

ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death—Executive Summary

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)

Developed in Collaboration With the European Heart Rhythm Association and the Heart Rhythm Society

WRITING COMMITTEE MEMBERS

Douglas P. Zipes, MD, MACC, FAHA, FESC, Co-Chair; A. John Camm, MD, FACC, FAHA, FESC, Co-Chair; Martin Borggrefe, MD, FESC; Alfred E. Buxton, MD, FACC, FAHA; Bernard Chaitman, MD, FACC, FAHA; Martin Fromer, MD; Gabriel Gregoratos, MD, FACC, FAHA; George Klein, MD, FACC; Arthur J. Moss, MD, FACC, FAHA†; Robert J. Myerburg, MD, FACC, FAHA; Silvia G. Priori, MD, PhD, FESC*; Miguel A. Quinones, MD, FACC; Dan M. Roden, MD, CM, FACC, FAHA; Michael J. Silka, MD, FACC, FAHA; Cynthia Tracy, MD, FACC, FAHA

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*European Heart Rhythm Association Official Representative.

†Heart Rhythm Society Official Representative.

‡Immediate Past Chair.

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PREAMBLE

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 ACC/AHA Task Force on Practice Guidelines, whose charge is to develop, update, or revise practice guidelines for important cardiovascular diseases and procedures, directs this effort. The Task Force is pleased to have this guideline developed in conjunction with the European Society of Cardiology (ESC). Writing committees are charged with the task of performing an assessment of the evidence and acting as an independent group of authors to develop or update written recommendations for clinical practice.

Experts in the subject under consideration have been selected from all 3 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 formal 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 might 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 ACC/AHA Task Force on Practice Guidelines and the ESC Committee for Practice Guidelines make every effort to avoid any actual, potential, or perceived conflict of interest that might arise as a result of an industry relationship or personal interest of the writing committee. Specifically, 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 might be perceived as real or potential conflicts of interest. Writing committee members are also strongly encouraged to declare a previous relationship with industry that might be perceived as relevant to guideline development. If a writing committee member develops a new relationship with industry during his or her tenure, he or she is required to notify guideline staff in writing. The continued participation of the writing committee member will be reviewed. These statements are reviewed by the parent task force, reported orally to all members of the writing committee at each meeting, and updated and reviewed by the writing committee as changes occur. Please refer to the methodology manuals for further description of the policies used in guideline development, including relationships with industry, which are available on the ACC, AHA, and ESC World Wide Web sites (http://www.acc.org/clinical/manual/manual_introltr.htm, <http://circ.ahajournals.org/manual/>, and <http://www.esccardio.org/knowledge/guidelines/Rules/>, respectively). Please see Appendix 1 for author relationships with industry and Appendix 2 for peer reviewer relationships with industry that are pertinent to these guidelines.

These practice guidelines are intended to assist healthcare providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis and management of specific diseases or conditions. These guidelines attempt to define practices that meet the needs of most patients in most circumstances. These guideline recommendations reflect a consensus of expert opinion after a thorough review of the available, current scientific evidence and are intended to improve patient care. If these guidelines are used as the basis for regulatory/payer decisions, the ultimate goal is quality of care and serving the patient's best interests. The ultimate judgment regarding care of a particular patient must be made by the healthcare provider and the patient in light of all of the circumstances presented by that patient. There are circumstances in which deviations from these guidelines are appropriate.

The guidelines will be reviewed annually by the ACC/AHA Task Force on Practice Guidelines and the ESC Committee for Practice Guidelines and will be considered current unless they are updated, revised, or sunsetted and withdrawn from distribution. The executive summary and recommendations are published in the September 5, 2006 issue of the *Journal of the American College of Cardiology*, the September 5, 2006 issue of *Circulation*, and the September 17, 2006 issue of the *European Heart Journal*. The full-text guideline is e-published in the September 5, 2006 issue of the *Journal of the American College of Cardiology*, the September 5, 2006 issue of *Circulation*, and the September 2006 issue of *Europace*, as well as posted on the ACC (www.acc.org), AHA (www.americanheart.org), and ESC (www.escardio.org) World Wide Web sites. Copies of the full text and the executive summary are available from all 3 organizations.

*Sidney C. Smith Jr., MD, FACC, FAHA, FESC,
Chair, ACC/AHA Task Force on Practice Guidelines*
*Silvia G. Priori, MD, PhD, FESC,
Chair, ESC Committee for Practice Guidelines*

I. INTRODUCTION

Several excellent guidelines already exist on treating patients who have ventricular arrhythmias (Table 1). The purpose of this document is to update and combine the previously published recommendations into one source approved by the major cardiology organizations in the United States and Europe. We have consciously attempted to create a streamlined document, not a textbook that would be useful specifically to locate recommendations on the evaluation and treatment of patients who have or may be at risk for ventricular arrhythmias. Thus, sections on epidemiology, mechanisms and substrates, and clinical presentations are brief, because there are no recommendations for those sections. For the other sections, the wording has been kept to a minimum, and clinical presentations have been confined to those aspects relevant to forming recommendations.

The reader should note that the recommendations, text, figures, and tables included in this executive summary represent a succinct summary of the more extensive evidence base, critical evaluation, supporting text, tables, figures, and references that are included in the full-text guidelines.

Table 1. Clinical Practice Guidelines and Policy Statements That Overlap With ACC/AHA/ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of SCD

Document	Sponsor	Citation
Guidelines		
SCD	ESC	Eur Heart J 2001;22:1374-450
Syncope	ESC	Eur Heart J 2004;25:2054-72
Exercise testing	ACC/AHA	Circulation 2002;106:1883-92
Cardiac pacemakers and antiarrhythmia devices	ACC/AHA/NASPE	Circulation 2002;106:2145-61
Echocardiography	ACC/AHA	J Am Coll Cardiol 2003;42:954-70
Supraventricular arrhythmias	ACC/AHA/ESC	Eur Heart J 2003;24:1857-97 J Am Coll Cardiol 2003;42:1493-531
SCD Update	ESC	Eur Heart J 2003;24:13-5
Congenital heart disease	ESC	Eur Heart J 2003;24:1035-84
European guidelines on CVD prevention	ESC	Eur J Cardiovasc Prev Rehab 2003;10 Suppl 1:S1-78
Infective endocarditis	ESC	Eur Heart J 2004;25:267-76
Pericardial disease	ESC	Eur Heart J 2004;25:587-610
Pulmonary arterial hypertension	ESC	Eur Heart J 2004;25:2243-78
AED use in Europe	ESC/ERC	Eur Heart J 2004;25:437-45
ST-elevation myocardial infarction	ACC/AHA	J Am Coll Cardiol 2004;44:e1-211
Chronic heart failure	ACC/AHA	J Am Coll Cardiol 2005;46:e1-82
Chronic heart failure	ESC	Eur Heart J 2005;26:1115-40
CPR and ECC	AHA/ILCOR	Circulation 2005;112:IV-1-203
Resuscitation	ERC	Resuscitation 2005;67 Suppl:539-86
Valvular heart disease	ACC/AHA	J Am Coll Cardiol 2006;48:e1-148
Statements		
Invasive electrophysiology studies, catheter ablation, and cardioversion	ACC/AHA	J Am Coll Cardiol 2000;36:1725-36
Hypertrophic cardiomyopathy	ACC/ESC	Eur Heart J 2003;24:1965-91 J Am Coll Cardiol 2003;42:1687-713
Cardiovascular disease during pregnancy	ESC	Eur Heart J 2003;24:761-81
Physical activity and recreational sports AHA for young patients with genetic CVD		Circulation 2004;109:2807-16
36th Bethesda Conference: Eligibility recommendations for competitive athletes with cardiovascular abnormalities	ACC	J Am Coll Cardiol 2005;45:1318-75

The guidelines from the ACC, AHA, and ESC are available at www.acc.org, www.americanheart.org, and www.escardio.org, respectively.

ACC = American College of Cardiology; AHA = American Heart Association; CVD = cardiovascular disease; CPR = cardiopulmonary resuscitation; ECC = emergency cardiovascular care; ERC = European Resuscitation Council; ESC = European Society of Cardiology; ILCOR = International Liaison Committee on Resuscitation; NASPE = Heart Rhythm Society (formerly North American Society for Pacing and Electrophysiology); SCD = sudden cardiac death.

Readers are strongly encouraged to refer to the full-text guidelines.

The final recommendations for indications for a diagnostic procedure, a particular therapy, or an intervention for management of patients with ventricular arrhythmias and prevention of sudden cardiac death summarize both clinical evidence and expert opinion. Classification of Recommendations and Level of Evidence are expressed in the ACC/AHA/ESC format as follows:

Classification of Recommendations

- **Class I:** Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.
- **Class II:** Conditions for which there is conflicting evidence and/or divergence of opinion about the usefulness/efficacy of a procedure or treatment.
 - **Class IIa:** Weight of evidence/opinion is in favor of usefulness/efficacy.
 - **Class IIb:** Usefulness/efficacy is less well established by evidence/opinion.
- **Class III:** Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

Level of Evidence

- **Level of Evidence A:** Data derived from multiple randomized clinical trials or meta-analyses.
- **Level of Evidence B:** Data derived from a single randomized trial or nonrandomized studies.
- **Level of Evidence C:** Only consensus opinion of experts, case studies, or standard-of-care.

The schema for classification of recommendations and level of evidence is summarized in Table 2, which also illustrates how the grading system provides an estimate of the size of treatment effect and an estimate of the certainty of the treatment effect.

Recommendations with respect to therapy have considered:

1. The therapy to be offered (implantable cardioverter-defibrillator [ICD], antiarrhythmic drugs, surgery, and miscellaneous other treatments)
2. The point at which therapy is offered (primary prevention for those who are at risk but have not yet suffered from a life-threatening ventricular arrhythmia or sudden cardiac "death" episode, or secondary for those patients who have already experienced such arrhythmias or events),
3. The purpose of therapy (life preservation or symptom reduction/improved quality of life)
4. The etiology of the arrhythmia substrate (coronary heart disease, cardiomyopathy, or other conditions)
5. The functional status of the patient (New York Heart Association [NYHA] class)

6. The state of left ventricular (LV) function (left ventricular ejection fraction [LVEF]), and
7. The specific arrhythmia concerned (e.g., sustained monomorphic ventricular tachycardia [VT], polymorphic VT, and ventricular fibrillation [VF])

Not all therapeutic combinations are clinically relevant and many have no evidence base and probably will not have in the future because of the lack of clinical relevance or the relative rarity of the particular grouping. In many instances, the probable value of therapy may be reasonably inferred by the response of similar patients to specific therapies.

A. Prophylactic Implantable Cardioverter-Defibrillator Recommendations Across Published Guidelines

The ACC/AHA/NASPE 2002 Guidelines Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices (1), the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (2), the ESC 2001 and 2003 Guidelines on Prevention of Sudden Cardiac Death (3,4), the ESC 2005 Guidelines for the Diagnosis and Treatment of Chronic Heart Failure (5) and the ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult (6) include a large number of recommendations on ICD therapy that merit attention.

Recommendations for prophylactic ICD implantation based on (EFs) have been inconsistent because clinical investigators have chosen different EFs for enrollment in trials of therapy, average values of the EF in such trials have been substantially lower than the cutoff value for enrollment, and subgroup analysis of clinical trial populations based on EF have not been consistent in their implications. Substantial differences among guidelines have resulted. However, no trial has randomized patients with an intermediate range of EFs. For instance, there is no trial that has specifically studied patients with a LVEF between 31% and 35%, and yet recommendations have been set for such patients on the basis of data derived from trials that studied groups with EFs less than or equal to 30%, others that enrolled patients with an EF less than or equal to 35%, and another that enrolled patients with an EF less than or equal to 40%. Recognizing these inconsistencies, this Guideline Writing Committee has decided to deal with the issue by constructing recommendations to apply to patients with an EF less than or equal to a range of values. The highest appropriate class of recommendation was then based on all trials that recruited patients with EFs within this range. In this way, potential conflicts between guidelines were reduced and errors due to drawing false conclusions relating to unstudied patient groups were minimized (see Table 3).

It is important to note that experts can review the same data and arrive at different interpretations. Attempting to homogenize heterogeneous trials invariably leads to varying interpretations of the trial data. Furthermore, differences

Table 2. Applying Classification of Recommendations and Level of Evidence†

		“SIZE of TREATMENT EFFECT”			
		Class I <i>Benefit >>> Risk</i>	Class IIa <i>Benefit >> Risk</i> Additional studies with focused objectives needed	Class IIb <i>Benefit ≥ Risk</i> Additional studies with broad objectives needed; Additional registry data would be helpful	Class III <i>Risk ≥ Benefit</i> No additional studies needed
“Estimate of Certainty (Precision) of Treatment Effect”	Level A Multiple (3-5) population risk strata evaluated* General consistency of direction and magnitude of effect	Procedure/Treatment SHOULD be performed/administered <ul style="list-style-type: none"> • Recommendation that procedure or treatment is useful/effective • Sufficient evidence from multiple randomized trials or meta-analyses 	IT IS REASONABLE to perform procedure/administer treatment <ul style="list-style-type: none"> • Recommendation in favor of treatment or procedure being useful/effective • Some conflicting evidence from multiple randomized trials or meta-analyses 	Procedure/Treatment MAY BE CONSIDERED <ul style="list-style-type: none"> • Recommendation’s usefulness/efficacy less well established • Greater conflicting evidence from multiple randomized trials or meta-analyses 	Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL <ul style="list-style-type: none"> • Recommendation that procedure or treatment not useful/effective and may be harmful • Sufficient evidence from multiple randomized trials or meta-analyses
	Level B Limited (2-3) population risk strata evaluated*	<ul style="list-style-type: none"> • Recommendation that procedure or treatment is useful/effective • Limited evidence from single randomized trial or non-randomized studies 	<ul style="list-style-type: none"> • Recommendation in favor of treatment or procedure being useful/ effective • Some conflicting evidence from single randomized trial or non-randomized studies 	<ul style="list-style-type: none"> • Recommendation’s usefulness/efficacy less well established • Greater conflicting evidence from single randomized trial or non-randomized studies 	<ul style="list-style-type: none"> • Recommendation that procedure or treatment not useful/effective and may be harmful • Limited evidence from single randomized trial or non-randomized studies
	Level C Very limited (1-2) population risk strata evaluated*	<ul style="list-style-type: none"> • Recommendation that procedure or treatment is useful/effective • Only expert opinion, case studies, or standard-of-care 	<ul style="list-style-type: none"> • Recommendation in favor of treatment or procedure being useful/ effective • Only diverging expert opinion, case studies, or standard-of-care 	<ul style="list-style-type: none"> • Recommendation’s usefulness/efficacy less well established • Only diverging expert opinion, case studies, or standard-of-care 	<ul style="list-style-type: none"> • Recommendation that procedure or treatment not useful/effective and may be harmful • Only expert opinion, case studies, or standard-of-care

†Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as gender, age, history of diabetes, history of heart failure, and prior aspirin use. †A recommendation with a Level of Evidence of 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. Even though randomized trials are not available, there may be a very clear consensus that a particular therapy is useful or effective.

Table 3. Inconsistencies Between ACC/AHA/ESC Guidelines for the Management of Patients With Ventricular Arrhythmias and the Prevention of SCD and Other Published ACC/AHA and ESC Guidelines With Respect to ICD Therapy for Primary Prevention to Reduce Total Mortality by a Reduction in SCD

Group Addressed in Recommendation	Guideline and Class of Recommendation With Level of Evidence* for Each Group				Comment From the ACC/AHA/ESC VA and SCD Guidelines
	2005 ACC/AHA HF	2005 ESC HF	2004 ACC/AHA STEMI	2002 ACC/AHA/NASPE PM and ICD	
LVD d/t MI, LVEF 30% or less, NYHA II, III	<i>Class I; LOE: B</i>	<i>Class I; LOE: A</i>	<i>Class IIa; LOE: B</i>	<i>Class IIa; LOE: B</i>	VA and SCD has combined all trials that enrolled patients with LVD d/t MI into one recommendation, <i>Class I; LOE: A</i>
LVD d/t MI, LVEF 30% to 35%, NYHA II, III	<i>Class IIa; LOE: B</i>	<i>Class I; LOE: A</i>	N/A	N/A	
LVD d/t MI, LVEF 30% to 40%, NSVT, positive EP study	N/A	N/A	<i>Class I; LOE: B</i>	<i>Class IIb; LOE: B</i>	
LVD d/t MI, LVEF 30% or less, NYHA I	<i>Class IIa; LOE: B</i>	N/A	N/A	N/A	VA and SCD has expanded the range of LVEF to 30% to 35% or less for patients with LVD d/t MI and NYHA functional class I into one recommendation, <i>Class IIa; LOE: B</i>
LVD d/t MI, LVEF 31% to 35% or less, NYHA I	N/A	N/A	N/A	N/A	
NICM, LVEF 30% or less, NYHA II, III	<i>Class I; LOE: B</i>	<i>Class I; LOE: A</i>	N/A	N/A	VA and SCD has combined all trials of NICM, NYHA II, III into one recommendation, <i>Class I; LOE: B</i>
NICM, LVEF 30% to 35%, NYHA II, III	<i>Class IIa; LOE: B</i>	<i>Class I; LOE: A</i>	N/A	N/A	
NICM, LVEF 30% or less, NYHA I	<i>Class IIb; LOE: C</i>	N/A	N/A	N/A	VA and SCD has expanded the range of LVEF to 30% to 35% or less for patients with NICM and NYHA functional class I into one recommendation, <i>Class IIb; LOE: B</i>
NICM, LVEF 31% to 35% or less, NYHA I	N/A	N/A	N/A	N/A	

*For an explanation of Class Recommendation and Level of Evidence, see Table 2. For further discussion, please see the Introduction.

ACC/AHA HF = ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult (6); ACC/AHA/NASPE PM and ICD = ACC/AHA/NASPE 2002 Guidelines Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices (1); ACC/AHA STEMI = ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (2); EP = electrophysiological; ESC HF = ESC 2005 Guidelines for the Diagnosis and Treatment of Chronic Heart Failure (5); LOE = level of evidence; LVD d/t MI = left ventricular dysfunction due to prior myocardial infarction; LVEF = left ventricular ejection fraction; N/A = populations not addressed; NICM = nonischemic cardiomyopathy; NSVT = nonsustained ventricular tachycardia; NYHA = New York Heart Association functional class; SCD = sudden cardiac death; VA = ventricular arrhythmias.

between the United States and Europe may modulate how recommendations are implemented. Guidelines are composed of recommendations on the basis of the best available medical science; however, implementation of these recommendations will be impacted by the financial, cultural, and societal differences among individual countries.

B. Classification of Ventricular Arrhythmias and Sudden Cardiac Death

This classification table is provided for direction and introduction to the guidelines (Table 4).

II. INCIDENCE OF SUDDEN CARDIAC DEATH

The geographic incidence of sudden cardiac death (SCD) varies as a function of coronary heart disease (CHD) prevalence in different regions (3). Estimates for the United States (9–13) range from less than 200 000 to more than 450 000 SCDs annually, with the most widely used estimates in the range of 300 000 to 350 000 SCDs annually (14). The variation is based, in part, on the inclusion criteria used in individual studies. Overall, event rates in Europe are similar to those in the United States (3), with significant geographic variations reported.

The temporal definition of SCD strongly influences epidemiological data (15). The proportion of all natural deaths due to SCD is 13% when a definition of 1 h from onset of symptoms is used. In contrast, the community-wide study in Maastricht, the Netherlands, reported that 18.5% of all deaths were SCD, using a 24-h definition (16). The

application of a 24-h definition of SCD increases the fraction of all natural deaths falling into the “sudden” category but reduces the proportion of all sudden natural deaths that are due to cardiac causes (15).

Approximately 50% of all CHD deaths are sudden and unexpected, occurring shortly (instantaneous to 1 h) after the onset of a change in clinical status, with some geographical variation in the fraction of coronary deaths that are sudden (17). The decreasing age-adjusted CHD mortality does not imply a decrease in absolute numbers of cardiac or SCDs (18,19) because of the growth and aging of the United States and European populations and the increasing prevalence of chronic heart disease (20).

Population Subgroups and Risk Prediction

Three factors affect the ability to identify subjects and population subgroups at risk and consideration of strategies for prevention of SCD:

- The absolute numbers and event rates (incidence) among population subgroups (Fig. 1)
- The clinical subgroups in which SCDs occur
- The time-dependence of risk (14).

The overall incidence of SCD in the United States is 1 to 2/1000 population (0.1% to 0.2%) per year, with some variations in estimates based on differences in various sources of data. This large population base includes those victims whose SCDs occur as a first cardiac event, as well as those whose SCDs can be predicted with greater accuracy because they are included in higher risk subgroups (Fig. 1).

Table 4. Classification of Ventricular Arrhythmias

Classification by Clinical Presentation			Reference
Hemodynamically stable	Asymptomatic	The absence of symptoms that could result from an arrhythmia.	(7)
	Minimal symptoms, e.g., palpitations	Patient reports palpitations felt in either the chest, throat, or neck as described by the following: <ul style="list-style-type: none"> ■ Heartbeat sensations that feel like pounding or racing ■ An unpleasant awareness of heartbeat ■ Feeling skipped beats or a pause 	(7)
Hemodynamically unstable	Presyncope	Patient reports presyncope as described by the following: <ul style="list-style-type: none"> ■ Dizziness ■ Lightheadedness ■ Feeling faint ■ “Graying out” 	(7)
	Syncope	Sudden loss of consciousness with loss of postural tone, not related to anesthesia, with spontaneous recovery as reported by the patient or observer. Patient may experience syncope when supine.	(7)
	Sudden cardiac death	Death from an unexpected circulatory arrest, usually due to a cardiac arrhythmia occurring within an hour of the onset of symptoms.	(7a)
	Sudden cardiac arrest	Death from an unexpected circulatory arrest, usually due to a cardiac arrhythmia occurring within an hour of the onset of symptoms, in whom medical intervention (e.g., defibrillation) reverses the event.	(7)
Classification by Electrocardiography			
Nonsustained VT		Three or more beats in duration, terminating spontaneously in less than 30 s. VT is a cardiac arrhythmia of three or more consecutive complexes in duration emanating from the ventricles at a rate of greater than 100 bpm (cycle length less than 600 ms)	(7)
	Monomorphic	Nonsustained VT with a single QRS morphology.	(7)
	Polymorphic	Nonsustained VT with a changing QRS morphology at cycle length between 600 and 180 ms.	(7)
Sustained VT		VT greater than 30 s in duration and/or requiring termination due to hemodynamic compromise in less than 30 s.	(7)
	Monomorphic	Sustained VT with a stable single QRS morphology.	(7)
	Polymorphic	Sustained VT with a changing or multiform QRS morphology at cycle length between 600 and 180 ms.	(7)
Bundle-branch re-entrant tachycardia		VT due to re-entry involving the His-Purkinje system, usually with LBBB morphology; this usually occurs in the setting of cardiomyopathy.	(7)
Bidirectional VT		VT with a beat-to-beat alternans in the QRS frontal plane axis, often associated with digitalis toxicity.	(7)
Torsades de pointes		Characterized by VT associated with a long QT or QTc, and electrocardiographically characterized by twisting of the peaks of the QRS complexes around the isoelectric line during the arrhythmia: <ul style="list-style-type: none"> ■ “Typical,” initiated following “short-long-short” coupling intervals. ■ Short coupled variant initiated by normal-short coupling. 	(7)
Ventricular flutter		A regular (cycle length variability 30 ms or less) ventricular arrhythmia approximately 300 bpm (cycle length—200 ms) with a monomorphic appearance; no isoelectric interval between successive QRS complexes.	(7)
Ventricular fibrillation		Rapid, usually more than 300 bpm/200 ms (cycle length 180 ms or less), grossly irregular ventricular rhythm with marked variability in QRS cycle length, morphology, and amplitude.	(7)
Classification by Disease Entity			
Chronic coronary heart disease			
Heart failure			
Congenital heart disease			
Neurological disorders			
Structurally normal hearts			
Sudden infant death syndrome			
Cardiomyopathies			
	Dilated cardiomyopathy		
	Hypertrophic cardiomyopathy		
	Arrhythmogenic right ventricular cardiomyopathy		

LBBB = left bundle-branch block; VT = ventricular tachycardia.

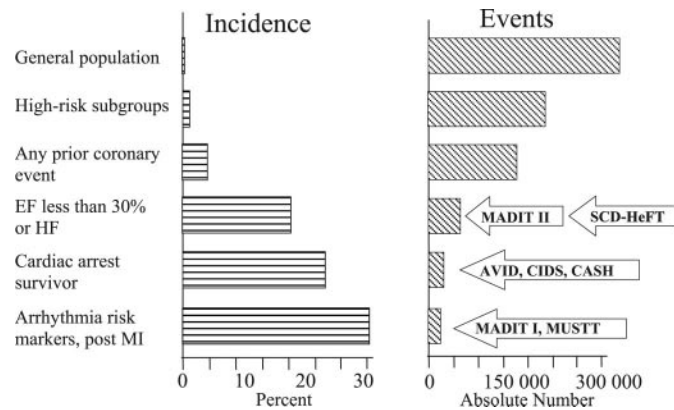


Figure 1. Absolute numbers of events and event rates of SCD in the general population and in specific subpopulations over 1 y. General population refers to unselected population age greater than or equal to 35 y, and high-risk subgroups to those with multiple risk factors for a first coronary event. Clinical trials that include specific subpopulations of patients are shown in the right side of the figure. AVID = Antiarrhythmics Versus Implantable Defibrillators; CASH, Cardiac Arrest Study Hamburg; CIDS = Canadian Implantable Defibrillator Study; EF = ejection fraction; HF = heart failure; MADIT = Multicenter Automatic Defibrillator Implantation Trial; MI = myocardial infarction; MUSTT = Multicenter UnSustained Tachycardia Trial; SCD-HeFT = Sudden Cardiac Death in Heart Failure Trial. Modified with permission from Myerburg RJ, Kessler KM, Castellanos A. SCD. Structure, function, and time-dependence of risk. *Circulation* 1992;85:12–10.

Higher levels of risk resolution can be achieved by identification of more specific subgroups. However, the corresponding absolute number of deaths becomes progressively smaller as the subgroups become more focused, limiting the potential impact of interventions to a much smaller fraction of the total population (21).

III. CLINICAL PRESENTATIONS OF PATIENTS WITH VENTRICULAR ARRHYTHMIAS AND SUDDEN CARDIAC DEATH

Ventricular arrhythmias can occur in individuals with or without cardiac disorders. There is a great deal of overlap between clinical presentations (Table 5) and severity and type of heart disease. For example, stable and well-tolerated VT can occur in the individual with previous myocardial infarction (MI) and impaired ventricular function. The prognosis and management are individualized according to symptom burden and severity of underlying heart disease in addition to the clinical presentation.

IV. RESTING ELECTROCARDIOGRAPHY

Recommendations

Class I

Resting 12-lead electrocardiogram (ECG) is indicated in all patients who are evaluated for ventricular arrhythmias. (Level of Evidence: A)

A standard resting 12-lead ECG allows not only identification of various congenital abnormalities associated with ventricular arrhythmias and SCD (e.g., long QT syndrome [LQTS], short QT syndrome, Brugada syndrome, arrhythmogenic right ventricular [RV] cardiomyopathy) but also identification of various other ECG parameters, such as those due to electrolyte disturbances, or evidence suggesting underlying structural disease such as bundle-branch block, atrioventricular

(AV) block, ventricular hypertrophy, and Q waves indicative of ischemic heart disease or infiltrative cardiomyopathy.

V. EXERCISE TESTING

Recommendations

Class I

- Exercise testing is recommended in adult patients with ventricular arrhythmias who have an intermediate or greater probability of having CHD by age, gender, and symptoms* to provoke ischemic changes or ventricular arrhythmias. (Level of Evidence: B) *See Table 4 in the ACC/AHA 2002 Guideline Update for Exercise Testing (22) for further explanation of CHD probability.
- Exercise testing, regardless of age, is useful in patients with known or suspected exercise-induced ventricular arrhythmias, including catecholaminergic VT to provoke the arrhythmia, achieve a diagnosis,

Table 5. Clinical Presentations of Patients With Ventricular Arrhythmias and Sudden Cardiac Death

- Asymptomatic individuals with or without electrocardiographic abnormalities
- Persons with symptoms potentially attributable to ventricular arrhythmias
 - Palpitations
 - Dyspnea
 - Chest pain
 - Syncope and presyncope
- Ventricular tachycardia that is hemodynamically stable
- Ventricular tachycardia that is not hemodynamically stable
- Cardiac arrest
 - Asystolic (sinus arrest, atrioventricular block)
 - Ventricular tachycardia
 - Ventricular fibrillation
 - Pulseless electrical activity

and determine the patient's response to tachycardia. (Level of Evidence: B)

Class IIa

Exercise testing can be useful in evaluating response to medical or ablation therapy in patients with known exercise-induced ventricular arrhythmias. (Level of Evidence: B)

Class IIb

1. Exercise testing may be useful in patients with ventricular arrhythmias and a low probability of CHD by age, gender, and symptoms.* (Level of Evidence: C) *See Table 4 in the ACC/AHA 2002 Guideline Update for Exercise Testing (22) for further explanation of CHD probability.
2. Exercise testing may be useful in the investigation of isolated premature ventricular complexes (PVCs) in middle-aged or older patients without other evidence of CHD. (Level of Evidence: C)

Class III

See Table 1 in the ACC/AHA 2002 Guideline Update for Exercise Testing (22) for contraindications. (Level of Evidence: B)

Exercise ECG is commonly used in the evaluation of patients with ventricular arrhythmias. Its most common application is for detection of silent ischemia in patients suspected of having underlying CHD (22). In patients with known or silent CHD or cardiomyopathies, the presence of frequent PVCs during or after exercise has been associated with greater risk for serious cardiovascular events but not specifically to SCD (23–25). However, exercise-induced PVCs in apparently normal individuals should not be used to dictate therapy unless associated with documented ischemia or sustained VT.

VI. AMBULATORY ELECTROCARDIOGRAPHY

Recommendations

Class I

1. Ambulatory ECG is indicated when there is a need to clarify the diagnosis by detecting arrhythmias, QT-interval changes, T-wave alternans, or ST changes, to evaluate risk, or to judge therapy. (Level of Evidence: A)
2. Event monitors are indicated when symptoms are sporadic to establish whether they are caused by transient arrhythmias. (Level of Evidence: B)
3. Implantable recorders are useful in patients with sporadic symptoms suspected to be related to arrhythmias such as syncope when a symptom–rhythm correlation cannot be established by conventional diagnostic techniques. (Level of Evidence: B)

The use of continuous or intermittent ambulatory recording techniques can be very helpful in diagnosing a suspected

arrhythmia, establishing its frequency and relating symptoms to the presence of the arrhythmia. Silent myocardial ischemic episodes may also be detected.

VII. ELECTROCARDIOGRAPHIC TECHNIQUES AND MEASUREMENTS

Recommendations

Class IIa

It is reasonable to use T-wave alternans for improving the diagnosis and risk stratification of patients with ventricular arrhythmias or who are at risk for developing life-threatening ventricular arrhythmias. (Level of Evidence: A)

Class IIb

ECG techniques such as signal-averaged ECG, heart rate variability, baroflex sensitivity, and heart rate turbulence may be useful for improving the diagnosis and risk stratification of patients with ventricular arrhythmias or who are at risk of developing life-threatening ventricular arrhythmias. (Level of Evidence: B)

ICD trials, especially Multicenter Automatic Defibrillator Implantation Trial (MADIT) II, have highlighted the need to develop novel tools in order to identify patients at highest risk of ventricular arrhythmias and SCD. Numerous modalities exist at present for assessing this risk but only 2 are currently approved by the U.S. Food and Drug Administration: signal-averaged ECG and T-wave alternans. However, heart rate variability and baroflex sensitivity also show considerable promise.

VIII. LEFT VENTRICULAR FUNCTION AND IMAGING

Recommendations

Class I

1. Echocardiography is recommended in patients with ventricular arrhythmias who are suspected of having structural heart disease. (Level of Evidence: B)
2. Echocardiography is recommended for the subset of patients at high risk for development of serious ventricular arrhythmias or SCD, such as those with dilated, hypertrophic, or RV cardiomyopathies, acute MI survivors, or relatives of patients with inherited disorders associated with SCD. (Level of Evidence: B)
3. Exercise testing with an imaging modality (echocardiography or nuclear perfusion [single-photon emission computed tomography [SPECT]]) is recommended to detect silent ischemia in patients with ventricular arrhythmias who have an intermediate probability of having CHD by age, symptoms, and gender and in whom ECG assessment is less reliable

because of digoxin use, LV hypertrophy, greater than 1-mm ST-segment depression at rest, Wolff-Parkinson-White syndrome, or left bundle-branch block. (*Level of Evidence: B*)

4. Pharmacological stress testing with an imaging modality (echocardiography or myocardial perfusion SPECT) is recommended to detect silent ischemia in patients with ventricular arrhythmias who have an intermediate probability of having CHD by age, symptoms, and gender and are physically unable to perform a symptom-limited exercise test. (*Level of Evidence: B*)

Class IIa

1. Magnetic resonance imaging (MRI), cardiac computed tomography (CT), or radionuclide angiography can be useful in patients with ventricular arrhythmias when echocardiography does not provide accurate assessment of LV and RV function and/or evaluation of structural changes. (*Level of Evidence: B*)
2. Coronary angiography can be useful in establishing or excluding the presence of significant obstructive CHD in patients with life-threatening ventricular arrhythmias or in survivors of SCD, who have an intermediate or greater probability of having CHD by age, symptoms, and gender. (*Level of Evidence: C*)
3. LV imaging can be useful in patients undergoing biventricular pacing. (*Level of Evidence: C*)

A. Echocardiography

Echocardiography is the imaging technique most commonly used because it is inexpensive in comparison with other techniques such as MRI and cardiac CT, is readily available, and provides accurate diagnosis of myocardial, valvular, and congenital heart disorders associated with ventricular arrhythmias and SCD (26,27) (Table 6). In addition, LV systolic function and regional wall motion can be evaluated, and in a majority of patients, EF can be determined (28).

B. Radionuclide Techniques

Myocardial perfusion SPECT using exercise or pharmacological agents is applicable for a selected group of patients suspected of having ventricular arrhythmias triggered by ischemia and who are unable to exercise or have resting

Table 6. Conditions Associated With Ventricular Arrhythmias That Can Be Diagnosed With Echocardiography

Disease Entity	Diagnostic Accuracy
Dilated cardiomyopathy	High
Ischemic cardiomyopathy	High
Hypertension with moderate to severe LVH	High
Hypertrophic cardiomyopathy	High
Valvular heart disease	High
ARVC	Moderate
Brugada syndrome	Poor

ARVC = arrhythmogenic right ventricular cardiomyopathy; LVH = left ventricular hypertrophy.

ECG abnormalities that limit the accuracy of ECG for ischemia detection.

C. Coronary Angiography

In patients with life-threatening ventricular arrhythmias or in survivors of SCD, coronary angiography plays an important diagnostic role in establishing or excluding the presence of significant obstructive CHD.

IX. ELECTROPHYSIOLOGICAL TESTING

Electrophysiological (EP) testing with intracardiac recording and electrical stimulation at baseline and with drugs has been used for arrhythmia assessment and risk stratification for SCD. EP testing is used to document inducibility of VT, guide ablation, evaluate drug effects, assess the risks of recurrent VT or SCD, evaluate loss of consciousness in selected patients with arrhythmias suspected as a cause, and assess the indications for ICD therapy (29–32).

A. Electrophysiological Testing in Patients With Coronary Heart Disease

Recommendations

Class I

1. EP testing is recommended for diagnostic evaluation of patients with remote MI with symptoms suggestive of ventricular tachyarrhythmias including palpitations, presyncope, and syncope. (*Level of Evidence: B*)
2. EP testing is recommended in patients with CHD to guide and assess efficacy of VT ablation. (*Level of Evidence: B*)
3. EP testing is useful in patients with CHD for the diagnostic evaluation of wide-QRS-complex tachycardias of unclear mechanism. (*Level of Evidence: C*)

Class IIa

EP testing is reasonable for risk stratification in patients with remote MI, nonsustained VT, and LVEF equal to or less than 40%. (*Level of Evidence: B*)

Drug testing for assessing antiarrhythmic drug efficacy has largely been abandoned. The prognostic value of inducible ventricular flutter and fibrillation is still controversial. Limited data on the prognostic value of inducible ventricular flutter suggest that it may be an important end point (33,34).

B. Electrophysiological Testing in Patients With Syncope

Recommendations

Class I

EP testing is recommended in patients with syncope of unknown cause with impaired LV function or structural heart disease. (*Level of Evidence: B*)

Class IIa

EP testing can be useful in patients with syncope when bradyarrhythmias or tachyarrhythmias are suspected and in whom noninvasive diagnostic studies are not conclusive. (Level of Evidence: B)

Syncope is a transient symptom that may be caused by an underlying rhythm disorder with or without an associated cardiac disease. EP testing is used to document or exclude the arrhythmic cause of syncope. It is most useful in patients with CHD and LV dysfunction. EP testing is usually not the first evaluation step but rather complementary to a full syncope work-up. Lack of correlation between symptoms and a documented arrhythmia elicited during EP testing may lead to overinterpretation or underinterpretation of the predictive value of the results. Transient drug effects that can provoke syncope may remain undetected. Other causes such as a neurological etiology need to be considered in some patients.

X. VALUE OF ANTIARRHYTHMIC DRUGS

Use of antiarrhythmic drugs in the acute setting is described in Section XIII on Acute Management of Specific Arrhythmias.

The available antiarrhythmic drugs can be classified by the Vaughan Williams 4-level schema (type I: fast sodium channel blockers, type II: beta blockers, type III: repolarization potassium current blockers, type IV: calcium channel antagonists) (35), or by the more mechanistic and clinically relevant Sicilian Gambit (36). The Vaughan Williams schema is somewhat outdated because antiarrhythmic drugs have complex actions that do not easily fit into 1 of the 4 specified classes of drug effects. This classification is of limited usefulness when choosing an antiarrhythmic drug to manage a specific arrhythmia. The Sicilian Gambit, introduced in 1991, was an attempt to provide a classification of antiarrhythmic drugs based on their mechanism of action and on arrhythmogenic mechanisms.

A. Beta Blockers

These drugs are effective in suppressing ventricular ectopic beats and arrhythmias as well as reducing SCD in a spectrum of cardiac disorders in patients with and without heart failure (HF). Beta blockers are safe and effective antiarrhythmic agents that can be considered the mainstay of antiarrhythmic drug therapy (37,38).

B. Amiodarone and Sotalol

The overall long-term survival benefit from amiodarone is controversial, with most studies showing no clear advantage over placebo. A few studies and one meta-analysis of several large studies have shown reduction in SCD using amiodarone for LV dysfunction due to prior MI and nonischemic dilated cardiomyopathy (DCM) (39–41), but the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) showed

no survival benefit from amiodarone when compared with placebo (8,42).

Sotalol, like amiodarone, is effective in suppressing ventricular arrhythmias, but it has greater proarrhythmic effects and has not been shown to provide a clear increase in survival.

XI. SPECIAL CONSIDERATIONS WHERE ANTIARRHYTHMIC DRUGS MAY BE INDICATED

Amiodarone therapy may be considered in special situations (43); secondary subset analyses indicate possible survival benefit when amiodarone is combined with beta blockers (44,45).

A. Patients With Ventricular Tachyarrhythmias Who Do Not Meet Criteria for an Implantable Cardioverter-Defibrillator

Beta blockers are the first-line therapy, but if this therapy at full therapeutic dose is not effective, then amiodarone or sotalol can be tried with monitoring for adverse effects during administration.

B. Patients With Implantable Cardioverter-Defibrillators Who Have Recurrent Ventricular Tachycardia/Ventricular Fibrillation With Frequent Appropriate Implantable Cardioverter-Defibrillator Firing

This scenario, in its extreme, has been called defibrillator (tachycardia) storm, and it requires the addition of antiarrhythmic drugs and/or catheter ablation for control of the recurrent VT and associated ICD shocks. Sotalol is effective in suppressing atrial and ventricular arrhythmias (46), the combination of beta blockers and amiodarone is an alternative approach. Intravenous amiodarone has been useful.

XII. IMPLANTABLE AND EXTERNAL CARIOVERTER DEVICES

Several prospective multicenter clinical trials have documented improved survival with ICD therapy in high-risk patients with LV dysfunction due to prior MI and nonischemic cardiomyopathy (8,47–53) (Figure 2). ICD therapy compared with conventional or traditional antiarrhythmic drug therapy has been associated with mortality reductions from 23% to 55% depending on the risk group participating in the trial, with the improvement in survival due almost exclusively to a reduction in SCD. The trials may be subcategorized into 2 types: primary prevention (prophylactic) trials in which the subjects have not experienced a life-threatening ventricular arrhythmia or a symptomatic equivalent and secondary prevention trials involving subjects who have had an abortive cardiac arrest, a life-threatening VT, or unexplained syncope with work-up suggesting a high probability that a ventricular tachyarrhythmia was the cause of the syncope.

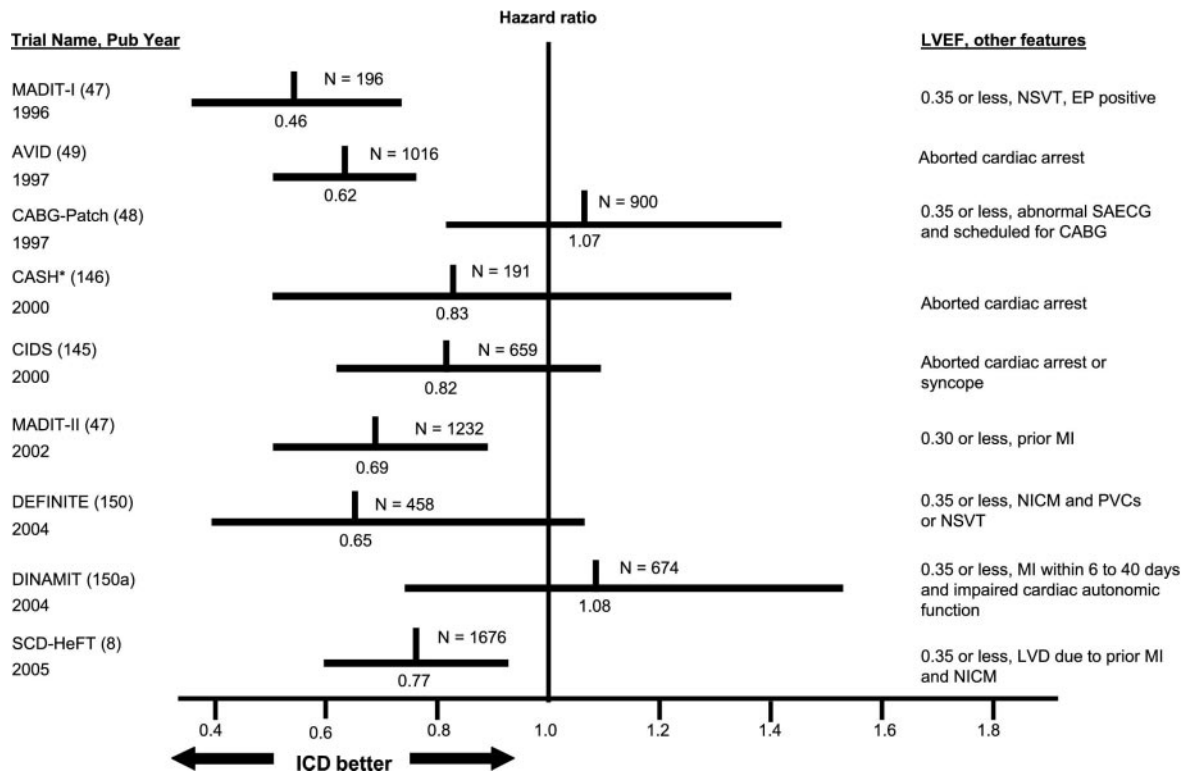


Figure 2. Major implantable cardioverter-defibrillator (ICD) trials. Hazard ratios (vertical line) and 95% confidence intervals (horizontal lines) for death from any cause in the ICD group compared with the non-ICD group. *Includes only ICD and amiodarone patients from CASH. For expansion of trial names, see Appendix 3. CABG = coronary artery bypass graft surgery; EP = electrophysiological study; LVD = left ventricular dysfunction; LVEF = left ventricular ejection fraction; MI = myocardial infarction; N = number of patients; NICM = nonischemic cardiomyopathy; NSVT = nonsustained ventricular tachycardia; PVCs = premature ventricular complexes; SAECG = signal-averaged electrocardiogram.

A. Automated External Defibrillator

The automated external defibrillator (AED) saves lives when external defibrillation can be rendered within minutes of onset of VF. The AED represents an efficient method of delivering defibrillation to persons experiencing out-of-hospital cardiac arrest, and its use by both traditional and nontraditional first responders appears to be safe and effective (54,55). Appropriate device location to reduce time delay after onset of cardiac arrest is critical. Federal, state, and community efforts have been effective in placing AEDs in schools, sporting events, high-density residential sites, and airports as well as on airplanes and in police and fire department vehicles (56–58).

B. Ablation

Recommendations

Class I

1. Ablation is indicated in patients who are otherwise at low risk for SCD and have sustained predominantly monomorphic VT that is drug resistant, who are drug intolerant, or who do not wish long-term drug therapy. (Level of Evidence: C)
2. Ablation is indicated in patients with bundle-branch reentrant VT. (Level of Evidence: C)

3. Ablation is indicated as adjunctive therapy in patients with an ICD who are receiving multiple shocks as a result of sustained VT that is not manageable by reprogramming or changing drug therapy or who do not wish long-term drug therapy (59,60). (Level of Evidence: C)
4. Ablation is indicated in patients with Wolff-Parkinson-White syndrome resuscitated from sudden cardiac arrest due to atrial fibrillation and rapid conduction over the accessory pathway causing VF (61). (Level of Evidence: B)

Class IIa

1. Ablation can be useful therapy in patients who are otherwise at low risk for SCD and have symptomatic nonsustained monomorphic VT that is drug resistant, who are drug intolerant, or who do not wish long-term drug therapy. (Level of Evidence: C)
2. Ablation can be useful therapy in patients who are otherwise at low risk for SCD and have frequent symptomatic predominantly monomorphic PVCs that are drug resistant, who are drug intolerant, or who do not wish long-term drug therapy. (Level of Evidence: C)
3. Ablation can be useful in symptomatic patients with Wolff-Parkinson-White syndrome who have acces-

sory pathways with refractory periods less than 240 ms in duration (61). (*Level of Evidence: B*)

Class IIb

1. Ablation of Purkinje fiber potentials may be considered in patients with ventricular arrhythmia storm consistently provoked by PVCs of similar morphology (62). (*Level of Evidence: C*)
2. Ablation of asymptomatic PVCs may be considered when the PVCs are very frequent to avoid or treat tachycardia-induced cardiomyopathy (63). (*Level of Evidence: C*)

Class III

Ablation of asymptomatic relatively infrequent PVCs is not indicated. (*Level of Evidence: C*)

The specific application of radiofrequency ablation to VT has evolved as the technology has developed. Radiofrequency ablation can be applied in the treatment of VT in patients with ischemic disease, cardiomyopathy, bundle-branch re-entry, and various forms of idiopathic VT (64–76).

C. Antiarrhythmic Surgery

In patients with recurrent VT refractory to drugs, implanted defibrillators, and radiofrequency catheter ablation, direct surgical ablation or resection of the arrhythmogenic focus is an approach that continues to be used in experienced centers. Surgery requires accurate preoperative and intraoperative mapping to determine the site or sites of the tachycardia. Some centers use a scar-based approach to resecting arrhythmogenic sites.

Left cervicothoracic sympathetic ganglionectomy is associated with reduction in the frequency of arrhythmogenic syncope in the congenital LQTS and may be useful as adjunctive therapy in high-risk patients with long QT who have recurrent syncope and/or aborted cardiac arrest despite combined ICD and beta-blocker therapy or in patients with long QT who cannot tolerate beta blockers (77).

D. Revascularization for Arrhythmia Management

A review of coronary revascularization studies reveals improved survival and reduction in SCD during long-term follow-up (78,79). If obstructive CHD is complicated by ventricular arrhythmias, especially in patients with left main and proximal left anterior descending coronary artery disease, there is a reasonable likelihood that revascularization will reduce the frequency and complexity of the arrhythmias and, in some patients, will eliminate such arrhythmias.

XIII. ACUTE MANAGEMENT OF SPECIFIC ARRHYTHMIAS

A. Management of Cardiac Arrest

Cardiac arrest is characterized by an abrupt loss of effective blood flow, sufficient to cause immediate loss of

consciousness, leading immediately to death if untreated. The most common electrical mechanisms for cardiac arrest are VF and pulseless VT (see Section 4 in the full-text guidelines), but substantial numbers of cardiac arrests begin as severe bradyarrhythmias, asystole, or pulseless electrical activity.

Recommendations

Class I

1. After establishing the presence of definite, suspected, or impending cardiac arrest, the first priority should be activation of a response team capable of identifying the specific mechanism and carrying out prompt intervention. (*Level of Evidence: B*)
2. Cardiopulmonary resuscitation (CPR) should be implemented immediately after contacting a response team. (*Level of Evidence: A*)
3. In an out-of-hospital setting, if an AED is available, it should be applied immediately and shock therapy administered according to the algorithms contained in the documents on CPR (80,81) developed by the American Heart Association (AHA) in association with the International Liaison Committee on Resuscitation (ILCOR) and/or the European Resuscitation Council (ERC). (*Level of Evidence: C*)
4. For victims with ventricular tachyarrhythmic mechanisms of cardiac arrest, when recurrences occur after a maximally defibrillating shock (generally 360 J for monophasic defibrillators), intravenous amiodarone should be the preferred antiarrhythmic drug for attempting a stable rhythm after further defibrillations. (*Level of Evidence: B*)
5. For recurrent ventricular tachyarrhythmias or non-tachyarrhythmic mechanisms of cardiac arrest, it is recommended to follow the algorithms contained in the documents on CPR (80,81) developed by the AHA in association with ILCOR and/or the ERC. (*Level of Evidence: C*)
6. Reversible causes and factors contributing to cardiac arrest should be managed during advanced life support, including management of hypoxia, electrolyte disturbances, mechanical factors, and volume depletion. (*Level of Evidence: C*)

Class IIa

For response times greater than or equal to 5 min, a brief (less than 90 to 180 s) period of CPR is reasonable prior to attempting defibrillation. (*Level of Evidence: B*)

Class IIb

A single precordial thump may be considered by healthcare professional providers when responding to a witnessed cardiac arrest. (*Level of Evidence: C*)

Advanced life support activities, other than those directly related to electrical methods for control of tachyarrhythmias, led to the generation of complex protocols to guide responders. These documents, published by the AHA (80) and the ERC (81), cover the broad expanse of clinical circumstances and considerations of mechanisms. They provide management information, stratified for special circumstances such as age of the victim (from infancy to the elderly), pathophysiological status, and survival probabilities. The response algorithms to these various circumstances are complex and the reader is referred to the source documents for details (80,81). As management guidelines, these documents are classified as Level of Evidence C, but they are derived from a combination of varied studies and opinion that range from Levels of Evidence A, B, or C. Abbreviated versions for tachyarrhythmias and nontachyarrhythmic mechanisms are shown in Figure 3 in the full-text guidelines.

B. Arrhythmias Associated With Acute Coronary Syndromes

The incidence of VF (occurring within 48 h of the onset of the acute coronary syndrome [ACS]) may be decreasing owing to aggressive revascularization limiting infarct size and to increased beta-blocker use (82). VF occurring early in the ACS has been associated with an increase in hospital mortality but not with increased long-term mortality (83). Prophylaxis with lidocaine may reduce the incidence of VF in the ACS but appears to be associated with increased mortality, likely owing to bradycardia, and this treatment has largely been abandoned (84). Use of prophylactic beta blockers in the setting of acute MI reduces the incidence of VF, and this practice is encouraged when appropriate. Similarly, correction of hypomagnesemia and hypokalemia is encouraged because of the potential contribution of electrolyte disturbances to VF (85).

C. Ventricular Tachycardia Associated With Low Troponin Myocardial Infarction

Recommendations

Class I

Patients presenting with sustained VT in whom low-level elevations in cardiac biomarkers of myocyte injury/necrosis are documented should be treated similarly to patients who have sustained VT and in whom no biomarker rise is documented. (Level of Evidence: C)

D. Sustained Monomorphic Ventricular Tachycardia

Recommendations

Class I

- 1. Wide-QRS tachycardia should be presumed to be VT if the diagnosis is unclear. (Level of Evidence: C)**

- 2. Direct-current cardioversion with appropriate sedation is recommended at any point in the treatment cascade in patients with suspected sustained monomorphic VT with hemodynamic compromise. (Level of Evidence: C)**

Class IIa

- 1. Intravenous procainamide (or ajmaline in some European countries) is reasonable for initial treatment of patients with stable sustained monomorphic VT. (Level of Evidence: B)**
- 2. Intravenous amiodarone is reasonable for patients with sustained monomorphic VT that is hemodynamically unstable, refractory to conversion with countershock, or recurrent despite procainamide or other agents. (Level of Evidence: C)**
- 3. Transvenous catheter pace termination can be useful to treat patients with sustained monomorphic VT that is refractory to cardioversion or is frequently recurrent despite antiarrhythmic medication. (Level of Evidence: C)**

Class IIb

Intravenous lidocaine might be reasonable for initial treatment of patients with stable sustained monomorphic VT specifically associated with acute myocardial ischemia or infarction. (Level of Evidence: C)

Class III

Calcium channel blockers such as verapamil and diltiazem should not be used in patients to terminate wide-QRS-complex tachycardia of unknown origin, especially in patients with a history of myocardial dysfunction. (Level of Evidence: C)

Correction of potentially causative or aggravating conditions such as hypokalemia and ischemia is an early priority. Timely termination is usually desirable even if VT is well tolerated. This can be achieved with cardioversion, antiarrhythmic medications, or pacing techniques.

Initial treatment often includes the administration of intravenous antiarrhythmic medication. The advantages include the lack of necessity for anesthesia and ready availability.

Intravenous amiodarone is not ideal for early conversion of stable monomorphic VT. Intravenous procainamide is more appropriate when early slowing of the VT rate and termination of monomorphic VT are desired (86,87). Close monitoring of blood pressure and cardiovascular status is recommended in the presence of congestive HF or severe LV dysfunction as intravenous procainamide can cause transient hypotension (88). Lidocaine is effective when VT is thought to be related to myocardial ischemia (89,90).

E. Repetitive Monomorphic Ventricular Tachycardia

Recommendations

Class IIa

Intravenous amiodarone, beta blockers, and intravenous procainamide (or sotalol or ajmaline in Europe) can be useful for treating repetitive monomorphic VT in the context of coronary disease (91) and idiopathic VT. (Level of Evidence: C)

Repetitive monomorphic VT is characterized electrocardiographically by frequent ventricular ectopy and salvos of nonsustained ventricular tachycardia (NSVT) with intervening sinus rhythm. It typically occurs at rest and is self-terminating, although the arrhythmia can be present for much of the time (92). Although this terminology can refer to mechanistically diverse arrhythmias, it generally refers to idiopathic VT, most frequently the RV outflow type (93–95). This tachycardia can cause palpitations or, rarely, tachycardia-related cardiomyopathy (96). Many patients have no symptoms related to the arrhythmia. In some patients, tachycardia is provoked by exercise (97). An electrocardiographically similar presentation is less frequent in patients with structural heart disease and, specifically, previous MI (91).

Beta-blocking agents or calcium channel blockers are often effective. Ablation is generally successful in problematic RV outflow tachycardia (98).

F. Polymorphic Ventricular Tachycardia

Recommendations

Class I

1. **Direct current cardioversion with appropriate sedation as necessary is recommended for patients with sustained polymorphic VT with hemodynamic compromise and is reasonable at any point in the treatment cascade. (Level of Evidence: B)**
2. **Intravenous beta blockers are useful for patients with recurrent polymorphic VT especially if ischemia is suspected or cannot be excluded. (Level of Evidence: B)**
3. **Intravenous loading with amiodarone is useful for patients with recurrent polymorphic VT in the absence of abnormal repolarization related to congenital or acquired LQTS. (Level of Evidence: C)**
4. **Urgent angiography with a view to revascularization should be considered for patients with polymorphic VT when myocardial ischemia cannot be excluded. (Level of Evidence: C)**

Class IIb

Intravenous lidocaine may be reasonable for treatment of polymorphic VT specifically associated with acute myocardial ischemia or infarction. (Level of Evidence: C)

Polymorphic VT may be sustained, generally requiring urgent electrical cardioversion or self-terminating with interludes of sinus rhythm.

Intravenous beta blockers are useful in this context and improve mortality in the setting of recurrent polymorphic VT with acute MI (99). Intravenous loading with amiodarone is also useful (80,81,100–102). Urgent coronary angiography should be considered in the setting of recurrent polymorphic VT when ischemia is suspected or cannot be excluded (103).

G. Torsades de Pointes

Recommendations

Class I

1. **Withdrawal of any offending drugs and correction of electrolyte abnormalities are recommended in patients presenting with torsades de pointes. (Level of Evidence: A)**
2. **Acute and long-term pacing is recommended for patients presenting with torsades de pointes due to heart block and symptomatic bradycardia. (Level of Evidence: A)**

Class IIa

1. **Management with intravenous magnesium sulfate is reasonable for patients who present with LQTS and few episodes of torsades de pointes. Magnesium is not likely to be effective in patients with a normal QT interval. (Level of Evidence: B)**
2. **Acute and long-term pacing is reasonable for patients who present with recurrent pause-dependent torsades de pointes. (Level of Evidence: B)**
3. **Beta blockade combined with pacing is reasonable acute therapy for patients who present with torsades de pointes and sinus bradycardia. (Level of Evidence: C)**
4. **Isoproterenol is reasonable as temporary treatment in acute patients who present with recurrent pause-dependent torsades de pointes who do not have congenital LQTS. (Level of Evidence: B)**

Class IIb

1. **Potassium repletion to 4.5 to 5 mM/L may be considered for patients who present with torsades de pointes. (Level of Evidence: B)**
2. **Intravenous lidocaine or oral mexiletine may be considered in patients who present LQT3 and torsades de pointes. (Level of Evidence: C)**

Marked QT interval prolongation and the morphologically distinctive polymorphic VT torsades de pointes occur in 3 common settings: congenital LQTS, a drug-associated form, and in patients with advanced conduction system disease that has progressed to heart block.

H. Incessant Ventricular Tachycardia

Recommendations

Class I

Revascularization and beta blockade followed by intravenous antiarrhythmic drugs such as procainamide or amiodarone are recommended for patients with recurrent or incessant polymorphic VT due to acute myocardial ischemia. (*Level of Evidence: C*)

Class IIa

Intravenous amiodarone or procainamide followed by VT ablation can be effective in the management of patients with frequently recurring or incessant monomorphic VT. (*Level of Evidence: B*)

Class IIb

1. Intravenous amiodarone and intravenous beta blockers separately or together may be reasonable in patients with VT storm. (*Level of Evidence: C*)
2. Overdrive pacing or general anesthesia may be considered for patients with frequently recurring or incessant VT. (*Level of Evidence: C*)
3. Spinal cord modulation may be considered for some patients with frequently recurring or incessant VT. (*Level of Evidence: C*)

I. Clinical Features

The syndrome of very frequent episodes of VT requiring cardioversion has been termed "VT storm."

Management guidelines for these syndromes rely on anecdotal evidence because they are rare, there are multiple potential underlying mechanisms, and no randomized trials have been conducted.

Intravenous beta blockade should be considered for a polymorphic VT storm as it is the single most effective therapy. It is of utmost importance to try and understand the substrate of incessant arrhythmias because if a diagnosis is established, a targeted treatment may be possible.

XIV. VENTRICULAR ARRHYTHMIA AND SUDDEN CARDIAC DEATH RELATED TO SPECIFIC PATHOLOGY

A. Left Ventricular Dysfunction Due to Prior Myocardial Infarction

Recommendations

Class I

1. Aggressive attempts should be made to treat HF that may be present in some patients with LV dysfunction due to prior MI and ventricular tachyarrhythmias. (*Level of Evidence: C*)
2. Aggressive attempts should be made to treat myocardial ischemia that may be present in some pa-

tients with ventricular tachyarrhythmias. (*Level of Evidence: C*)

3. Coronary revascularization is indicated to reduce the risk of SCD in patients with VF when direct, clear evidence of acute myocardial ischemia is documented to immediately precede the onset of VF. (*Level of Evidence: B*)
4. If coronary revascularization cannot be carried out, and there is evidence of prior MI and significant LV dysfunction, the primary therapy of patients resuscitated from VF should be the ICD in patients who are receiving chronic optimal medical therapy and those who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: A*)
5. ICD therapy is recommended for primary prevention to reduce total mortality by a reduction in SCD in patients with LV dysfunction due to prior MI who are at least 40 d post-MI, have an LVEF less than or equal to 30% to 40%, are NYHA functional class II or III, are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: A*) (See Section IA.)
6. The ICD is effective therapy to reduce mortality by a reduction in SCD in patients with LV dysfunction due to prior MI who present with hemodynamically unstable sustained VT, who are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: A*)

Class IIa

1. Implantation of an ICD is reasonable in patients with LV dysfunction due to prior MI who are at least 40 d post-MI, have an LVEF of less than or equal to 30% to 35%, are NYHA functional class I on chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: B*) (See Section IA.)
2. Amiodarone, often in combination with beta blockers, can be useful for patients with LV dysfunction due to prior MI and symptoms due to VT unresponsive to beta-adrenergic-blocking agents. (*Level of Evidence: B*)
3. Sotalol is reasonable therapy to reduce symptoms resulting from VT for patients with LV dysfunction due to prior MI unresponsive to beta-blocking agents. (*Level of Evidence: C*)
4. Adjunctive therapies to the ICD, including catheter ablation or surgical resection, and pharmacological therapy with agents such as amiodarone or sotalol are reasonable to improve symptoms due to frequent episodes of sustained VT or VF in patients with LV dysfunction due to prior MI. (*Level of Evidence: C*)

5. **Amiodarone is reasonable therapy to reduce symptoms due to recurrent hemodynamically stable VT for patients with LV dysfunction due to prior MI who cannot or refuse to have an ICD implanted. (Level of Evidence: C)**
6. **ICD implantation is reasonable for treatment of recurrent sustained VT in patients post-MI with normal or near normal ventricular function who are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: C)**

Class IIb

1. **Curative catheter ablation or amiodarone may be considered in lieu of ICD therapy to improve symptoms in patients with LV dysfunction due to prior MI and recurrent hemodynamically stable VT whose EF is greater than 40%. (Level of Evidence: B)**
2. **Amiodarone may be reasonable therapy for patients with LV dysfunction due to prior MI with an ICD indication, as defined above, in patients who cannot or refuse to have an ICD implanted. (Level of Evidence: C)**

Class III

1. **Prophylactic antiarrhythmic drug therapy is not indicated to reduce mortality in patients with asymptomatic nonsustained ventricular arrhythmias. (Level of Evidence: B)**
2. **Class IC antiarrhythmic drugs in patients with a past history of MI should not be used. (Level of Evidence: A)**

Patients with chronic CHD manifest 3 general types of ventricular tachyarrhythmias: NSVT (defined as 3 or more repetitive ventricular beats in a row lasting up to 30 s in duration at a rate greater than 100 beats per minute), sustained VT, and cardiac arrest resulting from VT or VF. The cardiac mortality of patients with all types of ventricular tachyarrhythmias is high. The high mortality results from nonsudden, as well as sudden, cardiac death. These arrhythmias may result from myocardial ischemia, or effects of HF, in addition to primary electrical abnormalities.

Most NSVT in patients with chronic CHD is brief and does not cause symptoms. There is no evidence that suppression of asymptomatic NSVT prolongs life. The treatment of sustained VT in patients with chronic CHD should be tempered by the clinical manifestations produced by the tachycardia, as well as the frequency of episodes. Patients experiencing cardiac arrest due to VF that does not occur within the first 24 to 48 h of acute MI may be at risk for recurrent cardiac arrest.

All patients with CHD are at risk for SCD, and most SCD occurs in patients without severe LV dysfunction. ICD therapy is indicated to reduce the risk of SCD in 2

patient groups: patients whose LVEF is less than or equal to 40% as a result of prior MI and who have spontaneous NSVT and sustained monomorphic VT inducible by EP testing (50) and patients whose LVEF is less than 30% as a result of an MI that occurred greater than or equal to 40 d earlier when HF (NYHA functional class II or III symptoms) is present (51). The use of antiarrhythmic agents may predispose the patient to proarrhythmic complications that might pose significant threats to life. Increasingly, the ICD is being used effectively to treat these arrhythmias, which in themselves may not be life-threatening, in order to avoid the relative ineffectiveness and adverse complications of pharmaceutical therapy.

B. Valvular Heart Disease

Recommendations

Class I

Patients with valvular heart disease and ventricular arrhythmias should be evaluated and treated following current recommendations for each disorder. (Level of Evidence: C)

Class IIb

The effectiveness of mitral valve repair or replacement to reduce the risk of SCD in patients with mitral valve prolapse, severe mitral regurgitation and serious ventricular arrhythmias is not well established. (Level of Evidence: C)

To date, there are insufficient data demonstrating reduction in ventricular arrhythmias as a result of valve repair or replacement in most patients with valvular disease. For these reasons, patients with valvular heart disease and ventricular arrhythmias should be evaluated and treated following current recommendations for each disorder (104).

C. Congenital Heart Disease

Recommendations

Class I

1. **ICD implantation is indicated in patients with congenital heart disease who are survivors of cardiac arrest after evaluation to define the cause of the event and exclude any reversible causes. ICD implantation is indicated in patients who are receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: B)**
2. **Patients with congenital heart disease and spontaneous sustained VT should undergo invasive hemodynamic and EP evaluation. Recommended therapy includes catheter ablation or surgical resection to**

eliminate VT. If that is not successful, ICD implantation is recommended. (Level of Evidence: C)

Class IIa

Invasive hemodynamic and EP evaluation is reasonable in patients with congenital heart disease and unexplained syncope and impaired ventricular function. In the absence of a defined and reversible cause, ICD implantation is reasonable in patients who are receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: B)

Class IIb

EP testing may be considered for patients with congenital heart disease and ventricular couplets or NSVT to determine the risk of a sustained ventricular arrhythmia. (Level of Evidence: C)

Class III

Prophylactic antiarrhythmic therapy is not indicated for asymptomatic patients with congenital heart disease and isolated PVCs. (Level of Evidence: C)

Congenital heart disease represents a diverse spectrum of anatomic and physiological defects with significant differences in respect to natural history, pre- and postoperative physiology as well as the risk of arrhythmias, appropriate therapies and risk of late SCD.

During infancy and childhood, greater than 75% of deaths in patients with congenital heart disease are in-hospital events, most occurring during the perioperative period (105). The remaining deaths occur as out-of-hospital or emergency department events, often in patients with other congenital anomalies or sepsis.

Beyond 20 y of age, there is a progressive increase in the incidence of sudden and total cardiac mortality in postoperative congenital heart disease patients (106).

Five congenital heart defects have been associated with the greatest risks of late SCD: tetralogy of Fallot, d- and l-transposition of the great arteries, aortic stenosis, and functional single ventricle (106–108). The largest number of late SCD studies in postoperative patients with congenital heart disease have been for tetralogy of Fallot.

In general, postoperative patients with unexplained syncope should undergo both hemodynamic and EP evaluation. A positive response to EP testing, independent of the clinical indication, may identify patients with a high risk of late SCD (109). In the absence of ventricular dysfunction or symptoms, isolated ventricular ectopy has minimal prognostic significance, and the risks of antiarrhythmic drug treatment can exceed any potential benefit (110).

The most common congenital coronary artery anomaly causing SCD in the young is anomalous origin of the left coronary artery from the right sinus of Valsalva. The

proposed mechanism of SCD is that either acute angulation of the coronary ostium or compression of the left coronary artery as it traverses the region between the aortic wall and RV outflow tract results in acute myocardial ischemia and the development of VT or VF. Definitive diagnosis by coronary angiography is an indication for surgical revascularization.

Although disorders in this category are important causes of life-threatening ventricular arrhythmias, the occurrence of VT/SCD is relatively rare and, hence, in most cases, there are few trial data as to how the arrhythmias should best be managed. Data relating to the prevention of life-threatening ventricular arrhythmias are even sparser.

Acute emergencies, as a consequence of any underlying ailment in this section, should be managed conventionally.

D. Metabolic and Inflammatory Conditions

1. Myocarditis, Rheumatic Disease, and Endocarditis

Recommendations

Class I

1. **Temporary pacemaker insertion is indicated in patients with symptomatic bradycardia and/or heart block during the acute phase of myocarditis. (Level of Evidence: C)**
2. **Acute aortic regurgitation associated with VT should be treated surgically unless otherwise contraindicated. (Level of Evidence: C)**
3. **Acute endocarditis complicated by aortic or annular abscess and AV block should be treated surgically unless otherwise contraindicated. (Level of Evidence: C)**

Class IIa

1. **ICD implantation can be beneficial in patients with life-threatening ventricular arrhythmias who are not in the acute phase of myocarditis, as indicated in the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices (1) who are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: C)**
2. **Antiarrhythmic therapy can be useful in patients with symptomatic NSVT or sustained VT during the acute phase of myocarditis. (Level of Evidence: C)**

Class III

ICD implantation is not indicated during the acute phase of myocarditis. (Level of Evidence: C)

Myocarditis is an inflammatory process affecting the cardiac myocardium and is most often related to infection.

Cardiac arrhythmias associated with acute myocarditis can range from conduction abnormalities to difficult to suppress life-threatening ventricular arrhythmias. Death can

occur related to HF and arrhythmias including heart block (111–118). Patients with arrhythmias or syncope may require antiarrhythmic drugs and/or device therapy (119). Temporary pacemaker insertion is indicated in patients with acute myocarditis who present with symptomatic heart block as it would be in other causes of acute symptomatic heart block.

Lyme carditis patients can develop varying degrees of AV conduction abnormalities. Persistent heart block is rare, but in such cases permanent pacing may be needed (120,121).

Chagas' disease is caused by the protozoan *Trypanosoma cruzi* and transmitted by an insect vector and is common in Central and South America. Acute myocarditis is rare, but over one third develop late myocardial damage with progressive HF and poor survival. Conduction defects with progression to complete heart block are common. Life-threatening ventricular arrhythmias are common. Amiodarone appears to be effective in treating ventricular tachyarrhythmias, and death occurs as a result of either refractory HF or arrhythmias (122). Device therapy including the ICD is frequently used in the late phase (123).

Acute rheumatic fever, complete heart block, and ventricular arrhythmias are rare (124–126). The development of cardiac rhythm disturbances portends poorly in infective endocarditis (127).

2. Infiltrative Cardiomyopathies

Recommendations

Class I

In addition to managing the underlying infiltrative cardiomyopathy, life-threatening arrhythmias should be treated in the same manner that such arrhythmias are treated in patients with other cardiomyopathies, including the use of ICD and pacemakers in patients who are receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: C)

The association between the infiltrative cardiomyopathies and VT/SCD is well documented. In all cases, where appropriate, treatment of the underlying condition must accompany management of cardiac manifestations.

3. Endocrine Disorders and Diabetes

Recommendations

Class I

- 1. The management of ventricular arrhythmias secondary to endocrine disorders should address the electrolyte (potassium, magnesium, and calcium) imbalance and the treatment of the underlying endocrinopathy. (Level of Evidence: C)**

- 2. Persistent life-threatening ventricular arrhythmias that develop in patients with endocrine disorders should be treated in the same manner that such arrhythmias are treated in patients with other diseases, including use of ICD and pacemaker implantation as required in those who are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: C)**
- 3. Patients with diabetes with ventricular arrhythmias should generally be treated in the same manner as patients without diabetes. (Level of Evidence: A)**

Endocrine disorders can induce VT/SCD by excess or insufficient hormone activity on myocardial receptors (e.g., pheochromocytoma, hypothyroidism). The endocrinopathy can also cause myocardial changes (e.g., acromegaly) or electrolyte disturbances produced by hormone excess (e.g., hyperkalemia in Addison's disease and hypokalemia in Conn's syndrome) and certain endocrine disorders can accelerate the progression of conditions such as underlying structural heart disease secondary to dyslipidemia or hypertension, increasing the risk of serious arrhythmias.

4. End-Stage Renal Failure

Recommendations

Class I

- 1. The acute management of ventricular arrhythmias in end-stage renal failure should immediately address hemodynamic status and electrolyte (potassium, magnesium, and calcium) imbalance. (Level of Evidence: C)**
- 2. Life-threatening ventricular arrhythmias, especially in patients awaiting renal transplantation, should be treated conventionally, including the use of ICD and pacemaker implantation as required, in patients who are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: C)**

Cardiovascular causes account for at least 40% of deaths in patients with end-stage renal failure and 20% of these are sudden.

5. Obesity, Dieting, and Anorexia

Recommendations

Class I

Life-threatening ventricular arrhythmias in patients with obesity, anorexia, or when dieting should be treated in the same manner that such arrhythmias are treated in patients with other diseases, including ICD and pacemaker implantation as required. Patients receiving ICD implantation should be receiv-

ing chronic optimal medical therapy and have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: C*)

Class IIa

Programmed weight reduction in obesity and carefully controlled re-feeding in anorexia can effectively reduce the risk of ventricular arrhythmias and SCD. (*Level of Evidence: C*)

Class III

Prolonged, unbalanced, very low calorie, semistarvation diets are not recommended; they may be harmful and provoke life-threatening ventricular arrhythmias. (*Level of Evidence: C*)

Extreme disorders of eating, and overzealous methods of rectifying them quickly, are all associated with SCD. In overweight individuals, this risk is particularly evident in the severely obese with a 40 to 60 times higher incidence compared to that in the age-matched general population (128,129).

Obstructive sleep apnea may play a role in the genesis of arrhythmias and HF in obese individuals (130).

Reported mortality rates in anorexia nervosa fluctuate from 5% to 20%, but the actual rate is likely to be around 6% (131). Up to a third of these deaths, including those occurring during re-feeding, are said to be due to cardiac causes but no precise data exist on SCD.

E. Pericardial Diseases

Recommendations

Class I

Ventricular arrhythmias that develop in patients with pericardial disease should be treated in the same manner that such arrhythmias are treated in patients with other diseases, including ICD and pacemaker implantation as required. Patients receiving ICD implantation should be receiving chronic optimal medical therapy and have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: C*)

F. Pulmonary Arterial Hypertension

Recommendations

Class III

Prophylactic antiarrhythmic therapy generally is not indicated for primary prevention of SCD in patients with pulmonary arterial hypertension or other pulmonary conditions. (*Level of Evidence: C*)

SCD is responsible for 30% to 40% of mortality in patients with pulmonary arterial hypertension.

G. Transient Arrhythmias of Reversible Cause

Recommendations

Class I

1. Myocardial revascularization should be performed, when appropriate, to reduce the risk of SCD in patients experiencing cardiac arrest due to VF or polymorphic VT in the setting of acute ischemia or MI. (*Level of Evidence: C*)
2. Unless electrolyte abnormalities are proved to be the cause, survivors of cardiac arrest due to VF or polymorphic VT in whom electrolyte abnormalities are discovered in general should be evaluated and treated in a similar manner to that of cardiac arrest without electrolyte abnormalities. (*Level of Evidence: C*)
3. Patients who experience sustained monomorphic VT in the presence of antiarrhythmic drugs or electrolyte abnormalities should be evaluated and treated in a manner similar to that of patients with VT without electrolyte abnormalities or antiarrhythmic drugs present. Antiarrhythmic drugs or electrolyte abnormalities should not be assumed to be the sole cause of sustained monomorphic VT. (*Level of Evidence: B*)
4. Patients who experience polymorphic VT in association with prolonged QT interval due to antiarrhythmic medications or other drugs should be advised to avoid exposure to all agents associated with QT prolongation. A list of such drugs can be found on the Web sites www.qtdrugs.org and www.torsades.org. (*Level of Evidence: B*)

The mortality of cardiac arrest survivors is high, even when the cause of the initial arrest appears to be a transient or correctable abnormality, and much of the mortality appears due to recurrent cardiac arrest (132, 133).

Observational studies suggest that

- Sustained monomorphic VT in patients with prior MI is unlikely to be affected by revascularization (134).
- Myocardial revascularization is sufficient therapy only in patients surviving VF in association with myocardial ischemia when ventricular function is normal and there is no history of MI (135).

XV. VENTRICULAR ARRHYTHMIAS ASSOCIATED WITH CARDIOMYOPATHIES

A. Dilated Cardiomyopathy (Nonischemic)

Recommendations

Class I

1. EP testing is useful to diagnose bundle-branch reentrant tachycardia and to guide ablation in patients with nonischemic DCM. (*Level of Evidence: C*)

2. EP testing is useful for diagnostic evaluation in patients with nonischemic DCM with sustained palpitations, wide-QRS-complex tachycardia, presyncope, or syncope. (*Level of Evidence: C*)
3. An ICD should be implanted in patients with nonischemic DCM and significant LV dysfunction who have sustained VT or VF, who are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: A*)
4. ICD therapy is recommended for primary prevention to reduce total mortality by a reduction in SCD in patients with nonischemic DCM who have an LVEF less than or equal to 30% to 35%, who are NYHA functional class II or III, who are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: B*) (See Section IA.)

Class IIa

1. ICD implantation can be beneficial for patients with unexplained syncope, significant LV dysfunction, and nonischemic DCM who are receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: C*)
2. ICD implantation can be effective for termination of sustained VT in patients with normal or near normal ventricular function and nonischemic DCM who are receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: C*) (See Section IA.)

Class IIb

1. Amiodarone may be considered for sustained VT or VF in patients with nonischemic DCM. (*Level of Evidence: C*)
2. Placement of an ICD might be considered in patients who have nonischemic DCM, who have LVEF of less than or equal to 30% to 35%, who are NYHA functional class I receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: C*)

Considerations taken by the Writing Committee in formulating recommendations for this section are discussed in detail in the Introduction.

Risk Stratification

The 5-y mortality for DCM has been recently estimated at 20% with SCD accounting for approximately 30% (8% to 51%) of deaths (136,137). Ventricular arrhythmias, both symptomatic and asymptomatic, are common, but syncope and SCD are infrequent initial

manifestations of the disease (138,139). The incidence of SCD is highest in patients with indicators of more advanced cardiac disease who are also at highest risk of all-cause mortality. Although VT and/or VF is considered the most common mechanism of SCD, bradycardia, pulmonary embolus, electromechanical dissociation, and other causes account for up to 50% of SCD in patients with advanced HF (140–142).

In controlled trials, amiodarone reduced the incidence of SCD in a population of patients with predominately nonischemic DCM (143) but not in a study of HF patients where the majority had CHD (144). The ICD has been shown to be superior to amiodarone for secondary prevention of VT and VF in studies where the majority of patients had CHD (49,145,146). The subgroup with nonischemic DCM in these studies benefited from the ICD more than those with CHD (147).

The Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial (148–150) randomized 458 patients with nonischemic DCM, EF less than 35%, and frequent PVCs or NSVT to receive best medical therapy with or without ICD. There was a trend toward reduction of mortality with ICD therapy, but this was not significant.

Genetic Analysis

The clinical applicability of genetic analysis to DCM is still limited as knowledge in this area does not allow genotyping most individuals clinically affected by the disease. Patients with DCM and AV block and patients with DCM and skeletal muscle diseases have higher probability of being successfully genotyped. When a pathogenetic mutation is identified, it becomes possible to establish a presymptomatic diagnosis of the disease among family members and provide them with genetic counseling to monitor progression of the disease and to assess the risk of transmitting the disease to offspring. Based on current knowledge, genetic analysis does not contribute to risk stratification in DCM.

B. Hypertrophic Cardiomyopathy

Recommendations

Class I

ICD therapy should be used for treatment in patients with hypertrophic cardiomyopathy (HCM) who have sustained VT and/or VF and who are receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: B*)

Class IIa

1. **ICD implantation can be effective for primary prophylaxis against SCD in patients with HCM who have one or more major risk factor (see Table 7) for**

Table 7. Risk Factors for Sudden Cardiac Death in Hypertrophic Cardiomyopathy

Major Risk Factors	Possible in Individual Patients
Cardiac arrest (VF)	AF
Spontaneous sustained VT	Myocardial ischemia
Family history of premature sudden death	LV outflow obstruction
Unexplained syncope	High-risk mutation
LV thickness greater than or equal to 30 mm	Intense (competitive) physical exertion
Abnormal exercise BP	
Nonsustained spontaneous VT	

Modified with permission from 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.

AF = atrial fibrillation; BP = blood pressure; LV = left ventricular; VF = ventricular fibrillation; VT = ventricular tachycardia.

SCD and who are receiving chronic optimal medical therapy and in patients who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: C)

2. Amiodarone therapy can be effective for treatment in patients with HCM with a history of sustained VT and/or VF when ICD is not feasible. (Level of Evidence: C)

Class IIb

1. EP testing may be considered for risk assessment for SCD in patients with HCM. (Level of Evidence: C)
2. Amiodarone may be considered for primary prophylaxis against SCD in patients with HCM who have one or more major risk factor for SCD (see Table 7), if ICD implantation is not feasible. (Level of Evidence: C)

Risk Stratification

Most individuals with HCM are asymptomatic and the first manifestation may be SCD (151–157). SCD is usually related to ventricular arrhythmia with a variable contribution of triggers such as ischemia, outflow obstruction, or atrial fibrillation (153–156,158). This relatively low incidence creates a challenge for risk stratification since the false-positive results for any stratifier may overwhelm the true-positive results (159). In one study, 23 of 480 patients died suddenly over a mean follow-up of 6.5 y (160). The risk of SCD was directly related to LV wall thickness with essentially no mortality over 20 y with wall thickness less than 20 mm and almost 40% for wall thickness greater than or equal to 30 mm.

A consensus document on HCM from the ACC and ESC categorized the known risk factors for SCD as “major” and “possible in individual patients” (161) as follows in Table 7.

Management

The mainstay of pharmacological management for the symptomatic patient has been beta blockers or verapamil, which probably exert their effect by reducing heart rate and decreasing contractility (153,162). Amiodarone is widely used and considered the most effective antiarrhythmic

agent, although large controlled comparative trials are not available (163,164).

Although there are no randomized studies available, the ICD has been used in patients with cardiac arrest, sustained VT or VF with a high percentage of patients receiving appropriate discharge during follow-up at a rate of 11% per year (165).

Genetic Analysis

Genetic analysis is useful in families with HCM because whenever a pathogenetic mutation is identified, it becomes possible to establish a presymptomatic diagnosis of the disease among family members and to provide them with genetic counseling to assess the risk of disease development and transmission of the disease to offspring. Genetic analysis may contribute to risk stratification in selected circumstances.

C. Arrhythmogenic Right Ventricular Cardiomyopathy

Recommendations

Class I

ICD implantation is recommended for prevention of SCD in patients with arrhythmogenic RV cardiomyopathy with documented sustained VT or VF who are receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: B)

Class IIa

1. ICD implantation can be effective for prevention of SCD in patients with arrhythmogenic RV cardiomyopathy with extensive disease, including those with LV involvement, one or more affected family member with SCD, or undiagnosed syncope when VT or VF has not been excluded as the cause of syncope, who are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: C)
2. Amiodarone or sotalol can be effective for treatment of sustained VT or VF in patients with arrhythmogenic RV cardiomyopathy when ICD implantation is not feasible. (Level of Evidence: C)
3. Ablation can be useful as adjunctive therapy in management of patients with arrhythmogenic RV cardiomyopathy with recurrent VT, despite optimal antiarrhythmic drug therapy. (Level of Evidence: C)

Class IIb

EP testing might be useful for risk assessment of SCD in patients with arrhythmogenic RV cardiomyopathy. (Level of Evidence: C)

Risk Stratification

Patients with arrhythmogenic RV cardiomyopathy (“dysplasia”) have ventricular arrhythmias with left bundle-branch block morphology that span the spectrum of simple

ventricular ectopy, sustained and NSVT, or VF. Unfortunately, SCD is frequently the first manifestation of the disease (167–169).

Management

The ICD has been used in patients with unexplained syncope, sustained VT, or VF with a high incidence of appropriate shocks (170). Although there are no specific large randomized trials in arrhythmogenic RV cardiomyopathy to support this, the situation is sufficiently “similar” to those disease states such as previous MI where these indications are well established (49,171–173).

Genetic Analysis

Genetic analysis is useful in families with RV cardiomyopathy because whenever a pathogenetic mutation is identified, it becomes possible to establish a presymptomatic diagnosis of the disease among family members and to provide them with genetic counseling to monitor the development of the disease and to assess the risk of transmitting the disease to offspring. Based on current knowledge, genetic analysis does not contribute to risk stratification of arrhythmogenic RV cardiomyopathy.

D. Neuromuscular Disorders

Recommendations

Class I

Patients with neuromuscular disorders who have ventricular arrhythmias should generally be treated in the same manner as patients without neuromuscular disorders. (Level of Evidence: A)

Class IIb

Permanent pacemaker insertion may be considered for neuromuscular diseases such as myotonic muscular dystrophy, Kearns-Sayre syndrome, Erb’s 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)

The inherited neuromuscular disorders may predispose to atrial arrhythmias, conduction defects, advanced AV block, monomorphic VT, polymorphic VT, and SCD (174–183).

The clinical presentation, indicating the potential substrate for SCD, is quite variable because SCD is a well-recognized complication of some of the neuromuscular diseases and progression of the conduction abnormalities may be unpredictable (184–190). Once cardiac involvement occurs, particularly with the muscular dystrophies, the clinician should maintain a low threshold for investigating symptoms or ECG findings to determine the need for pacemaker insertion, invasive EP studies, or ICD implantation.

XVI. HEART FAILURE

Recommendations

Class I

1. **ICD therapy is recommended for secondary prevention of SCD in patients who survived VF or hemodynamically unstable VT, or VT with syncope and who have an LVEF less than or equal to 40%, who are receiving chronic optimal medical therapy and who have a reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: A)**
2. **ICD therapy is recommended for primary prevention to reduce total mortality by a reduction in SCD in patients with LV dysfunction due to prior MI who are at least 40 d post-MI, have an LVEF less than or equal to 30% to 40%, are NYHA functional class II or III, are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: A) (See Section IA.)**
3. **ICD therapy is recommended for primary prevention to reduce total mortality by a reduction in SCD in patients with nonischemic heart disease who have an LVEF less than or equal to 30% to 35%, are NYHA functional class II or III receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: B) (See Section IA.)**
4. **Amiodarone, sotalol and/or other beta blockers are recommended pharmacological adjuncts to ICD therapy to suppress symptomatic ventricular tachyarrhythmias (both sustained and nonsustained) in otherwise optimally treated patients with HF. (Level of Evidence: C)**
5. **Amiodarone is indicated for the suppression of acute hemodynamically compromising ventricular or supraventricular tachyarrhythmias when cardioversion and/or correction of reversible causes have failed to terminate the arrhythmia or prevent its early recurrence. (Level of Evidence: B)**

Class IIa

1. **ICD therapy combined with biventricular pacing can be effective for primary prevention to reduce total mortality by a reduction in SCD, in patients with NYHA functional class III or IV receiving optimal medical therapy, in sinus rhythm with a QRS complex of at least 120 ms and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: B)**
2. **ICD therapy is reasonable for primary prevention to reduce total mortality by a reduction in SCD in patients with LV dysfunction due to prior MI who are at least 40 d post-MI, have an LVEF of less than**

or equal to 30% to 35%, are NYHA functional class I, are receiving chronic optimal medical therapy, and have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: B*) (See Section IA.)

3. ICD therapy is reasonable in patients who have recurrent stable VT, a normal or near normal LVEF, and optimally treated HF and who have a reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: C*)
4. Biventricular pacing in the absence of ICD therapy is reasonable for the prevention of SCD in patients with NYHA functional class III or IV HF, an LVEF less than or equal to 35% and a QRS complex equal to or wider than 160 ms (or at least 120 ms in the presence of other evidence of ventricular dyssynchrony) who are receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: B*)

Class IIb

1. Amiodarone, sotalol, and/or beta blockers may be considered as pharmacological alternatives to ICD therapy to suppress symptomatic ventricular tachyarrhythmias (both sustained and nonsustained) in optimally treated patients with HF for whom ICD therapy is not feasible. (*Level of Evidence: C*)
2. ICD therapy may be considered for primary prevention to reduce total mortality by a reduction in SCD in patients with nonischemic heart disease who have an LVEF of less than or equal to 30% to 35%, are NYHA functional class I receiving chronic optimal medical therapy, and who have a reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: B*) (See Section IA.)

Considerations taken by the Writing Committee in formulating recommendations for this section are discussed in detail in the Introduction.

Ventricular arrhythmias and SCD are common in patients with symptomatic acute and chronic HF and LV systolic dysfunction. The cause of HF likely influences the mechanisms and types of ventricular arrhythmias. The guidelines and comments in this section refer to patients with symptomatic HF; not just abnormal LVEF (refer to the ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult for definitions [6]).

In the setting of acute HF, ventricular arrhythmias may be especially poorly tolerated and early cardioversion should be performed, rather than attempting pharmacological termination of arrhythmia.

There is no evidence that suppression of NSVT has a favorable effect on prognosis in patients with HF (144). Thus, asymptomatic NSVT should not be treated by antiarrhythmic medication. If NSVT causes symptoms that

require therapy, amiodarone is probably the safest agent to use for treatment.

SCD accounts for approximately 50% of deaths in patients with HF. However, there is little evidence that empiric antiarrhythmic therapy can reduce the risk of SCD.

The SCD-HeFT trial showed no survival benefit to patients with HF (NYHA functional class II and III) and LVEF less than or equal to 35% treated with amiodarone empirically (8).

ICD therapy has not improved survival of patients with HF due to nonischemic DCM in 2 small trials (191,192). However, the SCD-HeFT trial demonstrated a 23% reduction in total mortality with ICD treatment in comparison to placebo (8). These results are consistent with results of DEFINITE and earlier trials of patients with CHD and LV dysfunction, some of whom had symptomatic HF (47,50,51). ICD in combination with biventricular pacing may improve survival and improve symptoms of patients with advanced HF (NYHA functional class III and IV) over short-term follow-up (1 to 2 y).

The value of biventricular pacing without additional ICD support for the reduction of SCD remains controversial (193,194).

XVII. GENETIC ARRHYTHMIA SYNDROMES

A. General Concepts for Risk Stratification

LQTS, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia (Online Mendelian Inheritance in Man [OMIM] Nos. 192500, 152427, 603830, 600919, 176261, 603796, 601144, and 604772) (195) are inherited arrhythmogenic diseases. They share genetically determined susceptibility to VT and SCD in the absence of recognizable structural abnormalities of the heart. These syndromes are by definition rare diseases because they have an estimated prevalence below 5 in 10 000 (196).

B. Long QT Syndrome

Recommendations

Class I

1. **Lifestyle modification is recommended for patients with an LQTS diagnosis (clinical and/or molecular).** (*Level of Evidence: B*)
2. **Beta blockers are recommended for patients with an LQTS clinical diagnosis (i.e., in the presence of prolonged QT interval).** (*Level of Evidence: B*)
3. **Implantation of an ICD along with use of beta blockers is recommended for LQTS patients with previous cardiac arrest and who have reasonable expectation of survival with a good functional status for more than 1 y.** (*Level of Evidence: A*)

Class IIa

1. **Beta blockers can be effective to reduce SCD in patients with a molecular LQTS analysis and normal QT interval.** (*Level of Evidence: B*)

2. **Implantation of an ICD with continued use of beta blockers can be effective to reduce SCD in LQTS patients experiencing syncope and/or VT while receiving beta blockers and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: B)**

Class IIb

1. **Left cardiac sympathetic neural denervation may be considered for LQTS patients with syncope, torsades de pointes, or cardiac arrest while receiving beta blockers. (Level of Evidence: B)**
2. **Implantation of an ICD with use of beta blockers may be considered for prophylaxis of SCD for patients in categories possibly associated with higher risk of cardiac arrest such as LQT2 and LQT3 and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: B)**

Even before the identification of the genetic subtypes, QT interval duration was identified as the strongest predictor of risk for cardiac events (syncope, SCD) in LQTS (197), and it remains so. A normal QT interval in an ungenotyped family member portends a good prognosis (198). A QTc exceeding 500 ms (corresponding to the upper QTc quartile among affected genotyped individuals) identifies patients with the highest risk of becoming symptomatic by age 40 y (199). Patients with the Jervell Lange-Nielsen and other homozygous syndromes and patients with LQTS associated with syndactyly (200,201) are at higher risk.

Patients resuscitated from SCD have an especially ominous prognosis with a relative risk of 12.9 of experiencing another cardiac arrest (202). Syncope in LQTS patients is usually attributed to severe ventricular arrhythmias, although other causes can occur.

Lifestyle Changes

It is recommended that all patients affected by LQTS avoid competitive sports activity (203). For LQT1 patients, swimming should be specifically limited or performed under supervision. LQT2 patients should avoid exposure to acoustic stimuli especially during sleep (avoidance of telephone and alarm clock on the nightstand). All patients with LQTS should avoid drugs known to prolong the QT interval and those that deplete potassium/magnesium.

Genetic Analysis

Genetic analysis is very important for identifying all mutation carriers within an LQTS family: Once identified, silent carriers of LQTS genetic defects may be treated with beta blockers for prophylaxis of life-threatening arrhythmias. Furthermore, silent mutation carriers should receive genetic counseling to learn about the risk of transmitting LQTS to offspring.

In patients affected by LQTS, genetic analysis is useful for risk stratification (199) and for making therapeutic decisions (204). Although genetic analysis is not yet widely available, it is advisable to try to make it accessible to LQTS patients.

Andersen Syndrome

Little is known about risk stratification and management of patients with Andersen syndrome. Patients seem to have ventricular arrhythmias but not a high incidence of cardiac arrest: The benefit of prophylactic treatment with beta blockers has not been defined even if most patients with prolonged QT are usually treated with these agents on empiric grounds. The beneficial role of calcium channel blockers has also been proposed on the basis of the arrhythmia-suppression observed in a single patient (205).

C. Short QT Syndrome and Brugada Syndrome

Recommendations

Class I

An ICD is indicated for Brugada syndrome patients with previous cardiac arrest receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: C)

Class IIa

1. **An ICD is reasonable for Brugada syndrome patients with spontaneous ST-segment elevation in V1, V2, or V3 who have had syncope with or without mutations demonstrated in the SCN5A gene and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: C)**
2. **Clinical monitoring for the development of a spontaneous ST-segment elevation pattern is reasonable for the management of patients with ST-segment elevation induced only with provocative pharmacological challenge with or without symptoms. (Level of Evidence: C)**
3. **An ICD is reasonable for Brugada syndrome patients with documented VT that has not resulted in cardiac arrest and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: C)**
4. **Isoproterenol can be useful to treat an electrical storm in the Brugada syndrome. (Level of Evidence: C)**

Class IIb

1. **EP testing may be considered for risk stratification in asymptomatic Brugada syndrome patients with spontaneous ST elevation with or without a mutation in the SCN5A gene. (Level of Evidence: C)**

2. **Quinidine might be reasonable for the treatment of electrical storm in patients with Brugada syndrome.** (*Level of Evidence: C*)

The Brugada syndrome is associated with a characteristically abnormal ECG and a high risk of SCD in individuals with a structurally normal heart (206).

SCD is caused by rapid polymorphic VT or VF frequently occurring at rest or during sleep. Quinidine and isoproterenol may be useful in patients with arrhythmia storm even in the presence of an ICD (207–209).

Genetic Analysis—Brugada Syndrome

Genetic analysis may help identify silent carriers of Brugada syndrome–related mutations so that they can remain under clinical monitoring to detect early manifestations of the syndrome. Furthermore, once identified, silent mutation carriers should receive genetic counseling and discuss the risk of transmitting the disease to offspring. Based on current knowledge, genetic analysis does not contribute to risk stratification.

Genetic Analysis—Short QT Syndrome

Genetic analysis may help identify silent carriers of short QT syndrome related mutations; however, the risk of cardiac events in genetically affected individuals with a normal ECG is currently not known. The risk is also unknown because of the limited number of patients with short QT syndrome identified to date. At present, genetic analysis does not contribute to risk stratification.

D. Catecholaminergic Polymorphic Ventricular Tachycardia

Recommendations

Class I

1. **Beta blockers are indicated for patients who are clinically diagnosed with catecholaminergic polymorphic VT on the basis of the presence of spontaneous or documented stress-induced ventricular arrhythmias.** (*Level of Evidence: C*)
2. **Implantation of an ICD with use of beta blockers is indicated for patients with catecholaminergic polymorphic VT who are survivors of cardiac arrest and who have reasonable expectation of survival with a good functional status for more than 1 y.** (*Level of Evidence: C*)

Class IIa

1. **Beta blockers can be effective in patients without clinical manifestations when the diagnosis of catecholaminergic polymorphic VT is established during childhood based on genetic analysis.** (*Level of Evidence: C*)
2. **Implantation of an ICD with use of beta blockers can be effective for affected patients with catecholaminergic polymorphic VT with syncope**

and/or documented sustained VT while receiving beta blockers and who have reasonable expectation of survival with a good functional status for more than 1 y. (*Level of Evidence: C*)

Class IIb

Beta blockers may be considered for patients with catecholaminergic polymorphic VT who were genetically diagnosed in adulthood and never manifested clinical symptoms of tachyarrhythmias. (*Level of Evidence: C*)

Catecholaminergic polymorphic VT is characterized by ventricular tachyarrhythmias that develop during physical activity or acute emotion in the presence of an unremarkable resting ECG (210).

Genetic Analysis

Genetic analysis may help identify silent carriers of catecholaminergic VT related mutations; once identified, silent carriers may be treated with beta blockers to reduce the risk of cardiac events and may receive appropriate genetic counseling to assess the risk of transmitting the disease to offspring. Based on current knowledge, genetic analysis does not contribute to further risk stratification.

XVIII. ARRHYTHMIAS IN STRUCTURALLY NORMAL HEARTS

A. Idiopathic Ventricular Tachycardia

Recommendations

Class I

Catheter ablation is useful in patients with structurally normal hearts with symptomatic, drug refractory VT arising from the RV or LV or in those who are drug intolerant or who do not desire long-term drug therapy. (*Level of Evidence: C*)

Class IIa

1. **EP testing is reasonable for diagnostic evaluation in patients with structurally normal hearts with palpitations or suspected outflow tract VT.** (*Level of Evidence: B*)
2. **Drug therapy with beta blockers and/or calcium channel blockers (and/or IC agents in RV outflow tract [RVOT] VT) can be useful in patients with structurally normal hearts with symptomatic VT arising from the right ventricle.** (*Level of Evidence: C*)
3. **ICD implantation can be effective therapy for termination of sustained VT in patients with normal or near normal ventricular function and no structural heart disease who are receiving chronic optimal medical therapy and who have reasonable expectation of survival for more than 1 y.** (*Level of Evidence: C*)

Demographics and Presentation of Outflow Tract Ventricular Tachycardia

VT arising from the right ventricle is the most common form of VT in apparently healthy people and is associated with a good prognosis in those without overt structural heart disease (73,76,93,97,211–221). This VT usually has a left bundle-branch, inferior axis morphology.

Clinical treatment of RVOT or LVOT VT often involves beta and calcium-channel blockers. Type IC antiarrhythmic drugs have been found useful in RVOT VT (97,214,222–225). In patients who remain symptomatic or who fail drug therapy, catheter ablation of the arrhythmia focus in the RVOT should be considered.

So-called idiopathic LV VT can arise from the LVOT or from the fascicles of the specialized conduction system. Left fascicular VT typically is reentrant and may respond to beta blockers or to calcium-channel blockers.

B. Electrolyte Disturbances

Recommendations

Class I

Potassium (and magnesium) salts are useful in treating ventricular arrhythmias secondary to hypokalemia (or hypomagnesemia) resulting from diuretic use in patients with structurally normal hearts. (Level of Evidence: B)

Class IIa

1. It is reasonable to maintain serum potassium levels above 4.0 mM/L in any patient with documented life-threatening ventricular arrhythmias and a structurally normal heart. (Level of Evidence: C)
2. It is reasonable to maintain serum potassium levels above 4.0 mM/L in patients with acute MI. (Level of Evidence: B)
3. Magnesium salts can be beneficial in the management of VT secondary to digoxin toxicity in patients with structurally normal hearts. (Level of Evidence: B)

A rapid rise in extracellular potassium, hypokalemia (less than 3.5 mM), and hypomagnesemia are all associated with ventricular arrhythmias and SCD in patients with structurally normal hearts (some of whom may have underlying channelopathies) and in an acute MI setting (226–240). Hypomagnesemia is classically associated with polymorphic VT or torsades de pointes, which together with ventricular arrhythmias in an acute MI setting, may respond to intravenous magnesium (241–244). Hypokalemia with or without hypomagnesemia may be responsible for ventricular arrhythmias in subjects with hypertension and congestive cardiac failure (precipitated by the use of thiazide and loop diuretics) (227,228,245), acute starvation (246), acute alcohol toxicity/withdrawal, and those with ventricular arrhythmias associated with digoxin and other Vaughan Williams class III antiarrhythmic drugs (238,247,248). Significant hypocalcemia can prolong the QT interval.

C. Physical and Toxic Agents

Recommendations

Class I

1. Complete abstinence from alcohol is recommended in cases where there is a suspected correlation between alcohol intake and ventricular arrhythmias. (Level of Evidence: C)
2. Persistent life-threatening ventricular arrhythmias despite abstinence from alcohol should be treated in the same manner that such arrhythmias are treated in patients with other diseases, including an ICD, as required, in patients receiving chronic optimal medical therapy and who have reasonable expectation of survival for more than 1 y. (Level of Evidence: C)

The relationship between alcohol ingestion and VT/SCD is indisputable; what is controversial however, is its exact nature (249). A number of studies claim a J-shaped relationship with risk lowest in individuals with low alcohol intake (i.e., 2 to 6 drinks per week) compared to those who rarely or never consume alcohol (250) and those with a high alcohol intake (i.e., greater than 3 to 5 drinks per day) (251,252) and binge drinking habits, the so called “holiday heart syndrome” (253–256).

D. Smoking

Recommendations

Class I

Smoking should be strongly discouraged in all patients with suspected or documented ventricular arrhythmias and/or aborted SCD. (Level of Evidence: B)

Cigarette smoking is an independent risk factor for SCD irrespective of underlying CHD (257–261). Cessation of smoking significantly reduces risk of SCD.

E. Lipids

Recommendations

Class I

Statin therapy is beneficial in patients with CHD to reduce the risk of vascular events, possibly ventricular arrhythmias, and SCD. (Level of Evidence: A)

Class IIb

n-3 polyunsaturated fatty acid supplementation may be considered for patients with ventricular arrhythmias and underlying CHD. (Level of Evidence: B)

The association of high total, VLDL, or LDL cholesterol levels, a low HDL cholesterol level together with high triglyceride and apolipoprotein B levels with increased risk of VT/SCD is almost entirely due to concurrent CHD. The effect of lipid lowering on SCD in primary prevention has

not been addressed but a relative risk reduction of 30% to 40% would be expected in parallel with the reduction in the risk of CHD death (262,263).

Free fatty acid or nonesterified fatty acid levels are also an independent risk factors for SCD but not fatal MI (264).

XIX. VENTRICULAR ARRHYTHMIAS AND SUDDEN CARDIAC DEATH RELATED TO SPECIFIC POPULATIONS

A. Athletes

Recommendations

Class I

1. **Preparticipation history and physical examination, including family history of premature or SCD and specific evidence of cardiovascular diseases such as cardiomyopathies and ion channel abnormalities is recommended in athletes. (Level of Evidence: C)**
2. **Athletes presenting with rhythm disorders, structural heart disease, or other signs or symptoms suspicious for cardiovascular disorders, should be evaluated as any other patient but with recognition of the potential uniqueness of their activity. (Level of Evidence: C)**
3. **Athletes presenting with syncope should be carefully evaluated to uncover underlying cardiovascular disease or rhythm disorder. (Level of Evidence: B)**
4. **Athletes with serious symptoms should cease competition while cardiovascular abnormalities are being fully evaluated. (Level of Evidence: C)**

Class IIb

Twelve-lead ECG and possibly echocardiography may be considered as preparticipation screening for heart disorders in athletes. (Level of Evidence: B)

It is generally accepted that preparticipation screening for medical conditions should be a requirement for clearance to participate in competitive athletics, but there are no uniformly accepted standards for screening.

The major causes of SCD in athletes are HCM (36%) and coronary artery anomalies (19%), arrhythmogenic RV cardiomyopathy, and myocarditis.

Screening of athletes is a difficult task. The low incidence of anomalies makes screening not very cost effective, although one study has suggested that ECG screening is more cost effective than echocardiographic screening (265,266).

B. Gender and Pregnancy

Recommendations

Class I

1. **Pregnant women developing hemodynamically unstable VT or VF should be electrically cardioverted or defibrillated. (Level of Evidence: B) (See Section XIII.)**

2. **In pregnant women with the LQTS who have had symptoms, it is beneficial to continue beta-blocker medications throughout pregnancy and afterward, unless there are definite contraindications. (Level of Evidence: C)**

QT Interval

Typically, women have longer QT intervals than do men, and this difference is more pronounced at slower heart rates. The incidence of both congenital and acquired forms of long QT intervals and resultant torsades de pointes is higher in women than in men (197,267). Palpitations are extremely common during pregnancy and several studies have shown an increase in the symptoms of supraventricular tachycardia (SVT) during pregnancy (268–270).

VT occurs in the absence of overt structural heart disease and may be related to elevated catecholamines (271). As such, these arrhythmias may be beta-blocker sensitive. In women presenting with new onset VT during the last 6 wk of pregnancy or in the early postpartum period, the possibility of postpartum cardiomyopathy should be ruled out (272).

Potentially life-threatening ventricular tachyarrhythmias should be terminated by electrical cardioversion. Beta 1–selective beta blockers alone, amiodarone alone (noting cautions about birth defects above) or in combination may be used, and ICD may be needed as its presence does not contraindicate future pregnancies.

C. Elderly Patients

Recommendations

Class I

1. **Elderly patients with ventricular arrhythmias should generally be treated in the same manner as younger individuals. (Level of Evidence: A)**
2. **The dosing and titration schedule of antiarrhythmic drugs prescribed to elderly patients should be adjusted to the altered pharmacokinetics of such patients. (Level of Evidence: C)**

Class III

Elderly patients with projected life expectancy less than 1 y due to major comorbidities should not receive ICD therapy. (Level of Evidence: C)

Ventricular arrhythmias are common in elderly populations and the incidence increases in the presence of structural heart disease (273–276).

Complex ventricular arrhythmias often presage new major coronary events and SCD in patients with CHD and other types of structural heart disease (277,278). The incidence of SCD increases with advancing age (279,280).

The management of ventricular arrhythmias and the prevention of SCD in elderly patients do not differ appreciably from that recommended for the general population. Despite the demonstrated efficacy in reducing all-cause mortality and SCD, beta blockers are underused in the elderly.

Several randomized, prospective trials have demonstrated the efficacy of ICDs in reducing SCD in patients with CHD at high risk for SCD (primary prevention) and in patients resuscitated from SCD (secondary prevention) when compared with antiarrhythmic drug therapy across all age groups (47,49–51,145,146).

All previously referenced studies included substantial numbers of patients over the age of 65 y. Subgroup analysis in Antiarrhythmics Versus Implantable Defibrillators (AVID) and MADIT II trials demonstrated equivalent benefits from ICD implantation in older and younger patients (49,51).

Several observational studies have shown that the invasive approach in managing patients with life-threatening ventricular arrhythmias is equally beneficial in the elderly and in younger patients (281–283). Very elderly patients with multiple comorbidities and limited life expectancy may not be appropriate candidates for ICD therapy even if they meet standard criteria.

D. Pediatric Patients

Recommendations

Class I

1. **An ICD should be implanted in pediatric survivors of a cardiac arrest, when a thorough search for a correctable cause is negative and the patients are receiving optimal medical therapy and have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: C)**
2. **Hemodynamic and EP evaluation should be performed in the young patient with symptomatic, sustained VT. (Level of Evidence: C)**
3. **ICD therapy in conjunction with pharmacological therapy is indicated for high-risk pediatric patients with a genetic basis (ion channel defects or cardiomyopathy) for either SCD or sustained ventricular arrhythmias. The decision to implant an ICD in a child must consider the risk of SCD associated with the disease, potential equivalent benefit of medical therapy as well as risk of device malfunction, infection or lead failure and that there is reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: C)**

Class IIa

1. **ICD therapy is reasonable for pediatric patients with spontaneous sustained ventricular arrhythmias associated with impaired (LVEF of 35% or less) ventricular function receiving chronic optimal medical therapy and who have reasonable expectation of survival with a good functional status for more than 1 y. (Level of Evidence: B)**
2. **Ablation can be useful in pediatric patients with symptomatic outflow tract or septal VT that is**

drug resistant, when the patient is drug intolerant or wishes not to take drugs. (Level of Evidence: C)

Class III

1. **Pharmacological treatment of isolated PVCs in pediatric patients is not recommended. (Level of Evidence: C)**
2. **Digoxin or verapamil should not be used for treatment of sustained tachycardia in infants when VT has not been excluded as a potential diagnosis. (Level of Evidence: C)**
3. **Ablation is not indicated in young patients with asymptomatic NSVT and normal ventricular function. (Level of Evidence: C)**

The incidence of SCD due to cardiovascular disease is significantly less in pediatric than adult patients.

Several groups of young patients have been identified who are at an increased risk of SCD compared to the general population. These include patients with congenital heart disease, coronary artery anomalies, cardiomyopathies, and primary arrhythmic diagnoses such as the LQTSs (284). Sustained ventricular arrhythmias may also occur in infants, most commonly an accelerated idioventricular rhythm. VF and SCD have been reported in these infants, most often following the administration of intravenous digoxin or verapamil for a presumptive diagnosis of SVT (285,286). Beyond the first year of life, most children with complex ectopy or hemodynamically tolerated VT appear to have a good prognosis (287,288).

The role and benefit of ICD implantation for prevention of SCD in young children with advanced ventricular dysfunction have not been defined. In older children and adolescents, prophylactic ICD implantation may be considered, based on data derived from adult randomized clinical trials of similar patients (8,42).

E. Patients With Implantable Cardioverter-Defibrillators

Recommendations

Class I

1. **Patients with implanted ICDs should receive regular follow-up and analysis of the device status. (Level of Evidence: C)**
2. **Implanted ICDs should be programmed to obtain optimal sensitivity and specificity. (Level of Evidence: C)**
3. **Measures should be undertaken to minimize the risk of inappropriate ICD therapies. (Level of Evidence: C)**
4. **Patients with implanted ICDs who present with incessant VT should be hospitalized for management. (Level of Evidence: C)**

Class IIa

1. Catheter ablation can be useful for patients with implanted ICDs who experience incessant or frequently recurring VT. (*Level of Evidence: B*)
2. In patients experiencing inappropriate ICD therapy, EP evaluation can be useful for diagnostic and therapeutic purposes. (*Level of Evidence: C*)

The placement of an ICD does not, in itself, decrease the incidence of arrhythmias, although the patient is protected from the consequences of the arrhythmias.

SVT may trigger ICD action due to fulfilling programmed ventricular or SVT detection criteria. Atrial fibrillation is the most frequent culprit arrhythmia.

Dual-chamber ICDs provide improved atrial diagnostic features with recording of local atrial electrograms, regularity of atrial signals, and cycle lengths.

High drug concentrations due to overdose or drug interactions generally increase risk of drug-induced arrhythmias. Table 8 lists examples of drug interactions that may cause arrhythmias.

F. Digitalis Toxicity**Recommendations****Class I**

An antidigitalis antibody is recommended for patients who present with sustained ventricular arrhythmias, advanced AV block, and/or asystole that are considered due to digitalis toxicity. (*Level of Evidence: A*)

Class IIa

1. Patients taking digitalis who present with mild cardiac toxicity (e.g., isolated ectopic beats only), can be managed effectively with recognition, continuous monitoring of cardiac rhythm, withdrawal of digitalis, restoration of normal electrolyte levels (including serum potassium greater than 4 mM/L) and oxygenation. (*Level of Evidence: C*)
2. Magnesium or pacing is reasonable for patients who take digitalis and present with severe toxicity (sustained ventricular arrhythmias, advanced AV block, and/or asystole). (*Level of Evidence: C*)

Class IIb

Dialysis for the management of hyperkalemia may be considered for patients who take digitalis and present with severe toxicity (sustained ventricular arrhythmias, advanced AV block, and/or asystole). (*Level of Evidence: C*)

Class III

Management by lidocaine or phenytoin is not recommended for patients taking digitalis and who present with severe toxicity (sustained ventricular arrhyth-

mias, advanced AV block, and/or asystole). (*Level of Evidence: C*)

Certain arrhythmias are typical: enhanced atrial, junctional, or ventricular automaticity (with ectopic beats or tachycardia) often combined with AV block.

In mild cases, management includes discontinuing the drug, monitoring rhythm, and maintaining normal serum potassium. Occasionally, temporary pacing may be needed. For more severe intoxication (serum digoxin concentration greater than 4 to 5 ng/mL, and with serious arrhythmias), the treatment of choice is digoxin-specific Fab antibody (290).

G. Drug-Induced Long QT Syndrome**Recommendations****Class I**

In patients with drug-induced LQTS, removal of the offending agent is indicated. (*Level of Evidence: A*)

Class IIa

1. Management with intravenous magnesium sulfate is reasonable for patients who take QT-prolonging drugs and present with few episodes of torsades de pointes in which the QT remains long. (*Level of Evidence: B*)
2. Atrial or ventricular pacing or isoproterenol is reasonable for patients taking QT-prolonging drugs who present with recurrent torsades de pointes. (*Level of Evidence: B*)

Class IIb

Potassium ion repletion to 4.5 to 5 mM/L may be reasonable for patients who take QT-prolonging drugs and present with few episodes of torsades de pointes in which the QT remains long. (*Level of Evidence: C*)

Marked QT prolongation, often accompanied by the morphologically distinctive polymorphic VT "torsades de pointes," occurs in 1% to 10% of patients receiving QT prolonging antiarrhythmic drugs, and much more rarely in patients receiving "noncardiovascular" drugs with QT prolonging potential. Table 9 lists those generally recognized as having QT prolonging potential. An up-to-date list is maintained at www.torsades.org and www.qt4drugs.org.

QT intervals, uncorrected for rate, are generally greater than 500 msec, prominent U waves are common, and marked QTU prolongation may only be evident on post-pause beats. Major risk factors for drug-induced torsades de pointes are listed in Table 10; often more than one is present. Drugs can expose subclinical congenital LQTS; in addition, some studies have implicated more common DNA variants (polymorphisms, with fre-

Table 8. Drug Interactions Causing Arrhythmias

Drug	Interacting Drug	Effect
Increased Concentration of Arrhythmogenic Drug		
Digoxin	Some antibiotics	By eliminating gut flora that metabolize digoxin, some antibiotics may increase digoxin bioavailability. Note: some antibiotics also interfere with P-glycoprotein (expressed in the intestine and elsewhere), another effect that can elevate digoxin concentration
Digoxin	Amiodarone	Increased digoxin bioavailability, reduced biliary and renal excretion due to P-glycoprotein inhibition
	Quinidine	
	Verapamil	
	Cyclosporine	Digoxin toxicity
	Itraconazole	
	Erythromycin	
Quinidine	Ketoconazole	Increased drug levels
Cisapride	Itraconazole	
Terfenadine, astemizole	Erythromycin*	
	Clarithromycin	
	Some calcium blockers*	
	Some HIV protease inhibitors (especially ritanovir)	
Beta blockers, propafenone	Quinidine (even ultra-low dose)	Increased beta blockade
	Fluoxetine	Increased beta blockade
Flecainide	Some tricyclic antidepressants	Increased adverse effects
		Decreased analgesia (due to failure of biotransformation to the active metabolite morphine)
Dofetilide	Verapamil	Increased plasma dofetilide concentration due to inhibition of renal excretion
	Cimetidine	
	Trimethoprim	
	Ketoconazole	
	Megestrol	
Decreased Concentration of Antiarrhythmic Drug		
Digoxin	Antacids	Decreased digoxin effect due to decreased absorption
	Rifampin	Increased P-glycoprotein activity
Quinidine, mexiletine	Rifampin, barbiturates	Induced drug metabolism
Synergistic Pharmacological Activity Causing Arrhythmias		
QT-prolonging antiarrhythmics	Diuretics	Increased torsades de pointes risk due to diuretic-induced hypokalemia
Beta blockers	Amiodarone, clonidine, digoxin, diltiazem, verapamil	Bradycardia when used in combination
Digoxin	Amiodarone, beta blockers, clonidine, diltiazem, verapamil	
Verapamil	Amiodarone, beta blockers, clonidine, digoxin, diltiazem	
Diltiazem	Amiodarone, beta blockers, clonidine, digoxin, verapamil	
Clonidine	Amiodarone, beta blockers, digoxin, diltiazem, verapamil	
Amiodarone	Beta blockers, clonidine, digoxin, diltiazem, verapamil	
Sildenafil	Nitrates	Increased and persistent vasodilation; risk of myocardial ischemia

*These may also accumulate to toxic levels with co-administration of inhibitor drugs like ketoconazole. Data are from Roden DM, Anderson ME. Proarrhythmia. In: Kass RS, Clancy CE, editors. Handbook of Experimental Pharmacology: vol. 171. Basis and Treatment of Cardiac Arrhythmias. Boston: Springer Verlag, 2006:288–304 (289).

Table 9. Examples of Drugs Causing Torsades de Pointes*

Frequent (greater than 1%) (e.g., hospitalization for monitoring recommended during drug initiation in some circumstances)

- Disopyramide
- Dofetilide
- Ibutilide
- Procainamide
- Quinidine
- Sotalol
- Ajmaline

Less frequent

- Amiodarone
- Arsenic trioxide
- Bepridil
- Cisapride
- Anti-infectives: clarithromycin, erythromycin, halofantrine, pentamidine, sparfloxacin
- Antiemetics: domperidone, droperidol
- Antipsychotics: chlorpromazine, haloperidol, mesoridazine, thioridazine, pimozide
- Opioid dependence agents: methadone

*See www.torsades.org for up-to-date listing. Adapted with permission from Roden DM. Drug-induced prolongation of the QT interval. *N Engl J Med* 2004;350:1013–22. Copyright © 2004 Massachusetts Medical Society (294).

quencies ranging up to 15% of some populations) (291,292).

Intravenous magnesium can suppress episodes of torsades de pointes without necessarily shortening QT, even when serum magnesium is normal (293). Temporary pacing is highly effective in managing torsades de pointes that is recurrent after potassium repletion and magnesium supplementation.

H. Sodium Channel Blocker–Related Toxicity

Recommendations

Class I

In patients with sodium channel blocker–related toxicity, removal of the offending agent is indicated. (Level of Evidence: A)

Class IIa

1. **Stopping the drug, reprogramming the pacemaker or repositioning leads can be useful in patients taking sodium channel blockers who present with elevated defibrillation thresholds or pacing requirement. (Level of Evidence: C)**
2. **In patients taking sodium channel blockers who present with atrial flutter with 1:1 AV conduction, withdrawal of the offending agent is reasonable. If the drug needs to be continued, additional A-V nodal blockade with diltiazem, verapamil or beta blocker or atrial flutter ablation can be effective. (Level of Evidence: C)**

Class IIb

Administration of a beta blocker and a sodium bolus may be considered for patients taking sodium chan-

nel blockers if the tachycardia becomes more frequent or more difficult to cardiovert. (Level of Evidence: C)

Arrhythmias caused by sodium channel blocking drugs are included in Table 11. Antiarrhythmic drugs are the most common precipitants, although other agents, notably tricyclic antidepressants and cocaine, may produce some of their toxicities through these mechanisms. In large clinical trials, sodium channel blocking drugs have increased mortality among patients convalescing from myocardial infarction.

Animal and clinical anecdotes suggest that administration of sodium, as sodium chloride or sodium bicarbonate, may be effective in the reversing conduction slowing or frequent or cardioversion-resistant VT (295,296). Beta blockers have also been used successfully (297).

I. Tricyclic Antidepressant Overdose

Tricyclic antidepressants are second only to analgesics as a cause of serious overdose toxicity. Typical cardiac manifestations include sinus tachycardia, and PR and QRS prolongation and occasionally a Brugada syndrome-like ECG (298).

QRS duration can be shortened in experimental animals and in humans by administration of NaHCO₃ or NaCl boluses (299). Antipsychotic agents well known to produce marked QT prolongation and torsades de pointes include thioridazine and haloperidol.

J. Other Drug-Induced Toxicity

Recommendations

Class I

1. **High intermittent doses and cumulative doses exceeding the recommended levels should be avoided in patients receiving anthracyclines such as doxorubicin. (Level of Evidence: B)**

Table 10. Risk Factors for Drug-Induced Torsades de Pointes

- Female gender
- Hypokalemia
- Bradycardia
- Recent conversion from atrial fibrillation
- Congestive heart failure
- Digitalis therapy
- High drug concentrations (*exception: quinidine*), often due to drug interactions
- Rapid rate of intravenous drug administration
- Baseline QT prolongation
- Ventricular arrhythmia
- Left ventricular hypertrophy
- Congenital long QT syndrome
- Certain DNA polymorphisms
- Severe hypomagnesemia
- Concomitant use of 2 or more drugs that prolong the QT interval
- Combination of QT-prolonging drug with its metabolic inhibitor

Adapted with permission from Roden DM. Drug-induced prolongation of the QT interval. *N Engl J Med* 2004;350:1013–22. Copyright © 2004 Massachusetts Medical Society (294).

DNA = deoxyribonucleic acid.

Table 11. Syndromes of Drug-Induced Arrhythmia and Their Management

Drugs	Clinical Setting	Management*
Digitalis	Mild cardiac toxicity (isolated arrhythmias only) Severe toxicity: sustained ventricular arrhythmias; advanced AV block; asystole	Anti-digitalis antibody Pacing Dialysis for hyperkalemia
QT-prolonging drugs	Torsades de pointes: few episodes, QT remains long Recurrent torsades de pointes	IV magnesium sulfate (MgSO ₄) Replete potassium (K ⁺) to 4.5 to 5 mEq/L Ventricular pacing Isoproterenol
Sodium channel blockers	Elevated defibrillation or pacing requirement Atrial flutter with 1:1 AV conduction Ventricular tachycardia (more frequent; difficult to cardiovert) Brugada syndrome	Stop drug; reposition leads Diltiazem, verapamil, beta blocker (IV) Beta blocker; sodium Stop drug; treat arrhythmia

*Always includes recognition, continuous monitoring of cardiac rhythm, withdrawal of offending agents, restoration of normal electrolytes (including serum potassium to greater than 4 mEq/L), and oxygenation. The order shown is not meant to represent the preferred sequence when more than one treatment is listed.
AV = atrioventricular; IV = intravenous.

- All patients receiving 5-fluorouracil therapy should receive close supervision and immediate discontinuation of the infusion if symptoms or signs of myocardial ischemia occur. Further treatment with 5-fluorouracil must be avoided in these individuals. (Level of Evidence: C)**
- Patients with known cardiac disease should have a full cardiac assessment including echocardiography, which should be undertaken prior to use of anthracyclines such as doxorubicin, and regular long-term follow up should be considered. (Level of Evidence: C)**

Anthracycline cardiotoxicity is dose dependent with intermittent high doses and higher cumulative doses increasing the risk of cardiomyopathy and lethal arrhythmias (300,301). Risk factors include younger age, female gender, and use of trastuzimab (300,302–304). This form of cardiomyopathy can occur acutely soon after treatment, within a few months of treatment (the so called subacute) form, or many years later (301,305–311).

5-Fluorouracil causes lethal and potentially fatal arrhythmias irrespective of underlying coronary disease during the acute infusion period, the vast majority during the first administration (312). Cardiac monitoring during the infusion period, especially the first, is recommended for all patients receiving 5-fluorouracil therapy.

Cocaine has both slow offset sodium channel–blocking properties as well as QT-prolonging (I_{Kr}-blocking) properties. Arrhythmias associated with cocaine ingestion include wide-complex tachycardias suggestive of sodium channel block (and responding to sodium infusion) as well as torsades de pointes. Cocaine also causes other cardiovascular complications that can lead to arrhythmias, notably myocarditis and coronary spasm.

XX. CONCLUSIONS

SCD continues to be a major cause of mortality in all developed countries. Using an evidence-based approach, this document attempts to summarize the latest information addressing the problem, trying as much as possible to provide recommendations consistent with previous documents. However, it is important to stress that the field is evolving and recommendations will certainly change as we learn more about the problem. The lengthy list of references serves as an indication of the large amount of research addressing SCD already, and undoubtedly, the list will continue to grow in the future. Timely updates of this information will be critical as we try to care for patients at risk of SCD.

APPENDIX 1. Author Relationships With Industry for the ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death

Committee Member	Research Grant	Speakers Bureau	Stock Ownership	Board of Directors	Consultant/Advisory Member
Martin Borggrefe, MD	• Medtronic Inc.	None	None	None	• Procter & Gamble • Impulse Dynamics • Synecor
Alfred E. Buxton, MD	• Medtronic Inc. • Guidant Corp. • St. Jude Medical	None	None	None	• Medtronic Inc. • General Electric
A. John Camm, MD	• Pfizer Inc.	• St. Jude Medical • Medtronic Inc. • Vitatron	• Cameron Health (small number of share options, less than US \$5000)	None	• Vitatron • St. Jude Medical • Procter & Gamble • Servier • GlaxoSmithKline • Guidant Corp. • Wyeth • Johnson & Johnson • Sanofi-Aventis • Cardiome • Astellas • Cryocor • Point • CV Therapeutics Inc.
Bernard R. Chaitman, MD	• Pfizer Inc. • Aventis Inc. • Berlex • Procter & Gamble • CV Therapeutics Inc.	• Pfizer Inc. • Merck Inc.	None	None	• Aventis Inc. • CV Therapeutics Inc.
Martin Fromer, MD	None	None	None	None	None
Gabriel Gregoratos, MD	None	• Pfizer Inc.	None	None	• CV Therapeutics Inc. • GlaxoSmithKline
George J. Klein, MD	None	None	None	• Cryocath Technologies	• Medtronic Inc.
Arthur J. Moss, MD	• Guidant Corp. • Medtronic Inc.	None	None	None	• CV Therapeutics Inc.
Robert J. Myerburg, MD	None	• Berlex • Procter & Gamble • Guidant Corp. • Reliant Pharmaceuticals	None	None	• Berlex • Procter & Gamble • Reliant Pharmaceuticals • Medifacts Corp.
Silvia G. Priori, MD	• Medtronic Inc.	None	None	None	• Pfizer Inc. • CV Therapeutics Inc. • Guidant Corp. • Medtronic Inc.
Miguel A. Quinones, MD	None	None	None	None	• Procter & Gamble
Dan M. Roden, MD	• Co-investigator for colleagues who have grants from Medtronic Inc., St. Jude Medical, receives no compensation from these grants	None	• No stocks valued greater than \$10,000	None	• Abbott • Alza • Arpida • Astra-Zeneca • Bristol-Myers Squibb • EBR Systems • First Genetic Trust • Lexicon • Lundbeck • Medtronic Inc.

APPENDIX 1. Continued

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Dan M. Roden, MD (continued)					<ul style="list-style-type: none"> • Merck Inc. • NPS Pharmaceuticals • Novartis • Pfizer Inc. • Johnson & Johnson • GlaxoSmithKline • CV Therapeutics Inc. • Genzyme • Sanofi-Synthelabo Groupe • Solvay Pharmaceuticals • Thornton Medical • Wyeth • Yamanouchi
Michael J. Silka, MD	None	None	None	None	<ul style="list-style-type: none"> • General Electric
Cynthia M. Tracy, MD	<ul style="list-style-type: none"> • Medtronic Inc. • Guidant Corp. 	None	None	None	None
Douglas P. Zipes, MD	<ul style="list-style-type: none"> • Medtronic Inc. 	None	<ul style="list-style-type: none"> • MVMD 	None	<ul style="list-style-type: none"> • Michael Marcus and Associates Science Partners, LLC, limited partner • GMP Companies Inc. • Medtronic Inc. • Aderis Pharmaceuticals Inc. • Terumo Cardiovascular Systems Corp. • Life Sentry • CV Therapeutics Inc. • Burrill and Company • Genzyme • Cardiofocus • Solvay Pharmaceuticals • Physical Logic

This table represents the relevant relationships of authors with industry to this topic that were reported orally at the initial writing committee meeting in May 2003 and updated in conjunction with all meetings and conference calls of the writing committee. It does not reflect any actual or potential relationships at the time of publication.

APPENDIX 2. External Peer Review Relationships With Industry for the ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death

Committee Member*†	Representation	Research Grant	Speakers Bureau	Stock Ownership	Board of Directors	Consultant/Advisory Member
Dr. John Di Marco	• Official Reviewer—AHA	• Guidant	• Guidant	None	None	• Novartis
Dr. John Field	• Official Reviewer—AHA	None	None	None	None	None
Dr. Bruce Lindsay	• Official Reviewer—ACCF Board of Trustees	None	None	None	None	• Guidant • Medtronic
Dr. Richard L. Page	• Official Reviewer—ACC/AHA Task Force on Practice Guidelines	None	None	None	None	• Procter & Gamble (no longer very active, less than \$10,000 last 2 years)
Dr. Karl Stajduhar	• Official Reviewer—ACCF Board of Governors	• Sanofi	None	None	None	None
Dr. Elliott M. Antman	• Content Reviewer—ACC/AHA Task Force on Practice Guidelines	None	None	None	None	None
Dr. Angelo Auricchio	• Content Reviewer—ESC	None	None	None	None	None
Dr. Jean-Jacques Blanc	• Content Reviewer—ESC	None	None	None	None	None
Dr. Guenther Breithardt	• Content Reviewer—ESC	• Guidant • Medtronic • Biotran	• Guidant • Medtronic			• Guidant • Medtronic • Abbott • Johnson & Johnson
Dr. Mark Carlson	• Content Reviewer—ACCF Clinical EP Committee	None	None	• Atricure	None	• Atricure • Cameron Health • St. Jude Medical • St. Jude Medical
Dr. Paolo Della Bella	• Content Reviewer—ESC	None	None	None	None	None
Dr. Andrew Epstein	• Content Reviewer—ACC/AHA/HRS Pacemaker Guidelines	• Guidant • Medtronic • St. Jude Medical	• Guidant • Medtronic • St. Jude Medical	None	None	None
Dr. Sharon Hunt	• Content Reviewer—ACC/AHA HF Guidelines, ACC/AHA Task Force on Practice Guidelines	None	None	None	None	None
Dr. Guillaume Jondeau	• Content Reviewer—ESC	None	None	None	None	None
Dr. Alan Kadish	• Content Reviewer—Individual Reviewer	• St. Jude Medical	St. Jude Medical	• Medtronic • St. Jude Medical	None	None
Dr. Cecilia Linde	• Content Reviewer—ESC	• Medtronic	None	None	None	• St. Jude Medical
Dr. Jonathan Linder	• Content Reviewer—ACCF Task Force on Clinical Expert Consensus Documents	None	None	• Targeson	None	None

APPENDIX 2. Continued

Committee Member*†	Representation	Research Grant	Speakers Bureau	Stock Ownership	Board of Directors	Consultant/Advisory Member
Dr. Christine Albert	• Content Reviewer—AHA, ECG & Arrhythmias Committee	None	None	None	None	None
Dr. Carina Blomstrom-Lundquist	• Content Reviewer—ESC, ACC/AHA/ESC Supraventricular Arrhythmias Guidelines	None	None	None	None	None
Dr. Ali Oto	• Content Reviewer—ESC	None	None	None	None	None
Dr. Alexander Parkomenko	• Content Reviewer—ESC	None	None	None	None	None
Dr. Richard Sutton	• Content Reviewer—ESC	None	None	None	None	None
Dr. Josep Brugada Terradellas	• Content Reviewer—ESC	None	None	None	None	None
Dr. Panos Vardas	• Content Reviewer—ESC	None	None	None	None	None
Dr. Sami Viskin	• Content Reviewer—ESC	None	None	None	None	None
Dr. David Wilber	• Content Reviewer—Individual Reviewer	• Biosense/ Webster • BAND • Guidant • Medtronic • St. Jude Medical	• Medtronic	None	None	• Biosense/Webster • Guidant
Dr. Antonio ZaZa	• Content Reviewer—ESC	None	None	None	None	None
Dr. L. Brent Mitchell	• Organizational Reviewer—HRS	None	None	None	None	None
Dr. Thomas Munger	• Organizational Reviewer—HRS	None	None	None	None	None

This table represents the relevant relationships of peer reviewers with industry to this topic that were disclosed at the time of peer review of this guideline. It does not necessarily reflect relationships with industry at the time of publication. *Participation in the peer review process does not imply endorsement of the document. †Names are listed in alphabetical order within each category of review.

APPENDIX 3

Ventricular Arrhythmias and SCD Acronyms and Abbreviations

- ACS = acute coronary syndromes
- AED = automated external defibrillator
- AMIOVERT = Amiodarone Versus Implantable Cardioverter-Defibrillator
- AV = atrioventricular
- AVID = Antiarrhythmics Versus Implantable Defibrillators
- CABG Patch Trial = Coronary Artery Bypass Graft Patch Trial
- CASH = Cardiac Arrest Study Hamburg
- CHD = coronary heart disease
- CT = computed tomography

- DCM = dilated cardiomyopathy
- DEFINITE = Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation
- ECG = electrocardiogram
- EF = ejection fraction
- EP = electrophysiological
- HCM = hypertrophic cardiomyopathy
- HF = heart failure
- ICD = implantable cardioverter-defibrillator
- LV = left ventricular
- LVEF = left ventricular ejection fraction
- LVOT = left ventricular outflow tract
- LQTS = long QT syndrome
- MADIT II = Multicenter Automatic Defibrillator Implantation Trial II

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MI = myocardial infarction
 MRI = magnetic resonance imaging
 MUSTT = Multicenter UnSustained Tachycardia Trial
 NSVT = nonsustained ventricular tachycardia
 NYHA = New York Heart Association
 PVC = premature ventricular complex
 RV = right ventricular
 RVOT = right ventricular outflow tract
 SCD = sudden cardiac death
 SCD-HeFT = Sudden Cardiac Death in Heart Failure Trial
 SCN5A = cardiac sodium channel gene
 SPECT = single-photon emission computed tomography
 SVT = supraventricular tachycardia
 VF = ventricular fibrillation
 VT = ventricular tachycardia

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