 2004 and 2005. Coronary Heart Disease. Chapter 8. Arrhythmias and Sudden Cardiac Death. Prepared by the Cardiac Networks Device Survey Group. Available at: http://www.c2c.nhs.uk/media/{09BDF807-67DA-4BB1-AF09-DF0B008E2E98}.pdf. Accessed February 2, 2007.
311. Crossley GH, Gayle DD, Simmons TW, et al. Reprogramming pacemakers enhances longevity and is cost-effective. Circulation. 1996;94:II245–7.
312. Bernstein AD, Irwin ME, Parsonnet V, et al. Report of the NASPE Policy Conference on antibradycardia pacemaker follow-up: effectiveness, needs, and resources. North American Society of Pacing and Electrophysiology. Pacing Clin Electrophysiol. 1994;17:1714–29.
313. Levine PA, Belott PH, Bilitch M, et al. Recommendations of the NASPE Policy Conference on pacemaker programmability and follow-up. Pacing Clin Electrophysiol. 1983;6:1222–3.
314. Fraser JD, Gillis AM, Irwin ME, Nishimura S, Tyers GF, Philippon F. Guidelines for pacemaker follow-up in Canada: a consensus statement of the Canadian Working Group on Cardiac Pacing. Can J Cardiol. 2000;16:355–76.
315. U.S. Department of Health and Human Services. 1984 Health Care Financing Administration. Available at: http://www.cms.hhs.gov/. Accessed November 2007.
316. Schoenfeld MH, Markowitz HT. Device follow-up in the age of automaticity. Pacing Clin Electrophysiol. 2000;23:803–6.
317. Pub 100–04 Medicare Claims Processing. Available at: http://www.hrsonline.org/uploadDocs/CMS%20Remote%20Monitoring%20Transmittal.pdf. Accessed June 9, 2006.
318. Mirowski M, Reid PR, Mower MM, et al. Termination of malignant ventricular arrhythmias with an implanted automatic defibrillator in human beings. N Engl J Med. 1980;303:322–4.
319. The Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. N Engl J Med. 1997;337:1576–83.
320. Wever EF, Hauer RN, van Capelle FL, et al. Randomized study of implantable defibrillator as first-choice therapy versus conventional strategy in postinfarct sudden death survivors. Circulation. 1995;91:2195–203.
321. Siebels J, Kuck KH. Implantable cardioverter defibrillator compared with antiarrhythmic drug treatment in cardiac arrest survivors (the Cardiac Arrest Study Hamburg). Am Heart J. 1994;127:1139–44.
322. Connolly SJ, Gent M, Roberts RS, et al. Canadian implantable defibrillator study (CIDS): a randomized trial of the implantable cardioverter defibrillator against amiodarone. Circulation. 2000;101:1297–302.
323. Kuck KH, Cappato R, Siebels J, Ruppel R. Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest: the Cardiac Arrest Study Hamburg (CASH). Circulation. 2000;102:748–54.
324. Connolly SJ, Hallstrom AP, Cappato R, et al. Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials. AVID, CASH and CIDS studies. Antiarrhythmics vs Implantable Defibrillator study. Cardiac Arrest Study Hamburg. Canadian Implantable Defibrillator Study. Eur Heart J. 2000;21:2071–8.
325. Ezekowitz JA, Armstrong PW, McAlister FA. Implantable cardioverter defibrillators in primary and secondary prevention: a systematic review of randomized, controlled trials. Ann Intern Med. 2003;138:445–52.
326. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. JAMA. 2003;290:2581–7.
327. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for

ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. N Engl J Med. 1996;335:1933–40.
328. Bigger JT Jr. Prophylactic use of implanted cardiac defibrillators in patients at high risk for ventricular arrhythmias after coronary-artery bypass graft surgery. Coronary Artery Bypass Graft (CABG) Patch Trial Investigators. N Engl J Med. 1997;337:1569–75.
329. Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G. A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. N Engl J Med. 1999;341:1882–90.
330. Kadish A, Quigg R, Schaechter A, Anderson KP, Estes M, Levine J. Defibrillators in nonischemic cardiomyopathy treatment evaluation. Pacing Clin Electrophysiol. 2000;23:338–43.
331. Hohnloser SH, Kuck KH, Dorian P, et al. Prophylactic use of an implantable cardioverter-defibrillator after acute myocardial infarction. N Engl J Med. 2004;351:2481–8.
332. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med. 2002;346:877–83.
333. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med. 2005;352:225–37.
334. Hammill SC, Stevenson LW, Kadish AH, et al. Review of the Registry's first year, data collected, and future plans. Heart Rhythm. 2007;4:1260–3.
335. Fogoros RN, Elson JJ, Bonnet CA, Fiedler SB, Burkholder JA. Efficacy of the automatic implantable cardioverter-defibrillator in prolonging survival in patients with severe underlying cardiac disease. J Am Coll Cardiol. 1990;16:381–6.
336. Powell AC, Fuchs T, Finkelstein DM, et al. Influence of implantable cardioverter-defibrillators on the long-term prognosis of survivors of out-of-hospital cardiac arrest. Circulation. 1993;88:1083–92.
337. Domanski MJ, Sakseena S, Epstein AE, et al. Relative effectiveness of the implantable cardioverter-defibrillator and antiarrhythmic drugs in patients with varying degrees of left ventricular dysfunction who have survived malignant ventricular arrhythmias. AVID Investigators. Antiarrhythmics Versus Implantable Defibrillators. J Am Coll Cardiol. 1999;34:1090–5.
338. Moss AJ. Implantable cardioverter defibrillator therapy: the sickest patients benefit the most. Circulation. 2000;101:1638–40.
339. Maron BJ, Shen WK, Link MS, et al. Efficacy of implantable cardioverter-defibrillators for the prevention of sudden death in patients with hypertrophic cardiomyopathy. N Engl J Med. 2000;342:365–73.
340. Begley DA, Mohiddin SA, Tripodi D, Winkler JB, Fananapazir L. Efficacy of implantable cardioverter defibrillator therapy for primary and secondary prevention of sudden cardiac death in hypertrophic cardiomyopathy. Pacing Clin Electrophysiol. 2003;26:1887–96.
341. Link MS, Haugh CJ, Costeas XF, et al. Implantable cardioverter defibrillator in arrhythmogenic right ventricular dysplasia; short and long term results. Pacing Clin Electrophysiol. 1995;19:717.
342. Corrado D, Leoni L, Link MS, et al. Implantable cardioverter-defibrillator therapy for prevention of sudden death in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia. Circulation. 2003;108:3084–91.
343. Pezawas T, Stix G, Kastner J, Schneider B, Wolzt M, Schmidinger H. Ventricular tachycardia in arrhythmogenic right ventricular dysplasia/cardiomyopathy: clinical presentation, risk stratification and results of long-term follow-up. Int J Cardiol. 2006;107:360–8.
344. Gillis AM, Sheldon RS, Wyse DG, Duff HJ, Cassidy MR, Mitchell LB. Clinical and electrophysiologic predictors of ventricular tachyarrhythmia recurrence in patients with implantable cardioverter defibrillators. J Cardiovasc Electrophysiol. 2003;14:492–8.
345. Hodgkinson KA, Parfrey PS, Bassett AS, et al. The impact of implantable cardioverter-defibrillator therapy on survival in autosomal-dominant arrhythmogenic right ventricular cardiomyopathy (ARVD5). J Am Coll Cardiol. 2005;45:400–8.
346. Roguin A, Bomma CS, Nasir K, et al. Implantable cardioverter-defibrillators in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy. J Am Coll Cardiol. 2004;43:1843–52.
347. Tavernier R, Gevaert S, De SJ, et al. Long term results of cardioverter-defibrillator implantation in patients with right ventricular dysplasia and malignant ventricular tachyarrhythmias. Heart. 2001;85:53–6.
348. Wichter T, Paul M, Wollmann C, et al. Implantable cardioverter/defibrillator therapy in arrhythmogenic right ventricular cardiomyopathy: single-center experience of long-term follow-up and complications in 60 patients. Circulation. 2004;109:1503–8.
349. Zareba W, Moss AJ, Daubert JP, Hall WJ, Robinson JL, Andrews M. Implantable cardioverter defibrillator in high-risk long QT syndrome patients. J Cardiovasc Electrophysiol. 2003;14:337–41.
350. Viskin S. Implantable cardioverter defibrillator in high-risk long QT syndrome patients. J Cardiovasc Electrophysiol. 2003;14:1130–1.
351. Goel AK, Berger S, Pelech A, Dhala A. Implantable cardioverter defibrillator therapy in children with long QT syndrome. Pediatr Cardiol. 2004;25:370–8.
352. Monnig G, Kobe J, Loher A, et al. Implantable cardioverter-defibrillator therapy in patients with congenital long-QT syndrome: a long-term follow-up. Heart Rhythm. 2005;2:497–504.
353. Goldenberg I, Mathew J, Moss AJ, et al. Corrected QT variability in serial electrocardiograms in long QT syndrome: the importance of the maximum corrected QT for risk stratification. J Am Coll Cardiol. 2006;48:1047–52.
354. Hobbs JB, Peterson DR, Moss AJ, et al. Risk of aborted cardiac arrest or sudden cardiac death during adolescence in the long-QT syndrome. JAMA. 2006;296:1249–54.
355. Schimpf R, Wolpert C, Bianchi F, et al. Congenital short QT syndrome and implantable cardioverter defibrillator treatment: inherent risk for inappropriate shock delivery. J Cardiovasc Electrophysiol. 2003;14:1273–7.
356. Brugada R, Hong K, Dumaine R, et al. Sudden death associated with short-QT syndrome linked to mutations in HERG. Circulation. 2004;109:30–5.
357. Garcia-Moran E, Mont L, Cuesta A, Matas M, Brugada J. Low recurrence of syncope in patients with inducible sustained ventricular tachyarrhythmias treated with an implantable cardioverter-defibrillator. Eur Heart J. 2002;23:901–7.
358. Brodsky MA, Mitchell LB, Halperin BD, Raitt MH, Hallstrom AP. Prognostic value of baseline electrophysiology studies in patients with sustained ventricular tachyarrhythmia: the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial. Am Heart J. 2002;144:478–84.
359. LeLorier P, Krahn AD, Klein GJ, Yee R, Skanes AC. Comparison of patients with syncope with left ventricular dysfunction and negative electrophysiologic testing to cardiac arrest survivors and patients with syncope and preserved left ventricular function and impact of an implantable defibrillator. Am J Cardiol. 2002;90:77–9.
360. Grimm W, Herzum I, Muller HH, Christ M. Value of heart rate variability to predict ventricular arrhythmias in recipients of prophylactic defibrillators with idiopathic dilated cardiomyopathy. Pacing Clin Electrophysiol. 2003;26:411–5.
361. Pezawas T, Stix G, Kastner J, et al. Unexplained syncope in patients with structural heart disease and no documented ventricular arrhythmias: value of electrophysiologically guided implantable cardioverter defibrillator therapy. Europace. 2003;5:305–12.
362. Farmer DM, Swygman CA, Wang PJ, Mark EN III, Link MS. Evidence that nonsustained polymorphic ventricular tachycardia causes syncope (data from implantable cardioverter defibrillators). Am J Cardiol. 2003;91:606–9.
363. Brembilla-Perrot B, Suty-Selton C, Claudon O, et al. Significance of inducible ventricular flutter-fibrillation after myocardial infarction. Pacing Clin Electrophysiol. 2005;28:938–43.
364. Brilakis ES, Friedman PA, Maounis TN, et al. Programmed ventricular stimulation in patients with idiopathic dilated cardiomyopathy and syncope receiving implantable cardioverter-defibrillators: a case series and a systematic review of the literature. Int J Cardiol. 2005;98:395–401.
365. Guttigoli AB, Wilner BF, Stein KM, et al. Usefulness of prolonged QRS duration to identify high-risk ischemic cardiomyopathy patients with syncope and inducible ventricular tachycardia. Am J Cardiol. 2005;95:391–4.
366. Sanchez JM, Katsiyiannis WT, Gage BF, et al. Implantable cardioverter-defibrillator therapy improves long-term survival in patients with unexplained syncope, cardiomyopathy, and a negative electrophysiologic study. Heart Rhythm. 2005;2:367–73.
367. Anderson JL, Hallstrom AP, Epstein AE, et al. Design and results of the antiarrhythmics vs implantable defibrillators (AVID) registry. The AVID Investigators. Circulation. 1999;99:1692–9.
368. Nanthakumar K, Epstein AE, Kay GN, Plumb VJ, Lee DS. Prophylactic implantable cardioverter-defibrillator therapy in patients with left ventricular systolic dysfunction: a pooled analysis of 10 primary prevention trials. J Am Coll Cardiol. 2004;44:2166–72.

369. Kadish A, Dyer A, Daubert JP, et al. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. N Engl J Med. 2004;350:2151–8.
370. Levine JH, Waller T, Hoch D, Greenberg S, Goldberger J, Kadish A. Implantable cardioverter defibrillator: use in patients with no symptoms and at high risk. Am Heart J. 1996;131:59–65.
371. Knight BP, Goyal R, Pelosi F, et al. Outcome of patients with nonischemic dilated cardiomyopathy and unexplained syncope treated with an implantable defibrillator. J Am Coll Cardiol. 1999;33:1964–70.
372. Fonarow GC, Feliciano Z, Boyle NG, et al. Improved survival in patients with nonischemic advanced heart failure and syncope treated with an implantable cardioverter-defibrillator. Am J Cardiol. 2000;85:981–5.
373. Russo AM, Verdino R, Schorr C, et al. Occurrence of implantable defibrillator events in patients with syncope and nonischemic dilated cardiomyopathy. Am J Cardiol. 2001;88:1444–6.
374. Grimm W, Hoffmann JJ, Muller HH, Maisch B. Implantable defibrillator event rates in patients with idiopathic dilated cardiomyopathy, nonsustained ventricular tachycardia on Holter and a left ventricular ejection fraction below 30%. J Am Coll Cardiol. 2002;39:780–7.
375. Rankovic V, Karha J, Passman R, Kadish AH, Goldberger JJ. Predictors of appropriate implantable cardioverter-defibrillator therapy in patients with idiopathic dilated cardiomyopathy. Am J Cardiol. 2002;89:1072–6.
376. Singh SK, Link MS, Wang PJ, Homoud M, Estes NA III. Syncope in the patient with nonischemic dilated cardiomyopathy. Pacing Clin Electrophysiol. 2004;27:97–100.
377. Bansch D, Antz M, Boczor S, et al. Primary prevention of sudden cardiac death in idiopathic dilated cardiomyopathy: the Cardiomyopathy Trial (CAT). Circulation. 2002;105:1453–8.
378. Strickberger SA, Hummel JD, Bartlett TG, et al. Amiodarone versus implantable cardioverter-defibrillator:randomized trial in patients with nonischemic dilated cardiomyopathy and asymptomatic nonsustained ventricular tachycardia—AMIOVIRT. J Am Coll Cardiol. 2003;41:1707–12.
379. Desai AS, Fang JC, Maisel WH, Baughman KL. Implantable defibrillators for the prevention of mortality in patients with nonischemic cardiomyopathy: a meta-analysis of randomized controlled trials. JAMA. 2004;292:2874–9.
380. Tamburro P, Wilber D. Sudden death in idiopathic dilated cardiomyopathy. Am Heart J. 1992;124:1035–45.
381. Makati KJ, Fish AE, England HH, Tighiouart H, Estes NA III, Link MS. Equivalent arrhythmic risk in patients recently diagnosed with dilated cardiomyopathy compared with patients diagnosed for 9 months or more. Heart Rhythm. 2006;3:397–403.
382. Garson A Jr, Dick M, Fournier A, et al. The long QT syndrome in children. An international study of 287 patients. Circulation. 1993;87:1866–72.
383. Shah M, Akar FG, Tomaselli GF. Molecular basis of arrhythmias. Circulation. 2005;112:2517–29.
384. Moss AJ, Zareba W, Hall WJ, et al. Effectiveness and limitations of beta-blocker therapy in congenital long-QT syndrome. Circulation. 2000;101:616–23.
385. Priori SG, Napolitano C, Schwartz PJ, et al. Association of long QT syndrome loci and cardiac events among patients treated with beta-blockers. JAMA. 2004;292:1341–4.
386. Zareba W, Moss AJ, Schwartz PJ, et al. Influence of genotype on the clinical course of the long-QT syndrome. International Long-QT Syndrome Registry Research Group. N Engl J Med. 1998;339:960–5.
387. Groh WJ, Silka MJ, Oliver RP, Halperin BD, McAnulty JH, Kron J. Use of implantable cardioverter-defibrillators in the congenital long QT syndrome. Am J Cardiol. 1996;78:703–6.
388. Chatrath R, Porter CB, Ackerman MJ. Role of transvenous implantable cardioverter-defibrillators in preventing sudden cardiac death in children, adolescents, and young adults. Mayo Clin Proc. 2002;77:226–31.
389. Rashba EJ, Zareba W, Moss AJ, et al. Influence of pregnancy on the risk for cardiac events in patients with hereditary long QT syndrome. LQTS Investigators. Circulation. 1998;97:451–6.
390. Moss AJ, Zareba W, Kaufman ES, et al. Increased risk of arrhythmic events in long-QT syndrome with mutations in the pore region of the human ether-a-go-go-related gene potassium channel. Circulation. 2002;105:794–9.
391. Schwartz PJ, Priori SG, Spazzolini C, et al. Genotype-phenotype correlation in the long-QT syndrome: gene-specific triggers for life-threatening arrhythmias. Circulation. 2001;103:89–95.
392. Moss AJ, Robinson JL, Gessman L, et al. Comparison of clinical and genetic variables of cardiac events associated with loud noise versus swimming among subjects with the long QT syndrome. Am J Cardiol. 1999;84:876–9.
393. Priori SG, Schwartz PJ, Napolitano C, et al. Risk stratification in the long-QT syndrome. N Engl J Med. 2003;348:1866–74.
394. Daubert JP, Zareba W, Rosero SZ, Budzikowski A, Robinson JL, Moss AJ. Role of implantable cardioverter defibrillator therapy in patients with long QT syndrome. Am Heart J. 2007;153:53–8.
395. Maron BJ, McKenna WJ, Danielson GK, et al. American College of Cardiology/European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents and the European Society of Cardiology Committee for Practice Guidelines. J Am Coll Cardiol. 2003;42:1687–713.
396. Maron BJ. Contemporary considerations for risk stratification, sudden death and prevention in hypertrophic cardiomyopathy. Heart. 2003;89:977–8.
397. Maron BJ, Estes NA III, Maron MS, Almquist AK, Link MS, Udelson JE. Primary prevention of sudden death as a novel treatment strategy in hypertrophic cardiomyopathy. Circulation. 2003;107:2872–5.
398. McKenna WJ, Mogensen J, Elliott PM. Role of genotyping in risk factor assessment for sudden death in hypertrophic cardiomyopathy. J Am Coll Cardiol. 2002;39:2049–51.
399. Elliott PM, Gimeno JR, Tome MT, et al. Left ventricular outflow tract obstruction and sudden death risk in patients with hypertrophic cardiomyopathy. Eur Heart J. 2006;27:1933–41.
400. Almquist AK, Montgomery JV, Haas TS, Maron BJ. Cardioverter-defibrillator implantation in high-risk patients with hypertrophic cardiomyopathy. Heart Rhythm. 2005;2:814–9.
401. Cecchi F, Olivotto I, Montereggi A, Santoro G, Dolara A, Maron BJ. Hypertrophic cardiomyopathy in Tuscany: clinical course and outcome in an unselected regional population. J Am Coll Cardiol. 1995;26:1529–36.
402. Spirito P, Rapezzi C, Autore C, et al. Prognosis of asymptomatic patients with hypertrophic cardiomyopathy and nonsustained ventricular tachycardia. Circulation. 1994;90:2743–7.
403. Colan SD, Lipshultz SE, Lowe AM, et al. Epidemiology and cause-specific outcome of hypertrophic cardiomyopathy in children: findings from the Pediatric Cardiomyopathy Registry. Circulation. 2007;115:773–81.
404. Ikeda H, Maki S, Yoshida N, et al. Predictors of death from congestive heart failure in hypertrophic cardiomyopathy. Am J Cardiol. 1999;83:1280–3.
405. Maki S, Ikeda H, Muro A, et al. Predictors of sudden cardiac death in hypertrophic cardiomyopathy. Am J Cardiol. 1998;82:774–8.
406. Marian AJ, Mares A Jr, Kelly DP, et al. Sudden cardiac death in hypertrophic cardiomyopathy. Variability in phenotypic expression of beta-myosin heavy chain mutations. Eur Heart J. 1995;16:368–76.
407. Takagi E, Yamakado T, Nakano T. Prognosis of completely asymptomatic adult patients with hypertrophic cardiomyopathy. J Am Coll Cardiol. 1999;33:206–11.
408. Kyriakidis M, Triposkiadis F, Anastasakis A, et al. Hypertrophic cardiomyopathy in Greece: clinical course and outcome. Chest. 1998;114:1091–6.
409. Wichter T, Breithardt G. Implantable cardioverter-defibrillator therapy in arrhythmogenic right ventricular cardiomyopathy: a role for genotyping in decision-making?. J Am Coll Cardiol. 2005;45:409–11.
410. Priori SG, Aliot E, Blomstrom-Lundqvist C, et al. Task Force on Sudden Cardiac Death of the European Society of Cardiology. Eur Heart J. 2001;22:1374–450.
411. Corrado D, Basso C, Schiavon M, Thiene G. Screening for hypertrophic cardiomyopathy in young athletes. N Engl J Med. 1998;339:364–9.
412. Hulot JS, Jouven X, Empana JP, Frank R, Fontaine G. Natural history and risk stratification of arrhythmogenic right ventricular dysplasia/cardiomyopathy. Circulation. 2004;110:1879–84.
413. Pignatelli RH, McMahon CJ, Dreyer WJ, et al. Clinical characterization of left ventricular noncompaction in children: a relatively common form of cardiomyopathy. Circulation. 2003;108:2672–8.
414. Oechslin EN, Attenhofer Jost CH, Rojas JR, Kaufmann PA, Jenni R. Long-term follow-up of 34 adults with isolated left ventricular noncompaction: a distinct cardiomyopathy with poor prognosis. J Am Coll Cardiol. 2000;36:493–500.
415. Jenni R, Oechslin E, Schneider J, Attenhofer JC, Kaufmann PA. Echocardiographic and pathoanatomical characteristics of isolated left

ventricular non-compaction: a step towards classification as a distinct cardiomyopathy. Heart. 2001;86:666–71.
416. Petersen SE, Selvanayagam JB, Wiesmann F, et al. Left ventricular non-compaction: insights from cardiovascular magnetic resonance imaging. J Am Coll Cardiol. 2005;46:101–5.
417. Chin TK, Perloff JK, Williams RG, Jue K, Mohrmann R. Isolated noncompaction of left ventricular myocardium. A study of eight cases. Circulation. 1990;82:507–13.
418. Ichida F, Hamamichi Y, Miyawaki T, et al. Clinical features of isolated noncompaction of the ventricular myocardium: long-term clinical course, hemodynamic properties, and genetic background. J Am Coll Cardiol. 1999;34:233–40.
419. Ritter M, Oechslin E, Sutsch G, Attenhofer C, Schneider J, Jenni R. Isolated noncompaction of the myocardium in adults. Mayo Clin Proc. 1997;72:26–31.
420. Yasukawa K, Terai M, Honda A, Kohno Y. Isolated noncompaction of ventricular myocardium associated with fatal ventricular fibrillation. Pediatr Cardiol. 2001;22:512–4.
421. Celiker A, Kafali G, Dogan R. Cardioverter defibrillator implantation in a child with isolated noncompaction of the ventricular myocardium and ventricular fibrillation. Pacing Clin Electrophysiol. 2004;27:104–8.
422. Hermida JS, Lemoine JL, Aoun FB, Jarry G, Rey JL, Quiret JC. Prevalence of the Brugada syndrome in an apparently healthy population. Am J Cardiol. 2000;86:91–4.
423. Sarkozy A, Boussy T, Kourgiannides G, et al. Long-term follow-up of primary prophylactic implantable cardioverter-defibrillator therapy in Brugada syndrome. Eur Heart J. 2007;28:334–44.
424. Brugada P, Brugada J. Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome. A multicenter report. J Am Coll Cardiol. 1992; 20:1391–6.
425. Brugada J, Brugada R, Brugada P. Brugada syndrome. Arch Mal Coeur Vaiss. 1999;92:847–50.
426. Antzelevitch C, Brugada P, Borggrefe M, et al. Brugada syndrome: report of the second consensus conference: endorsed by the Heart Rhythm Society and the European Heart Rhythm Association. Circulation. 2005;111:659–70.
427. Martin GR, Silverman NH, Soifer SJ, Lutin WA, Scagnelli SA. Tricuspid regurgitation in children: a pulsed Doppler, contrast echocardiographic and angiographic comparison. J Am Soc Echocardiogr. 1988;1:257–63.
428. Leenhardt A, Lucet V, Denjoy I, Grau F, Ngoc DD, Coumel P. Catecholaminergic polymorphic ventricular tachycardia in children. A 7–year follow-up of 21 patients. Circulation. 1995;91:1512–9.
429. Lahat H, Pras E, Eldar M. RYR2 and CASQ2 mutations in patients suffering from catecholaminergic polymorphic ventricular tachycardia. Circulation. 2003;107:e29.
430. Laitinen PJ, Brown KM, Piippo K, et al. Mutations of the cardiac ryanodine receptor (RyR2) gene in familial polymorphic ventricular tachycardia. Circulation. 2001;103:485–90.
431. Marks AR, Priori S, Memmi M, Kontula K, Laitinen PJ. Involvement of the cardiac ryanodine receptor/calcium release channel in catecholaminergic polymorphic ventricular tachycardia. J Cell Physiol. 2002;190:1–6.
432. Priori SG, Pandit SV, Rivolta I, et al. A novel form of short QT syndrome (SQT3) is caused by a mutation in the KCNJ2 gene. Circ Res. 2005;96:800–7.
433. Klein LS, Shih HT, Hackett FK, Zipes DP, Miles WM. Radiofrequency catheter ablation of ventricular tachycardia in patients without structural heart disease. Circulation. 1992;85:1666–74.
434. Stevenson LW, Desai AS. Selecting patients for discussion of the ICD as primary prevention for sudden death in heart failure. J Card Fail. 2006;12:407–12.
435. Hauptman PJ, Masoudi FA, Weintraub WS, Pina I, Jones PG, Spertus JA. Variability in the clinical status of patients with advanced heart failure. J Card Fail. 2004;10:397–402.
436. Levy WC, Mozaffarian D, Linker DT, et al. The Seattle Heart Failure Model: prediction of survival in heart failure. Circulation. 2006;113: 1424–33.
437. Mozaffarian D, Anker SD, Anand I, et al. Prediction of mode of death in heart failure: the Seattle Heart Failure Model. Circulation. 2007;116: 392–8.
438. The Seattle Heart Failure Model. Available at: http://www.seattleheartfailuremodel.org. Accessed January 2008.
439. Kozak LJ, Owings MF, Hall MJ. National Hospital Discharge Survey: 2002 annual summary with detailed diagnosis and procedure data. Vital Health Stat 13. 2005;1–199.
440. Silka MJ, Kron J, Dunnigan A, Dick M. Sudden cardiac death and the use of implantable cardioverter-defibrillators in pediatric patients. The Pediatric Electrophysiology Society. Circulation. 1993;87:800–7.
441. Liberthson RR. Sudden death from cardiac causes in children and young adults. N Engl J Med. 1996;334:1039–44.
442. Eisenberg M, Bergner L, Hallstrom A. Epidemiology of cardiac arrest and resuscitation in children. Ann Emerg Med. 1983;12:672–4.
443. Hamilton RM, Dorian P, Gow RM, Williams WG. Five-year experience with implantable defibrillators in children. Am J Cardiol. 1996;77: 524–6.
444. Alexander ME, Cecchin F, Walsh EP, Triedman JK, Bevilacqua LM, Berul CI. Implications of implantable cardioverter defibrillator therapy in congenital heart disease and pediatrics. J Cardiovasc Electrophysiol. 2004;15:72–6.
445. Choi GR, Porter CB, Ackerman MJ. Sudden cardiac death and channelopathies: a review of implantable defibrillator therapy. Pediatr Clin North Am. 2004;51:1289–303.
446. Khairy P, Landzberg MJ, Gatzoulis MA, et al. Value of programmed ventricular stimulation after tetralogy of fallot repair: a multicenter study. Circulation. 2004;109:1994–2000.
447. Karamlou T, Silber I, Lao R, et al. Outcomes after late reoperation in patients with repaired tetralogy of Fallot: the impact of arrhythmia and arrhythmia surgery. Ann Thorac Surg. 2006;81:1786–93.
448. Nugent AW, Daubeney PE, Chondros P, et al. Clinical features and outcomes of childhood hypertrophic cardiomyopathy: results from a national population-based study. Circulation. 2005;112:1332–8.
449. Silka MJ, Hardy BG, Menashe VD, Morris CD. A population-based prospective evaluation of risk of sudden cardiac death after operation for common congenital heart defects. J Am Coll Cardiol. 1998;32:245–51.
450. Oechslin EN, Harrison DA, Connelly MS, Webb GD, Siu SC. Mode of death in adults with congenital heart disease. Am J Cardiol. 2000;86: 1111–6.
451. Kammeraad JA, van Deurzen CH, Sreeram N, et al. Predictors of sudden cardiac death after Mustard or Senning repair for transposition of the great arteries. J Am Coll Cardiol. 2004;44:1095–102.
452. Graham TP Jr, Bernard YD, Mellen BG, et al. Long-term outcome in congenitally corrected transposition of the great arteries: a multi-institutional study. J Am Coll Cardiol. 2000;36:255–61.
453. Ghai A, Silversides C, Harris L, Webb GD, Siu SC, Therrien J. Left ventricular dysfunction is a risk factor for sudden cardiac death in adults late after repair of tetralogy of Fallot. J Am Coll Cardiol. 2002;40:1675–80.
454. Dubin AM, Berul CI, Bevilacqua LM, et al. The use of implantable cardioverter-defibrillators in pediatric patients awaiting heart transplantation. J Card Fail. 2003;9:375–9.
455. Evans RW, Manninen DL, Dong FB, Frist WH, Kirklin JK. The medical and surgical determinants of heart transplantation outcomes: the results of a consensus survey in the United States. J Heart Lung Transplant. 1993;12:42–5.
456. Sears SF Jr, Conti JB. Quality of life and psychological functioning of ICD patients. Heart. 2002;87:488–93.
457. Vlay SC, Olson LC, Fricchione GL, Friedman R. Anxiety and anger in patients with ventricular tachyarrhythmias. Responses after automatic internal cardioverter defibrillator implantation. Pacing Clin Electrophysiol. 1989;12:366–73.
458. Luderitz B, Jung W, Deister A, Marneros A, Manz M. Patient acceptance of the implantable cardioverter defibrillator in ventricular tachyarrhythmias. Pacing Clin Electrophysiol. 1993;16:1815–21.
459. Thomas SA, Friedmann E, Kao CW, et al. Quality of life and psychological status of patients with implantable cardioverter defibrillators. Am J Crit Care. 2006;15:389–98.
460. Irvine J, Dorian P, Baker B, et al. Quality of life in the Canadian Implantable Defibrillator Study (CIDS). Am Heart J. 2002;144:282–9.
461. Germano JJ, Reynolds M, Essebag V, Josephson ME. Frequency and causes of implantable cardioverter-defibrillator therapies: is device therapy proarrhythmic?. Am J Cardiol. 2006;97:1255–61.
462. Alter P, Waldhans S, Plachta E, Moosdorf R, Grimm W. Complications of implantable cardioverter defibrillator therapy in 440 consecutive patients. Pacing Clin Electrophysiol. 2005;28:926–32.
463. Rosenqvist M, Beyer T, Block M, Den DK, Minten J, Lindemans F. Adverse events with transvenous implantable cardioverter-defibrillators: a prospective multicenter study. European 7219 Jewel ICD investigators. Circulation. 1998;98:663–70.

464. Al-Ahmad A, Wang PJ, Homoud MK, Estes NA III, Link MS. Frequent ICD shocks due to double sensing in patients with bi-ventricular implantable cardioverter defibrillators. J Interv Card Electrophysiol. 2003;9:377–81.
465. Friedman PA, McClelland RL, Bamlet WR, et al. Dual-chamber versus single-chamber detection enhancements for implantable defibrillator rhythm diagnosis: the detect supraventricular tachycardia study. Circulation. 2006;113:2871–9.
466. Williams JL, Shusterman V, Saba S. A pilot study examining the performance of polynomial-modeled ventricular shock electrograms for rhythm discrimination in implantable devices. Pacing Clin Electrophysiol. 2006;29:930–9.
467. Gunderson BD, Gillberg JM, Wood MA, Vijayaraman P, Shepard RK, Ellenbogen KA. Development and testing of an algorithm to detect implantable cardioverter-defibrillator lead failure. Heart Rhythm. 2006; 3:155–62.
468. Gunderson BD, Patel AS, Bounds CA, Shepard RK, Wood MA, Ellenbogen KA. An algorithm to predict implantable cardioverter-defibrillator lead failure. J Am Coll Cardiol. 2004;44:1898–902.
469. Sears SF Jr, Shea JB, Conti JB. Cardiology patient page. How to respond to an implantable cardioverter-defibrillator shock. Circulation. 2005; 111:e380–e382.
470. Shah RV, Lewis EF, Givertz MM. Epicardial left ventricular lead placement for cardiac resynchronization therapy following failed coronary sinus approach. Congest Heart Fail. 2006;12:312–6.
471. Koos R, Sinha AM, Markus K, et al. Comparison of left ventricular lead placement via the coronary venous approach versus lateral thoracotomy in patients receiving cardiac resynchronization therapy. Am J Cardiol. 2004;94:59–63.
472. Gabor S, Prenner G, Wasler A, Schweiger M, Tscheliessnigg KH, Smolle-Juttner FM. A simplified technique for implantation of left ventricular epicardial leads for biventricular re-synchronization using video-assisted thoracoscopy (VATS). Eur J Cardiothorac Surg. 2005; 28:797–800.
473. Navia JL, Atik FA, Grimm RA, et al. Minimally invasive left ventricular epicardial lead placement: surgical techniques for heart failure resynchronization therapy. Ann Thorac Surg. 2005;79:1536–44.
474. Mair H, Sachweh J, Meuris B, et al. Surgical epicardial left ventricular lead versus coronary sinus lead placement in biventricular pacing. Eur J Cardiothorac Surg. 2005;27:235–42.
475. DeRose JJ, Ashton RC, Belsley S, et al. Robotically assisted left ventricular epicardial lead implantation for biventricular pacing. J Am Coll Cardiol. 2003;41:1414–9.
476. Jansens JL, Jottrand M, Preumont N, Stoupel E, de Cannière D. Robotic-enhanced biventricular resynchronization: an alternative to endovenous cardiac resynchronization therapy in chronic heart failure. Ann Thorac Surg. 2003;76:413–7.
477. Mizuno T, Tanaka H, Makita S, Tabuchi N, Arai H, Sunamori M. Biventricular pacing with coronary bypass and Dor's ventriculoplasty. Ann Thorac Surg. 2003;75:998–9.
478. Sachweh JS, Vazquez-Jimenez JF, Schondube FA, et al. Twenty years experience with pediatric pacing: epicardial and transvenous stimulation. Eur J Cardiothorac Surg. 2000;17:455–61.
479. Walsh EP, Cecchin F. Recent advances in pacemaker and implantable defibrillator therapy for young patients. Curr Opin Cardiol. 2004;19: 91–6.
480. Cohen MI, Rhodes LA, Spray TL, Gaynor JW. Efficacy of prophylactic epicardial pacing leads in children and young adults. Ann Thorac Surg. 2004;78:197–202.
481. Vogt PR, Sagdic K, Lachat M, Candinas R, von Segesser LK, Turina MI. Surgical management of infected permanent transvenous pacemaker systems: ten year experience. J Card Surg. 1996;11:180–6.
482. Huang DT, Sesselberg HW, McNitt S, et al. Improved survival associated with prophylactic implantable defibrillators in elderly patients with prior myocardial infarction and depressed ventricular function: a MADIT-II substudy. J Cardio Electro. 2007;18:833–8.
483. Koplan BA, Epstein LM, Albert CM, Stevenson WG. Survival in octogenarians receiving implantable defibrillators. Am Heart J. 2006; 152:714–9.
484. Lee DS, Tu JV, Austin PC, et al. Effect of cardiac and noncardiac conditions on survival after defibrillator implantation. J Am Coll Cardiol. 2007;49:2408–15.
485. Healey JS, Hallstrom AP, Kuck KH, et al. Role of the implantable defibrillator among elderly patients with a history of life-threatening ventricular arrhythmias. Eur Heart J. 2007;28:1746–9.
486. Mueller PS, Hook CC, Hayes DL. Ethical analysis of withdrawal of pacemaker or implantable cardioverter-defibrillator support at the end of life. Mayo Clin Proc. 2003;78:959–63.
487. Lewis WR, Luebke DL, Johnson NJ, Harrington MD, Costantini O, Aulisio MP. Withdrawing implantable defibrillator shock therapy in terminally ill patients. Am J Med. 2006;119:892–6.
488. Gostin LO. Law and medicine. JAMA. 1997;277:1866–7.
489. Weiss JP, Saynina O, McDonald KM, McClellan MB, Hlatky MA. Effectiveness and cost-effectiveness of implantable cardioverter defibrillators in the treatment of ventricular arrhythmias among Medicare beneficiaries. Am J Med. 2002;112:519–27.
490. O'Brien BJ, Connolly SJ, Goeree R, et al. Cost-effectiveness of the implantable cardioverter-defibrillator: results from the Canadian Implantable Defibrillator Study (CIDS). Circulation. 2001;103:1416–21.
491. Larsen G, Hallstrom A, McAnulty J, et al. Cost-effectiveness of the implantable cardioverter-defibrillator versus antiarrhythmic drugs in survivors of serious ventricular tachyarrhythmias: results of the Antiarrhythmics Versus Implantable Defibrillators (AVID) economic analysis substudy. Circulation. 2002;105:2049–57.
492. Hlatky MA, Sanders GD, Owens DK. Evidence-based medicine and policy: the case of the implantable cardioverter defibrillator. Health Aff (Millwood). 2005;24:42–51.
493. Saksena S, Madan N, Lewis C. Implanted cardioverter-defibrillators are preferable to drugs as primary therapy in sustained ventricular tachyarrhythmias. Prog Cardiovasc Dis. 1996;38:445–54.
494. Kupersmith J, Hogan A, Guerrero P, et al. Evaluating and improving the cost-effectiveness of the implantable cardioverter-defibrillator. Am Heart J. 1995;130:507–15.
495. Larsen GC, Manolis AS, Sonnenberg FA, Beshansky JR, Estes NA, Pauker SG. Cost-effectiveness of the implantable cardioverter-defibrillator: effect of improved battery life and comparison with amiodarone therapy. J Am Coll Cardiol. 1992;19:1323–34.
496. Owens DK, Sanders GD, Harris RA, et al. Cost-effectiveness of implantable cardioverter defibrillators relative to amiodarone for prevention of sudden cardiac death. Ann Intern Med. 1997;126:1–12.
497. Sanders GD, Hlatky MA, Owens DK. Cost-effectiveness of implantable cardioverter-defibrillators. N Engl J Med. 2005;353:1471–80.
498. Owens DK, Sanders GD, Heidenreich PA, McDonald KM, Hlatky MA. Effect of risk stratification on cost-effectiveness of the implantable cardioverter defibrillator. Am Heart J. 2002;144:440–8.
499. Sears SE Jr, Conti JB. Understanding implantable cardioverter defibrillator shocks and storms: medical and psychosocial considerations for research and clinical care. Clin Cardiol. 2003;26:107–11.
500. Schron EB, Exner DV, Yao Q, et al. Quality of life in the antiarrhythmics versus implantable defibrillators trial: impact of therapy and influence of adverse symptoms and defibrillator shocks. Circulation. 2002;105:589–94.
501. Namerow PB, Firth BR, Heywood GM, Windle JR, Parides MK. Quality-of-life six months after CABG surgery in patients randomized to ICD versus no ICD therapy: findings from the CABG Patch Trial. Pacing Clin Electrophysiol. 1999;22:1305–13.
502. Exner DV. Quality of life in patients with life-threatening arrhythmias: does choice of therapy make a difference?. Am Heart J. 2002;144:208–11.
503. Sears SF, Todaro JF, Urizar G, et al. Assessing the psychosocial impact of the ICD: a national survey of implantable cardioverter defibrillator health care providers. Pacing Clin Electrophysiol. 2000;23:939–45.
504. Wyman BT, Hunter WC, Prinzen FW, Faris OP, McVeigh ER. Effects of single- and biventricular pacing on temporal and spatial dynamics of ventricular contraction. Am J Physiol Heart Circ Physiol. 2002;282: H372–9.
505. Yu Y, Kramer A, Spinelli J, Ding J, Hoersch W, Auricchio A. Biventricular mechanical asynchrony predicts hemodynamic effect of uni- and biventricular pacing. Am J Physiol Heart Circ Physiol. 2003;285:H2788–96.
506. Sweeney MO. The nature of the game. J Cardiovasc Electrophysiol. 2005;16:483–5.
507. Wathen MS, Sweeney MO, DeGroot PJ, et al. Shock reduction using antitachycardia pacing for spontaneous rapid ventricular tachycardia in patients with coronary artery disease. Circulation. 2001;104:796–801.
508. Wathen MS, DeGroot PJ, Sweeney MO, et al. Prospective randomized multicenter trial of empirical antitachycardia pacing versus shocks for spontaneous rapid ventricular tachycardia in patients with implantable cardioverter-defibrillators: Pacing Fast Ventricular Tachycardia Reduces Shock Therapies (PainFREE Rx II) trial results. Circulation. 2004;110: 2591–6.

JACC Vol. 61, No. 3, 2013
January 22, 2013:e6–75

509. Fisher JD, Mehra R, Furman S. Termination of ventricular tachycardia with bursts of rapid ventricular pacing. Am J Cardiol. 1978;41:94–102.
510. Gillis AM, Leitch JW, Sheldon RS, et al. A prospective randomized comparison of autodecremental pacing to burst pacing in device therapy for chronic ventricular tachycardia secondary to coronary artery disease. Am J Cardiol. 1993;72:1146–51.
511. Schaumann A, von zur Mühlen F, Herse B, Gonska BD, Kreuzer H. Empirical versus tested antitachycardia pacing in implantable cardioverter defibrillators: a prospective study including 200 patients. Circulation. 1998;97:66–74.
512. Wilkoff BL, Hess M, Young J, Abraham WT. Differences in tachyarrhythmia detection and implantable cardioverter defibrillator therapy by primary or secondary prevention indication in cardiac resynchronization therapy patients. J Cardiovasc Electrophysiol. 2004;15:1002–9.
513. Schoenfeld MH. Contemporary pacemaker and defibrillator device therapy: challenges confronting the general cardiologist. Circulation. 2007;115:638–53.
514. Scheinman M, Akhtar M, Brugada P, et al. Teaching objectives for fellowship programs in clinical electrophysiology. J Am Coll Cardiol. 1988;12:255–61.
515. Faust M, Fraser J, Schurig L, et al. Educational guidelines for the clinically associated professional in cardiac pacing and electrophysiology. Pacing Clin Electrophysiol. 1990;13:1448–55.
516. Senges-Becker JC, Klostermann M, Becker R, et al. What is the "optimal" follow-up schedule for ICD patients?. Europace. 2005;7:319–26.
517. Schoenfeld MH, Compton SJ, Mead RH, et al. Remote monitoring of implantablecardioverter defibrillators: a prospective analysis. Pacing Clin Electrophysiol. 2004;27:757–63.
518. Fetter JG, Stanton MS, Benditt DG, Trusty J, Collins J. Transtelephonic monitoring and transmission of stored arrhythmia detection and therapy data from an implantable cardioverter defibrillator. Pacing Clin Electrophysiol. 1995;18:1531–9.
519. Winters SL, Packer DL, Marchlinski FE, et al. Consensus statement on indications, guidelines for use, and recommendations for follow-up of implantable cardioverter defibrillators. North American Society of Electrophysiology and Pacing. Pacing Clin Electrophysiol. 2001;24:262–9.
520. Epstein AE, Miles WM, Benditt DG, et al. Personal and public safety issues related to arrhythmias that may affect consciousness: implications for regulation and physician recommendations. A medical/scientific statement from the American Heart Association and the North American Society of Pacing and Electrophysiology. Circulation. 1996;94:1147–66.
521. Jung W, Luderitz B. European policy on driving for patients with implantable cardioverter defibrillators. Pacing Clin Electrophysiol. 1996;19:981–4.
522. Epstein AE, Baessler CA, Curtis AB, et al. Addendum to "Personal and public safety issues related to arrhythmias that may affect consciousness: implications for regulation and physician recommendations: a medical/scientific statement from the American Heart Association and the North American Society of Pacing and Electrophysiology": public safety issues in patients with implantable defibrillators: a scientific statement from the American Heart Association and the Heart Rhythm Society. Circulation. 2007;115:1170–6.
523. Maron BJ, Zipes DP. Introduction: eligibility recommendations for competitive athletes with cardiovascular abnormalities-general considerations. J Am Coll Cardiol. 2005;45:1318–21.
524. Practice advisory for the perioperative management of patients with cardiac rhythm management devices: pacemakers and implantable cardioverter-defibrillators: a report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Rhythm Management Devices. Anesthesiology. 2005;103:186–98.
525. Gould PA, Krahn AD. Complications associated with implantable cardioverter-defibrillator replacement in response to device advisories. JAMA. 2006;295:1907–11.
526. Amin MS, Matchar DB, Wood MA, Ellenbogen KA. Management of recalled pacemakers and implantable cardioverter-defibrillators: a decision analysis model. JAMA. 2006;296:412–20.
527. Hauser RG, Kallinen LM, Almquist AK, Gornick CC, Katsiyiannis WT. Early failure of a small-diameter high-voltage implantable cardioverter-defibrillator lead. Heart Rhythm. 2007;4:892–6.

2012 Device-Based Therapy Focused Update References (Corresponds to Sections 2.4.1 and 2.8.3)

540. Barsheshet A, Wang PJ, Moss AJ, et al. Reverse remodeling and the risk of ventricular tachyarrhythmias in the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy). J Am Coll Cardiol. 2011;57:2416–23.
541. Wilkoff BL, Auricchio A, Brugada J, et al. HRS/EHRA expert consensus on the monitoring of cardiovascular implantable electronic devices (CIEDs): description of techniques, indications, personnel, frequency and ethical considerations. Heart Rhythm. 2008;5:907–25.
542. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med. 2002;346:1845–53.
543. Bristow MR, Saxon LA, Boehmer J, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. 2004;350:2140–50.
544. Cleland JGF, Daubert J-C, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med. 2005;352:1539–49.
545. Goldstein NE, Lampert R, Bradley E, Lynn J, Krumholz HM. Management of implantable cardioverter defibrillators in end-of-life care. Ann Intern Med. 2004;141:835–8.
546. Moss AJ, Hall WJ, Cannom DS, et al. Cardiac-resynchronization therapy for the prevention of heart-failure events. N Engl J Med. 2009;361:1329–38.
547. Tang ASL, Wells GA, Talajic M, et al. Cardiac-resynchronization therapy for mild-to-moderate heart failure. N Engl J Med. 2010;363:2385–95.
548. Linde C, Abraham WT, Gold MR, et al. Randomized trial of cardiac resynchronization in mildly symptomatic heart failure patients and in asymptomatic patients with left ventricular dysfunction and previous heart failure symptoms. J Am Coll Cardiol. 2008;52:1834–43.
549. Brignole M, Gammage M, Puggioni E, et al. Comparative assessment of right, left, and biventricular pacing in patients with permanent atrial fibrillation. Eur Heart J. 2005;26:712–22.
550. Brignole M, Botto G, Mont L, et al. Cardiac resynchronization therapy in patients undergoing atrioventricular junction ablation for permanent atrial fibrillation: a randomized trial. Eur Heart J. 2011;32:2420–9.
551. Doshi RN, Daoud EG, Fellows C, et al. Left ventricular-based cardiac stimulation post AV nodal ablation evaluation (the PAVE study). J Cardiovasc Electrophysiol. 2005;16:1160–5.
552. Gasparini M, Auricchio A, Regoli F, et al. Four-year efficacy of cardiac resynchronization therapy on exercise tolerance and disease progression: the importance of performing atrioventricular junction ablation in patients with atrial fibrillation. J Am Coll Cardiol. 2006;48:734–43.
553. Wilton SB, Leung AA, Ghali WA, et al. Outcomes of cardiac resynchronization therapy in patients with versus those without atrial fibrillation: a systematic review and meta-analysis. Heart Rhythm. 2011;8:1088–94.
554. Wilkoff BL, Cook JR, Epstein AE, et al. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. JAMA. 2002;288:3115–23.
555. Adelstein E, Schwartzman D, Gorcsan J 3rd, Saba S. Predicting hyperresponse among pacemaker-dependent nonischemic cardiomyopathy patients upgraded to cardiac resynchronization. J Cardiovasc Electrophysiol. 2011;22:905–11.
556. Vatankulu MA, Goktekin O, Kaya MG, et al. Effect of long-term resynchronization therapy on left ventricular remodeling in pacemaker patients upgraded to biventricular devices. Am J Cardiol. 2009;103:1280–4.
557. Rickard J, Bassiouny M, Cronin EM, et al. Predictors of response to cardiac resynchronization therapy in patients with a non-left bundle branch block morphology. Am J Cardiol. 2011;108:1576–80.
558. Masci PG, Marinelli M, Piacenti M, et al. Myocardial structural, perfusion, and metabolic correlates of left bundle branch block mechanical derangement in patients with dilated cardiomyopathy: a tagged cardiac magnetic resonance and positron emission tomography study. Circ Cardiovasc Imaging. 2010;3:482–90.
559. Kashani A, Barold SS. Significance of QRS complex duration in patients with heart failure. J Am Coll Cardiol. 2005;46:2183–92.
560. Doval HC, Nul DR, Grancelli HO, et al. Randomised trial of low-dose amiodarone in severe congestive heart failure: Grupo de Estudio de la

Sobrevida en la Insuficiencia Cardiaca en Argentina (GESICA). Lancet. 1994;344:493–8.
561. Bleeker GB, Schalij MJ, Molhoek SG, et al. Relationship between QRS duration and left ventricular dyssynchrony in patients with end-stage heart failure. J Cardiovasc Electrophysiol. 2004;15:544–9.
562. Blanc JJ, Etienne Y, Gilard M, et al. Evaluation of different ventricular pacing sites in patients with severe heart failure: results of an acute hemodynamic study. Circulation. 1997;96:3273–7.
563. Prinzen FW, Vernooy K, De Boeck BWL, et al. Mechano-energetics of the asynchronous and resynchronized heart. Heart Fail Rev. 2011;16: 215–24.
564. Ukkonen H, Sundell J, Knuuti J. Effects of CRT on myocardial innervation, perfusion and metabolism. Europace. 2008;10 Suppl 3: iii114–7.
565. Cazeau S, Leclercq C, Lavergne T, et al. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. N Engl J Med. 2001;344:873–80.
566. Stellbrink C, Breithardt OA, Franke A, et al. Impact of cardiac resynchronization therapy using hemodynamically optimized pacing on left ventricular remodeling in patients with congestive heart failure and ventricular conduction disturbances. J Am Coll Cardiol. 2001;38:1957–65.
567. Bradley DJ, Bradley EA, Baughman KL, et al. Cardiac resynchronization and death from progressive heart failure: a meta-analysis of randomized controlled trials. JAMA. 2003;289:730–40.
568. Haghjoo M, Bagherzadeh A, Fazelifar AF, et al. Prevalence of mechanical dyssynchrony in heart failure patients with different QRS durations. Pacing Clin Electrophysiol. 2007;30:616–22.
569. Stavrakis S, Lazzara R, Thadani U. The benefit of cardiac resynchronization therapy and QRS duration: a meta-analysis. J Cardiovasc Electrophysiol. 2012;23:163–8.
570. Sipahi I, Carrigan TP, Rowland DY, et al. Impact of QRS duration on clinical event reduction with cardiac resynchronization therapy: meta-analysis of randomized controlled trials. Arch Intern Med. 2011;171: 1454–62.
571. Sipahi I, Chou JC, Hyden M, et al. Effect of QRS morphology on clinical event reduction with cardiac resynchronization therapy: meta-analysis of randomized controlled trials. Am Heart J. 2012;163:260–7.
572. Bilchick KC, Kamath S, DiMarco JP, Stukenborg GJ. Bundle-branch block morphology and other predictors of outcome after cardiac resynchronization therapy in Medicare patients. Circulation. 2010;122:2022–30.
573. Adelstein EC, Saba S. Usefulness of baseline electrocardiographic QRS complex pattern to predict response to cardiac resynchronization. Am J Cardiol. 2009;103:238–42.
574. Rickard J, Kumbhani DJ, Gorodeski EZ, et al. Cardiac resynchronization therapy in non-left bundle branch block morphologies. Pacing Clin Electrophysiol. 2010;33:590–5.
575. Upadhyay GA, Choudhry NK, Auricchio A, et al. Cardiac resynchronization in patients with atrial fibrillation: a meta-analysis of prospective cohort studies. J Am Coll Cardiol. 2008;52:1239–46.
576. Beshai JF, Grimm RA, Nagueh SF, et al. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. N Engl J Med. 2007;357:2461–71.
577. Ariga R, Tayebjee MH, Benfield A, et al. Greater three-dimensional ventricular lead tip separation is associated with improved outcome after cardiac resynchronization therapy. Pacing Clin Electrophysiol. 2010;33: 1490–6.
578. Singh JP, Klein HU, Huang DT, et al. Left ventricular lead position and clinical outcome in the multicenter automatic defibrillator implantation trial-cardiac resynchronization therapy (MADIT-CRT) trial. Circulation. 2011;123:1159–66.
579. Linde C, Leclercq C, Rex S, et al. Long-term benefits of biventricular pacing in congestive heart failure: results from the MUltisite STimulation in cardiomyopathy (MUSTIC) study. J Am Coll Cardiol. 2002;40:111–8.
580. Sweeney MO, Prinzen FW. A new paradigm for physiologic ventricular pacing. J Am Coll Cardiol. 2006;47:282–8.
581. Sharma AD, Rizo-Patron C, Hallstrom AP, et al. Percent right ventricular pacing predicts outcomes in the DAVID trial. Heart Rhythm. 2005;2:830–4.
582. Steinberg JS, Fischer A, Wang P, et al. The clinical implications of cumulative right ventricular pacing in the Multicenter Automatic Defibrillator Trial II. J Cardiovasc Electrophysiol. 2005;16:359–65.
583. Lindenfeld J, Feldman AM, Saxon L, et al. Effects of cardiac resynchronization therapy with or without a defibrillator on survival and hospitalizations in patients with New York Heart Association class IV heart failure. Circulation. 2007;115:204–12.
584. Amin MS, Fox AD, Kalahasty G, et al. Benefit of primary prevention implantable cardioverter-defibrillators in the setting of chronic kidney disease: a decision model analysis. J Cardiovasc Electrophysiol. 2008; 19:1275–80.
585. Abraham WT, Young JB, León AR, et al. Effects of cardiac resynchronization on disease progression in patients with left ventricular systolic dysfunction, an indication for an implantable cardioverter-defibrillator, and mildly symptomatic chronic heart failure. Circulation. 2004;110: 2864–8.
586. Daubert C, Gold MR, Abraham WT, et al. Prevention of disease progression by cardiac resynchronization therapy in patients with asymptomatic or mildly symptomatic left ventricular dysfunction: insights from the European cohort of the REVERSE (Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction) trial. J Am Coll Cardiol. 2009;54:1837–46.
587. Singh JP, Gras D. Biventricular pacing: current trends and future strategies. Eur Heart J. 2012;33:305–13.
588. Stevenson WG, Hernandez AF, Carson PE, et al. Indications for cardiac resynchronization therapy: 2011 update from the Heart Failure Society of America Guideline Committee. J Card Fail. 2012;18:94–106.
589. Dickstein K, Vardas PE, Auricchio A, et al. 2010 Focused update of ESC guidelines on device therapy in heart failure: an update of the 2008 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure and the 2007 ESC guidelines for cardiac and resynchronization therapy. Eur Heart J. 2010;31:2677–87.
590. Dubner S, Auricchio A, Steinberg JS, et al. ISHNE/EHRA expert consensus on remote monitoring of cardiovascular implantable electronic devices (CIEDs). Europace. 2012;14:278–93.
591. Crossley GH, Chen J, Choucair W, et al. Clinical benefits of remote versus transtelephonic monitoring of implanted pacemakers. J Am Coll Cardiol. 2009;54:2012–9.
592. Crossley GH, Boyle A, Vitense H, et al. The CONNECT (Clinical Evaluation of Remote Notification to Reduce Time to Clinical Decision) trial: the value of wireless remote monitoring with automatic clinician alerts. J Am Coll Cardiol. 2011;57:1181–9.
593. Varma N, Epstein AE, Irimpen A, et al. Efficacy and safety of automatic remote monitoring for implantable cardioverter-defibrillator follow-up: the Lumos-T Safely Reduces Routine Office Device Follow-up (TRUST) trial. Circulation. 2010;122:325–32.
594. Mabo P, Victor F, Bazin P, et al. A randomized trial of long-term remote monitoring of pacemaker recipients (the COMPAS trial). Eur Heart J. 2012;33:1105–11.
595. Saxon LA, Hayes DL, Gilliam FR, et al. Long-term outcome after ICD and CRT implantation and influence of remote device follow-up: the ALTITUDE survival study. Circulation. 2010;122:2359–67.

KEY WORDS: ACCF/AHA Practice Guidelines ■ arrhythmia ■ cardiomyopathy ■ cardiac resynchronization ■ device-based therapy ■ focused update ■ heart failure ■ pacing.

Appendix 1. 2008 Author Relationships With Industry and Other Entities (Relevant)—ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities

Committee Member	Consulting Fees/Honoraria	Speakers' Bureau	Ownership/ Partnership/ Principal	Research Grants	Institutional or Other Financial Benefit
Andrew E. Epstein*	• Boston Scientific • CryoCath • Medtronic • Sanofi-Aventis • St. Jude†	• Boston Scientific • Medtronic • Reliant Pharmaceuticals • Sanofi-Aventis • St. Jude	None	• Biotronik† • Boston Scientific† • C. R. Bard/Electrophysiology Division† • Irving Biomedical† • Medtronic† • St. Jude†	Electrophysiology fellowship support from: • Medtronic† • St. Jude†
John P. DiMarco*	• Boston Scientific† • CV Therapeutics† • Daiichi Sankyo • Medtronic† • Novartis† • Sanofi-Aventis • Solvay • St. Jude	None	None	• Boston Scientific† • CV Therapeutics† • Medtronic • Sanofi-Aventis • St. Jude	None
Kenneth A. Ellenbogen*	• Ablation Frontiers • Atricure • Biosense Webster • Biotronik • Boston Scientific • Medtronic • Sorin/ELA • St. Jude	• Reliant Pharmaceuticals • Sanofi-Aventis	None	• Biosense Webster • Boston Scientific† • Cameron Medical • Impulse Dynamics • Medtronic† • St. Jude	None
N.A. Mark Estes III	• Medtronic	• Boston Scientific • Medtronic • St. Jude	None	None	None
Roger A. Freedman*	• Boston Scientific • Medtronic • Sorin/ELA • St. Jude	• Boston Scientific • St. Jude	• St. Jude	• Boston Scientific† • Medtronic† • St. Jude†	University of Utah Division of Cardiology receives electrophysiology fellowship support grants from: • Boston Scientific† • Medtronic† • St. Jude†
Leonard S. Gettes	None	None	None	None	None
A. Marc Gillinov*	• AtriCure • Edwards† • Medtronic	• Guidant • St. Jude	• Viacor†	None	None
Gabriel Gregoratos	None	None	None	None	None
Stephen C. Hammill	• Biosense Webster	• Boston Scientific	None	• Medtronic	None
David L. Hayes*	• Al Semi • Blackwell/Futura† • Boston Scientific† • Medtronic† • Sorin/ELA • St. Jude	None	None	• Boston Scientific† • Medtronic† • St. Jude	• Biotronik • Boston Scientific† • Medtronic† • Sorin/ELA • St. Jude
Mark A. Hlatky	• Blue Cross/Blue Shield Technology Evaluation Center	None	None	None	None
L. Kristin Newby	• AstraZeneca/Atherogenics • Biosite • CV Therapeutics • Johnson & Johnson • Novartis • Procter & Gamble • Roche Diagnostics	None	None	• Adolor • American Heart Association† • BG Medicine • Bristol-Myers Squibb/Sanofi† • Inverness Medical† • Medicure† • Schering-Plough†	None
Richard L. Page	• Astellas • Berlex • Pfizer • Sanofi-Aventis†	None	None	• Procter & Gamble	• Boston Scientific† • Medtronic† • St. Jude†

(Continued)

Appendix 1. Continued

Committee Member	Consulting Fees/Honoraria	Speakers' Bureau	Ownership/ Partnership/ Principal	Research Grants	Institutional or Other Financial Benefit
Mark H. Schoenfeld	None	None	None	None	None
Michael J. Silka	None	None	None	None	None
Lynne Warner Stevenson	• Biosense Webster‡ • Boston Scientific‡ • CardioMEMS • Medtronic • Medtronic‡ • Scios	None	None	• Biosense Webster‡ • Medtronic	None
Michael O. Sweeney	• Medtronic†	• Boston Scientific • Medtronic†	None	None	None

This table represents the relationships of committee members with industry that were reported orally at the initial writing committee meeting and updated in conjunction with all meetings and conference calls of the writing committee during the document development process (last revision, January 16, 2008). It does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of 5% or more of the voting stock or share of the business entity, or ownership of $10,000 or more of the fair market value of the business entity, or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships noted in this table are modest unless otherwise noted.

*Recused from voting on guideline recommendations.

†Indicates significant-level relationship (more than $10,000).

‡Indicates spousal relationship.

Appendix 2. 2008 Reviewer Relationships With Industry and Other Entities (Relevant)—ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities

Peer Reviewer*	Representation	Consulting Fees/Honoraria	Speakers' Bureau	Ownership/ Partnership/ Principal	Research Grant	Institutional or Other Financial Benefit
Mina K. Chung	Official—Heart Rhythm Society	• American College of Cardiology Foundation • Boston Medical Center • Boston Scientific (honoraria donated) • Elsevier • Medtronic (honoraria donated) • Nexcura (no honoraria received) • University of Texas Health Science Center • WebMD Health (for CryoCath Technologies, Inc.)	None	None	• Biotronik† (research grants to electrophysiology section, Cleveland Clinic) • Boston Scientific† (research grants to electrophysiology section, Cleveland Clinic) • Medtronic† (research grants to electrophysiology section, Cleveland Clinic) • Reliant Pharmaceuticals† (research grants to electrophysiology section, Cleveland Clinic) • St. Jude Medical† (research grants to electrophysiology section, Cleveland Clinic)	None
Fred Kusumoto	Official—Heart Rhythm Society	• Boston Scientific • Medtronic	None	None	None	None
Bruce Lindsay	Official—American College of Cardiology Board of Trustees	None	None	None	None	None
Samir Saba	Official—American Heart Association	None	None	None	• Boston Scientific • Medtronic • St. Jude Medical	None
Paul Wang	Official—American Heart Association; Content—American Heart Association Electrocardiography and Arrhythmias Committee	• Boston Scientific† • Lifewatch† • Medtronic • St. Jude	• Boston Scientific† • Medtronic • St. Jude	• Hansen Medical†	• Boston Scientific† • Medtronic • St. Jude	None
Stuart Winston	Official—American College of Cardiology Board of Governors	• Boston Scientific	None	None	None	None
Patrick McCarthy	Organizational—Society of Thoracic Surgeons	• CV Therapeutics† • Medtronic	None	None	None	None
Mandeep Mehra	Organizational—Heart Failure Society of America	• Astellas • Boston Scientific • Cordis • Debiopharma • Medtronic • Novartis • Roche Diagnostics • Scios • Solvay • St. Jude	None	None	• Maryland Industrial Partnerships† • National Institutes of Health† • Other Tobacco-Related Diseases†	• University of Maryland† (salary); • Legal consultant
Jennifer Cummings	Content—American College of Cardiology Foundation Clinical Electrophysiology Committee	• Reliant • Signalife • St. Jude • Zin	None	None	None	None
Christopher Fellows	Content—American College of Cardiology Foundation Clinical Electrophysiology Committee	• Boston Scientific • St. Jude	None	None	None	None
Nora Goldschlager	Content—Individual	• St. Jude	None	None	None	None

(Continued)

Appendix 2. Continued

Peer Reviewer*	Representation	Consulting Fees/Honoraria	Speakers' Bureau	Ownership/ Partnership/ Principal	Research Grant	Institutional or Other Financial Benefit
Peter Kowey	Content—American College of Cardiology Foundation Clinical Electrophysiology Committee	None	• Medtronic†	• CardioNet†	None	None
Rachel Lampert	Content—Heart Rhythm Society Scientific and Clinical Documents Committee	None	None	None	• Boston Scientific† • Medtronic† • St. Jude†	None
J. Philip Saul	Content—Pediatric Expert and American College of Cardiology Foundation Clinical Electrophysiology Committee	None	None	None	None	None
George Van Hare	Content—Individual	• St. Jude	None	None	• Medtronic† (fellowship funding)	None
Edward P. Walsh	Content—Individual Pediatric Expert	None	None	None	None	None
Clyde Yancy	Content—American College of Cardiology/American Heart Association Lead Task Force Reviewer and 2005 Chronic Heart Failure Guideline Writing Committee	• AstraZeneca • GlaxoSmithKline • Medtronic • NitroMed • Otsuka • Scios	• GlaxoSmithKline • Novartis	None	• GlaxoSmithKline • Medtronic • NitroMed • Scios	None

This table represents the relationships of reviewers with industry that were reported at peer review. It does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of 5% or more of the voting stock or share of the business entity, or ownership of $10,000 or more of the fair market value of the business entity, or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships noted in this table are modest unless otherwise noted.

*Names are listed in alphabetical order within each category of review. Participation in the peer review process does not imply endorsement of this document.

†Indicates significant-level relationship (more than $10,000).

Appendix 3. Abbreviations List

ACC = American College of Cardiology

ACCF = American College of Cardiology Foundation

AF = Atrial fibrillation

AHA = American Heart Association

AMI = Acute myocardial infarction

AMIOVIRT = Amiodarone Versus Implantable Defibrillator in Patients with Nonischemic Cardiomyopathy and Asymptomatic Nonsustained Ventricular Tachycardia

ARVD/C = Arrhythmogenic right ventricular dysplasia/cardiomyopathy

ATP = Antitachycardia pacing

AV = Atrioventricular

AVID = Antiarrhythmics Versus Implantable Defibrillators

CABG-Patch = Coronary Artery Bypass Graft-Patch

CARE-HF = Cardiac Resynchronization in Heart Failure

CASH = Cardiac Arrest Study Hamburg

CAT = Cardiomyopathy Trial

CI = Confidence interval

CIDS = Canadian Implantable Defibrillator Study

CIED = Cardiovascular implantable electronic devices

CARE-HF = Cardiac Resynchronization in Heart Failure

COMPANION = Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure Trial

CRT = Cardiac resynchronization therapy

CRT-D = Cardiac resynchronization therapy device incorporating both pacing and defibrillation capabilities

CRT-P = Cardiac resynchronization device providing pacing but not defibrillation capability

CTOPP = Canadian Trial of Physiologic Pacing

DAVID = Dual Chamber and VVI Implantable Defibrillator

DCM = Dilated cardiomyopathy

DDD = Dual-chamber pacemaker that senses/paces in the atrium/ventricle and is inhibited/triggered by intrinsic rhythm

DEFINITE = Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation

DINAMIT = Defibrillator in Acute Myocardial Infarction Trial

ECG = Electrocardiograph

GDMT = Guideline-directed medical therapy

HCM = Hypertrophic cardiomyopathy

(Continued)

Appendix 3. Continued

HR = Hazard ratio

HRS = Heart Rhythm Society

ICD = Implantable cardioverter-defibrillator

LBBB = Left bundle-branch block

LV = Left ventricular/left ventricle

LVEF = Left ventricular ejection fraction

MADIT-CRT = Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy

MADIT I = Multicenter Automatic Defibrillator Implantation Trial I

MADIT II = Multicenter Automatic Defibrillator Implantation Trial II

MI = Myocardial infarction

MIRACLE ICD II = Multicenter InSync ICD Randomized Clinical Evaluation II

MOST = Mode Selection Trial

MUSTT = Antiarrhythmic Drug Therapy in the Multicenter UnSustained Tachycardia Trial

NYHA = New York Heart Association

PainFREE Rx II = Pacing Fast VT Reduces Shock Therapies Trial II

PASE = Pacemaker Selection in the Elderly

PAVE = Left Ventricular-Based Cardiac Stimulation Post AV Nodal Ablation Evaluation Study

QOL = Quality of life

RAFT = Resynchronization-Defibrillation for Ambulatory Heart Failure Trial

REVERSE = Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction

RR = Relative risk

RV = Right ventricular/right ventricle

RVA = Right ventricular apical

RWI = Relationships with industry and other entities

SCD = Sudden cardiac death

SCD-HeFT = Sudden Cardiac Death in Heart Failure Trial

SND = Sinus node dysfunction

SVT = Supraventricular tachycardia

TF = Task Force

TTM = Transtelephonic monitoring

UK-PACE = United Kingdom Pacing and Cardiovascular Events

VF = Ventricular fibrillation

VPS = Vasovagal Pacemaker Study I

VPS-II = Vasovagal Pacemaker Study II

VT = Ventricular tachycardia

Appendix 4. 2012 Author Relationships With Industry and Other Entities (Relevant)—2012 ACCF/AHA/HRS Focused Update Incorporated Into the ACCF/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities

Committee Member	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Cynthia M. Tracy, Chair	George Washington University Medical Center—Associate Director and Professor of Medicine	None	None	None	None	None	None	None
Andrew E. Epstein, Vice Chair	University of Pennsylvania—Professor of Medicine Philadelphia VA Medical Center—Chief, Cardiology Section	• Boston Scientific (DSMB)‡ • Medtronic‡ • Medtronic/Cryocath (DSMB) • St. Jude Medical (DSMB)‡ • Zoll—Advisory Board	None	None	• Biotronik • Boston Scientific‡ • Cameron Health‡ • Medtronic‡ • St. Jude Medical‡	• Boston Scientific, Medtronic, St. Jude Medical—industry supporters of fellowship program	None	2.4.1
Dawood Darbar	Vanderbilt University School of Medicine—C. Sydney Burwell Associate Professor Medicine Pharmacology Vanderbilt Arrhythmia Service—Director	None	None	None	None	None	None	None
John P. DiMarco	University of Virginia—Director, Clinical EP Laboratory	• Medtronic • St. Jude Medical	None	None	• Boston Scientific	None	None	2.4.1
Sandra B. Dunbar	Emory University, Nell Hodgson Woodruff School of Nursing—Associate Dean for Academic Advancement, Charles Howard Candler Professor	None	None	None	None	None	None	None
N.A. Mark Estes III	Tufts University—Professor of Medicine	• Boston Scientific‡ • Boston Scientific, EP Fellowship Educational Symposium‡ • Medtronic	None	None	• Boston Scientific—MADIT-RIT (Co-PI)	None	None	2.4.1
T. Bruce Ferguson, Jr	East Carolina University—Professor of Surgery and Physiology	• United Healthcare—Advisory Board	None	None	None	None	None	2.4.1
Stephen C. Hammill	Mayo Clinic—Professor of Medicine	None	None	None	None	None	None	None
Pamela E. Karasik	Georgetown University Medical School—Associate Professor of Medicine VA Medical Center, Washington, DC—Acting Chief of Cardiology	None	None	None	None	None	None	None
Mark S. Link	Tufts Medical Center—Professor of Medicine	None	None	None	• Boston Scientific—MADIT-RIT (Co-PI)	None	None	2.4.1
Joseph E. Marine	Johns Hopkins University—Associate Professor of Medicine	None	None	None	None	None	None	None
Mark H. Schoenfeld	Yale University School of Medicine—Clinical Professor of Medicine	• United Healthcare Advisory Board	None	None	None	None	None	2.4.1
Amit J. Shanker	Center for Advanced Arrhythmia Medicine—Director Columbia University College of Physicians and Surgeons—Assistant Professor of Medicine	None	None	None	None	None	None	None

(Continued)

Appendix 4. Continued

Committee Member	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Michael J. Silka	University of Southern California—Professor of Pediatrics Children's Hospital Los Angeles—Chief, Division of Cardiology	None	None	None	None	None	None	None
Lynne Warner Stevenson	Brigham & Women's Hospital—Director, Cardiomyopathy and Heart Failure	None	None	None	• Biosense Webster†	None	None	2.4.1
William G. Stevenson	Brigham & Women's Hospital—Director, Clinical Cardiac EP	None	None	None	• Biosense Webster†	None	None	2.4.1
Paul D. Varosy	VA Eastern Colorado Health Care System—Director of Cardiac Electrophysiology University of Colorado Denver—Assistant Professor of Medicine	None	None	None	None	None	None	None

This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing group during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or if the interest represents ownership of ≥$10,000 of the fair market value of the business entity, or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted.

*Writing group members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply.

†No financial benefit.

‡Indicates significant relationship.

According to the ACCF/AHA, a person has a *relevant* relationship IF: (a) the *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or (b) the *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document* or makes a competing drug or device addressed in the *document*; or (c) the *person or a member of the person's household* has a reasonable potential for financial, professional, or other personal gain or loss as a result of the issues or content addressed in the *document*.

DSMB indicates Data Safety Monitoring Board; EP, electrophysiology; HRS, Heart Rhythm Society; MADIT-RIT, Multicenter Automatic Defibrillator Implantation Trial–Reduce Inappropriate Therapy; PI, principal investigator; and VA, Veterans Affairs.

Appendix 5. 2012 Reviewer Relationships With Industry and Other Entities (Relevant)—2012 ACCF/AHA/HRS Focused Update Incorporated Into the ACCF/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities

Peer Reviewer	Representation	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Sana Al-Khatib	Official Representative—AHA	Duke Clinical Research Institute and Duke University Medical Center	None	• Medtronic	None	None	None	None
Hugh Calkins	Official Representative—HRS	Johns Hopkins Hospital	• Biosense Webster • Boston Scientific • Medtronic*	None	None	• Boston Scientific* • Medtronic* • St. Jude Medical*	None	None
James R. Edgerton	Official Representative—STS	The Heart Hospital Baylor Plano	None	None	None	None	None	None
Michael M. Givertz	Official Representative—HFSA	Brigham and Women's Hospital	None	None	None	None	None	None
Jonathan L. Halperin	Official Representative—ACCF/AHA Task Force on Practice Guidelines Lead Reviewer	Mount Sinai Medical Center	• Biotronik*	None	None	None	None	None
Bradley P. Knight	Official Representative—HRS	Northwestern Medical Center	• Boston Scientific • Cameron Health†	• Biosense Webster • Biotronik • Boston Scientific • Medtronic	None	• Cameron Health*	None	None
Thomas J. Lewandowski	Official Representative—ACCF Board of Governors	Appleton Cardiology Thedacare	None	None	None	None	None	None
Henry M. Spotnitz	Official Representative—AATS	Columbia University	None	None	• Strategic Pacing Systems†	None	None	None
C. Michael Valentine	Official Representative—ACCF Board of Trustees	The Cardiovascular Group	• Medtronic*	None	None	None	None	None
Paul J. Wang	Official Representative—AHA	Stanford University Medical Center	• Medtronic	None	None	• Medtronic*	None	None
John F. Beshai	Content Reviewer—ACCF EP Committee	University of Chicago Medical Center	None	None	None	None	• Medtronic* • St. Jude Medical*	None
George H. Crossley	Content Reviewer	St. Thomas Heart	• Boston Scientific • Medtronic	• Boston Scientific • Medtronic	None	None	• Boston Scientific • Medtronic*	None
Jennifer E. Cummings	Content Reviewer—ACCF EP Committee	University of Toledo	None	• Boston Scientific • Medtronic • St. Jude	None	None	None	None
Kenneth A. Ellenbogen	Content Reviewer	Virginia Commonwealth University Medical Center	• Cameron Health • Boston Scientific • Medtronic	• Biotronik • Boston Scientific • Medtronic • St. Jude Medical	None	None	• Biosense Webster* • Boston Scientific* • Medtronic* • St. Jude Medical*	None
Roger A. Freedman	Content Reviewer	University of Utah Health Sciences Center	• Boston Scientific • Sorin • Spectranetics • St. Jude Medical	None	None	• Medtronic* • St. Jude Medical*	None	• Defendant, 2011, pacemaker battery depletion
Gabriel Gregoratos	Content Reviewer	University of California–San Francisco	None	None	None	None	None	None
David L. Hayes	Content Reviewer	Mayo Clinic	• Biotronik • Boston Scientific • Medtronic* • Sorin • St. Jude Medical	None	None	None	None	None
Mark A. Hlatky	Content Reviewer	Stanford University School of Medicine	None	None	None	None	None	None
Sandeep K. Jain	Content Reviewer	University of Pittsburgh Physicians, UPMC Heart and Vascular Institute	None	None	None	• Medtronic*	None	None
Samuel O. Jones	Content Reviewer	San Antonio Military Medical Center	None	None	None	None	• Medtronic† • St. Jude Medical†	None

(Continued)

Appendix 5. Continued

Kousik Krishnan	Content Reviewer	Rush University Medical Center	• Boston Scientific • St. Jude Medical	None	None	None	• Biotronik* • Boston Scientific—Multicenter MADIT-RIT study* • Medtronic*	None
Michael Mansour	Content Reviewer	Cardiovascular Physicians	None	None	None	None	None	None
Steven M. Markowitz	Content Reviewer—ACCF EP Committee	New York Hospital	• Biotronik • Boston Scientific • Medtronic • St. Jude Medical	None	None	None	• Biosense Webster* • Boston Scientific* • Medtronic* • St. Jude Medical*	None
Marco A. Mercader	Content Reviewer	George Washington University	None	None	None	None	•None	None
Simone Musco	Content Reviewer	Saint Patrick Hospital	• Boston Scientific	None	None	None	None	None
L. Kristin Newby	Content Reviewer	Duke University Medical Center	None	None	None	None	None	None
Brian Olshansky	Content Reviewer—ACCF EP Committee	University of Iowa Hospitals	• Boston Scientific–Guidant • Medtronic	None	None	None	None	None
Richard L. Page	Content Reviewer	University of Wisconsin Hospital and Clinics	None	None	None	None	None	None
Allen J. Solomon	Content Reviewer	Medical Faculty Associates	None	None	None	None	None	None
John S. Strobel	Content Reviewer	Internal Medicine Associates	None	None	None	• Medtronic*	None	None
Stephen L. Winters	Content Reviewer	Morristown Medical Center	• Biosense Webster	None	None	None	• Boston Scientific • Medtronic • St. Jude Medical	• Defendant, 2011, complication of ICD placement

This table represents the relationships of reviewers with industry and other entities that were disclosed at the time of peer review and determined to be relevant. It does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or if the interest represents ownership of ≥$10,000 of the fair market value of the business entity, or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Names are listed in alphabetical order within each category of review.

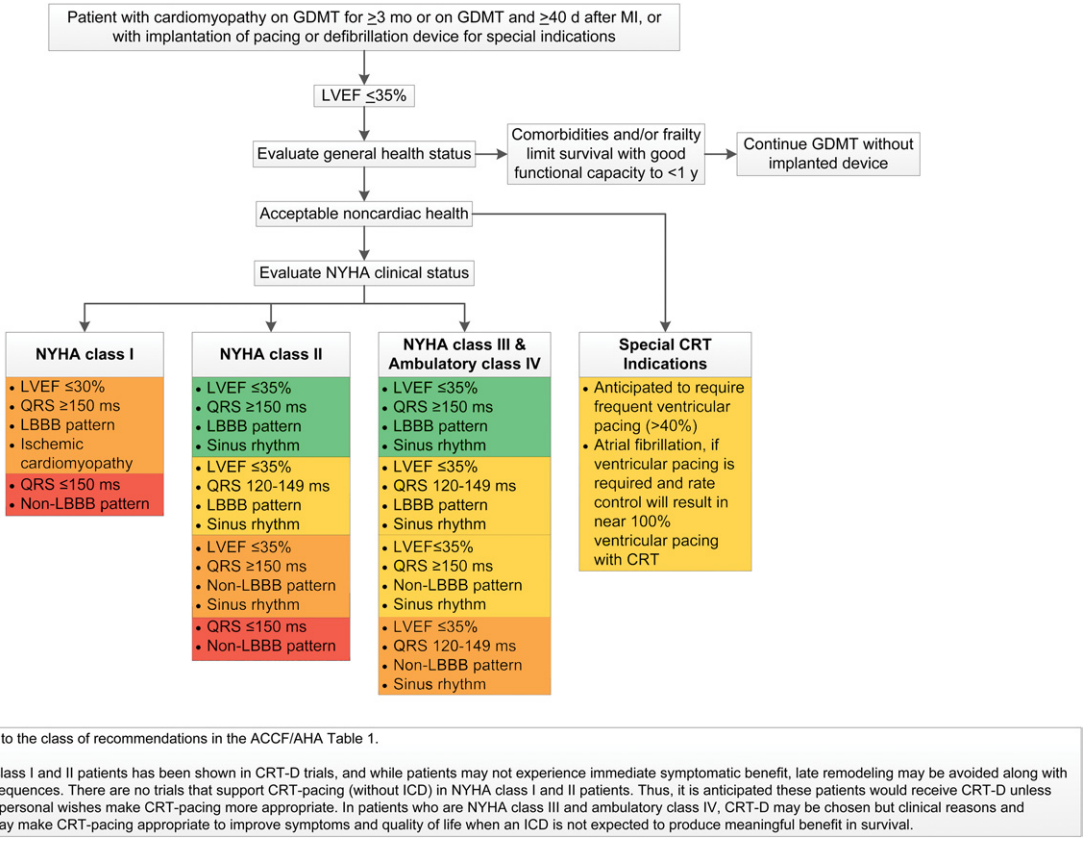
*Significant relationship.

†No financial benefit.

According to the ACCF/AHA, a person has a *relevant* relationship IF: (a) the *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or (b) the *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document* or makes a competing drug or device addressed in the *document*; or (c) the *person or a member of the person's household* has a reasonable potential for financial, professional, or other personal gain or loss as a result of the issues or content addressed in the *document*.

AATS indicates American Association for Thoracic Surgery; ACCF, American College of Cardiology Foundation; AHA, American Heart Association; EP, Emergency Physicians; 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.

Appendix 6. 2012 Indications for CRT Therapy—Algorithm



Colors correspond to the class of recommendations in the ACCF/AHA Table 1.

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; IV, intravenous; LV, left ventricular; LVEF, left ventricular ejection fraction; LBBB, left bundle-branch block; MI, myocardial infarction; and NYHA, New York Heart Association.