DEVICE THERAPY

REVIEW ARTICLE

Indications for ICD Therapy for the Primary Prevention of Sudden Death in Patients With Left Ventricular Dysfunction and a Narrow QRS Complex

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ABSTRACT. There is a growing trend to implant cardiac devices (including implantable cardioverter-defibrillator (ICDs) for primary prevention) based on earlier identification of serious disease and earlier intervention. All current guidelines depend on two findings: 1) structural changes reflecting the degree of systolic left ventricular (LV) dysfunction; and 2) functional status using the New York Heart Association (NYHA) classification. The latter, as a surrogate for heart failure (HF), is a much weaker criterion than the clinical findings of congestion. There is almost no evidence that the ICD reduction of sudden death depends on the severity of congestion or NYHA class, and there is no evidence that ICDs prevent sudden cardiac death more efficiently in symptomatic HF patients than in asymptomatic ones. The various guidelines do not as yet support these concepts. The requirements for “on optimal medical treatment” for 3 months or 9 months for non-ischemic cardiomyopathy are difficult to comprehend and should be revised as there are no mortality data comparing optimal versus suboptimal medical treatment. “Optimal medical therapy” in the context of ICD therapy has never been defined, and may vary from patient to patient. In future, ICD indications will most probably depend primarily on the degree of LV dysfunction alone rather than symptomatic LV dysfunction.

KEYWORDS. heart failure, implantable cardioverter-defibrillator, left ventricular systolic dysfunction, sudden cardiac death.

Introduction

Sudden death continues to cause 20–50% of deaths in cardiomyopathy or systolic heart failure (HF).1–3 Ventricular arrhythmias are common in patients with HF. Sudden death (unexpected death occurring within 1 h of onset of symptoms if any) is mostly due to a ventricular tachyarrhythmia, which may or may not be related to acute ischemia, and much less frequently due to bradyarrhythmias and electromechanical dissociation. Mortality rates increase the higher the New York Heart Association (NYHA) class, but the proportion of patients dying suddenly and unexpectedly due to ventricular tachyarrhythmias (rather than from progressive pump failure) is highest among those with less severe HF and milder symptoms (NYHA class II or III).4 To date, no single test reliably predicts arrhythmic risk in patients with HF. The severity of left ventricular (LV) dysfunction, not the severity of symptoms, seems to be the best predictor of sudden cardiac death. In this respect, the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) conducted in class II and class III HF patients with LV ejection fraction (LVEF) ≤35% showed improved mortality in class II NYHA patients, but no survival benefit in NYHA class III patients.5 Early trials where the LVEF arbitrarily varied from 30% to 40% strongly suggest that stable reduction of LVEF should most probably be the
only indication for implantable cardioverter-defibrillator (ICD) implantation regardless of symptoms or NYHA class, but excluding patients with a poor life expectancy from heart diseases or other causes.

A recent study of 756 patients who received an ICD for primary prevention (follow-up 3.4 years) revealed that 107 patients (14%) had died. The mode of death was obtained in 79% of the patients. The cause of death was HF in 37%, non-cardiac death in 35%, and sudden death in 7%. Remarkably, the sudden death rate was comparable in ICD patients with primary prevention and those with secondary prevention, thereby providing impressive results of ICD therapy which altered the mode of death to mostly pump failure and non-cardiac causes.6

Basis of the guidelines

All current indications for ICD implantation depend on two findings:1) structural changes reflecting the degree of systolic dysfunction such as decreased left ventricular ejection fraction (LVEF); and 2) functional status using the NYHA classification as a measure of severity of HF symptoms. The NYHA class as a surrogate for HF is a much weaker criterion for HF than the clinical findings of congestion.8

Is there a gold standard for measuring left ventricular ejection fraction?

Results from non-invasive techniques such as echocardiography, radionuclide ventriculography, and cardiovascular magnetic resonance are not exactly interchangeable.9–11 Each technique has individual strengths and limitations. There is no "gold standard." The choice of a particular technique in clinical practice is often governed by the availability of local resources. The important practical issue is not which technique is best, but rather, which technique is available at a particular institution and possesses reasonable accuracy and reproducibility.11 Echocardiography has been widely used for the evaluation of LVEF as it is readily available and relatively less expensive than other techniques.

American College of Cardiology/American Heart Association/Heart Rhythm Society guidelines 2008

The 2008 American College of Cardiology/American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) guidelines recommend an ICD as a class I indication in a NYHA class I patient with LVEF ≤30% 40 days post myocardial infarction (MI).12 However, the guidelines contain no mention of an ICD indication for the post-MI patient with LVEF ≤35% in NYHA class I. It would be prudent to consider an ICD in such patients. In this respect a recently published arrhythmia book clearly assigned a class I indication for an ICD in this very situation.13 One might argue that there is a margin of error in the imaging techniques to determine an LVEF of 30% versus 35%, and the fact that LVEF is generally approximated in 5% increments.9–11 On the other hand, the mean LVEF in the trials were much lower than the thresholds described in the guidelines. In any case, the dilemma disappears by looking at the 2006 ACC/AHA/ESC (European society of Cardiology) guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden death.14 This document is more flexible and realistic by recommending an ICD in the post-MI patient NYHA class I with LVEF 30–35% and on optimal treatment.

The 2008 ACC/AHA/HRS guidelines offer an ICD for patients with a non-ischemic cardiomyopathy and LVEF ≤35% with NYHA class II/III as a class I indication.14 Yet, the same situation in a NYHA class I patient is relegated to a IIb ICD indication for no good reason except that data about this group of patients are not as extensive as in the ischemic group.14

Heart Failure Society of America 2010

The Heart Failure Society of America (HFSA) guidelines indicate that prophylactic ICD placement should be considered in patients with an LVEF ≤35% and mild to moderate HF symptoms: ischemic etiology and non-ischemic etiology.15 The guidelines indicate that if an ICD is considered due to LV dysfunction which is of recent onset, LV function should be reassessed ideally after 3–6 months. The guidelines state that ICD placement is not recommended in chronic, severe refractory HF when there is no reasonable expectation for improvement or in patients with a life expectancy of less than 1 year. We interpret this statement to mean that an ICD could be considered in selected ambulatory NYHA class IV HF patients.

The HFSA guidelines do not advocate an ICD in class I NYHA patients. The guidelines emphasize that the decision to implant an ICD be made in light of functional status and prognosis based on severity of underlying HF and comorbid conditions.

European Society of Cardiology 2012

In these guidelines, an ICD is recommended in patients with symptomatic HF (NYHA class II and class III) and LVEF ≤35% despite ≥3 months of optimal pharmacological therapy, (and expected to survive for >1 year with good functional status) in the following situations: 1) ischemic cardiomyopathy >40 days after acute MI; 2) non-ischemic cardiomyopathy after a period of optimization of medical therapy (at least 3 months) and only if the LVEF is persistently low.16

Centers for Medicare and Medicaid Services

According to the current guidelines (2005) an ICD is approved for the following conditions:17
1. Patients with ischemic dilated cardiomyopathy (IDCM), documented prior MI, NYHA Class II and III heart failure, and measured LVEF <35%.

2. Patients with non-ischemic dilated cardiomyopathy (NIDCM) >9 months, NYHA class II and class III HF, and measured LVEF <35%.

All Centers for Medicare and Medicaid Services (CMS) indications must meet the following criteria:

a. Patients must not have irreversible brain damage from preexisting cerebral disease.

b. MIs must be documented and defined according to the consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the Redefinition of MI.18

The indications must also meet the following criteria:

a. Patients must be able to give informed consent.

b. Patients must not have:
   
   • cardiogenic shock or symptomatic hypotension while in a stable baseline rhythm
   • had a coronary bypass surgery or coronary angioplasty within the past 3 months
   • had an acute MI within the past 40 days
   • clinical symptoms or findings that would make them a candidate for coronary revascularization
   • any disease, other than cardiac disease (e.g., cancer, uremia, liver failure), associated with a likelihood of survival less than 1 year

c. LVEFs must be measured by angiography, radionuclide scanning, or echocardiography

d. MIs must be documented as above18

The CMS indications do not carry class I NYHA patients. They contain no statement about optimal medical therapy, yet reimbursement has been denied by CMS presumably in the absence of optimal medical therapy. Thus, optimal medical management is implied in the CMS guidelines.

**New York Heart Association Classification**

All ICD trials determined NYHA class only once at baseline. Yet, many adequately treated patients with HF return to a NYHA class I status. It means that they are currently asymptomatic but they were symptomatic in the past. The guidelines are based on the patients’ NYHA class upon enrolling into the various trials upon which the guidelines are based. Thus, a patient who started with class III NYHA HF and improves to class I of the NYHA would be considered a class I NYHA patient as far as the guidelines are concerned. Although it makes sense that such a patient should probably be considered for an ICD on the basis of the past history, this action would violate some of the present guidelines.

Many of the randomized controlled trials have excluded patients in NYHA class IV patients. This group has not really been well characterized or studied. Therefore, these patients are not candidates for ICD therapy according to the above guidelines presumably because they have too high a non-sudden death rate. This makes decisions for use of therapeutic strategies for sudden cardiac death more difficult in those patients with the worst prognosis. Automatic denial of ICD therapy for this group cannot always be justified at present, and ICD therapy should be individualized according to the clinical circumstances.

**Optimal medical therapy**

Some guidelines require candidates for an ICD to be “on optimal medical treatment.” We are unaware of any trials randomizing patients to optimal versus suboptimal medical treatment and calculating mortality difference after medical therapy. It is LV dysfunction, decreased LVEF, and reverse ventricular remodeling that determine prognosis and longevity. Congestion, or symptoms, or NYHA class, and the requirement of being on “optimal medical therapy” should no longer be the part of the guidelines. “Optimal medical therapy” in the context of ICD therapy has never been defined, and may vary from patient to patient. All patients should receive standard medical therapy and undergo ICD implantation as soon they are sufficiently stable to undergo the procedure safely, to prevent undue delay imposed by the search of “optimal medical therapy” for HF by trial and error to attain this rather elusive goal. The requirement of optimal therapy of HF for 3 months in some of the guidelines is not based on any published data. Little is known about the evolution of the LVEF in HF patients. We believe that this requirement is best worded in terms of “optimal therapy which may take as long as 3 months in some patients.” The waiting time of 9 months for patients with non-ischemic cardiomyopathy in the CMS guidelines does not make sense. However, patients with non-ischemic cardiomyopathy may be considered for an ICD after 3 months as part of a strictly defined research protocol.

**Conclusion**

The number of ICDs implanted for primary prevention is growing and far exceeds the number for secondary prevention. The indications for ICDs should be based on the earlier identification of serious disease and earlier intervention. The patients in the primary prevention trials who experienced benefit from ICD therapy had a significantly lower LVEF than the values that appear in all the guidelines. There is almost no evidence that the reduction of sudden death with an ICD depends on severity of congestion or NYHA class, and there is no evidence that ICDs prevent sudden cardiac death more efficiently in symptomatic HF patients than in asymptomatic ones. At present, the different categories of ICD...
indications in the various guidelines do not support the belief that ICD indications should depend primarily on the degree of LV dysfunction, and that symptoms or lack thereof should not be the deciding factor to implant an ICD. Decreased LV systolic function, or decreased LVEF or cardiomyopathy, should be the primary target for device therapy regardless of symptoms. We believe that in future the various guidelines will incorporate these concepts. With regard to HF guidelines promulgated by HF societies, one could argue that they need not address NHHA class I patients because they do not have HF. ICD implants are not without complications. With expanding indications the benefit of device therapy in asymptomatic or minimally symptomatic patients must be carefully weighed against the potential risk of lifelong device ICD complications. The often heard statement that implanting an ICD is similar to implanting a pacemaker is simply not true. It is important in patients who receive an ICD for primary prevention to avoid right ventricular pacing and program the device to avoid inappropriate shocks.

References

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