Hypertrophic cardiomyopathy (HCM) is a genetic disease with a prevalence estimated to be 1:500 in a general population of young adults, based on clinical and echocardiographic criteria.[i] HCM is associated with an increased risk of cardiac arrhythmias, including atrial fibrillation (AF), nonsustained ventricular tachycardia (NSVT), and sustained ventricular tachycardia (VT). Presence of cardiac arrhythmias has an important effect on the prognosis of HCM patients, especially with respect to ventricular arrhythmias as a major cause of sudden cardiac death (SCD). The 2014 European Society of Cardiology (ESC) guidelines for HCM[ii] include a calculator which estimates a 5-year risk of SCD, based on a prognostic model derived from a retrospective, multicenter longitudinal cohort study.[iii] The 2011 American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) guidelines[iv] as well as the 2017 AHA/ACC/ Heart Rhythm Society (HRS) guidelines[v] utilize presence of various clinical factors such as unexplained syncope, left ventricular wall thickness, family history of SCD, NSVT, and/or abnormal blood pressure response during exercise to recommend implantable cardioverter-defibrillator (ICD) implant for primary prevention of SCD.

In this issue of *Journal of Cardiovascular Electrophysiology*, Magnusson and Mörner describe the incidence of NSVT, AF, and bradycardia in thirty patients (mean age of 50 years of age) at relatively low risk of SCD by utilizing an implantable cardiac monitor (ICM).[vi] Of note, most patients (29/30) had a 5-year SCD risk score of <4% (mean of 2.3%), as calculated by the ESC SCD risk calculator. Patients with a high risk of SCD (>6% over five years) were excluded as ICD implant should be considered in this group.

Analyzing data from an ICM (Confirm Rx; Abbott/St. Jude Medical) implanted for 18 months, 7 (23%) patients had NSVT. No patients had sustained VT. Nine patients (30%) had

evidence of AF (>2 minutes in duration), all within the first 12 months. Of note, only three patients with AF had symptoms. Lastly, asymptomatic sinus bradycardia or pauses were also seen in 13 patients (43%). Sinus bradycardia occurred, typically at 30-40 BPM (with ICM cutoff for detection set at 40 BPM), with longest pause recorded of 3.1 seconds. Most bradycardia episodes occurred during nighttime, and did not meet criteria for pacemaker implantation. Thus, the clinical significance of these findings is minimal.

This is the first study utilizing an ICM for arrhythmia detection in an HCM population. A relatively high incidence of NSVT and AF was detected in patients at low risk for SCD. Perhaps this is not surprising, given the prolonged nature of ICM monitoring compared to ambulatory cardiac monitoring. Almost all patients had newly detected arrhythmias; only 2 of 7 patients with NSVT having had prior documentation on Holter, and only 2 of 9 with AF. Thus, out of 30 patients, a new arrhythmia diagnosis was made in 5 patients that impacts their calculated SCD risk and in 7 patients in whom anticoagulation is now indicated.

NSVT on Holter monitoring has been associated with increased risk of SCD in HCM patients. Monserrat et al. found that 20% of 531 patients with HCM had evidence of NSVT on ambulatory electrocardiogram monitoring.[vii] Over a mean follow-up of 70 months, 32 patients had SCD. The odds ratio (OR) for SCD in patients with NSVT was 2.8, with higher risk in those $\leq$ 30 years of age (OR 4.35; p = 0.006) than those over 30 (OR 2.16; p = 0.1). Interestingly, no relationship was found between SCD risk and frequency, duration, or rate of NSVT episodes.

SCD risk assessment remains a challenge. Risk assessment models have been largely based on retrospective cohort studies, and there is debate about which model is “best”,

weighing sensitivity and specificity of predicting SCD. However, presence of NSVT remains a risk factor in both the European and American models.

AF is the most common arrhythmia in HCM patients, and has been thought to be associated with an increased risk of HCM-related death, with Olivotto et al. reporting an OR of 3.7, due to excess of deaths related to heart failure, in 480 consecutive HCM patients.[viii] In this series, patients with AF also had a higher risk of stroke (OR 17.7). AF was documented after symptom onset, or incidentally at time of routine examination. Regarding incidence of AF, during a mean follow-up of 9 years, AF occurred in 107 patients (22%; annual incidence of 2%). However, a more recent report by Rowin et al.[ix] demonstrated that the overall prognosis of patients with AF and HCM may not be so dire. 304 patients with AF with at least one clinically overt episode of AF requiring medical attention were included in the cohort study. Over a follow-up of 4.8 years, 91% were alive, with 89% having only New York Heart Association class I or II symptoms. In this group, the incidence of severe heart failure was similar to the cohort group. These contrasting results may be in part due to the improvements in treatment of HCM patients, including the use of ICDs, catheter ablation of AF, percutaneous and surgical interventions for outflow tract obstruction, and greater use of anticoagulation, including direct oral anticoagulants. Nevertheless, AF in HCM patients is considered a class I indication for anticoagulation, as per the 2011 ACCF/AHA guidelines[iv] as well as the 2014 ESC guidelines,[ii] unless contraindicated, and thus, its diagnosis carries significant implications.

The authors certainly provide useful background information of arrhythmia burden in a low risk HCM cohort. What is not well defined, however, is what one should do with this information. Most would agree that the bradyarrhythmias detected during sleeping hours

would not warrant pacemaker implantation. However, it is unclear if these events represent parasympathetic physiology of sleep, or can be ascribed to undiagnosed/untreated obstructive sleep apnea (OSA). This would have import, as the second arrhythmia finding, atrial fibrillation, can be instigated by OSA. Magnussen and Mörner acted upon the finding of AF (by recommending anticoagulation), but they did not act on the other findings. In this low risk HCM population, the documented NSVT did not increase the ESC risk score sufficiently to recommend ICD implant for any of the patients, and thus the value of this information is unclear. That said, the ACCF/AHA HCM guidelines do list NSVT as a class IIb indication for ICD in the absence of other risk factors, especially if risk modifiers are utilized (such as delayed enhancement on MRI). Additionally, the definition of NSVT (>8 beats at >160 BPM) is not the standard definition used for HCM risk stratification (> 3 beats at >120 BPM) and therefore may lack sensitivity. Lastly, SCD risk in HCM patients is generally considered in multi-year intervals (5 years for the ESC risk score). Therefore, the decision to remove the ICM after 1.5 years is curious, and suggests that the arrhythmia burden reported in the present study may be somewhat incomplete. Modern ICM have battery lives at least twice this. Having longer monitoring periods could allow for even more NSVT detection. Perhaps this is more ubiquitous than previously thought and as such may have little prognostic significance after all. Or perhaps NSVT is most predictive in intermediate risk HCM patients, in whom a decision regarding ICD implantation is more ambiguous than the cohort described in this study.

The first step in determining appropriate treatment strategies for arrhythmias in HCM is to define the scope of the problem; to observe and report. The authors have provided the first

real glimpse into continuous monitoring in this patient population. However, in order to protect and serve our patients, we need more complete information.

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