Sudden cardiac death risk in hypertrophic cardiomyopathy

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This editorial refers to ‘Disease penetrance and risk stratification for sudden cardiac death in asymptomatic hypertrophic cardiomyopathy mutation carriers’1, by M. Michels et al., on page 2593 and ‘Exercise-induced ventricular arrhythmias and risk of sudden cardiac death in patients with hypertrophic cardiomyopathy’2, by J.R. Gimeno et al., on page 2599

It is well recognized that sudden cardiac death (SCD) is an infrequent, unpredictable, but catastrophic complication of hypertrophic cardiomyopathy (HCM). In population-based studies the overall SCD rate is ~1% per year among patients with a clinical diagnosis of HCM. A crucial aspect of the management of patients with HCM is an assessment of each individual patient’s risk for SCD so that preventative strategies may be considered. Data on the effectiveness of any pharmacological strategy to prevent SCD are at best conflicting so that ultimately SCD risk stratification in hypertrophic cardiomyopathy comes down to assessing whether patients are potential candidates to receive implantable cardioverter defibrillators (ICDs). The ICD, while undeniably effective in aborting SCD, is associated with a considerable morbidity, especially in younger patients, and the decision to implant should not be taken lightly.2–4

Despite decades of investigation, our ability to risk stratify for SCD is imperfect at best, as evidenced by the fact that, even among patients with no discernible risk factors, SCD occurs at a rate of just less than 1% per year; patients with ≥ 3 risk factors appear to have event rates that approach 5% per year, whereas even survivors of prior SCD have a rate of subsequent SCD of ~10% per year.4 This low positive predictive value of current risk models means that in all risk categories most patients are unlikely to experience an arrhythmogenic event in any given year. The problem is compounded by a lack of consistent quantitative data or even definitions for specific risk factors (Figure 1). Family history of SCD has a paucity of data to support its use, and whether deaths should be considered only in primary relatives or extended to more distant relations has varied in the literature. In the end, the choice of whether to pursue an ICD comes down to whether individual patients and their physicians perceive that the risk for SCD outweighs the risk of device placement. That we need a better understanding of the triggers for ventricular arrhythmias in HCM and better risk stratification algorithms is obvious, but the tools are lacking.

Two separate investigative teams have recently reported findings relevant to risk stratification in HCM. Gimeno et al.5 describe the impact of exercise-induced ventricular arrhythmias on subsequent SCD rates in HCM patients. While the results are somewhat intuitive (exercise-induced arrhythmia portending subsequent arrhythmogenic events), this concept had been only partially addressed in prior publications.6 One could question whether exercise-induced ventricular arrhythmias represent a new risk factor, or whether this is simply an additional method of assessing for non-sustained ventricular tachycardia; an SCD risk factor with varied data on its prognostic value.7–11 Nevertheless, the current study appears to provide an important message confirming that clinicians need to pay attention to the electrocardiogram whether this is the resting ECG, the ambulatory ECG, or the ECG recorded during exercise testing. Ventricular arrhythmias, in any setting, appear to have potentially ominous implications for some HCM patients.

The second study by Michels et al.12 actually introduces a new dilemma for cardiologists caring for families with HCM. Specifically, these investigators found that patients who had inherited an HCM-associated mutation could have conventional risk factors for SCD even in the absence of left ventricular hypertrophy. Prior to this publication, there has been an uneasy consensus that HCM genotype-positive, phenotype-negative individuals were unlikely to be at increased risk for adverse events.13 In other words, SCD, representing one of the phenotypic expressions of HCM, is unlikely in the absence of any other phenotypic expression of the disease. However, it remains possible that among prior population-based autopsy series, some of the ‘unexplained’ sudden deaths may represent individuals with occult HCM-associated mutations in the absence of hypertrophy. It would be interesting to consider a molecular genetic component to post-mortem examination in cases of unexplained sudden death.

The fact that risk factors for SCD can exist in the absence of hypertrophy certainly provides a counselling challenge. Specifically,
the question may now be raised as to whether an HCM-associated mutation in the presence of risk factors for SCD is sufficient to warrant placement of an ICD. Current guidelines and consensus documents do not support this notion, nor does the current study answer that question.\textsuperscript{13,14} We will need sufficient follow-up time of patients with HCM mutations in the absence of hypertrophy who truly experience SCD prior to the onset of hypertrophy; and such patients are uncommon. It is intriguing that an arrhythmic substrate may be present without the classical features of the phenotype and, if other studies confirm this finding, it illustrates the dichotomy between phenotypes and the complexity of SCD in HCM.

In summary, these two studies illustrate different facets of this intriguing but at times frustrating disease, which defies attempts at simplification from a clinical, morphological, electrophysiological, and genetic standpoint. Physicians need to help each individual patient and family gain an understanding of the complexities so that they may participate in decision making.

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References