MIOCARDIOPATIA IPETROFICA

Prevenzione morte improvvisa secondo

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

Recommendations

Class I

ICD therapy should be used for treatment in patients with 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 ofEvidence: B)*

Class IIa

1. **ICD implantation can be effective for primary prophylaxis against SCD in patients with HCM who have 1 or more major risk factor (see Table 7)** for 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 an 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 1 or more major risk factor for SCD (see Table 7) if ICD implantation is not feasible. ***(Level of Evidence: C)***

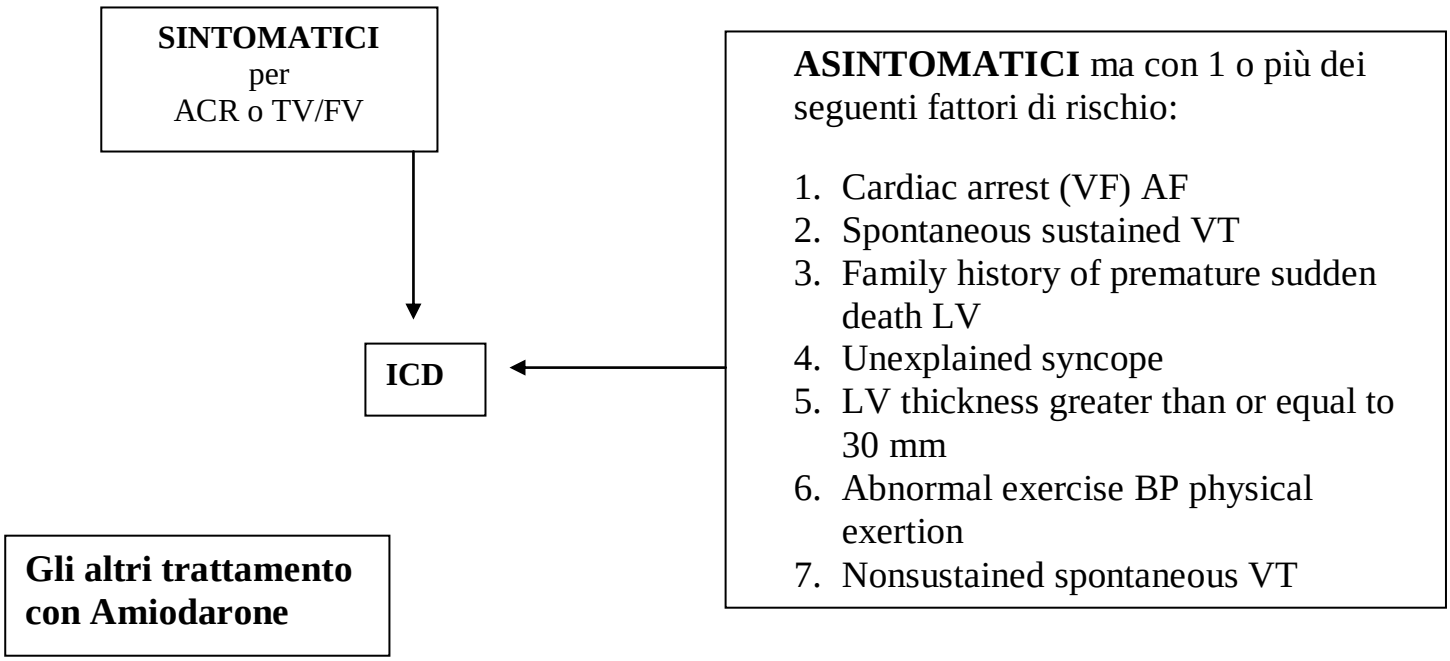
Table 7. Risk Factors for Sudden Cardiac Death in Hypertrophic Cardiomyopathy

Major Risk Factors

1. **Cardiac arrest (VF) AF**
2. **Spontaneous sustained VT**
3. **Family history of premature sudden death LV**
4. **Unexplained syncope**
5. **LV thickness greater than or equal to 30 mm**
6. **Abnormal exercise BP physical exertion**
7. **Nonsustained spontaneous VT**

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

	I	*IIA*	*IIB*
Prevenzione priamria		**ICD implantation** can be effective for primary prophylaxis against SCD in patients with HCM **who have 1 or more major risk factor (see Table 7)** for 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)*	**Amiodarone** may be considered for primary prophylaxis against SCD in patients with HCM **who have 1 or more major risk factor for SCD (see Table 7) if ICD implantation is not feasible.** *(Level of Evidence: C)*
Prevenzione secondaria	**ICD therapy should be used for treatment in patients with 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 ofEvidence: B)*	**2. Amiodarone therapy can be effective for treatment in patients with HCM with a history of sustained VT and/or VF when an ICD is not feasible.** *(Level of Evidence: C)*	



Risk Stratification

Most individuals with HCM are asymptomatic and the first manifestation may be SCD . SCD is usually related to ventricular arrhythmia with varying contribution of triggers such as ischemia, outflow obstruction, or AF. SCD is less frequently due to bradycardia. The annual mortality from HCM has been estimated as high as 6% from tertiary centers , but community-based studies suggest a more benign disease in the majority of individuals, **with an annual mortality in the range of 1% or less**. This relatively low incidence creates a challenge for risk stratification because the false positive values for any stratifier may overwhelm the true positive values. Features suggesting higher risk of SCD have been derived from observational studies. In one study, 23 of 480 patients died suddenly over a mean follow-up of 6.5 y.

The risk of SCD

1) was directly related to LV wall thickness with essentially no mortality over 20 y with wall thickness less than 20 mm and **mortality of almost 40% for wall thickness greater than or equal to 30 mm.** Patients with such extreme wall thickness were the youngest and frequently asymptomatic. Five of 12 patients in this category under the age of 18 died suddenly. Others have suggested that patients with extreme septal hypertrophy also have other risk factors, and the independent value of extreme septal hypertrophy is less clear. The degree of outflow obstruction has been shown to predict cardiovascular death but not SCD. Athletes with HCM should not participate in most competitive sports with the possible exception of sports of low dynamic and low static intensity . Participation in low-to-moderate athletic activities may be allowed in selected low-risk patients .Cardiac MRI and CT have been suggested to be helpful in assessing extent of disease and predicting SCD**.**

2) A history of SCD in one or more family members has been considered to signify higher risk . This is intuitively logical and related closely to the suggestion that

3) certain specific genetic abnormalities have been associated with increased risk of SCD ; the role of genetic testing as a predictor of SCD is likely to increase .

4) Syncope has been associated with increased risk of SCD

The severity of other symptoms such as dyspnea, chest pain, and effort intolerance has not been correlated with increased risk of SCD. A flat or

5) hypotensive response to upright or supine exercise testing in patients younger than 40 y has been shown to be a risk factor for SCD, although the positive predictive value of this finding is low . A normal blood pressure response identifies a low-risk group.

4)The presence of VT on Holter monitoring has been associated with a higher risk of SCD, although the positive predictive accuracy is relatively low. The absence of VT appears to have good negative predictive value. VT induced in the EP laboratory has also been associated with a higher risk of SCD, although others have suggested that VT induced in this setting with aggressive stimulation techniques is not specific.A consensus document on HCM from the American College of Cardiology and European Society of Cardiology categorized known risk factors for SCD as "major" and "possible in individual patients"

It is clear that many of the risk factors listed in Table 7 are interdependent, and the major independent risk factors may prove to be the extent of disease and the genetic abnormality.The absence of risk factors identifies a low-risk group, but the positive predictive value of any single risk factor is limited. Risk stratification based on incorporation of multiple risk factors would likely improve positive predictive accuracy .

Electrophysiological Testing

The value of EP testing in HCM has been controversial. In 1989, Fananapazir et al. showed by using 2 premature stimuli that only 16% of patients with cardiac arrest or syncope in the setting of HCM had inducible sustained VT. In a later study, the same group published data on 230 patients, including 155 patients reported earlier. Patients with inducible VT had a poorer prognosis than those without inducible VT. Induced VT was often polymorphic. The response to EP testing was considered to be an important predictive factor for outcome, together with a history of syncope or cardiac arrest. In a prospective study of 29 patients with HCM, 8 of them presenting with syncope, EP testing with up to 3 extrastimuli at 3 cycle lengths including LV stimulation failed to distinguish patients with from those without syncope. In patients who received an ICD for primary prevention, the estimated appropriate discharge rate was 5% per year .

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 . Disopyramide has been similarly used presumably for its negative inotropic effect. AF can be especially problematic, with sudden clinical deterioration as a result of high ventricular rates and loss of atrial filling. In addition, it is associated with increased risk of embolism, HF, and death. The high rate of

embolism warrants anticoagulation with warfarin even though this has not been validated in this group of patients by a large randomized trial. Amiodarone is widely used and considered the most effective antiarrhythmic agent, although large controlled comparative trials are not available . Medical therapy has not been proved to e294 Zipes et al. JACC Vol. 48, No. 5, 2006 ACC/AHA/ESC Practice Guidelines September 5, 2006:e247–e346 be beneficial in the prevention of disease progression in the asymptomatic individual and is generally not indicated. Nonetheless, treatment with beta blockers and/or calcium antagonists is tempting even in asymptomatic individuals if they are younger and have severe hypertrophy or significant gradients . It is intuitively reasonable that optimal medical therapy and control of comorbidities will also reduce the risk of SCD, although this has not been rigidly demonstrated. Although no randomized studies are 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. The ICD implanted in a subgroup of patients for primary prophylaxis on the basis of perceived high risk for SCD (syncope, family history of SCD, NSVT, inducible VT, septal thickness greater than or equal to 30 mm) resulted in a lower rate of appropriate discharge of 5% per year. Amiodarone has been shown useful in prevention of SCD in nonrandomized studies while other studies have suggested symptomatic improvement but have not shown complete prevention of SCD . Placebo-controlled studies or studies that compared ICD with amiodarone are not available, and the role of amiodarone in prevention of SCD is unclear. Amiodarone is unlikely to be superior to the ICD for this purpose, and a comparative study may never be done . The ICD is not indicated in the majority of asymptomatic patients with HCM, who will have relatively benign course. Its role is individualized in the patient considered to be at high risk for SCD. Although precise risk stratification has not been validated, patients with multiple risk factors (especially severe septal hypertrophy, greater than or equal to 30 mm) and those with SCD (especially multiple SCDs)
in close relatives appear to be at sufficiently high risk to merit consideration of ICD therapy.

Genetic Analysis

Genetic analysis is useful in families with HCM becausewhenever 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.