Arrhythmias in Hypertrophic Cardiomyopathy and 2014 ESC Guidelines

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Hypertrophic cardiomyopathy (HCM) is a leading cause of sudden cardiac death (SCD) in young adults. The latest ESC consensus guidelines broadly define HCM by the presence of increased left ventricular (LV) wall thickness in one or more myocardial segments that is not explained by abnormal loading conditions [1]. This is a purely morphological definition that doesn’t make assumptions about aetiology or myocardial pathology.

The population prevalence of HCM is approximately 0.2% and there are no major ethnic differences [2]. The 12-lead ECG can be normal at presentation in a small proportion of patients but more commonly shows a variable combination of Sokolow-Lyon voltage criteria for left ventricular hypertrophy (LVH), ST- and T-wave abnormalities, and pathological Q-waves [3]. Diagnostic workup should include, in addition to thorough history and examination, resting and ambulatory ECGs, comprehensive evaluation of the LV with 2D echocardiography, cardiopulmonary exercise testing, cardiac MRI (with late gadolinium enhancement), and genetic testing [1,4].

Arrhythmias in HCM

The incidence of arrhythmias in HCM appears to be age-related. Asymptomatic NSVT has been observed on Holter monitoring in approximately a quarter of adults with HCM. The presence of non-sustained VT (NSVT) is associated with a substantial increase in the risk of SCD in young patients with HCM (odds ratio of 4.35), although no relationship has been seen between the duration, frequency or rate of NSVT and prognosis [5].

Supraventricular tachyarrhythmias are observed in up to 40% of patients. Atrial fibrillation (AF) is commonly associated with HCM [6]. Symptomatic bradyarrhythmias caused by sinus node dysfunction and AV block are relatively uncommon in HCM and should raise suspicion of particular genetic subtypes in younger patients, or Fabry disease in older patients. Chronotropic incompetence is common in Fabry disease and can cause exercise limitation. The management of bradyarrhythmias in HCM is no different to that in other patient groups, although the role of rate-responsive pacing in treating exercise intolerance in this patient group is uncertain [1].

In a systematic review of over 7000 HCM patients, the overall prevalence of AF was found to be 20-25% [7]. The prevalence of thromboembolic events in HCM patients with AF was found to be nearly 30%, with a reported incidence of 3.75% per 100 patients per year. For this reason, ambulatory ECG monitoring is vital at initial clinical assessment to assess both the risk of SCD and stroke. Left atrial dimension and age are common predictors for risk of AF and thromboembolism in HCM [1,7].

Owing to the younger age of HCM patients with AF compared to the general population, the CHADS-VASc scoring system should not be used to assess thromboembolic risk in this patient group. All HCM patients with documented AF should routinely receive lifelong anticoagulation unless contraindicated. Non-vitamin K antagonist oral anticoagulants (NOACs) are only recommended if warfarin is not tolerated, as there is no data supporting the use of NOACs in HCM. Digoxin should be avoided in patients with left ventricular outflow tract (LVOT) obstruction and class 1C antiarrhythmics such as flecainide are not recommended as these may increase the risk of further arrhythmias [1].

Risk assessment

Factors that have been shown to influence risk of SCD in HCM include: presence of unexplained syncope, documented NSVT, severe LVH or LVOT obstruction on echocardiography, abnormal blood pressure response to exercise, and family history of SCD at a young age. Some, such as NSVT and unexplained syncope, appear to be more important in younger patients [1,8]. In addition, left atrial size
has also been shown to be an independent predictor of SCD in a cohort of nearly 1500 Italian HCM patients [9].

There have, however, been no randomised studies or validated prospective risk prediction models to guide implantable cardioverter-defibrillator (ICD) implantation for primary prevention in HCM. There has been concern that binary risk assessment approaches traditionally used in HCM patients to decide appropriateness of primary prevention ICD implantation are inconsistent, don’t take into account different effect size of individual risk factors, and provide only crude estimates of risk [10,11]. Furthermore, a large proportion of ICD recipients have experienced inappropriate shocks and device-related complications [12].

In 2014, O’Mahony et al proposed the first validated prognostic risk prediction model for SCD in HCM (called HCM risk-SCD) based on data from a retrospective, multi-centre longitudinal cohort study [13]. The investigators predict that, if 16 HCM patients receive an ICD as a result of a 5-year SCD risk estimate of ≥ 4% using their prediction tool, one death will be prevented at 5 years [13,14]. Interestingly, this model excludes abnormal blood pressure response as a risk marker. It should also be noted that, using this model, the calculated risk of SCD falls in patients with severe LVH greater than 35mm. The fall in risk in patients with extreme LVH may have been confounded by small numbers of patients in this category, but this phenomenon has also been observed in a previous study [8]. The risk prediction tool has only been validated in European patients, and it cannot be used in patients who have had a myomectomy or alcohol septal ablation. Further, it cannot be used in paediatric patients, elite athletes, patients who have metabolic/infiltrative diseases such as Fabry disease, and patients who have syndromes such as Noonan syndrome [1,13].

The risk estimate calculated using HCM risk-SCD decreases with increasing patient age. The 1% to 99% centiles of the patient cohort on which the model was derived from was 16.9 years to 81.4 years (mean ± standard deviation 48±17 years), showing that it has been reasonably validated in older patients [13]. Such a fall in risk with age is clinically plausible, as patients who had survived longer with the condition or who express the phenotype at a later age are expected to have inherently at lower disease-related risk compared to patients who express a similar phenotype at a younger age. In 2013, Maron et al showed that HCM patients surviving into the seventh decade of life are at low risk of SCD even with conventional risk factors, and that other cardiac and non-cardiac comorbidities have greater impact on survival than HCM in older patients [15].

**Managing the risk of SCD**

There are no randomised controlled trials or other convincing evidence to support the use of antiarrhythmic pharmacotherapy for prevention of SCD in HCM and pharmacological therapy is administered on an empirical basis to improve functional capacity, reduce symptoms and prevent disease progression rather than for antiarrhythmic properties [1].

Avoidance of competitive sports is recommended in patients with HCM. Fatal, exercise-induced ventricular arrhythmias are however rare, especially in asymptomatic patients, and the vast majority of appropriate ICD therapies have been shown to occur in the absence of physical exertion or tachycardia [16,17].

ICD implantation is recommended for high risk patients. The 2014 ESC guidelines recommend that ICD implantation should be considered in patients with an estimated 5-year risk of SCD of ≥6% and a life expectancy of 1 year, and they recommend that the 5-year risk of SCD should be re-evaluated at 1-2 year intervals or whenever there is a change in clinical status [1]. Patients who have had previous sustained ventricular arrhythmia or aborted SCD are at particularly high risk of subsequent lethal cardiac arrhythmias and should routinely be offered ICD implantation for secondary prevention.

Most patients only require a single ventricular lead, although patients with LVOT obstruction may benefit from an atrial lead to provide the option of short AV delay pacing, and resynchronisation therapy should be considered in those with impaired ventricular function. The VF zone of the device should be programmed at >220/min to minimise shocks from rapidly conducted AF. Anti-tachycardia pacing can be effective at terminating ventricular arrhythmias, although it doesn’t reduce the incidence of appropriate shocks [1,18]. Beta blockers and/or amiodarone are recommended in
patients who continue to have symptomatic ventricular arrhythmias or recurrent shocks despite optimal device reprogramming. Some patients may require electrophysiological studies to identify and treat any ablatable arrhythmic substrate if they continue to get supraventricular tachyarrhythmias that lead to inappropriate ICD shocks [1].

Conclusions

The 2014 ESC guidelines provide comprehensive recommendations on risk stratification and management of arrhythmias in HCM using both current best evidence and consensus expert opinion. The recommendations are patient-centred with particular focus on individualised assessment and therapy, but also set the benchmark for optimal management of these patients.

References


