Risk Stratification in Hypertrophic Cardiomyopathy
Fact or Fiction?*
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Hypertrophic cardiomyopathy (HCM) is an inherited cardiac muscle disease that affects sarcomeric proteins, resulting in severe hypertrophy, myofibrillar disorganization, and enhanced interstitial fibrosis. The disease is often familial, with autosomal-dominant transmission. More than 100 different mutations in 10 genes that encode sarcomeric proteins have been described (1–3). Hypertrophy typically affects the interventricular septum, but may be concentric or apically located. The main hemodynamic feature is diastolic dysfunction with increased filling pressures, delayed relaxation, and increased muscle stiffness. Approximately 25% of all patients have dynamic left ventricular (LV) outflow tract obstruction with a systolic pressure gradient.

The great threat of the disease is that affected children and young adults may die suddenly. However, the incidence is low: 2% to 3% per year in adults and 4% to 6% in children. It is the most common cause of sudden death in athletes and its occurrence is often associated with exercise. Thus, risk stratification has become a major issue in HCM (4,5). Approximately 60% to 70% of all patients with HCM die suddenly. It is generally assumed, although not established, that sudden death is due to ventricular arrhythmias (6). The arrhythmic substrate is a combination of several factors, including hypertrophy, myocardial fiber disarray, and interstitial fibrosis. Accepted triggers for ventricular arrhythmias are ischemia, physical exercise, and excessive sympathetic stimulation. The following risk factors have been associated with an increased risk of sudden death.

1. Family history of HCM with sudden cardiac death
2. History of syncope or presyncope
3. Massive LV hypertrophy (septal wall thickness >30 mm)
4. Survived sudden cardiac death
5. Nonsustained ventricular tachyarrhythmias (NSVT)
6. Abnormal blood pressure response to exercise

Several other risk factors have been described, but the severity of the outflow tract obstruction, the degree of functional limitation, and cardiac symptoms in general did not correlate with the risk of sudden cardiac death.

In this issue of the journal, the report by Monserrat et al. (7), the prognostic importance of repetitive, prolonged, and symptomatic NSVT has been examined and related to age and prognosis. A total of 531 patients with HCM were studied using Holter monitoring (mean 41 ± 11 h). A total of 104 patients (19.6%) had NSVT, which increased with age (p = 0.008), LV wall thickness (p = 0.001), and left atrial size (p = 0.0001). Sixty-eight patients died during follow-up of 72 months; 32 died suddenly (47%). Mortality rate was highest in young patients (<30 years) with NSVT. Thus, it was concluded that sudden cardiac death is significantly increased in young patients with HCM and NSVT. A relation among frequency, duration, and rate of NSVT could not be demonstrated.

RECOMMENDATIONS

The implication of the study by Monserrat et al. (7) is that when NSVTs occur in young patients with HCM, it may justify implantation of an implantable cardioverter-defibrillator (ICD) to prevent sudden cardiac death. In contrast, NSVT in older patients does not justify therapy when it occurs without other risk factors, such as severe LV hypertrophy, history of presyncope or syncope, or abnormal blood pressure response to exercise. However, it should be kept in mind that Holter monitoring identifies only a small subset of patients at high risk and, therefore, the search for other risk factors is a must. The current practice for treating patients with HCM (Fig. 1) should be re-evaluated in the light that prophylactic implantation of an ICD is always an option when NSVTs are present.

![Figure 1. Therapeutic strategies in hypertrophic cardiomyopathy (HCM). ICD = implantable cardioverter-defibrillator; NSVT = nonsustained ventricular tachyarrhythmias.](image)
REFERENCES