Prevention of Sudden Death in Hypertrophic Cardiomyopathy

But Which Defibrillator for Which Patient?

Giuseppe Boriani, MD, PhD; Barry J. Maron, MD; Win-Kuang Shen, MD; Paolo Spirito, MD

Case presentation: A 14-year-old girl died suddenly and unexpectedly while exercising. Clinical and echocardiographic family screening identified hypertrophic cardiomyopathy (HCM) in her only sibling, an asymptomatic 17-year-old boy. In her brother, echocardiography showed extreme septal ventricular hypertrophy, 35 mm in thickness; left ventricular (LV) outflow obstruction was absent. Left atrial dimension was 42 mm. Holter monitoring showed 2 runs of nonsustained ventricular tachycardia (5 and 8 beats). Blood pressure response during exercise was normal. The patient was judged to be at high risk for sudden death and a candidate for an implantable cardioverter-defibrillator (ICD). The overall favorable clinical profile (ie, no symptoms, preserved systolic function, and low risk of developing atrial fibrillation [AF]) suggested that long-term survival principally relied on effective prevention of sudden death. Therefore, ICD selection centered on the long-term reliability of the ICD system, particularly the leads. A single-chamber ICD with a single-coil active-fixation lead was implanted to facilitate extraction should lead removal be required. Moreover, a high–shock output ICD was used because of the massive LV hypertrophy and possible high defibrillation threshold.

Background

During the past few years, interest has increased in the use of the ICD in genetic cardiac diseases associated with sudden cardiac death, such as HCM, long-QT syndrome, arrhythmogenic right ventricular cardiomyopathy, and Brugada syndrome. HCM is by far the most common of these cardiac conditions, with a prevalence of about 1:500 in the general population. Because most HCM patients at high risk for sudden death are young, with no or only mild symptoms and preserved systolic function, prevention of sudden death by the ICD may prolong life substantially in this disease and could offer a normal or near-normal life expectancy to many patients. Indeed, recent investigations have shown that the ICD is effective in preventing sudden death in HCM. In a multicenter study of high-risk HCM patients, the device intervened appropriately and terminated ventricular tachycardia or fibrillation at a rate of 5% per year for primary prevention and 11% per year for secondary prevention, over an average follow-up of 3 years. The number of HCM patients implanted with an ICD also has increased substantially over the past few years. Therefore, a large ICD cohort is now emerging that differs from the general ICD population because of younger age, lower rate of life-threatening events, and longer expected survival. Consequently, in such patients, the selection of the most appropriate ICD system with adequate long-term reliability has become critically important, and the complexity of such decisions is enhanced by the clinical heterogeneity of HCM.

The 2002 American College of Cardiology/American Heart Association/North American Society of Pacing and Electrophysiology consensus guidelines do not address the specific issue of lead and device selection in HCM and are largely based on trials per...
formed in older patients with coronary artery disease. Therefore, it would seem justified and timely to address the important clinical issue of ICD selection in HCM. Here, we focus on the potential criteria to select the device and leads rather than on the specific indications for ICD implantation. Risk stratification and identification of ICD candidates recently have been addressed in detail in the American College of Cardiology/European Society of Cardiology consensus guidelines for HCM.

**Considerations for ICD Selection in HCM**

Malfunction of transvenous leads over time is a particularly important issue for young ICD recipients, given the reported incidence of lead failure (largely fracture and erosion) of up to 20% to 35% after 5 years. Such lead problems usually compromise system function, causing inappropriate shocks, and require lead removal, which may be fraught with difficulty.

**Single-Chamber Versus Dual-Chamber ICD**

The dual-chamber ICD is often preferred over the single-chamber device because it preserves atrioventricular synchrony during pacing and allows better supraventricular arrhythmia discrimination, thus reducing the inappropriate interventions. However, the dual-chamber ICD may not always be the best option in HCM because it has higher potential for complications compared with the single-lead device. In addition, many young high-risk HCM patients do not have bradyarrhythmias or supraventricular tachyarrhythmias that would justify a lead for atrial pacing and sensing.

The single-chamber ICD may represent a more appropriate option for high-risk HCM patients whose long-term survival may depend largely on the effective prevention of sudden death (Figure 1). A profile suggesting this clinical course can be described as the following: no or only mild symptoms (New York Heart Association class I or II), absence of resting LV outflow obstruction, and nondilated left atrium (<45 mm) without a history of AF. This clinical profile is relatively frequent among young HCM patients at high risk of sudden death and is common in those patients with extreme LV hypertrophy (wall thickness ≥30 mm) or a family history of sudden death as the sole indicator of high-risk status.

A single-chamber ICD is indicated in all high-risk HCM patients with chronic permanent AF. In some HCM patients, the marked cycle variability that can occur during AF may be poorly tolerated and has been reported as an occasional trigger for life-threatening ventricular tachyarrhythmias (Figure 2). This alternation of short and long ventricular cycles often cannot be prevented reliably by β-blockers or calcium antagonists. However, regularization of ventricular rate is now possible by using specific pacing algorithms that are within the capabilities of single-chamber ICDs.

A dual-chamber ICD may be preferable in high-risk patients who have episodes of paroxysmal AF or who are likely to develop AF. This arrhythmia is relatively common in HCM, occurring in about 20% of patients (incidence 2%/year), and increases in direct relation to left atrial size and age. The dual-chamber ICD may discriminate paroxysmal AF from ventricular tachyarrhythmias more reliably than the single-chamber device, although a decrease in inappropriate ICD activations remains to be definitively proved. Furthermore, the latest generation of dual-chamber ICDs may reduce AF recurrences by applying specific algorithms that suppress atrial ectopies by continuous atrial pacing over the spontaneous atrial activity. The efficacy of these algorithms in the specific setting of HCM is presently unresolved and under investigation.

Paroxysmal AF may be poorly tolerated in HCM patients with severe...
diastolic dysfunction and an LV filling that depends to a great extent on effective atrial systole and duration of diastole. Dual-defibrillator devices (dual ICDs) are now available that have the capability to deliver a low-energy shock to interrupt AF selectively, in addition to the conventional shock for ventricular tachyarrhythmias (Figure 1). These shocks for atrial tachyarrhythmias can be activated by the patient or delivered automatically for arrhythmic episodes of a preprogrammed duration (Figure 3).

A history of syncope is not uncommon in HCM and may be caused by a number of mechanisms, including neurally mediated responses resulting in cardioinhibition, vasodepression, or both. Although controversy remains about whether dual-chamber pacing may be helpful in reducing the recurrence of neurally mediated syncope by maintaining a normal heart rate and atrial contribution to cardiac filling and output, a dual-chamber system could be considered in high-risk patients with HCM, diastolic dysfunction, and recurrent episodes of neurally mediated syncope who are candidates for an ICD (Figure 1).

**ICD Leads**

Shocking leads with different technical features are available, and lead selection generally is based on the patient’s clinical profile. With single-coil leads, the shock current travels from the ventricular coil to the device metal can. In dual-coil leads, the shock current follows 2 pathways: from the ventricular (distal) coil to the proximal coil, and from the distal coil to the device can. Dual-coil leads have the advantage of slightly lower defibrillation thresholds. However, should lead removal be required, extraction of a dual-coil lead is usually more difficult given the tight adherence of the proximal coil to the thin walls of the right atrium or vena cava. In view of these potential problems, a single-coil lead may be preferable in young HCM patients who are expected to survive for a long time and have a measured defibrillation threshold within the normal range.

The method of fixation of the lead tip to the atrial or ventricular wall also merits attention. Tip fixation may be ensured by either a tined lead tip that becomes progressively surrounded by fibrous tissue (passive fixation) or, alternatively, by a screw (active fixation). Leads with a screw are more easily removed and thus are advisable for ICD candidates with an extended life expectancy, such as most young HCM patients.

**Implantation Techniques**

The standard approach of ICD lead insertion through the subclavian vein occasionally may result in lead entrapment between subclavian muscle and costoclavicular ligament. This problem is more common in youthful active patients and may cause lead malfunction due to progressive erosion of the insulation layer or fracture of the lead (ie, “subclavian crush syndrome”). Therefore, in young HCM patients, it may be prudent to use a more lateral access to the central venous circulation through the cephalic vein or, in selected cases, the axillary vein, which requires a particular approach to venous puncture.

**ICD and Outflow Obstruction**

LV outflow tract obstruction is present under basal conditions in about 20% to 25% of HCM patients and is associated with increased risk of progressive heart failure and cardiovascular death. The left atrium often is enlarged as a consequence of augmented end-diastolic pressures and mitral valve regurgitation (due to systolic anterior motion of the valve). Therefore, in high-risk patients with outflow obstruction and a dilated
left atrium, the propensity to develop paroxysmal AF usually justifies a dual-chamber ICD.

Another reason for a 2-lead ICD system may come from the capability of dual-chamber pacing to reduce the outflow gradient and, in selected patients (usually the elderly), to improve symptoms.4,7 In the individual patient implanted with a dual-chamber ICD, a period of pacing then can determine whether the potential benefits on gradient and symptoms exceed the limitation of increased battery depletion due to continuous ventricular pacing and consequently more frequent device replacement.

ICD in End-Stage HCM
A small minority of patients with HCM (<5%) evolve into the end-stage phase, characterized by systolic dys-function, LV wall thinning, and cavity dilatation.3,4,15 This is virtually the only HCM subgroup with an indication for heart transplantation. Because of the considerable risk for sudden death in patients with end-stage congestive heart failure awaiting donor hearts, strong consideration should be given to an ICD as a bridge to transplantation. The single-chamber ICD is probably preferable in these patients, unless a prior history of paroxysmal AF or other conventional indications to dual-chamber pacing is present. Biventricular pacing (in combination with defibrillation capabilities) is another potential option, although its efficacy in end-stage HCM remains unknown.

ICD in Children With HCM
Implantation of ICDs in pediatric patients raises a number of dilemmas in clinical decision-making, such as the choice of implantation techniques.

Progressive decrease in the size of the ICD generator has now made transvenous implants possible in children as small as 20 to 25 kg.16 In an attempt to address the problem of lead stretching, fracture, and displacement due to body growth, transvenous techniques have been promoted in which the defibrillation lead is positioned in a loop within the inferior vena cava to provide residual catheter length, as a means of compensating for future body growth and reducing the risk of lead fracture. Interest is growing in the development of a generation of “leadless” ICDs, in which cardiac rhythm is sensed directly by the generator and defibrillation shocks are delivered through electrodes implanted in subcutaneous tissue.

High Defibrillation Threshold
A marked increase in LV wall thickness is common in HCM, the average being 20 to 22 mm.4,5 Furthermore, extreme LV hypertrophy (wall thickness ≥30 mm), reported in about 10% of patients, is an independent risk factor for sudden death in the young and a justification for a prophylactic ICD.5 Because LV mass is an important determinant of defibrillation threshold,6,17 increased defibrillation energy requirements have been identified in some HCM patients with severe hypertrophy, particularly when associated with amiodarone treatment.17 In some of these patients, the recommended 10-Joule safety margin between maximal ICD shock energy and minimum effective defibrillation energy may be difficult to achieve at the time of ICD implantation, and the option of a high-shock output device (36 to 41 Joule) can be considered. Alternative methods for reducing defibrillation threshold include positioning an additional coil-lead in the superior vena cava or a subcutaneous array lead on the chest.

ICDs in HCM: The Cost Issue
Difficult questions have been raised about the economic burden of ICDs on society, with cost being principally related to the total number of implantations. Although HCM probably accounts for <5% of all ICDs, cost containment cannot be ignored even in this disease. Given the lengthy expected survival of most HCM patients, potential ICD complications and generator replacements are likely to contribute significantly to the overall costs and merit careful evaluation. Therefore, in HCM patients with a favorable overall clinical profile whose long-term survival principally relies on effective prevention of sudden death, less expensive single-chamber ICDs that possibly are associated with fewer complications may be preferable to more complex devices (Figure 1). In the future, new ICD models with basic functions ("shock box") and an extended battery life might find application in selected HCM patients.

Conclusions
Most HCM patients who are at high risk for sudden death and are candidates for an ICD are young and asymptomatic, with preserved systolic function and the potential to survive for many decades. Because ICD selection remains hampered by the limited experience with long-term performance and complications of ICD lead systems, a prudent balance should be sought between the most sophisticated ICDs and the simpler devices that are likely to be associated with fewer complications. At present, the dual-chamber ICD may be preferable for patients with a history of paroxysmal AF or a clinical profile suggesting a high likelihood for developing this arrhythmia. The higher risk for complications with the 2-lead system probably is balanced by its potentially enhanced capability for discriminating supraventricular from ventricular tachyarrhythmias and the possibility of applying particular algorithms designed to prevent AF. The most advanced models, the dual ICDs, also can interrupt AF by delivering an atrial shock. In view of the expected lower rate of lead complications, the single-chamber ICD generally is preferred in children or adolescents, in patients without outflow obstruction or with a clinical profile suggesting low risk for paroxysmal AF, and in those patients with chronic permanent AF.

Many of the current uncertainties about ICD selection in HCM probably will be resolved by further technological progress toward increased long-term lead reliability. Reduction in lead-related complications will greatly
benefit young high-risk HCM patients, as well as patients with other arrhythmogenic cardiac disorders who can reasonably expect substantial prolongation of life with ICD protection from sudden death.

References
Prevention of Sudden Death in Hypertrophic Cardiomyopathy: But Which Defibrillator for Which Patient?
Giuseppe Boriani, Barry J. Maron, Win-Kuang Shen and Paolo Spirito

_Circulation._ 2004;110:e438-e442
doi: 10.1161/01.CIR.0000144463.65977.C9

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/110/15/e438

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/