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’†, by M. Michels et al., on page 2593 and ‘Exercise-induced ventricular arrhythmias and risk of sudden cardiac death in patients with hypertrophic cardiomyopathy’‡, 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.

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. 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 prognostic value. 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.† 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. 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.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