

The ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: Their Relevance to the Cardiologist, Internist and Family Physician

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The purpose of this review is to highlight the important and new features of the 2008 Guidelines published in *Circulation*, the *Journal of the American College of Cardiology* and *Heart Rhythm Journal* in 2008¹⁻³ and available online (<http://tinyurl.com/d9lygp>). This comprehensive document, coauthored by a committee of highly respected physicians, contains 527 references, the latest of which have been used to update the current recommendations. The salient features of the guidelines for internal cardioverter-defibrillators (ICDs) and permanent pacemakers (PPMs) will be emphasized.

Risk stratification was accomplished by weighing the evidence from published trials. The highest level of evidence (A) is derived from several randomized clinical trials in multiple populations. With limited populations from a single randomized trial or non-randomized studies, the level is graded as (B). With only limited populations, consensus or expert opinion, the level of evidence is (C). It is important to note that, in rare conditions, there may not be sufficient data for large randomized trials, and the consensus or expert opinion is the only data available.

The greater the potential benefit to the patient, the more reason there is to recommend the procedure. Thus, classes are established with the highest benefit >>> risk (Class I); benefit >> risk (Class IIA); benefit > or equal to risk (Class IIB). If the risk is \geq to the benefit, the procedure is contraindicated and should not be performed (Class III).

The language used in the document is very specific and has a very definite meaning for therapy: *Class I* (is indicated, is recommended); *Class Iia* (is reasonable); *Class Iib* (may be considered); *Class III* (is not recommended). For this reason, in this review, the same terminology will be used, as will specific language as it applies to the disorder discussed.

The proper selection of the patient for a particular procedure is crucial, not only for the best care of the patient, but also for the healthcare system. With the current financial crisis and limited resources, it is important to correctly risk-stratify patients so they will receive appropriate treatment, that those who will benefit from device therapy not be overlooked, and that those who will not benefit will not receive an unnecessary device that will not prolong meaningful life (the last is a triple-negative, but the meaning is clear!).

The author recommends that physicians have the guidelines readily available. As an example of how the recommendations are applied, note one of the changes from the 2002 Guidelines. The MADIT-II criteria for an ICD were upgraded from Class IIA to Class I. As the level of evidence increased with more review of the data, the committee determined that if the patient meets the criteria (remote myocardial infarction [MI], ischemic cardiomyopathy, left ventricular ejection fraction (LVEF) ≤ 0.30 , the procedure *should be performed* (rather than *is reasonable* to perform).

The committee made some general comments on the formulation of this document. Mortality refers to "all-cause mortality". Comorbidities, life expectancy (defined as "reasonable expectation of survival with a good functional status for more than one year") and quality of life should be addressed. Patients receiving devices should have a thorough search for all inciting causes (*e.g.*, nonessential drug therapy that could be eliminated). The committee recognized that patients have the right to decline a recommendation, even if guidelines are met. They emphasized that guidelines apply to most patients, but may require modification for a situation that only the primary treating physician can evaluate.

Internal Cardioverter-Defibrillators

The review will focus first on ICD therapy. The differences between ICDs and PPMs are not always recognized by the public. Sometimes this misperception is fostered by the media. Several years ago, a prominent politician received an ICD, but the press described it as a "pacemaker plus" (perhaps to allay concern for his health). For the lay public who may read this article, PPMs pace the heart when the heartbeat is too slow. ICDs perform this function, as well as having the ability to terminate life-threatening arrhythmias by shocking or pacing the heart back to normal. If a patient meets the criteria both for a PPM and for an ICD, the ICD is the device that should be implanted.

The indications for ICD implantation have expanded from preventing sudden death in ischemic, nonischemic and other cardiomyopathies, to their application in certain genetic disorders. The majority of studies have been performed in patients with coronary artery disease and fewer in patients with nonischemic cardiomyopathy. With various studies using different criteria for the populations studied, the line between primary and secondary prevention became less defined. Another difficulty arose with the different criteria for LVEF (0.30, 0.35, 0.40) along with the concerns about standardization in making this measurement. The committee recommended "that the clinician use the LVEF

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determination that they believe is the most clinically accurate and appropriate in their institution.”

In general, anyone who suffers a cardiac arrest or sustained ventricular tachycardia has an indication for an ICD, unless there is transient remediable cause. It holds true for patients with syncope who undergo an electrophysiology study (EPS) and demonstrate inducible ventricular tachycardia/ventricular fibrillation (VT/VF). Note that myocardial revascularization is not considered sufficient therapy in those with prior MI, but may be useful if the etiology of the event was acute myocardial ischemia in the absence of prior MI. Patients with electrolyte abnormalities discovered at the time of cardiac arrest should be considered the same as if these were absent, since some abnormalities are related to acute changes during the resuscitation. Similarly, in patients with modest enzyme elevation during the episode of sustained VT/VF, the physician should not assume that ischemia or an infarct was the primary event.

There is no longer any question that ICD therapy is the preferred strategy for patients with structural heart disease at risk for sudden cardiac death (SCD). Antiarrhythmic drug therapy is a second choice without any guarantees.

Coronary artery disease. The reader is referred to the article for an in-depth discussion of the multiple trials in patients with coronary artery disease. ICD is indicated and should be recommended to the following groups of patients: (a) prior MI (at least 40 days post infarct), LVEF < 0.30 in New York Heart Association (NYHA) Functional Class I (MADIT-II criteria); (b) prior MI (at least 40 days post infarct, LVEF < 0.35 due to prior MI, in New York Heart Association (NYHA) Functional Class II–III (SCD-HeFT criteria); (c) nonsustained VT, LVEF < 0.40 due to prior MI and inducible, sustained VT or VF at EPS (MUSTT).

Nonischemic dilated cardiomyopathy (DCM). Nonischemic DCM has been a problem diagnosis for the electrophysiologist, since risk stratification is not as simple as with coronary disease. A number of trials have demonstrated trends. Nevertheless, if the patient experienced cardiac arrest or sustained VT, ICD remains the treatment of choice and is also indicated for those with a LVEF < 0.35 in NYHA Functional Classes II–III (SCD-HeFT criteria). For those patients with unexplained syncope and significant LV dysfunction, ICD implantation is reasonable. It can be considered for patients with an LVEF < 0.35 in NYHA Functional Class I.

Hypertrophic cardiomyopathy (HCM). HCM is the diagnosis that immediately comes to mind when the young athlete suffers a cardiac arrest. However, HCM may be more prevalent than generally thought. The incidence is 1/500 in the general population. ICD therapy is again recommended for all survivors of sudden cardiac arrest. Major risk factors include prior cardiac arrest, spontaneous sustained or nonsustained VT, family history of SCD, syncope, LV thickness > 30 mm and an abnormal blood pressure response to exercise (flat or hypotensive). Other risk factors, perhaps of lesser importance, include atrial fibrillation (AF), myocardial ischemia, LV outflow obstruction, high-risk mutations and competitive physical exertion. ICD implantation is reasonable for those with one or more major risk factors.

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C). The committee recognized ARVD/C as a

reason for sudden death in young individuals during exercise. Interrogation of ICDs implanted in these individuals has demonstrated frequent appropriate shocks and a low incidence of death. Risk stratification is not complete in this disorder, but those with a previous cardiac arrest, syncope with VT, extensive RV disease or LV involvement, polymorphic VT, RV aneurysm (associated with a locus on chromosome 1q42–43) seem to have higher risk. Thus, ICD implantation is reasonable for ARVD/C patients with one or more risk factors for SCD.

Long QT, short QT, Brugada, PMVT syndromes. Patients with other genetic disorders including long QT, short QT, Brugada and catecholaminergic polymorphic VT syndromes with a risk of SCD benefit from ICD implantation, which is now recommended if the patient has experienced a prior cardiac arrest or syncope. Without any good medical alternatives, ICD implantation may be considered for primary prevention in those with a family history of early mortality.

Unexplained syncope. Some patients with syncope who do not fit into any recognized indication undergo an EPS. If inducible into sustained VT, this arrhythmia is presumed to be the cause of syncope, and these patients can be offered the protection of an ICD.

Permanent Pacemaker (PPM)

Indications for a PPM are more intuitive than some of the newer indications for an ICD. As a general rule, symptomatic bradycardia is an indication for a pacemaker. One of the most common reasons is sinus node dysfunction due to degeneration of the conduction system, often affecting distal conduction as well. The committee makes the important point that a physiological bradycardia, *e.g.*, due to training in an athlete is not an indication for a pacemaker.

Another extremely important point emphasized in the guidelines was the avoidance of unnecessary ventricular pacing. A number of studies, both in patients with PPM and ICD, demonstrated the deleterious effects of right ventricular apical pacing. Pacing from other RV sites has been performed but more comparative studies are needed before a definitive statement is made. (It is the belief of a number of electrophysiologists, including this author, that pacing from the RV outflow tract, rather than the apex, is preferable and advantageous).

Considerations regarding sinus node dysfunction. In sinus node dysfunction, a PPM is indicated for documented symptomatic bradycardia including frequent pauses resulting in symptoms, symptomatic chronotropic incompetence and symptomatic bradycardia as a result of needed drug therapy.

It is reasonable to implant a PPM if the heart rate is < 40 beats per minute (bpm), even if the relationship between symptoms and bradycardia is less well defined. It is known that electrophysiologic measures of sinus node function may exist in patients who are not symptomatic. However, with syncope and EPS-documented sinus node dysfunction, a PPM is reasonable.

A PPM may be considered in minimally symptomatic patients with a chronic heart rate of < 40 while awake.

A PPM is not indicated in asymptomatic patients with sinus node dysfunction when the symptoms are clearly not related to

the bradycardia and when medications causing bradycardia are nonessential and can be discontinued.

Considerations regarding atrioventricular (A-V) block.

A-V block can occur at different levels in the conduction system: above, within and below the His bundle, often with different outcomes. In complete heart block, a PPM should be considered, even when the ventricular response is > 40 beats per minute, since this numerical value was not derived from clinical trial data. The committee emphasizes that it is the site of origin of the escape rhythm that determines the outcome. The reader is referred to the article for an in-depth review.

Whereas sinus pauses of 3 seconds are considered a criterion for sinus node dysfunction, pauses of > 5 seconds are considered related to advanced second-degree A-V block in the patient with AF.

The P-R interval is important for some patients with markedly prolonged first-degree A-V block in which atrial contraction occurs before atrial filling is complete, resulting in hemodynamic abnormalities and a reduction in cardiac output.

The reader is warned about reversible causes of A-V block such as in Lyme disease, in which the problem should resolve spontaneously. Conversely, in some diseases such as cardiac sarcoid or amyloid, A-V block may be transient, but likely to recur and merit therapy.

A PPM is indicated for third-degree and advanced second-degree A-V block at any anatomic level: if the patient has symptomatic bradycardia (including heart failure) or related ventricular arrhythmias; if due to needed drug therapy; with documented ≥ 3 -second pauses in sinus rhythm; with ≥ 5 -second pauses in awake patients with AF; with escape rates < 40 bpm; with escape rhythms below the A-V node; after A-V junction ablation; with nonresolving A-V block post cardiac surgery; with certain neuromuscular disorders (myotonic muscular dystrophy, Kearns-Sayre syndrome, Erb dystrophy).

Other special circumstances in which a PPM is indicated include symptomatic bradycardia with second-degree A-V block, regardless of the site of block; asymptomatic third-degree A-V block with cardiomegaly or LV dysfunction; and exercise-induced second- or third-degree A-V block in the absence of ischemia.

Now for the patients in whom a PPM is reasonable: asymptomatic patients without cardiomegaly with third-degree A-V block and an escape rate > 40 bpm; asymptomatic individuals with second-degree A-V block and intra- or infra-His block at EPS; first- or second-degree block with symptoms similar to pacemaker syndrome (due to long A-V delays); and asymptomatic Type II second-degree A-V block with a narrow QRS.

Finally, the practitioner should consider a PPM for those patients with neuromuscular disorders, as mentioned above, even if they have only first-degree A-V block, since the progression of conduction system disease is unpredictable.

A PPM should not be implanted for asymptomatic first-degree A-V block; asymptomatic second-degree A-V block at the level of the A-V node (supra-His); or if A-V block is expected to resolve (*e.g.*, Lyme disease, toxicity, transient vagotonia or hypoxia in sleep apnea).

Bifascicular block. The take-home message for bifascicular block is that the number of patients with this conduction

disturbance is large, and the rate of progression to complete heart block is low.

A PPM is indicated when there is Type II or advanced second-degree or intermittent third-degree A-V block, or if there is alternating bundle branch block.

A PPM is reasonable if the patient experiences syncope without any other likely cause; if EPS reveals a markedly prolonged H-V interval (≥ 100 msec); or if EPS demonstrates pathological pacing-induced intra-His block.

A PPM may be considered for those neuromuscular disorders, as described above.

A PPM should not be implanted in the absence of A-V block (or only first-degree) or symptoms.

Special considerations for A-V block associated with acute MI. In most cases, the development of A-V block associated with the acute phase of MI represents extensive myocardial damage and will have prognostic indications. The physician must remember this fact, as it will have major implications if pacing is required. For the patient at high risk of sudden death, an ICD rather than a PPM may be indicated (sometimes with resynchronization therapy).

Permanent pacing is indicated after the acute phase of MI: with persistent second-degree A-V block in the His-Purkinje system; with alternating bundle branch block; or with third-degree A-V block within or below the His; for transient second- or third-degree infranodal A-V block and associated bundle branch block; and for symptomatic second- or third-degree A-V block.

The physician should consider pacing for persistent second- or third-degree A-V block at the level of the A-V node, even if the patient is asymptomatic.

Permanent pacing is not indicated for transient A-V block in the absence of intraventricular conduction defects; left anterior fascicular block; new bundle branch or fascicular block in the absence of A-V block; or asymptomatic first-degree block in the presence of bundle branch or fascicular block.

Neurocardiogenic syncope and hypersensitive carotid sinus syncope. Almost all patients referred for neurally mediated hypotension or hypersensitive carotid sinus syncope can be treated medically. The tilt-table test has been quite useful in assessing these patients. A variety of medications and liberalization of salt intake has been helpful in most situations. Pacing has little benefit with a primarily vasodepressor response. Nevertheless, there are rare patients who fail to respond and for whom pacing is a consideration. Patients at high risk include those with little or no prodrome, profound bradycardia or asystole. Pacemakers with rate-drop features can be particularly helpful.

A PPM is indicated in recurrent syncope caused by spontaneously occurring carotid sinus stimulation that induces ventricular asystole of > 3 seconds. It is reasonable, even if there are no clear provocative events and > 3 seconds of asystole. It may be considered for neurocardiogenic syncope associated with bradycardia documented spontaneously or at the time of tilt-table testing.

A PPM should not be implanted for situational vasovagal syncope in which avoidance behavior is effective and preferred, or if the cardio-inhibitory response to carotid sinus stimulation is asymptomatic or vague.

Cardiac Resynchronization Therapy (CRT)

As noted above, RV apical pacing may be deleterious, particularly in patients with impaired LV function. Native left bundle branch block (LBBB) also disturbs conduction and then results in adverse remodeling of LV contraction. As a result, the patient may develop congestive heart failure. The best strategy today is to avoid RV apical pacing. For those with heart failure due to LBBB conduction and remodeling (or possibly as a result of RV apical pacing — note the guidelines state that for this entity, there is current insufficient evidence), CRT may be beneficial. It is achieved by pacing the left ventricle through a branch vein of the coronary sinus. The reader is referred to the guidelines for a detailed review of the studies that indicated an improvement in clinical status and mortality.

Currently, CRT is indicated for patients with a LVEF \leq 0.35, a QRS $>$ 0.12 seconds, sinus rhythm and NYHA Functional Classes III–IV while on optimal medical therapy. It is reasonable if the patient has AF, or if the patient has frequent dependence on ventricular pacing. CRT may be considered if the LVEF is $<$ 0.35, with NYHA Functional Class I–II on optimal therapy, and if the patient is undergoing PPM or ICD implantation with anticipated frequent ventricular pacing.

CRT is not indicated for asymptomatic patients or for those whose functional status and life expectancy are limited by chronic noncardiac conditions.

It is expected that the CRT indications will be further defined and refined in the near future.

Other New Additions to the Guidelines

Also included are recommendations for the selection of PPM/ICD and for follow up, quality-of-life (QOL) considerations, comments about patient longevity/comorbidities, cost/efficacy and terminal care.

Selection of the pacing mode is addressed with an emphasis on avoiding unnecessary RV apical pacing. Alternate-site RV pacing or CRT should be considered. The use of antitachycardia pacing as the first-line therapy in ICD patients can reliably terminate slow VT in 85–90% of cases. All devices require proper follow up in the outpatient office. Today, follow up can be performed transtelephonically as well as face-to-face in the clinic. Specific recommendations are provided.

QOL issues are addressed and range from psychological issues to inappropriate shocks. In fact, ICD therapy in general has been well tolerated and may even be associated with a better QOL. Most inappropriate shocks have been associated with AF, with a rapid ventricular response fulfilling the rate criteria for ICD therapy. Better programming, improved discrimination algorithms and tailored drug therapy may minimize these occurrences.

The committee found that even though age is a factor in outcome, even octogenarians may have a survival of $>$ 4 years. Age alone should not be used as a criterion to withhold device therapy. The physician must include in the decision-making process the indication for the device (primary versus secondary prevention), the existing comorbidities and the patient's own preference.

The ICD is cost effective, provided that proper patient selection has been accomplished. Consequently, it is imperative that the physician be aware of the guidelines, select the appropriate candidates and refer them when the benefit is greater than the risk.

A difficult but sometimes unavoidable situation is how to manage terminally ill patients. The guidelines provide the appropriate guidance in this matter. It is important to know that withholding and withdrawing life-sustaining treatments from terminally ill patients who do not want the treatment is ethical and legal in the United States.

Dying patients and/or their healthcare proxy may request termination of ICD and/or pacing therapy. The physician must fully inform them of the consequences and document the conversation in the medical record. Deactivation of the device should be accompanied by a do-not-resuscitate order written in the medical record. Impaired decision-making capacity merits a psychiatric consultation. If clinicians disagree, an ethics consultation should be sought. If a clinician has personal beliefs that prevent deactivating a device, care of the patient may be transferred to a colleague.

Final Comments

A recent article in the *Journal of the American Medical Association*⁴ concluded that recommendations issued in current ACC/AHA clinical guidelines were largely developed from lower levels of evidence of expert opinion and suffer from a lack of conclusive evidence. The authors concluded there is a need to improve the process of writing guidelines and expanding the evidence base. There can be little disagreement that the better the scientific data and population data, the better the guidelines. However, the current guidelines represent the best data we have now, represent the best analyses from the experts in our field and currently sets the standards.

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