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ORIGINAL ARTICLE

Revisiting risk stratification in hypertrophic cardiomyopathy after the recent guidelines – Late gadolinium enhancement remains tough to beat

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Cardiac magnetic resonance;
Late gadolinium enhancement

Abstract
Introduction and objectives: Recommendations for implantable cardioverter-defibrillator (ICD) implantation to prevent sudden cardiac death (SCD) in hypertrophic cardiomyopathy (HCM) have evolved over time, with late gadolinium enhancement (LGE) emerging as an important additional risk marker. Our study aimed to evaluate changes in the accuracy and discriminative performance of international guidelines for ICD recommendations and to determine whether LGE can improve this risk stratification.
Methods: We conducted a multicenter retrospective observational study of HCM patients who underwent cardiac magnetic resonance (CMR) imaging for diagnosis or risk assessment. ICD eligibility was determined based on the ESC guidelines (2014, 2022, 2023) and the American College of Cardiology (ACC) guidelines (2011, 2020, 2024). Our primary endpoint was a composite of sudden cardiac death (SCD), appropriate ICD discharge, or sustained ventricular tachycardia (VT).
Results: A total of 531 patients (median age 49 years; 57% male) were included. During a median follow-up of 49 months, twenty-eight events occurred (15 SCDs, six appropriate ICD discharges, seven sustained VTs). Over time, both European and American guidelines demonstrated improved sensitivity, positive predictive value, and discriminatory ability, while maintaining a high negative predictive value. The agreement between the recent ESC and ACC guidelines was moderate ($\kappa \approx 0.6$, $p<0.001$). Late gadolinium enhancement (LGE) was present in 80% of patients and LGE% independently predicted arrhythmic events (adjusted hazard ratio 1.09 per 1% increase; $p<0.001$). A burden $\geq 8\%$ was the best predictor of events, while the absence of LGE identified patients without arrhythmic outcomes.

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Conclusions: The extent of LGE burden improves risk stratification for SCD, with the complete absence of LGE indicating a very low-risk subgroup. LGE thresholds should be individualized by integrating imaging results, clinical factors and the patient's context.
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PALAVRAS-CHAVE
Cardiomiopatia hipertrófica;
Morte súbita cardíaca;
Cardioversor-desfibrilhador implantável;
Guidelines;
Ressonância magnética cardíaca;
Realce tardio

Rever a estratificação de risco na cardiomiopatia hipertrófica após as *guidelines* recentes - realce tardio pelo gadolinio continua difícil de superar

Resumo
Introdução e objetivos: As recomendações para a implantação do cardioversor-desfibrilhador implantável (CDI) para prevenção da morte súbita cardíaca (MSC) na cardiomiopatia hipertrófica (CMH) evoluíram ao longo do tempo, tendo o realce tardio (RT) emergido como um marcador de risco. Este estudo teve como objetivo avaliar a evolução da precisão e do desempenho discriminativo das *guidelines* internacionais para as recomendações de implantação de CDI e determinar se o RT pode melhorar esta estratificação de risco.
Métodos: Foi realizado um estudo observacional retrospetivo e multicêntrico de doentes com CMH submetidos a ressonância magnética cardíaca (RMC) para diagnóstico ou avaliação de risco. A elegibilidade para CDI foi determinada de acordo com as orientações da ESC (2014, 2022, 2023) e da ACC (2011, 2020, 2024). O *outcome* primário foi um composto de MSC, descarga apropriada do CDI ou taquicardia ventricular (TV) sustentada.
Resultados: Foram incluídos no estudo um total de 531 doentes (idade mediana de 49 anos; 57% do sexo masculino). Durante um seguimento mediano de 49 meses, ocorreram 28 eventos (15 MSCs, 6 descargas apropriadas de CDI, 7 TVs sustentadas). Com o tempo, as *guidelines* europeias e americanas demonstraram uma melhoria na sensibilidade, no valor preditivo positivo e na capacidade discriminativa, mantendo um elevado valor preditivo negativo. A concordância entre as mais recentes *guidelines* da ESC e da ACC foi moderada ($\kappa \approx 0,6$, $p < 0,001$). Foi detetado realce tardio (RT) em 80% dos doentes, e a percentagem de RT foi um preditor independente de eventos arrítmicos (aHR 1,09 por aumento de 1%; $p < 0,001$). Uma carga $\geq$8% foi o melhor preditor de eventos, enquanto a ausência de RT identificou doentes sem desfechos arrítmicos.
Conclusões: A carga de RT refina a estratificação do risco de morte súbita cardíaca, sendo que a ausência completa de RT identifica um subgrupo de risco muito baixo. Os limiares de RT devem ser individualizados, integrando os dados de imagem, os fatores clínicos e o contexto do doente.
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Introduction

Hypertrophic cardiomyopathy (HCM) has been increasingly recognized as a prevalent form of cardiomyopathy. Recent advances in science have led to the development of targeted medical therapies for this clinical entity. However, the wide variability of disease expression amongst patients and even amongst relatives with the same pathogenic sarcomeric variant makes prediction of arrhythmic events a challenge in current clinical practice.

In recent decades, the recommendation for implantable cardioverter defibrillator (ICD) implantation for the primary prevention of sudden cardiac death (SCD) in both European and American HCM guidelines has been evolving. Over a decade ago, both the ESC 2014[1] and the ACC/AHA 2011[2] guidelines proposed a clinical indicator-based decision. Around 2019, observational studies showed that late gadolinium enhancement (LGE) was a good predictor of the risk of fatal arrhytmia, perhaps even superior to the clinical risk prediction model implemented at the time.[3]

Since then, LGE has been incorporated into the guidelines as a risk factor to be considered for ICD implantation. Both the 2022 ESC guidelines on ventricular arrhythmias[4] and SCD prevention and the ESC 2023 Cardiomyopathies guidelines[5] recommend a threshold of 15% of LGE (relative to the total LV mass) to consider the implantation of ICD. On the other hand, the American College of Cardiology/American Heart Association (ACC/AHA) HCM guidelines from 2020[6] and 2024[7] do not recommend a specific cut-off but use the broader term ''extensive LGE''.

Objectives

In this study, we aimed to (1) assess how the accuracy and discriminative ability of different guidelines (ESC 2014, ESC 2022, ESC 2023, ACC 2011, ACC 2020, and ACC 2024) for

predicting sudden cardiac death (SCD) have evolved and (2) determine whether LGE can further improve risk stratification for SCD.

Methods

Study population

We conducted an international multicentric retrospective analysis of consecutive HCM patients undergoing cardiac magnetic resonance (CMR) for diagnostic confirmation and/or risk stratification at Instituto do Coração (InCor), University of São Paulo (São Paulo, Brazil) and Hospital de Santa Cruz (Lisbon, Portugal). The Brazilian site included patients between 2003 and 2017, while the Portuguese site included patients between 2009 and 2022.

The diagnosis of HCM was made by experienced cardiologists and based on available clinical data and LV wall thickness $\geq$15 mm in the absence of loading conditions or other disease that could explain the ventricular hypertrophy.

Exclusion criteria were: (1) age <16 years; (2) alternative diagnosis such as athlete's heart, Anderson-Fabry disease, cardiac amyloidosis or sarcoidosis that could explain ventricular hypertrophy; (3) CMR inconsistent with HCM or with previously stated alternative diagnosis; (4) LGE pattern consistent with prior myocardial infarction; (5) missing essential echocardiographic and/or 24 h Holter monitoring data: (6) moderate or severe aortic/mitral disease; (7) indication for ICD for secondary prevention; (8) previously implanted intracardiac electronic device.

The study protocol was reviewed and approved by each institution's review board which waived the need for specific informed consent.

Definitions

Our primary endpoint was a composite of SCD, appropriate ICD discharge and sustained VT. SCD was defined as witnessed sudden death with or without documented ventricular arrhytmia (VA) or death within one hour of new onset symptoms or nocturnal death with no antecedent history of worsening symptoms. Events were ascertained by reviewing electronic medical records including ICD electrograms. When death occurred outside of the hospital, the circumstances of death were determined by phone call interview with a family member.

Echocardiography, 24h Holter monitoring and exercise stress test data within a six-month window to the CMR were collected from the patient files. If no left ventricular outflow obstruction (LVOTO) was identified, we assumed an LVOT gradient of 3 mmHg since this is the minimum accepted by the HCM Risk-SCD calculator. Left atrial diameter was determined by M-Mode or 2D in the parasternal long axis plane and maximal LV wall thickness (MWT) was defined as the greatest dimension at any site within the LV myocardium. Non-sustained ventricular tachycardia (NSVT) on 24 h Holter monitoring was defined as $\geq$3 consecutive ventricular beats at a rate of $\geq$120 beats per minute. Abnormal blood pressure response on stress test was defined as either a failure to increase $\geq$20 mmHg or a drop of $\geq$20 mmHg during exercise.

Hypertrophic cardiomyopathy risk sudden death score and eligibility criteria for implantable cardiac device

The five-year HCM Risk-SCD score was calculated for each patient. Eligibility criteria for ICD according to the ESC 2014 (HCM), ESC 2022 (ventricular arrhythmias − VAs), ESC 2023 (Cardiomyopathies), ACC 2011, ACC 2020 and ACC 2024 (all HCM guidelines) was determined for each patient and subdivided into three categories: Class IIa indication for ICD (ICD should be considered); Class IIb indication for ICD (ICD may be considered) and; Class III indication (ICD not recommended).

Cardiac magnetic resonance data

All CMR scans were performed using a 1.5 T system. Images were transferred to a core laboratory where an experienced cardiologist in CMR, blinded for clinical events, analyzed all CMR data using a dedicated software (Circle Cardiovascular Imaging®, Calgary, Canada). LV volume, mass and EF were measured by using a standard volumetric technique. LV endocardial and epicardial borders on cine images were manually adjusted to define the myocardium, taking care to exclude papillary muscles and the intertrabecular blood pool. LV maximal wall thickness (MWT) was defined as the greatest dimension at any site within the LV myocardium.

In both centers, LGE images were acquired 10 min after the administration of intravenous gadolinium chelate contrast agent in the dose of 0.2 mmol/kg, with breath-hold two-dimensional segmented inversion-recovery sequences. Imaging was performed in short-axis views of the LV with 8 mm slice thickness and 2 mm gaps. The typical in-plane spatial resolution was 1.5 mm$\times$1.5 mm. Inversion time was optimized to null normal myocardial signal. The LV short-axis LGE images were first visually accessed for the presence of LGE, followed by quantification if LGE was present.

Late gadolinium enhancement was defined as areas of signal intensity $\geq$6 standard deviations from normal myocardium and was expressed as the percentage of myocardial mass (LGE%). Any areas that were identified as LGE by the software, but visually deemed artefactual on visual analysis were manually excluded.

Statistical analysis

Categorical variables are presented as frequencies and percentages, while continuous variables are presented as the mean $\pm$ standard deviation for normally distributed data or as the median and interquartile range for non-normally distributed data. The Student's t-test, Mann−Whitney U test, and Fisher's exact test were used for comparisons, as appropriate.

Diagnostic accuracy statistics, including sensitivity, specificity, positive predictive value, and negative predictive value, were calculated for each individual set of guidelines and for various LGE cut-off points.

Weighted κ was used to assess concordance in risk assessment between different guidelines. The strength of agreement between each classification was considered poor

(κ<0.2), fair (κ=0.21–0.4); moderate (κ=0.41–0.6), good (κ=0.61–0.8) or very good (κ=0.81–1.0).

Univariate cox regression analysis was performed to determine predictors of arrhythmic events. Clinically relevant variables and/or variables with a p-value <0.10 on individual analysis were included in multivariate models. Net reclassification index (categorical NRI) was used to ascertain improvements in the risk stratification strategies over time in the American and European guidelines.

Kaplan–Meier survival curves were plotted for each guideline recommendation class classified per LGE% strata. The log-rank test was used to assess significant differences in time to endpoint between the risk strata.

Statistical significance was set at p-value <0.05 (two-sided). All analyses were performed using SPSS® 27.0 and MedCalc® 9.3.8.0.

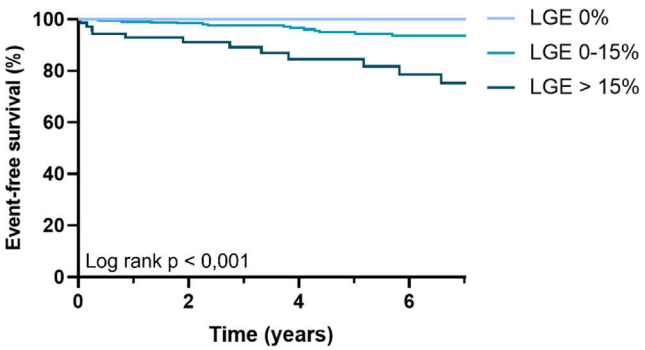

Figure 1 Kaplan–Meier curve showing event-free survival stratified by late gadolinium enhancement burden categories.

Results

Population characterization

We included a total of 531 patients (median age was 49 (IQR 35–61), 57% male). Over a median follow-up of 49 (IQR 21–88) months, 28 events occurred (15 SCDs, 6 appropriate ICD discharges and 7 sustained VTs).

Clinical risk factors were evaluated for each patient. In this cohort, 13% of patients had a Family history of SCD (n=71), 12% had had a recent episode of unexplained syncope which was deemed to be of possible cardiac etiology, and 19% (n=101) had at least one NSVT episode on Holter monitoring at the index evaluation.

Regarding transthoracic echocardiography parameters, median MWT was 19 (IQR 16–22) mm, LV gradient was 5 (IQR 3–50) mm and left atrium (LA) diameter was 43 (IQR 38–47) mm. Of these parameters, only LA diameter was significantly different between groups (47 [IQR 43–51] mm vs. 42 [IQR 38–47]mm; p=0.004).

The median HCM risk score in the cohort was 2.4 (IQR 1.6–4.1)%. Only 12% (n=65) of the patients had a calculated HCM Risk Score greater or equal to 6%. Although there is a numerical difference in the percentage of patients with an HCM risk score greater or equal to 6% between groups (21% vs. 12%), this did not achieve statistical significance (p=0.128). Table 1 shows the baseline population characteristics for our cohort separated by those who met the primary endpoint and those who did not.

Evolution of recommendations over time

The diagnostic accuracy statistics of the European and the American society guidelines have evolved similarly over time: sensitivity and positive predictive value increased, negative predictive value remained high and discriminative ability also increased (see Table 2 and Figure 4 for details).

The concordance in risk assessment is only moderate between the ESC 2022 and ACC 2020 (κ=0.60 (95% CI: 0.54–0.67); p<0.001) or the ESC 2023 and ACC 2024 guidelines (κ=0.56 (95% CI: 0.49–0.62); p<0.001).

The most recent 2020 (and 2024) AHA guidelines show a net reclassification index of 0.15 (p=0.01, mainly due to the correct reclassification of patients with arrhythmic events to receive an ICD [event 0.11; non-event 0.048]). When comparing the ESC's 2014 guidelines to the more recent recommendations in the 2022 and 2023 guidelines, reclassification also moved towards correctly classifying patients with arrhythmic events for ICD implantation. The NRI from the 2014 to the 2022 guidelines was 0.30 (p=0.027) (event 0.43; non-event −0.13), while the NRI from the 2014 to the 2023 guidelines was 0.17 (p=0.063) (event 0.21; non-event −0.05). However, the same cannot be said of the NRI from the 2022 to the 2023 ESC guidelines (NRI=−0.20 [p=0.039]; event 0.25; non-event 0.06).

Late gadolinium enhancement

Late gadolinium enhancement was present in 80% of patients, with a median LGE% of 3.2% (IQR 0.5–8.4%) and predicted arrhythmic events in this population (see Figure 1). LGE has remained an independent predictor of arrhythmic events after adjustment to known confounders (family history of SCD, unexplained syncope, NSVT, MWT, LVOT gradient, LA diameter, LVEF, apical aneurysm) with an aHR of 1.09 per 1% increase in LGE% (95% CI 1.05–1.12; p<0.001), and receiver operating characteristic analysis showed an AUC of 0.80 (0.72–0.88) (p<0.001) (see Figure 3).

The Youden test showed the best cut-off value for LGE burden in our cohort of 8.0% (Youden index 0.513), which represented a sensitivity of 75% and specificity of 76%, with negative and positive predictive values of 15% and 98%, respectively.

Alternatively, the cut-off used by the most recent ESC guidelines to define a high burden of LGE (>15%) showed to have high specificity (88%) at the expense of a much lower sensitivity (46%), with positive and negative predictive values of 16% and 97%, respectively.

Regardless of the guideline publisher, among patients with any recommendation for ICD (classes IIa and IIb), the absence of LGE identified those who experienced no arrhythmic events during follow-up (see Figure 2, top). Furthermore, among patients for whom ICD implantation is not recommended (class III), those who reached the endpoint (and therefore experienced arrhythmic events) all showed some degree of LGE on CMR (see Figure 2 – bottom).

Table 1 Baseline population characteristics.

	Total population n=531	Endpoint n=28	No endpoint n=503	p-Value
Age (years) [median (IQR)]	49 (35–61)	40 (30–65)	49 (35–61)	0.320
Sex – male [n (%)]	300 (57%)	13 (46%)	287 (57%)	0.270
Clinical risk factors				
Family history SCD [n (%)]	71 (13%)	5 (18%)	66 (13%)	0.474
Unexplained syncope [n (%)]	65 (12%)	3 (11%)	62 (12%)	0.800
NSVT [n (%)]	101 (19%)	9 (32%)	92 (18%)	0.069
ESC HCM risk score % [median (IQR)]	**2.4 (1.6–4.1)**	**3.9 (2.3–5.8)**	**2.3 (1.6–3.9)**	**0.004**
ESC HCM risk score ≥6% [n (%)]	65 (12%)	6 (21%)	59 (12%)	0.128
TTE				
MWT (mm) [median (IQR)]	19 (16–22)	20 (17–26)	19 (16–22)	0.108
LV gradient (mmHg) [median (IQR)]	5 (3–50)	7 (3–42)	5 (3–50)	0.917
LA diameter (mm) [median (IQR)]	**43 (38–47)**	**47 (43–51)**	**42 (38–47)**	**0.004**
CMR				
LV EDVi (mL/m^2) [median (IQR)]	72 (61–83)	73 (59–86)	72 (61–82)	0.639
LV ESVi (mL/m^2) [median (IQR)]	13 (11–17)	17 (12–20)	13 (11–17)	0.186
LVEF (%) [median (IQR)]	67 (60–70)	67 (56–70)	67 (61–70)	0.279
LVEF ≤50% [n (%)]	**19 (4%)**	**3 (11%)**	**16 (3%)**	**0.037**
LVM (g) [median (IQR)]	166 (133–207)	165 (137–230)	165 (132–204)	0.536
LVMi (g/m^2) [median (IQR)]	90 (73–112)	90 (79–116)	90 (73–112)	0.314
% LGE (%) [median (IQR)]	**3.2 (0.5–8.4)**	**12.0 (7.6–25.2)**	**2.8 (0.4–7.7)**	**< 0.001**
LGE >15% [n (%)]	**73 (14%)**	**13 (46%)**	**60(12%)**	**<0.001**
Apical aneurysm [n (%)]	8 (2%)	1 (4%)	7 (1%)	0.357

EDVi: indexed end-diastolic volume; ESC: European Society of Cardiology; ESVi: indexed end-systolic volume; LA: left atrium; LGE: late gadolinium enhancement; LV: left ventricle; LVEF: left ventricular ejection fraction; LVM: left ventricular mass; LVMi: indexed left ventricular mass; MWT: maximal wall thickness; NSVT: non-sustained ventricular tachycardia; SCD: sudden cardiac death.

Discussion

Although the implantation of an ICD as secondary prevention in patients with HCM has remained a stable class I indication, the risk stratification algorithms recommended by both European and American societies have evolved over time to improve their ability to discriminate risk. However, balancing the prevention of sudden cardiac death SCD in high risk individuals with minimizing the implantation of unnecessary devices has proven to be a difficult task.

Older guidelines, such as the 2011 AHA HCM guideline and the 2014 ESC HCM guideline, based their risk assessments on clinical and echocardiographic parameters. While the ESC adopted a calculation of risk based on the work of O'Mahony et al., [8] the AHA adopted a more dichotomic approach guiding ICD implantation by the presence of one or more risk factors for fatal arrhytmias. In our cohort, these

Table 2 Diagnostic accuracy statistics for all European Society of Cardiology and American Heart Association guidelines and for different cut-offs of late gadolinium enhancement.

	Sensitivity	Specificity	PPV	NPV	AUC
ESC 2014 HCM guidelines	50% (95CI 31–69%)	72% (95CI 68–76%)	9% (95CI 6–13%)	96% (95CI 95–97%)	0.61 (95 CI 0.50–0.72)
ESC 2022 VAs and SCD guidelines	71% (95CI 61–87%)	66% (95CI 61–70%)	10% (95CI 8–13%)	98% (95CI 96–99%)	0.71 (95CI 0.61–0.81)
ESC 2023 Cardiomyopathies guidelines	71% (95CI 61–87%)	67% (95CI 63–71%)	11% (95CI 9–14%)	98% (95CI 96–99%)	0.69 (95CI 0.59–0.79)
ACC 2011 HCM guidelines	64% (95CI 44–81%)	59% (95CI 55–63%)	8% (95CI 6–11%)	97% (95CI 95–98%)	0.61 (95CI 0.50–0.71)
ACC 2020 HCM guidelines	71% (95CI 51–87%)	54% (95CI 50–59%)	8% (95CI 6–10%)	97% (95CI 95–98%)	0.63 (95CI 0.53–0.74)
ACC 2024 HCM guidelines	71% (95CI 51–87%)	54% (95CI 50–59%)	8% (95CI 6–10%)	97% (95CI 95–98%)	0.63 (95CI 0.53–0.74)
LGE $\geq$8.0% (best cut-off)	75% (95CI 55–89%)	76% (95CI 72–80%)	15% (95CI 4–8%)	98% (95CI 97–99%)	
LGE $\geq$10%	67% (95CI 48–84%)	80% (95CI 76–83%)	16% (95CI 12–20%)	97% (95CI 96–99%)	
LGE $\geq$15%	46% (95CI 28–66%)	88% (95CI 85–91%)	18% (95CI 12–26%)	97% (95CI 95–98%)	

ACC: American College of Cardiology; ESC: European Society of Cardiology; HCM: hypertrophic cardiomyopathy; LGE: late gadolinium enhancement; SCD: sudden cardiac death; VAs: ventricular arrhythmias.

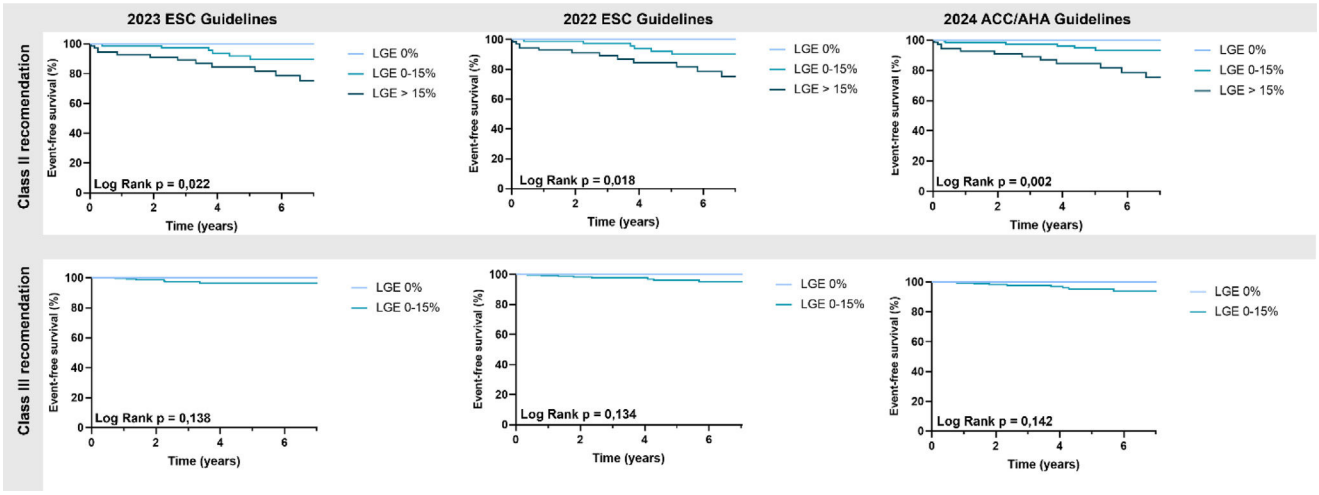

Figure 2 Kaplan–Meier curves showing event-free survival stratified by late gadolinium enhancement burden in patients with class II recommendation (IIa should be considered/IIb may be considered) (top) and class III recommendation (not recommended) (bottom) according to the different most recent iterations of the guidelines.

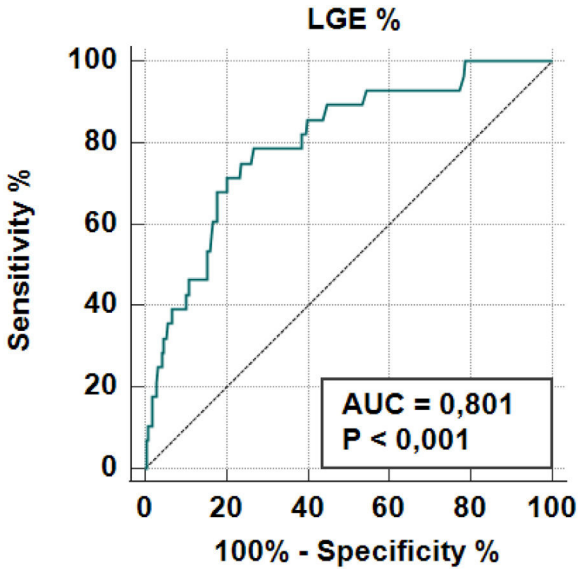

Figure 3 Receiver operator curve showing area under curve of late gadolinium enhancement burden.

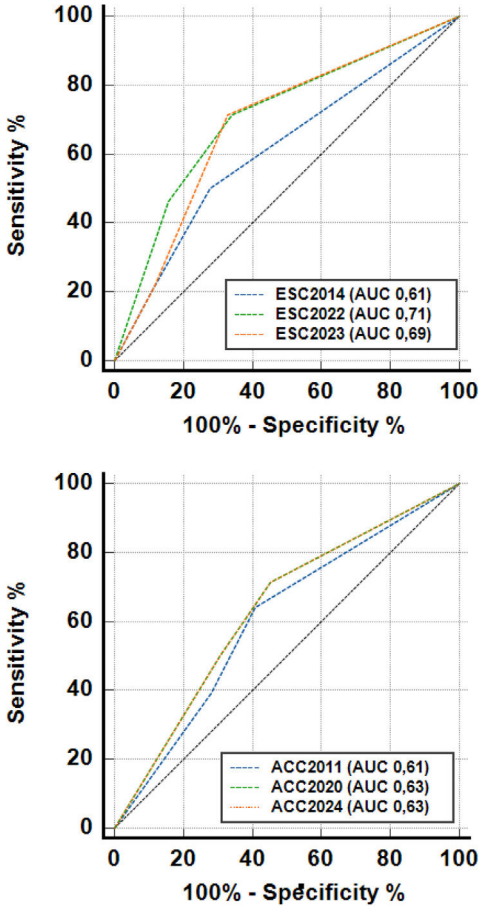

Figure 4 ROC curve showing AUC of the different iterations of the ESC (top) and ACC/AHA (bottom) guidelines.

older approaches showed the lowest predictive ability, with an AUC of 0.61 (95% CI 0.50–0.72) for the ESC approach and 0.61 (95% CI 0.50–0.71) for the AHA approach.

Over time, accumulating evidence has proven LGE to be a powerful tool for stratifying HCM patients based on the risk for development of ventricular arrythmias,[3] culminating in a recent meta-analysis from 2021,[9] which concluded that LGE is a strong predictor of arrhythmic events, and supports the use of LGE as a stratification tool on the most recent guidelines.

The inclusion of LGE as a stratification tool in the ESC's 2022 and 2023 guidelines, along with additional factors such as systolic dysfunction (defined as an LVEF <50%), resulted in a positive NRI in our cohort, as well as higher sensitivity and NPV (71% and 98%, respectively, compared to 50% and 96% in the previous 2014 version). Notably, although the 2022 guidelines also include additional modifiers for reclassification – namely, abnormal blood pressure response during a stress test, the presence of an LV apical aneurysm, and a pathogenic sarcomeric mutation – these factors did not lead

to a significant difference in sensitivity in our cohort. Sensitivity remained at 71% (95% CI 61–87%) for both the 2022 and 2023 recommendations.

There is still no consensus on the burden of LGE that warrants consideration for ICD implantation, resulting in a rather arbitrary cut-off in the European guidelines, of greater than 15%, and a broader definition in the American guidelines, which reference only ''extensive LGE'' without clarifying a cut-off.

Further risk stratification could be achieved by employing LGE% as an arbiter. In our cohort, the absence of LGE successfully identified patients at lower risk of arrhythmic events, even among those for whom current guidelines recommend considering ICD implantation for primary prevention (classes IIa and IIb). This observation is consistent with current evidence showing that patients without LGE on CMR experience a very low incidence of life-threatening arrhythmic events (SCD, aborted SCD, and appropriate device therapies).[9]

This dynamic underscores the complexity of applying a rigid cut-off universally, as the balance between these competing factors must be carefully weighed.

In this context, the complete absence of LGE emerges as an especially useful and pragmatic criterion, as it identifies a subgroup with consistently favorable outcomes across different studies. By identifying patients with an exceedingly low probability of arrhythmic events, this marker can provide reassurance to both clinicians and patients and help avoid the morbidity, psychological burden, and healthcare costs associated with ICD therapy when it is unlikely to confer benefit.

Limitations

Several limitations of this study should be acknowledged. First of all, patient inclusion was based on referral for CMR, making it likely that some form of referral bias is present in our sample. Comparisons between the different guidelines are also limited due to the small number of events in the population. Additionally, as rhythm documentation was unavailable for some SCD cases, some of these deaths may not have resulted from fatal arrhythmias.

Furthermore, the evaluation of risk was performed upon inclusion. Current guidelines recommend re-stratification at each visit, making it possible that some patients' risk increased during follow-up, which our study did not account for. Regarding LGE, there is also a possibility that its burden might increase over time in these patients, influencing risk assessment. Further studies are necessary to define the role of progression to a higher LGE burden during follow-up in predicting arrhythmic events, especially since the risk for these events seems to be inversely correlated with age and, hence, diminishes over time.

Conclusions

Current guidelines have shown increased sensitivity, PPV and discriminative power when compared with older counterparts. Although the notion of extensive LGE has been added as a predictor of arrhythmic events in the later iterations, the application of specific cutoffs entails a trade-off between sensitivity and specificity that is complex to balance.

Our study reinforces the complete absence of LGE in HCM patients as an especially useful tool for risk stratification, as it consistently identified a low-risk group.

Ultimately, the decision regarding which LGE% cut-off to apply should not be fixed but instead tailored to the clinical context and the individual patient's risk–benefit profile. This requires integrating imaging findings with other established risk markers, patient comorbidities, life expectancy, and personal preferences.

Conflicts of interest

The authors have no conflicts of interest to declare.

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