JAMA Clinical Guidelines Synopsis

Primary Prevention of Sudden Cardiac Death

Andrew D. Beaser, MD; Adam S. Cifu, MD; Hemal M. Nayak, MD

GUIDELINE TITLE 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death

RELEASE DATE September 25, 2018

PRIOR VERSIONS 2008 ACC/AHA/HRS Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities (specifically sections on indications for implantable cardioverter-defibrillators [ICDs])

DEVELOPER American College of Cardiology (ACC), American Heart Association (AHA), and Heart Rhythm Society (HRS)

FUNDING SOURCE ACC and AHA

TARGET POPULATION Adult patients with ventricular arrhythmias or at risk of sudden cardiac death

MAJOR RECOMMENDATIONS

- In patients with heart failure with reduced ejection fraction (<40%), guideline-directed medical therapy (GDMT) is recommended to reduce sudden cardiac death and all-cause mortality; GDMT includes β-blockers; mineralocorticoid receptor antagonists; and angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or angiotensin receptor–neprilysin inhibitors (class I, level A recommendation).
- In patients with left ventricular ejection fraction (LVEF) of 35% or less due to ischemic heart disease at least 40 days after myocardial infarction, at least 90 days after revascularization, and with New York Heart Association (NYHA) class II or III heart failure despite GDMT, an ICD is recommended if expected survival is greater than 1 year (class I, level A recommendation).
- In patients with LVEF of 30% or less due to ischemic heart disease at least 40 days after myocardial infarction, at least 90 days after revascularization, and with NYHA class I heart failure symptoms despite GDMT, an ICD is recommended if expected survival is greater than 1 year (class I, level A recommendation).
- In patients with nonischemic cardiomyopathy, NYHA class II to III symptoms, and LVEF of 35% or less despite GDMT, an ICD is recommended if expected survival is greater than 1 year (class I, level A recommendation).

Summary of the Clinical Problem

Ventricular arrhythmias range from benign premature ventricular contractions to ventricular fibrillation and can be asymptomatic or have sudden cardiac death as the first manifestation. Sudden cardiac death is a major public health problem, accounting for 50% of all cardiovascular death.[1] Although a plurality of sudden cardiac death occurs in the general population with no apparent cardiac risk factors, the risk is greatest in patients with LVEF of less than 30%, clinical heart failure, prior aborted cardiac arrest, or coronary artery disease.[2]

Characteristics of the Guideline Source

The guideline (**Table**) was developed and funded by the ACC, AHA, and HRS, which commissioned a task force of cardiologists and electrophysiologists with expertise in critical care, acute coronary syndromes, genetic cardiology, heart failure, and pediatrics and geriatricians with expertise in terminal care and shared decision-making. Writing committee members were selected to represent diverse perspectives. The guidelines were reviewed by nominees of the ACC, AHA, HRS, and Heart Failure Society of America, including a lay reviewer and individual content reviewers. Conflicts of interest were published with the final guideline document. Chairs and co-chairs were not allowed to have relevant relationships with industry and at least half of the committee members were required to be free of relevant relationships with industry. Committee members with relevant relationships recused themselves under the review of the chair.

Evidence Base

The guideline highlights the importance of medical therapy for primary prevention of sudden cardiac death and reiterates the importance of β-blockers; mineralocorticoid receptor antagonists; and angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or angiotensin receptor–neprilysin inhibitors to reduce all-cause mortality and sudden cardiac death. These recommendations are based on multiple randomized trials.

Prevention of sudden cardiac death can be classified as either primary for patients who are at elevated risk of sudden cardiac death or secondary for patients who have previously had sustained ventricular tachycardia and/or aborted sudden cardiac death. Primary

Table. Guideline Rating

Standard	Rating
Establishing transparency	Good
Management of conflict of interest in the guideline development group	Good
Guideline development group composition	Good
Clinical practice guideline–systematic review intersection	Good
Establishing evidence foundations and rating strength for each of the guideline recommendations	Good
Articulation of recommendations	Good
External review	Fair
Updating	Good
Implementation issues	Good

prevention recommendations are subdivided for patients with ischemic cardiomyopathy or nonischemic cardiomyopathy. For patients with LVEF of 35% or less due to ischemic heart disease, at least 40 days after myocardial infarction, at least 90 days after revascularization, and with NYHA class II or III chronic systolic heart failure despite GDMT, an ICD is recommended if meaningful survival of greater than 1 year is expected. These recommendations are based on 2 large randomized trials.[3,4] An ICD is also recommended for patients without symptoms (NYHA class 1) but with lower LVEF (<30%).

In patients with nonischemic cardiomyopathy, LVEF of 35% or less, NYHA class II to III heart failure, and GDMT for at least 3 months, ICD insertion is a class I recommendation. This is based on 2 pooled analyses from several randomized trials. The first analysis demonstrated a 31% relative risk reduction in all-cause mortality for ICD recipients vs those with medical therapy alone.[5] The second, more recent meta-analysis reviewed 6 randomized trials with a total of 2970 patients with nonischemic cardiomyopathy and demonstrated a 23% risk reduction in all-cause mortality with ICDs.[6] However, 58% of patients in the medical therapy group in the DANISH trial received cardiac resynchronization therapy with a pacemaker, thus questioning the generalizability of results to patients without cardiac resynchronization.[7] As it stands, LVEF remains the major risk predictor, and in conjunction with GDMT, ICDs are the mainstay for prevention of sudden cardiac death.

Benefits and Harms

Patients will benefit from the guideline's focus on maximizing GDMT before proceeding with device-based therapy. When GDMT fails to improve LVEF sufficiently, evidence-based use of ICDs results in reduction in sudden cardiac death. Surgical implantation of ICDs is not without risk of harm. Inappropriate ICD discharges or shocks remain an important problem and have been associated with significant physical and psychologic discomfort. Therefore, ICD implantation is not recommended for patients with end-stage heart failure with no advanced options for left ventricular assist device insertion or heart transplantation or those with expected survival of less than 1 year. Other potential harms related to ICD implantation include procedural complications as well as infection, potentially requiring ICD extraction.

Discussion

Notable changes from previous guidelines include the addition of angiotensin receptor–neprilysin inhibitors to GDMT. Controversy remains about this recommendation, which is based primarily on 1 randomized trial (PARADIGM-HF) with a control group receiving relatively low doses of enalapril. However, the demonstrated benefit of angiotensin receptor–neprilysin inhibitors led to its being added to the guideline.[8] As noted, the DANISH trial raised concerns about the role of ICDs in patients with nonischemic cardiomyopathy. The recommendation remains that patients with nonischemic cardiomyopathy with reduced LVEF and clinical heart failure while taking GDMT should receive ICDs.

In addition to the recommendations discussed above, this guideline discusses management of ventricular arrhythmias in many disease states other than ischemic cardiomyopathy and nonischemic cardiomyopathy.

Areas in Need of Future Study or Ongoing Research

As Myerburg et al[2] demonstrated, the highest prevalence of sudden cardiac death occurs in the general population. While this guideline focuses much of its sudden cardiac death prevention efforts on patients at higher risk (those with known cardiac disease), it is necessary to identify risk factors for sudden cardiac death in the general population. Furthermore, specific populations are underrepresented in data supporting the guidelines. The role of ICDs in these populations should be further defined via prospective studies. Other areas of ongoing research include identifying ICD-eligible patients most likely to benefit from an ICD and developing methods to identify and treat patients at high risk of sudden cardiac death who do not currently meet ICD eligibility criteria.

ARTICLE INFORMATION

Author Affiliations: University of Chicago, Chicago, Illinois.

Corresponding Author: Adam S. Cifu, MD, University of Chicago, 5841 S Maryland Ave, MC 3051, Chicago, IL 60637 (adamcifu@uchicago.edu).

Section Editor: Edward H. Livingston, MD, Deputy Editor, *JAMA*.

Published Online: June 13, 2019. doi:10.1001/jama.2019.7662

Conflict of Interest Disclosures: Dr Nayak reported receipt of speaker fees from Biotronik, institutional fellowship funding from Boston Scientific, Abbott, and Medtronic, and personal fees from Medtronic. No other disclosures were reported.

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