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REVIEW

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Evaluation of sudden cardiac death in hypertrophic cardiomyopathy

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Abstract

Hypertrophic cardiomyopathy has become a highly manageable condition due to recent therapeutic advances that have significantly reduced its overall mortality rate. However, sudden cardiac death continues to be a critical and unsolved threat, particularly in younger patients and competitive athletes. Even after recent updates to guidelines on sudden cardiac death risk evaluation in hypertrophic cardiomyopathy, new clinical evidence continues to emerge, further enriching our understanding of risk stratification and management. In this review, we summarize current research findings and explore recent advances to provide insights into future directions in the treatment of hypertrophic cardiomyopathy.

Keywords Hypertrophic cardiomyopathy, Sudden cardiac death, Pathophysiology, Etiology, Risk factors

Introduction

Hypertrophic cardiomyopathy (HCM), a globally prevalent primary cardiac disease with a genetic basis, has become a highly manageable condition due to recent advances in treatment [1, 2]. Since the initial pathologic insights by Teare [1, 3] and comprehensive clinical descriptions by Braunwauld et al. [4] in the early 1960 s, great progress has been achieved in the diagnosis and management of HCM. Current therapeutic strategies that target adverse pathways and can be tailored to individuals of all ages have significantly reduced annual HCM mortality, from 6% reported in the 1960 s to 0.5%, which is currently one of the lowest of all major disease-related risks (e.g., cancer, neurological disorders, congestive heart failure) [1, 5–8]. However, in adolescents and young adults, particularly in competitive athletes, HCM remains the leading cause of sudden cardiac death (SCD) [1, 9–12].

In the context of SCD, the implantable cardioverter-defibrillator (ICD) plays a central role in the management of HCM. A landmark study published in the *New England Journal of Medicine* in 2000 demonstrated that ventricular tachyarrhythmias were the primary cause of cardiac arrest in HCM patients, and that ICDs could reliably detect and terminate these life-threatening arrhythmias [13]. Consequently, ICD implantation has become a critical treatment strategy for preventing SCD in high-risk HCM patients [13]. Before the advent of the ICD, high-risk patients were administered cardioactive pharmacological agents (e.g., β-blockers and calcium channel blockers and antiarrhythmic agents such as amiodarone) for SCD prophylaxis [9].

As more patients are being diagnosed with HCM and as treatment strategies for HCM improve, identifying high-risk individuals has become more important. In this review, we focus on the pathophysiology, risk factors, and most recent advances in management strategies for SCD in patients with HCM.

Pathophysiology of SCD in HCM

Two mechanisms are proposed for pathogenesis of arrhythmic SCD in the treatment of HCM: proarrhythmic structural remodeling and ion channel abnormalities

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(Fig. 1). Structural remodeling in the form of cardiac hypertrophy, microvascular dysfunction, myocardial fibrosis, myocyte disarray, and apical aneurysm in HCM can also serve as a proarrhythmic substrate [14, 15]. In terms of cardiac hypertrophy, increased delayed afterdepolarizations (DADs) occur due to elevated cytosolic Ca^{2+} due to enhanced Ca^{2+} entry through L-type calcium channels and decreased exchange through Na^{+}/Ca^{2+} exchanger routes. This increase in DADs has been proposed as a mechanism for cardiac arrhythmias associated with hypertrophy in HCM [16, 17].

Microvascular dysfunction, frequently observed in HCM, is primarily driven by reduced arteriolar density, fibrosis, myocyte disarray, and elevated left ventricle (LV) end-diastolic pressure [18–21]. Structural abnormalities of small vessels in HCM have also been demonstrated [19]. These mechanisms, combined with inadequate myocardial blood flow reserve, predispose patients to myocardial ischemia. Ischemia then promotes abnormal automaticity by altering the resting membrane potential of the myocytes, lowering the threshold for depolarization and facilitating ventricular tachycardia (VT).

Myocardial fibrosis in HCM can be visualized by cardiac magnetic resonance (CMR) imaging using late gadolinium enhancement (LGE). Myocardial scar deposition can be a common reentry circuit for arrhythmic SCD events in HCM. Previous studies have revealed a significant relationship between LGE and VT on ambulatory monitoring [22, 23]. Additionally, a greater extent of myocardial fibrosis indicated by LGE leads to an increased risk of arrhythmic SCD events [24, 25].

Myocyte disarray, which has also been identified as a risk factor for ventricular arrhythmias in HCM, can be assessed by diffusion tensor imaging. Experimentally, myocardial disarray has been linked to altered transmural distribution of connexin 43, playing the role of a substrate for cardiac arrhythmias in HCM [26, 27].

LV apical aneurysm represents another important substrate for monomorphic VT. Rowin et al. [15] reported that the annual appropriate ICD therapy rate for primary prevention in patients with apical aneurysm was 4.0%, which is approximately five times higher than in those without apical aneurysm. Given the higher prevalence of apical-dominant HCM in Asian populations, understanding the characteristics of this phenomenon is critical [28–30]. The junction between scar formation at the aneurysm rim and the adjacent myocardium consistently gives rise to monomorphic VT, providing a rationale for catheter-based ablation therapy in patients with refractory VT [15, 31].

In terms of ion channel abnormalities, lethal arrhythmias can occur, even in the earlier stages of the disease, when structural remodeling is considerably less evident [32]. Preclinical in vivo and in vitro investigations of

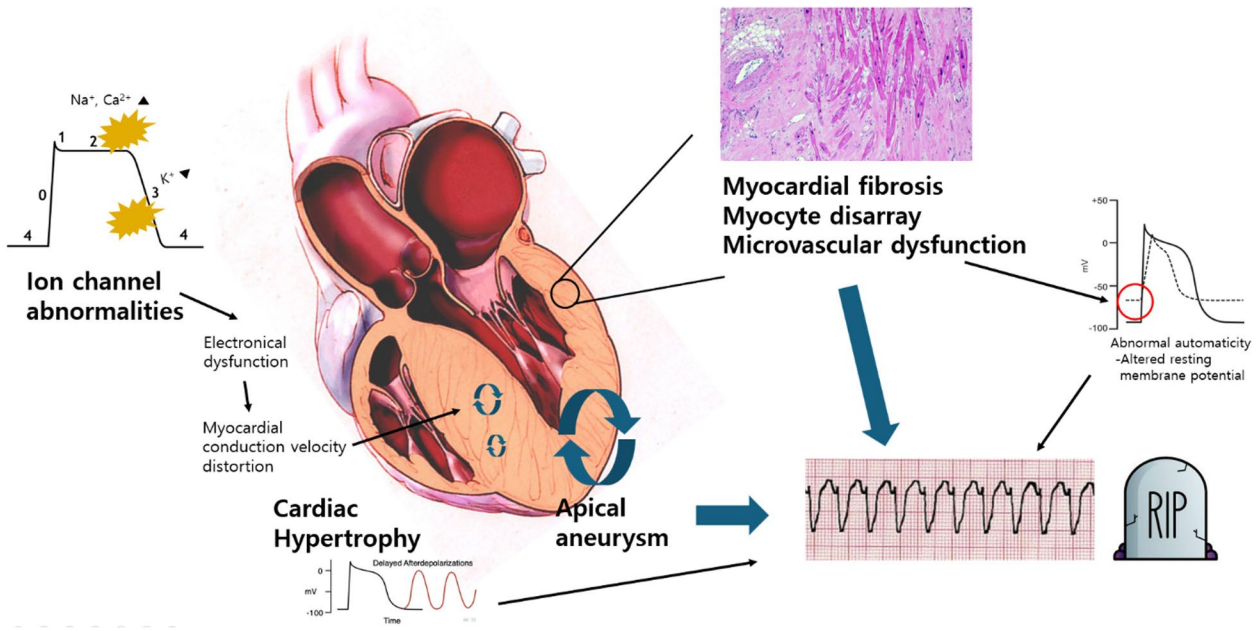

Fig. 1 Pathophysiology of sudden cardiac death (SCD) in hypertrophic cardiomyopathy. Prevention of SCD in hypertrophic cardiomyopathy primarily involves general measures, including recommendations on physical activity, and thorough risk factor evaluations. Selecting appropriate candidates for implantable cardioverter-defibrillator implantation requires careful assessment of various risk factors and, when indicated, the 5-year SCD risk estimation score. Additionally, clinicians must understand potential complications associated with implantable cardioverter-defibrillator implantation and incorporate these considerations into clinical decisions

sarcomeric mutations have revealed a spectrum of ion channel derangements [33–37]. Intracellular mechanisms, such as pathological changes in ion currents and intracellular Ca^{2+} homeostasis, play a role [38–41]. A few studies have found that altered intracellular Ca^{2+} homeostasis and increased late Na^{+} currents lead to an increased likelihood of early after-depolarizations and DADs, which contribute to arrhythmic events in diseased cardiomyocytes [17]. Recognizing this aspect, ranolazine, a potent and selective inhibitor of the cardiac late Na^{+} current, was administered to patients in the RESTYLE-HCM randomized controlled trial. The ranolazine group experienced a reduction in the 24-h burden of premature ventricular complexes, but no significant effects were seen on exercise performance, N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels, diastolic function, or quality of life [42]. As the authors themselves noted, given the study's small sample size and the weak association between ventricular contractions and hard clinical end points, these findings should be regarded as exploratory and hypothesis generating. Their results cast doubt on the pathogenic role of this current in HCM and warrant further investigation.

General management

Various pharmacological strategies, including the administration of prophylactic β-blockers or rhythm-modulating agents such as amiodarone, were once used to reduce the risk of SCD in young asymptomatic HCM patients [9]. These strategies are now considered part of the ICD era, with insufficient evidence to support their routine use [43].

Traditionally, patients with HCM have been advised to restrict exercise and avoid competitive sports. Recommendations are evolving, weighing the beneficial effects of mild to moderate physical activity in HCM patients, based on data from RESET-HCM clinical trial [44]. Although data addressing vigorous physical activity–related SCD are scarce, several studies have determined that vigorous physical activity is not associated with increased mortality or SCD events and may even reduce all-cause and cardiovascular mortality [45–48]. Lee et al. [49] reported that high-intensity physical activity–related SCD events were more common among younger patients, highlighting the importance of an individualized approach when prescribing exercise for HCM patients.

Prevention of SCD in HCM primarily involves general measures, including recommendations on physical activity and thorough evaluations of risk factors. Selecting appropriate candidates for ICD requires careful assessment of various risks and, when indicated, the 5-year SCD risk estimation score. Additionally, clinicians must fully understand the potential complications associated with ICDs and incorporate these considerations into clinical decision-making.

SCD risk stratification

Numerous studies have provided evidence supporting the significant role of ICD in preventing SCD in HCM patients. However, ICD implantation can lead to complications. For example, patients can experience inappropriate shocks, lead dysfunction, infections, bleeding, thrombosis, and lead-related tricuspid regurgitation [50]. The patient-selection criteria are important at this point, requiring consideration of general management strategies, ICD-related complications, and risk factors for SCD (Fig. 2).

Two major guidelines currently address ICD implantation in HCM patients: The 2024 guidelines from the American College of Cardiology (ACC) and American Heart Association (AHA) [51] and the 2023 European Society of Cardiology (ESC) guidelines [52]. Both guidelines strongly recommend that ICDs be considered for patients with documented cardiac arrest or hemodynamically significant ventricular arrhythmias, giving a class I indication for secondary prevention [53–57]. However, guidelines differ slightly regarding recommendations for primary prevention.

Historically, five major risk factors are considered when evaluating the risk of SCD in HCM patients: a family history of SCD, unexplained syncope, maximal LV wall thickness, nonsustained VT (NSVT) on ambulatory monitoring, and abnormal blood pressure during exercise tests. Echocardiography remains the primary imaging modality used to evaluate SCD risk in HCM, although it can underestimate maximal LV wall thickness and miss apical aneurysms [15, 58–61]. Development of new technologies, CMR imaging in particular, has offered diagnostic options to identify these risk factors. CMR can not only help quantify cardiac fibrosis by LGE or T1 mapping values, but it can also help physicians distinguish end stage (ES) HCM from other types of cardiomyopathies through echocardiography [62]. These advances, coupled with a lack of multivariate analyses demonstrating an association between abnormal blood pressure response and SCD, have led to the removal of abnormal blood pressure response from routine risk evaluation [63, 64].

Current ACC/AHA guidelines recommend that, for patients with one or more major risk factors, it is reasonable to use an estimate of the 5-year SCD risk to understand the magnitude of the individual risk associated with ICD decisions (Fig. 3) [11, 51]. The 5-year SCD risk score, which is well described in the ESC guidelines, is based on nine factors: age, unexplained syncope, LV outflow gradient, maximum LV wall thickness, left atrial diameter, NSVT, family history of SCD, LV systolic function, and

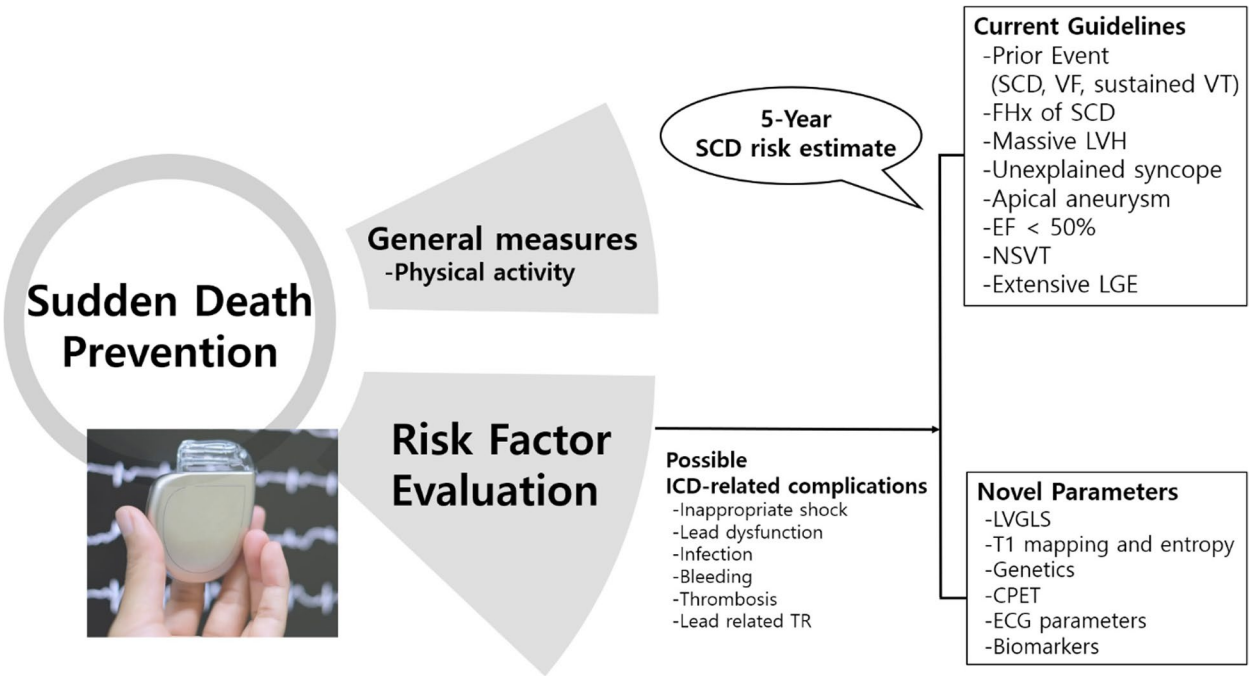

Fig. 2 Management for prevention of sudden cardiac death (SCD) in hypertrophic cardiomyopathy. Prevention of SCD in hypertrophic cardiomyopathy primarily involves general measures, including recommendations on physical activity, and thorough risk factor evaluation. Selecting appropriate candidates for implantable cardioverter-defibrillator (ICD) implantation requires careful assessment of various risk factors and, when indicated, the 5-year SCD risk estimation score. Additionally, clinicians must fully understand potential complications associated with ICD implantation and incorporate these considerations into clinical decisions. CPET, cardiopulmonary exercise testing; ECG, electrocardiography; EF, ejection fraction; LGE, late gadolinium enhancement; LVGLS, left ventricular global longitudinal strain; LVH, left ventricular hypertrophy; NSVT, nonsustained ventricular tachycardia; TR, tricuspid regurgitation; VF, ventricular fibrillation; VT, ventricular tachycardia

extent of myocardial scarring. An estimated 5-year risk less than 4% is regarded as low, while that of 6% or higher implies a high risk (Fig. 4) [52]. These guidelines share a class I indication for secondary prevention in those who have suffered from aborted SCD, VT, or ventricular fibrillation (VF). In addition, because the risk of SCD extends over many decades of life, periodic reevaluations of SCD risks every 1 to 2 years are recommended [51, 65, 66]. However, given the low incidence of SCD in patients older than 60 years, this approach is more suitable for young and middle-aged individuals.

These risk stratification strategies have been validated by multiple studies in Korea. Lee et al. [67] evaluated the performance of 2020 ACC/AHA guidelines and 2014 ESC guidelines for predicting SCD in HCM. Among 1,416 HCM patients, SCD risk was elevated in those with multiple risk factors but not in those with a single risk factor. The AHA/ACC and ESC guidelines had similar performance, with the 5-year time-dependent areas under the curve showing modest statistical power (0.677 and 0.724, respectively; P = 0.235). The ESC guidelines published in 2014 were validated by Choi et al. [68], who reported high negative predictive values and accuracy for predicting SCD or appropriate ICD therapy. However, as diagnostic techniques evolve and new parameters are introduced, further validation in the Korean population will be necessary.

Family history of sudden death from HCM

The effect of family history on SCD is based on the genetic nature of the disease. Relatives who exhibit the condition have the same genetic defect and, to some extent, share environmental factors. Several studies have examined the effects of family history as a predictor of SCD using survival analysis. Four of these studies, although they used different definitions of family history of SCD, found significant associations [69–72]. The average hazard ratio of family history of SCD (irrespective of definition) was 1.27 (95% confidence interval, 1.16–1.38) [10].

Definitions of family history of SCD continue to vary across guidelines. According to the 2023 ESC guidelines, family history is significant if at least one first-degree relative died suddenly before the age of 40 years with or without a diagnosis of HCM or when SCD occurred in a first-degree relative at any age with an established diagnosis of HCM [52]. In contrast, the 2024 AHA/ACC guidelines define a family history of SCD as a sudden death definitely or likely attributable to HCM in one or more

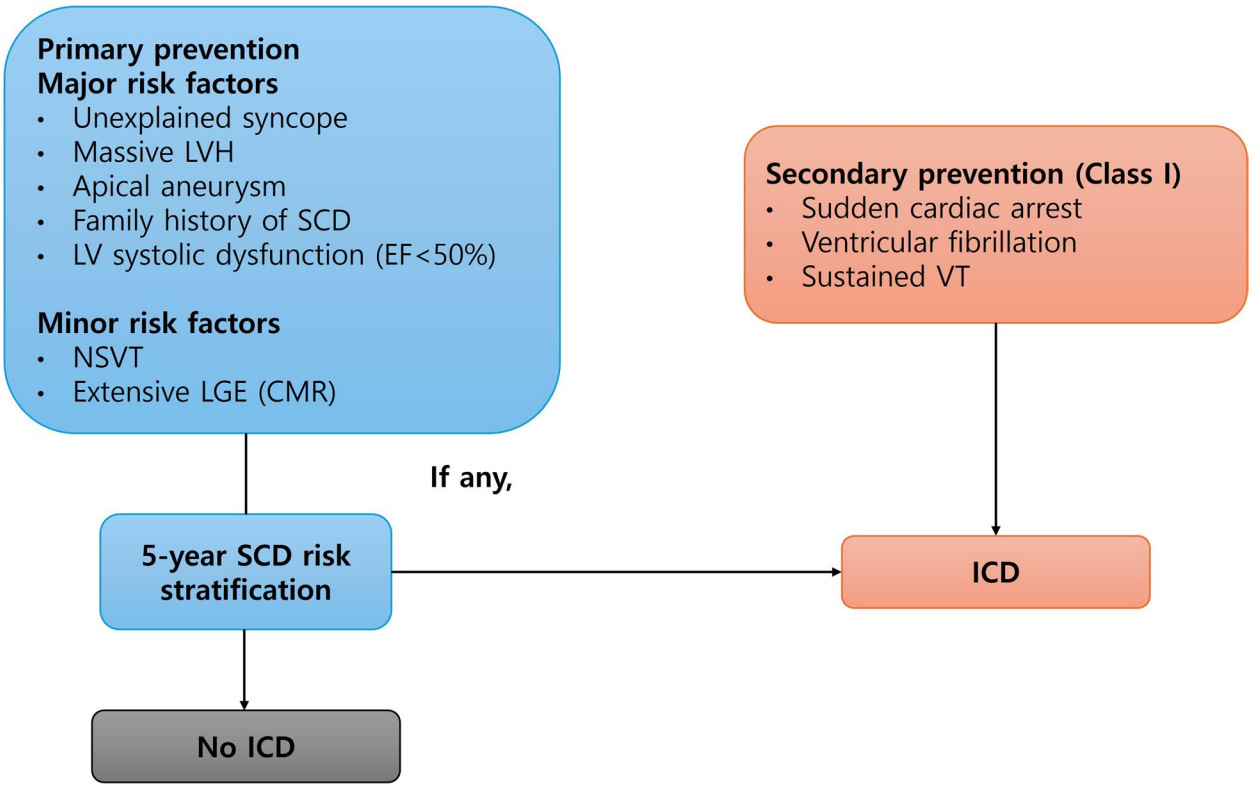

Fig. 3 Proposed algorithm for implantable cardioverter-defibrillator (ICD) implantation in hypertrophic cardiomyopathy. Both the American College of Cardiology/American Heart Association guidelines and the European Society of Cardiology guidelines suggest class 1 indication for ICD implantation in patients who have experienced aborted sudden cardiac death (SCD), ventricular tachycardia (VT), or ventricular fibrillation (VF). In cases of one or more risk factor for SCD, the 5-year SCD risk estimate can be considered when deciding whether to install an ICD. CMR, cardiac magnetic resonance imaging; EF, ejection fraction; FH, family history; LGE, late gadolinium enhancement; LVH, left ventricular hypertrophy; NSVT, non-sustained ventricular tachycardia.

first-degree or close relative aged 50 years or younger [51]. Close relatives would generally be second-degree relatives; however, multiple SCDs in tertiary relatives should also be considered. Multiple cases of SCD in a family history appeared to be a powerful risk factor ($P<0.0001$), predicting frequent SCDs in childhood and adolescence [73].

Massive left ventricular hypertrophy

LV hypertrophy (LVH) is associated with an increased prevalence of NSVT and exercise-induced ventricular arrhythmias [72, 74–76]. In HCM, both the severity and extent of LVH assessed by transthoracic echocardiogram are associated with risk of SCD [52, 74, 77, 78]. A maximum wall thickness of ≥ 30 mm in any segment within the chamber is generally regarded as the greatest risk for SCD in HCM patients, although, based on clinical judgment, a threshold of 28 mm may be a borderline value [11, 77, 79].

However, measurements from a transthoracic echocardiogram can be affected by observer variability and suboptimal imaging quality. Additionally, measuring only the maximum wall thickness may not adequately represent the full extent of myocardial hypertrophy. Under these circumstances, CMR serves as a robust additional diagnostic tool for comprehensive evaluation of LVH.

Unexplained syncope

Spirito et al. [80] conducted a systematic investigation of the prognostic significance of syncope in more than 1,500 HCM patients in 2009. Approximately 15% of the enrolled patients had a history of syncope, either neurally mediated (vasovagal) or unexplained. Neurally mediated syncope was not associated with an increased risk of SCD. In contrast, unexplained syncope showed a relative risk of 1.78 (P = 0.08), which indicates borderline significance. Nevertheless, the authors considered this association clinically significant, given the potential mechanisms underlying syncope in HCM.

Patients with recent unexplained syncope within 6 months before initial evaluation had a fivefold higher relative risk of SCD compared with patients without syncope, regardless of age. Remote episodes of syncope

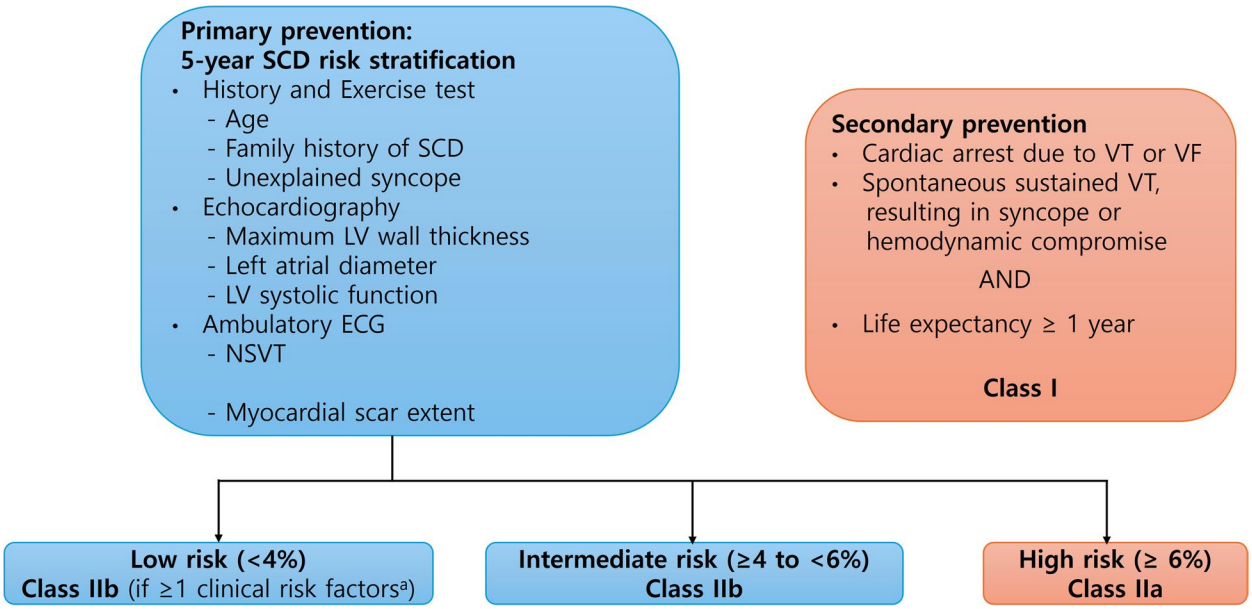

Fig. 4 Flowchart for implantation of a cardioverter defibrillator in patients with hypertrophic cardiomyopathy (HCM). 2D, two-dimensional; ECG, electrocardiogram; ICD, implantable cardioverter defibrillator; LV, left ventricular; NSVT, nonsustained ventricular tachycardia; SCD, sudden cardiac death; VF, ventricular fibrillation; VT, ventricular tachycardia. [a)]Clinical risk factors: extensive late gadolinium enhancement (> 15%) on cardiac magnetic resonance or LV ejection fraction < 50%.

(> 5 years before initial evaluation) showed no significant association in older patients.

Based on these results, current guidelines recommend treating one or more episodes of unexplained syncope, involving acute transient loss of consciousness and judged by history as unlikely to be related with neurally mediated syncope or left ventricular outflow tract obstruction as a major risk factor for SCD, particularly when occurring within 6 months of evaluation [51, 52].

LV apical aneurysm

LV apical aneurysms are defined as a discrete, thin-walled dyskinetic or akinetic segments at the most distal portion of the LV and are characterized by transmural scarring or LGE [15, 58]. The first descriptions of LV apical aneurysms in HCM suggested an association with sustained monomorphic VT, a relatively rare event in HCM [81]. Multiple studies have demonstrated that LV apical aneurysms are a significant marker of increased SCD risk [15, 82–84]. Based on these data, the updated 2024 ACC/AHA guidelines include an apical aneurysm as one of the major risk factors for SCD [51]. In contrast, the 2023 ESC guidelines for cardiomyopathy suggest that individualized ICD decisions be based on the 5-year SCD risk score (HCM Risk-SCD score), rather than solely on the presence of an apical aneurysm [52].

HCM with LV systolic dysfunction

HCM with LV systolic dysfunction, also known as the ES of HCM, is characterized by an ejection fraction (EF) < 50%, often accompanied by LV remodeling due to diffuse myocardial scarring [85, 86]. Numerous studies have highlighted the elevated risk of arrhythmic SCD in ES-HCM, raising concerns about the use of ICDs for primary prevention [53, 85–87]. According to the data from the Sarcomeric Human Cardiomyopathy Registry, HCM-LVSD affects about 8% of patients with HCM. Despite various natural history of HCM-LVSD, 75% of patients experienced adverse outcomes, including 35% experiencing a death equivalent (death, heart transplantation, or left ventricular assist device implantation) after a median time of 8.4 years since the development of systolic dysfunction. [88].

With advancements and aggressive implementation of various therapeutic approaches, including early evaluation for heart transplantation, cardiac resynchronization therapy, or ventricular assist devices, the annual mortality rate associated with ES-HCM has decreased from the previously reported 8% to 2%, about one-quarter of the original rate. However, according to Rowin et al. [89], ES-HCM still carries tenfold greater risk of mortality compared with HCM with preserved EF. Additionally, arrhythmic sudden death events (including appropriate ICD therapy for ventricular tachyarrhythmias, resuscitated cardiac arrest, and sudden death) were five times

more frequent in ES-HCM (2.4% per Year vs. 0.5% per year, $P=0.006$).

NSVT on ambulatory monitor

NSVT is defined as three or more consecutive ventricular beats at a minimum rate of 120 beats per minute, lasting less than 30 s, and not resulting in hemodynamic instability. NSVT is commonly documented in approximately 20% to 35% of HCM patients, usually with 24 to 48 h of ambulatory electrocardiogram monitoring [90]. Asymptomatic NSVT has been recognized as an SCD risk factor in HCM for nearly 40 years. However, discussions continue about the reliability of NSVT as a robust marker for individual risk assessment and selecting patients for ICDs for primary prevention.

NSVT becomes more frequent as cardiac hypertrophy progresses, which likely indicates a higher degree of fibrosis and myofibrillar disarray, both of which are important predictors of the disease's inherent arrhythmic risk [91]. Greater significance is attributed to NSVT that occurs repeatedly (three or more episodes), lasts longer (at least 10 beats), and is faster (200 beats per minute or higher), as observed over a 24- to 48-h extended ambulatory electrocardiography (ECG) monitoring period [51, 52]. Meanwhile, the value of short, single bursts of NSVT in predicting ICD-treated VT or VF remains uncertain without the presence of additional major risk factors [90].

Extensive LGE on CMR imaging

The introduction of LGE has improved risk stratification of SCD in HCM. While LGE is widely recognized as an prognostic marker across all cardiomyopathies, the accompanying myocardial fibrosis related with CMR findings is considered arrhythmogenic in HCM [23]. As expected, a greater extent of LGE in HCM is linked to a higher burden of NSVT and an increased risk of SCD.

Current guidelines define extensive LGE as comprising $\geq 15\%$ of LV mass, either quantified or estimated by visual inspection, based on evidence indicating a doubled risk of SCD compared with patients injected with smaller amounts of LGE [24, 51]. The ESC guidelines suggest using extensive LGE ($\geq 15\%$) in low- to intermediate-risk category patients, helping clinicians decide on use of prophylactic ICD implantation [52]. However, quantifying LGE in HCM can be challenging due to various scarring patterns and image quality. The standard deviation (SD) threshold method, which is typically preferred in HCM, defines LGE using a specific number of SDs above a normal reference region.

A recent meta-analysis study by Kiaos et al. [92] evaluated a single study of 5,550 patients with a median follow-up of 5.2 years. When the more extensively studied 6-SD technique is used, LGE greater than 10% was the optimal cutoff and could effectively reclassify intermediate-risk patients [92]. Still, given the complexity of arrhythmogenic mechanisms in HCM, the amount of LGE is not only the problem. The pattern and location may also play a role, and further studies are warranted.

Beyond these commonly cited risk factors, studies and results on novel parameters designed to more accurately predict SCD risk have emerged.

New perspectives on SCD risk assessment

Left ventricular global longitudinal strain

LV global longitudinal strain (LVGLS) is more sensitive than left ventricular EF in detecting LV systolic dysfunction, showing impairments in early stages of the disease or HCM with preserved EF. Studies have shown that impaired LVGLS is associated with a significantly increased risk of SCD events and is an independent predictor of appropriate ICD therapy [93–95]. Additionally, recent studies have incorporated machine learning into LVGLS analysis in an attempt to further refine ventricular arrhythmic risk subgroups [96].

T1 mapping and entropy on CMR in the evaluation of fibrosis

Entropy, a typical measure of image complexity, can be used to quantify tissue heterogeneity by analyzing all signal intensity values within the images. Not only LGE in CMR, but also extracellular volume fraction (ECV) and LV mean entropy derived from native T1 mapping can aid in detection of diffuse myocardial fibrosis and are independent predictors of SCD and cardiovascular disease in HCM patients [97–101]. However, T1/ECV mapping and entropy measurement have major differences. Conventional native T1 and ECV mapping derive mean values either from selected myocardial region of interests or by applying signal intensity thresholds. Even when averaged globally, both approaches may obscure regional heterogeneity. However, because entropy analysis incorporates the full distribution of voxel intensities across the entire LV, further studies are needed to determine whether entropy measurement adds incremental value over traditional region of interest or globally averaged T1/ECV metrics in detecting diffuse myocardial fibrosis in HCM.

Genetics

Like other types of cardiomyopathies, genetic testing has been widely used in HCM. Although numerous gene mutations have been identified in HCM, the most frequently reported variants are those in the genes that express myosin binding protein C (*MYBPC3*), β-myosin heavy chain (*MYH7*), and cardiac troponin T (*TNNT2*). Among these, *TNNT2* gene mutations, which affect thin myofilament

proteins, are associated with less severe hypertrophy but a higher risk of LV systolic dysfunction. By inducing severe myocyte disarray, these mutations can lead to a high incidence of SCD in younger patients [102–104].

According to a meta-analysis of 7,675 HCM patients, mutation-positive patients exhibited a higher risk of SCD by 5% (*MYPBPC3*), 11% (*MYH7*), and 17% (*TNNT2*), compared with a 0.4% risk in mutation-negative patients [105]. However, current guidelines suggest using genetic testing only for screening of HCM, not for risk stratification of SCD in HCM. In clinical practice, decisions for prophylactic ICD should not be based on genetics [51, 52].

Cardiopulmonary exercise testing

Magrì et al. [105, 106] conducted a prospective study about the use of cardiopulmonary exercise tests in improving contemporary strategies for SCD risk stratification. The study composite end point was SCD, aborted SCD, and appropriate ICD interventions. Multivariable analysis confirmed that the exercise ventilation (VE) to CO_2 output (VCO_2) relationship (VE/VCO_2 slope) was clinically significant. A VE/VCO_2 slope cutoff value of 31 showed the highest accuracy in predicting the SCD end point within the entire HCM cohort. However, given the need for standardized protocols for cardiopulmonary exercise tests, more studies should be conducted.

ECG parameters

Various ECG parameters can serve as predictive markers for SCD in HCM. T wave amplitude, myocardial infarction pattern (pseudo-ST segment elevation, QRS duration ≥ 120 ms, low QRS voltage), and both QRS fragmentation in ≥ 3 territories and a heart rate–corrected QT duration ≥ 460 ms were associated with ventricular arrhythmias and SCD in HCM patients [107–109]. Ventricular repolarization parameters including interval between the peak and end of the electrocardiographic T wave (Tpe) to corrected QT interval ratio and Tpe interval were also related to a higher risk of VT [110, 111].

Biomarkers

An increased level of NT-proBNP was an independent predictor of SCD in patients with HCM [112]. It was also significantly correlated with cardiac fibrosis, as detected by either LGE or Masson's trichrome staining in the myocardium.

Conclusions

With advances in our understanding of HCM using diagnostic modalities beyond echocardiography, updates have been incorporated into both ACC/AHA and ESC guidelines. Moreover, as genetics advances and artificial intelligence evolves, clinical studies are focusing on improving risk stratification. However, clinicians must not depend solely on single aspects of the disease. Instead, they must employ multiple tools to evaluate the risk of SCD in HCM patients. Last, as current guidelines suggest, it is important to reevaluate a patient's heart every 1 to 2 years, even in asymptomatic cases. Although some negative findings regarding longitudinal changes have been reported, the importance of regular follow-up remains indisputable [113].

Abbreviations

ACC	American College of Cardiology
AHA	American Heart Association
CMR	Cardiac magnetic resonance
DAD	Delayed after-depolarizations
ECG	Electrocardiography
ECV	Extracellular volume fraction
EF	Ejection fraction
ES	End stage
ESC	European Society of Cardiology
HCM	Hypertrophic cardiomyopathy
ICD	Implantable cardioverter-defibrillator
LGE	Late gadolinium enhancement
LV	Left ventricle
LVGLS	Left ventricular global longitudinal strain
LVH	Left ventricular hypertrophy
NSVT	Nonsustained ventricular tachycardia
NT-proBNP	N-terminal prohormone of brain natriuretic peptide
SCD	Sudden cardiac death
SD	Standard deviation
Tpe	Interval between the peak and end of the electrocardiographic T wave
VCO_2	CO_2 output
VE	Ventilation
VF	Ventricular fibrillation
VT	Ventricular tachycardia

Authors' contributions

SG Yoon wrote the main manuscript. GR Hong reviwed the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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