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Differing strategies for sudden death prevention in hypertrophic cardiomyopathy

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ABSTRACT

Sudden death (SD) has traditionally been the most visible and feared complication of hypertrophic cardiomyopathy (HCM). Substantial progress in reducing the occurrence of these catastrophic events represents a new paradigm in disease management. Prevention of SD in HCM has resulted from introduction of primary prevention ICDs that reliably terminate life-threatening ventricular tachyarrhythmias, as well as a matured risk stratification algorithm capable of reliably identifying those patients at highest risk. This initiative has been a major determinant of reducing HCM-related mortality to a low rate of 0.5%/year. In such a heterogeneous heart disease as HCM, no perfect risk stratification strategy is possible, and available approaches differ in terms of sensitivity and specificity for identifying patients with SD risk. Major cardiovascular societies, American Heart Association/American College of Cardiology in the USA and European Society of Cardiology in Europe have promoted different risk stratification guidelines creating the potential for judging SD risk in a given HCM patient differently based on commitment to a particular societal guideline or country of residence. In this review, we provide a critical but balanced assessment of these two divergent SD prevention strategies with regard to their respective strengths and weaknesses, as a guide to clinicians directly engaged in this important management issue.

INTRODUCTION

Sudden death (SD) has traditionally been the most visible and feared complication of hypertrophic cardiomyopathy (HCM) in physician and patient communities for >50 years[1–10] and has created an ominous prognostic narrative that appears to persist even today.[6–10] Historically, for many years, HCM was burdened by absence of a preventive treatment against SD,[1] although substantial progress in reducing the numbers of these catastrophic events now represents a new paradigm in disease management.

Indeed, during the last two decades, this disease has been transformed by contemporary management initiatives including the aggressive targeting of high-risk patients for prophylactically implanted cardioverter-defibrillators (ICDs).[10–17] As a result, the ICD has altered HCM clinical course for many patients throughout the world[11 12 14] and reduced the number of SDs, contributing to a substantially decreased mortality rate not thought possible even a few years ago for this disease.[1 18]

Nevertheless, risk stratification and selection of patients for ICDs in HCM has been periodically encumbered by a measure of scepticism, while at the same time overlooking the substantial life-saving progress already demonstrated with this initiative.[1 3 11–17] Nevertheless, certain 'gaps' in risk stratification remain important, including opportunity to decrease the number of apparently unnecessary implants that may place patients at increased risk for device-related complications.[19] Certainly, the interplay of traditional risk markers, modifiers and predictive statistical models has created a measure of uncertainty in the decision-making process for clinicians potentially confronted in their practice by HCM patients with arrhythmic risk.

Evidence of this dilemma are the two prominent but different risk stratification strategies that have emerged for the selection of patients deserving prophylactic ICD implants (table 1), supported independently by societal guidelines in the USA and Europe,[20–24] unavoidably raising the distinct possibility that patients with similar clinical profiles in different countries may not receive the same recommendation for the primary prevention of SD. In this review, we confront this unique clinical situation and assess in a balanced fashion those risk stratification approaches now employed in HCM practice.

DEMOGRAPHICS OF HCM-RELATED SD

Initially, SD events in HCM were thought to occur largely in young adults and adolescents.[1] This narrative was also driven by the early literature (and the media) showing HCM to be an important cause of SD in young competitive athletes.[25] However, based on ICD studies in HCM cohorts over 20 years, it is evident that arrhythmic SD events are also frequently delayed until later into midlife with the average age of first ICD therapy at 40 years.[16]

In reality, HCM can be considered a relatively low event rate disease. In hospital-based HCM cohorts, SD events are the least common of the major disease-related complications.[1 3 18] Furthermore, surveys and registries of SDs in clinically undiagnosed HCM patients also support the low prevalence of fatal events in this disease.[26 27]

UTILISATION OF ICDS IN HCM POPULATIONS

Historical context

After the initial comprehensive description of HCM by the Braunwald group at the National Institutes of Health in the early 1960s,[28] no effective protection from SD was available for many years. The earliest approaches to prevention were pharmacological with prophylactic administration of beta-blockers and verapamil and briefly an obsolete strategy in which antiarrhythmic drugs (eg, procainamide; quinidine) were combined with serial programmed ventricular stimulation to extinguish ventricular tachycardia (VT)/ventricular fibrillation (VF) episodes provoked in the laboratory.[6] However, such treatment strategies with

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Table 1 Comparison of AHA/ACC versus ESC strategies for sudden death prevention in HCM

Variables	AHA/ACC[21]	ESC[20]
ICD decisions	≥1 risk markers	Quantitative score
SDM in ICD decisions	Recommended	Objective score
Tested prospectively	yes	no
Annual event rate	Not used	Over 5 years
Prediction of SD events		
Sensitivity	95%	33%
Specificity	78%	92%
Flexible algorithm	+	Fixed
Number of ICDs needed to treat	6.6	7.2
Risk markers used		
Syncope	+	+
Massive LVH	+	+
NSVT	+	+
Family history: HCM-SD	+	+
LGE (fibrosis)	+	0
LV apical aneurysm	+	0
End stage (EF <50%)	+	0
CMR-related markers	+	0
Age*	+	+
LVOT obstruction 30 mm Hg	0	+
LA diameter	0	+

+=present.
0=absent.
*Age is not itself a major risk marker in the AHA/ACC method, but it is given important weight in the guidelines as a variable that can impact decisions regarding prophylactic ICD.
ACC, American College of Cardiology; AHA, American Heart Association; CMR, cardiovascular magnetic resonance; EF, ejection fraction; ESC, European Society of Cardiology; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; LA, left atrium; LGE, late gadolinium enhancement; LV, left ventricle; LVH, left ventricular hypertrophy; LVOT, left ventricular outflow tract; NSVT, nonsustained ventricular tachycardia; SD, sudden death; SDM, shared decision making.

drugs failed to generate strong antiarrhythmic effects, change the natural disease course or enhance longevity.

The ICD was inspired and designed by Mirowski and Mower at Sinai Hospital (Baltimore) in the 1970s for the prevention of SD in patients with ischaemic heart disease.[29] However, ICDs were initially employed sparingly in HCM until a landmark study in 2000,[15] showing device therapy reliably terminated potentially lethal ventricular tachyarrhythmia events and immediately restored sinus rhythm in high-risk patients.[10]

Efficacy

There is little debate over the efficacy of ICDs to abort life-threatening ventricular tachyarrhythmias in HCM.[11–17] The intervention rate for primary prevention therapy employing the individual risk factor strategy has been consistent at 3%–4%/year (10% /year for secondary prevention after cardiac arrest)[6] based on numerous multicentre and single institution studies and meta-analyses, in turn triggering dissemination of primary prevention ICDs to a multitude of countries and practices on all continents in patients of all ages, including children.[6 9 10 30] As a consequence, the ICD has been a major determinant of reduction in the HCM-related mortality rate to 0.5%/year (>10-fold lower than in the pre-ICD era), similar in all age groups including young patients generally considered to be at the highest risk.[6 18] Furthermore, survival with HCM has now been shown to exceed that of other cardiac or non-cardiac conditions that constitute the general risks of living.[31]

In HCM, there are often prolonged periods of device dormancy after implant before initial appropriate therapy that involves delays of 10 or more years in one-third of patients (ranging to 17 years). In contrast to ischaemic heart disease, after appropriate device interventions in patients with HCM, subsequent heart failure or disease progression is negligible.

Because all ICD implant decisions are theoretically life long, given the unpredicatability of the arrythmic substrate, the possibility of device-related complications[11] occurring over long periods of time must be considered, particularly for young patients,[9] including infection, lead failure and inappropriate shocks. However, inappropriate shocks triggered by atrial fibrillation, sinus tachycardia or T-wave oversensing have become less frequent (to about 1% / year) with standardised adjustments in device programming using high-rate cut-offs/thresholds and longer detection intervals. It is expected that the long-term risks from chronic indwelling venous leads will also be mitigated by increased employment of subcutaneous ICDs.[32] It is also notable that ICD implants do not appear to substantially impair overall psychological and physical well-being and may in select patients allow for an improved psychological outlook that would not be possible without device therapy.[17] In addition, sudden death risk can extend over long periods of time, with 36% of HCM patients who receive their first shock for life threatening VT/VF >10 years after the time of device implant.[16]

THE DEBATE: SELECTION OF PATIENTS FOR ICDS

In such a complex and heterogeneous heart disease as HCM, associated with a very low SD event rate, it is perhaps unrealistic to expect a risk stratification strategy in which all at-risk HCM patients appropriately receive prophylactic ICDs (and which interrupt potentially lethal ventricular tachyarrhythmias), while all those patients not at-risk avoid unnecessary lifelong device implants. For this reason, it is most appropriate to consider the results of risk stratification in HCM in terms of weighted balance ('seesaw' in figure 1), for example, with greater emphasis placed on identifying most at-risk patients (sensitivity) at the expense of some device-related overtreatment (specificity) versus greater weight placed on decreasing the number of ICDs implanted (and therefore potential device complications) allows that a greater number of true high-risk patients will remain unidentified and potentially unprotected from SD .

Emergence of two distinctly different methods for risk stratifying patients for primary prevention ICD implants (American Heart Association/American College of Cardiology vs European Society of Cardiology)[20 21] ultimately presents the managing cardiologist with the dilemma of which strategy to consider for each individual HCM patients (table 1). These decisions unavoidably involve which end of the treatment 'seesaw' (figure 1) both physician and patient prefer and/or accept, that is, a strategy that is more likely to protect a greater number of patients from SD risk at the cost of a small degree of overtreatment, or alternatively an approach that may miss some high-risk patients but is associated with less device overtreatment. It is within this framework that it is appropriate to assess here the two different methods available to identify high-risk HCM patients for primary prevention ICDs.[20 21]

MAJOR RISK MARKER STRATEGY (AHA/ACC)

The criteria for SD prevention with prophylactically implanted ICDs consistently promoted by ACC and AHA since the first (2003) HCM international consensus panel (with ESC)[23] rely on

Figure 1

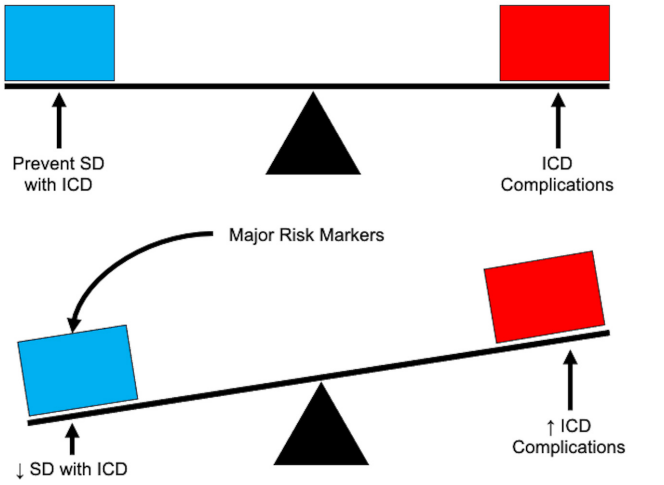

Figure 1 The 'seesaw' that governs ICD decision making in HCM. Risk stratification is a trade-off between preventing SD with ICDs and possible device-related complications. Shown here for American Heart Association/American College of Cardiology major risk marker strategy, using ≥1 risk factors in conjunction with clinical judgement and shared decision making, SDs are reduced (95% sensitivity), but concomitantly, the possibility of ICD complications (largely related to transvenous lead systems) are increased (specificity 78%). The seesaw for the European risk score would show a decrease in SDs (although more modest; sensitivity 33%) but with a significantly lower ICD complication rate (specificity 92%). HCM, hypertrophic cardiomyopathy; ICD, implanted cardioverter-defibrillator; SDs, sudden deaths.

traditional clinical approaches,[20–22] that is, presence of one or more acknowledged risk markers judged to be major within the clinical profile of the individual HCM patient can be sufficient to consider a primary prevention ICD[1 3–5 21–23] in conjunction with shared decision making and a measure of physician judgement when necessary (figure 2, table 2).

In this regard, the individual major risk marker strategy characterises SD risk based on available data and patient clinical

Figure 2

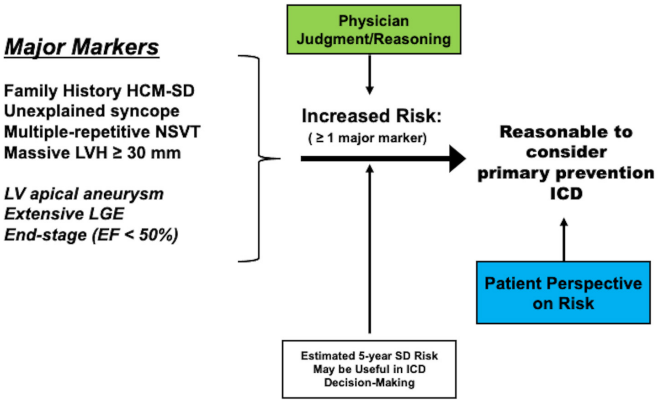

Figure 2 Risk stratification and ICD decision making for high-risk HCM patients based on the American Heart Association/American College of Cardiology guideline major risk marker strategy. EF, ejection fraction; ICD, implantable cardioverter defibrillator; LGE, late gadolinium enhancement; LVH, left ventricular hypertrophy; NSVT, non-sustained ventricular tachycardia; SD, sudden death.

profile to be judged unacceptably increased by both patients and physicians. While both SCD risk strategies can incorporate aspects of shared decision making and physician judgement, the major risk marker model would appear to offer greater opportunity to more easily implement patient-oriented approaches since management recommendations for ICDs are not predominantly based on assignment to a SCD risk estimate.

In this regard, the HCM risk factors that are generally accepted and dominate clinical decision making appear prominently in the literature, large registries and societal consensus guidelines: initially, the 2003 ACC/ESC consensus and thereafter 2011 ACC/AHA; 2014 ESC; 2017 AHA/ACC/HRS; and most recently 2020 AHA/ACC guidelines.[20–23]

Furthermore, over the last several decades, efficacy of the risk marker strategy has been extensively reported in adults and children selected for primary and secondary ICD therapy largely in retrospective clinical investigations predominantly from USA, Canada and Europe. These studies have consistently demonstrated that in high-risk HCM patients identified with the AHA/ACC risk marker strategy, primary prevention ICDs reliably terminated VT/VF (rate: 3%–4%/year) at an average age of 45 years with about one-third experiencing multiple device therapies.[11–16] However, these prior registry studies have for the most part been confined to select high-risk patient populations with ICDs with limited sensitivity and specificity for predicting future SD events.[4 5 10 15]

However, a number of contemporary studies have assessed the overall efficacy of the major risk factor strategy.[13 33 34] The largest of these efforts is a 17 -year consecutive prospective patient analysis, demonstrating with a sensitivity of 95%, the reliable selection of patients who subsequently experienced appropriate device therapy from prophylactically implanted ICDs, thereby aborting potential SD events and interrupting the natural history of the disease[13] (figure 3). Patients selected for ICDs and who received appropriate device therapy exceeded by 50-fold for those patients not selected for ICDs but who experienced SD events. Furthermore, 40% of the small number of patients who died suddenly were advised of their high-risk status but declined a prophylactic ICD.[13]

Notably, the AHA/ACC individual risk marker model[21] affords the necessary flexibility to allow addition of risk factors to the algorithm.[35 36] For example, with introduction of CMR to HCM, three novel markers have been identified, that is, LV apical aneurysm, extensive late gadolinium enhancement (LGE; fibrosis) and end stage with systolic dysfunction and diffuse LGE.[36–39] These new CMR markers account for an important 20% of appropriate ICD therapies, either solely or in combination with other risk factors but have not been incorporated into the ESC risk score[20 36] (figure 4). Of note, substantial LGE is also particularly helpful in resolving complex ICD decision making, acting as an arbitrator in selected patients for whom SD risk remains ambiguous, even after stratification with the other major markers. Alternatively, absence of LGE is associated with lower risk for adverse events, providing a measure of reassurance to patients and their healthcare providers.

Finally, the individual risk marker approach creates the opportunity to apply medical reasoning and physician judgement/intuition when necessary to assess the weight that certain risk factors deserve in the overall assessment of individual HCM patients, so important in a heterogeneous disease such as HCM in which ambiguities related to risk stratification arise not uncommonly.[21 35]

Specific examples may include: young HCM patients with maximal LV thickness that approaches but does not precisely meet the traditional ≥30 mm cut-off for massive LV hypertrophy as an independent SD risk marker[3 6 21 30]; syncopal episodes judged

Table 2 Major clinical markers recommended for current HCM risk stratification*†[21]

Family history of SD†[3 6]	Sudden death judged definitively or likely due to HCM, generally considered occurring in ≥1 first degree, or other close relatives, <50 years of age.
Extreme LV hypertrophy†[9 42]	Wall thickness ≥30 mm in any LV segment by echocardiography and/or CMR; consideration for this morphological marker is also given to borderline values of 28 mm or 29 mm in individual patients, at the discretion of the treating cardiologist.‡
Unexplained recent syncope†[43]	One or more recent and otherwise unexplained events involving loss of consciousness, judged by history unlikely to be neurally mediated (vasovagal) syncope.§
Non-sustained ventricular tachycardia (NVST)¶[3 6]	Three or more brief episodes of consecutive ventricular beats and/or ≥1 prolonged burst of ≥10 beats, at a rate of >130/min, usually over 24–48 hours continuous ambulatory ECG monitoring.
LGE (fibrosis)[39]	Diffuse and extensive LGE distribution representing fibrosis, either quantified or estimated by visual inspection as comprising about ≥15% of LV mass, either alone or in association with other risk markers, and a likely source of ventricular tachyarrhythmias.**
End-stage HCM[38]	Systolic dysfunction with ejection fraction <50% by echocardiography or CMR, usually in symptomatic patients without outflow obstruction who may be considered potential heart transplant candidates.
LV apical aneurysm[37]	Of variable size and characterised by akinetic-dyskinetic thinned wall. Usually identified by CMR (or contrast-enhanced echocardiography), with contiguous 'border-zone' myocardial scarring, often associated with apical hypertrophy and malignant ventricular tachyarrhythmias.

*Two other variables, abnormal blood pressure response to exercise and LV outflow obstruction (gradient ≥50 mm Hg at rest), can be used to selectively support ICD decisions in some patients with ≥1 other risk markers, but alone are not usually considered sufficient evidence to support ICD recommendations.
†Most important in risk stratification of children and adolescents.
‡Relationship between LV thickness and SD risk is linear, although mild LVH does not necessarily exclude SD risk; pattern of LVH does not predict HCM outcome, including development of heart failure.
§Episodes of near-syncope can also be considered, if judged likely to be arrhythmic in origin.
¶Prognostic power of NSVT as a risk factor is probably greater when associated with other markers, particularly substantial LGE, which can be responsible for ventricular tachyarrhythmias: it is also intuitive that long NSVT runs (≥ 10 beats) convey greater risk than brief runs.[6 21] Caution is appropriate when prognostic judgements rely solely on NSVT as an isolated risk factor because of its variability and also the difficulty in standardising for length of the monitoring period. Prolonged, frequent periods of palpitations can represent important ventricular tachyarrhythmias, particularly when associated with impaired consciousness but require documentation by ECG monitoring.
**In addition to the arbitrary cut-off of ≥15% of LV mass (exclusive of right ventricular insertion areas), a linear relationship is demonstrated between SD risk and LGE extent, suggesting that LGE of 10%–15% can be clinically relevant in some patients; absent or focal LGE (<5% of LV mass) is generally regarded as most consistent with low risk.
HCM, hypertrophic cardiomyopathy; ICD, implanted cardioverter-defibrillator; LGE, late gadolinium enhancement; LVH, left ventricular hypertrophy; SD, sudden death.

by clinical history as arrhythmic versus neurocardiogenic; or rapid, frequent but isolated long bursts of asymptomatic nonsustained ventricular tachycardia on ambulatory monitoring. This is an important principle, given that some individual HCM risk factors can be encumbered by uncertainty with variable definitions and interpretations that can impair consistency in judging risk stratification.[21 22]

ICD decisions require input from fully informed patients weighing the benefits and limitations of long-term device implants, important in HCM as underscored in the 2020 AHA/ACC guidelines.[21] This element of patient care known as shared decision making is particularly relevant in HCM for which the available clinical information may be ambiguous and/or insufficient to confidently support assignment of level of risk or recommendation of an ICD for a given patient. In this regard, ICD decisions should incorporate the wishes and desires of patients consistent with their personal preferences and values[21 35] (figure 2).

Notably, implementation of the major risk factor strategy with primary prevention ICDs over the last two decades has been a major determinant of the observed significant reduction in HCM-related mortality from as high as 6%/year in pre-ICD eras to the current low rate of 0.5%/year now reported from tertiary centres.[1 3–9 31] This SD prevention strategy has provided HCM patients with the opportunity for survival and possibility of normal or extended longevity.[6]

Figure 3

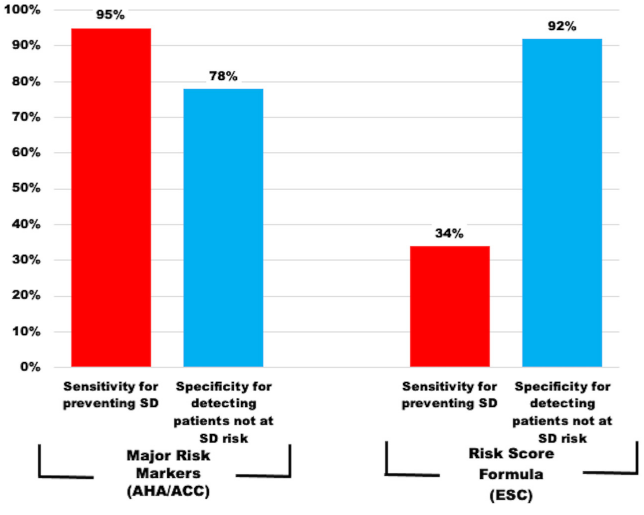

Figure 3 Sensitivity and specificity comparisons for the major risk marker and mathematical risk score strategies. SCD, sudden cardiac death.

Figure 4

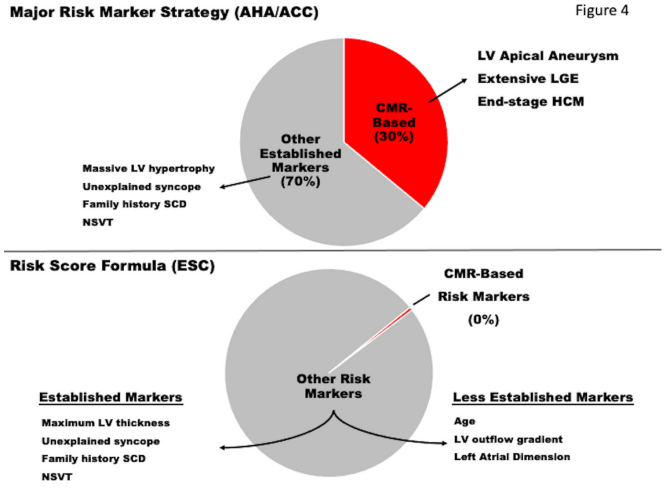

Figure 4 Proportion of high-risk HCM patients with ICD therapy, relative to CMR-based or other risk markers. HCM, hypertrophic cardiomyopathy; LV, left ventricular; LGE, late gadolinium enhancement; NSVT, nonsustained ventricular tachycardia; SCD, sudden cardiac death.

SCD RISK CALCULATOR/SCORE

More recently, another method have emerged to stratify risk for SD in patients with HCM. While European investigators had once adhered to the individual risk factor approach initially supported by the 2003 ESC consensus with ACC,[23] that approach was abandoned when the 2014 ESC guidelines[20] introduced a novel modelling approach with a highly statistically quantitative SD risk score (table 2).

By incorporating several disease-related features into a logistic regression equation, a 5-year SD risk is estimated over 5 years.[7 8 20] There are a number of attractive elements to the ESC risk score, namely ease of generating quantitative risk estimates assessed online quickly or by smart phone virtually anywhere at anytime and which can be used by clinicians having various levels of experience with HCM. The ESC SD risk score is composed of seven disease-related features that can be imputed online. Notably, four of the seven clinical variables in the ESC formula have prior independent association with SD risk, that is, unexplained syncope, massive hypertrophy, family history of HCM-related SD and non-sustained VT, while peak resting LV outflow gradient and left atrial diameter have not been documented in HCM as clearly associated with SD. Notably, CMR-related risk markers such as LV apical aneurysm and extensive LGE are important components of the AHA/ACC individual risk marker strategy but are not included in the ESC score (figure 4).[6–8 20 21]

The ESC SD risk score assigns management recommendations for primary prevention ICDs based on whether a patient falls into one of three risk categories: low (<4%: ICD not indicated), intermediate (4%–6%: ICD could be considered) or high (≥6%: ICD should be considered).[7 8 20] By virtue of the endorsement provided by ESC societal guidelines to >100 member or affiliated national cardiac societies serving countries with a combined population 20-fold that of the USA, the ESC risk score has been afforded substantial visibility in the international practising cardiovascular community.

Reproducibility of the ESC risk score model has been demonstrated in a number of HCM populations with respect to the C-statistic (ie, area under receiver operating characteristic (ROC) curve), where it has demonstrated at least modest discriminatory power for identifying HCM patients who experienced SD.[7 8] However, it has not yet been tested prospectively in an independent HCM population to determine its effectiveness either for risk stratification or prevention of SD by ICDs in 'real world' clinical practice.[6] Also, the utility of SD risk score is uncertain in patients following myectomy or alcohol septal ablation and is not recommended for risk stratification in children and adolescents.[20] This is a key age group in which HCM-related SDs occur not uncommonly, and major individual risk markers have been shown to be highly effective in preventing SDs in such young patients.[9 30] Recently, risk estimate scores have been developed for children with HCM (HCM Risk-Kids) but have not yet been prospectively assessed with clinical ICD decision making.[21]

Notably, a number of investigations have assessed the efficacy of the ESC risk score by its retrospective application to established HCM populations with known clinical outcome (with or without ICDs) and thereby encompassing 12 large cohorts from 15 countries.[13 33 34 40 41] In these analyses, the risk score yielded lower sensitivity (ie, 33%) for identifying patients with subsequent SD events,[13 33 34 40 41] a rate one-third that achieved with the AHA/ACC individual risk factor strategy (ie, with a sensitivity of 95%)[13 33 34] (figure 3). Using the risk score model as a primary strategy, only one-third of the patients who experienced appropriate ICD therapy had scores sufficiently high to justify an ICD recommendation (>6%/5 years).[41] Characteristics of the ESC-SD risk score that could in part explain its low sensitivity include exclusion of contemporary CMR-based risk markers that in contrast are incorporated into the AHA/ACC SD risk stratification strategy[36] (figure 4). These points underscore the challenge translating numerical outcome estimates obtained in patient subgroups to individual HCM patients for the purpose of making dichotomous treatment decisions.

Alternatively, the SD risk model supports an advantage of high specificity for ICD decisions, that is, 92% compared with 78% for AHA/ACC major risk marker strategy with the potential benefit of mitigating a 20% excess ICD use in lower risk young patients who otherwise may be subject to the risk for device complications over long implant periods(figures 1 and 3; table 1).[6] However, the number of ICDs needed to treat and save one life is similar with the two strategies (6.6 AHA/ACC vs 7.2 risk score) (table 1). Nevertheless, many clinicians are willing to accept more ICDs implants,[21] given the unique opportunity the ICD provides for prevention of SD. In addition, apparent ICD excess does not always represent unnecessary implants, since it is not uncommon for prophylactic ICDs to terminate life-threatening ventricular tachyarrhythmias unpredictably after many years.[13]

Finally, although it is difficult to envision directly combining the AHA/ACC and ESC strategies to derive recommendations for ICDs in the same patient, some cardiologists (and 2020 AHA/ACC HCM guidelines)[21] regard quantifying future risk with 5-year SD event rate estimates taken from the risk score as useful in ICD decision making (figure 2).

However, notably, there can be substantial variability in how individual patients perceive SD risk and the impact of this information on treatment decisions to prevent SD. For this reason, objectifying risk stratification by assigning strict ICD recommendations to binary risk estimates: high (ICD should be considered) versus low risk (ICD should not be considered) can be challenging for effectively implementing ICD decision making in a nuanced disease such as HCM. Also, many HCM patients find it difficult to personally relate to mortality rates in real-life terms, particularly considering that the difference in annual risk conveyed by the highest and lowest ESC risk score categories is only about 1%/year.[7 8 20]

In conclusion, ICDs have interrupted the course of HCM in many patients over the past 20 years, terminating potentially lethal ventricular–tachyarrhythmias and irrevocably altering the clinical landscape. The ICD is arguably the most important therapeutic innovation in this complex and often inherited heart disease.[3 11–16] The selection of high-risk HCM patients for ICD implants has evolved greatly with maturation of the AHA/ACC major risk maker strategy[21] and introduction of a novel statistical risk model from ESC.[20]

While these strategies differ in design, both have the same objective of preventing SDs and saving lives of HCM patients. Nevertheless, this situation has generated confusion and some controversy within the clinical cardiology community based on major societal guidelines each advancing different approaches to the same clinical problem. While there is probably no perfect risk stratification strategy achievable for a nuanced and heterogeneous disease such as HCM, it is most realistic to view risk stratification as a 'trade off' between preventing SD versus the possibility of device-related complications (figure 1).

All high-risk HCM patients deserve access to the most effective management strategy for SD prevention. In this review, we have provided a balanced assessment of the two divergent SD prevention strategies to guide those clinicians engaged in this challenging HCM management issue. We believe that with exposure to all available information, clinicians will select the most persuasive approach to identify those high-risk HCM patients in their practice with the best opportunity to experience prevention of SD, independent of allegiance to a particular societal guideline.

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