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Original Article

The role of global longitudinal strain in predicting fatal arrhythmic events in hypertrophic cardiomyopathy: An up-to-date systematic review and Meta-analysis



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ARTICLE INFO

Article history:

Received 1 March 2026

Received in revised form 24 April 2026

Accepted 26 April 2026

Available online 3 May 2026

Keywords:

Global longitudinal strain

Hypertrophic cardiomyopathy

Ventricular arrhythmias

Sudden cardiac death

ABSTRACT

Background: Sudden cardiac death (SCD) remains a leading cause of mortality in patients with hypertrophic cardiomyopathy (HCM). Accurate identification of individuals at high risk is essential for guiding implantable cardioverter-defibrillator (ICD) therapy. Global longitudinal strain (GLS), an echocardiographic parameter derived from speckle-tracking imaging, reflects subclinical left ventricular systolic dysfunction and may serve as an adjunctive risk marker for fatal ventricular arrhythmias (VAs).

Methods: A systematic review and meta-analysis were conducted following PRISMA guidelines. PubMed and the Cochrane Library were searched from inception to April 2025 for studies assessing the association between GLS and SCD and/or fatal VAs in HCM.

Results: Out of 1050 identified records, seven studies comprising 2167 patients (mean age 54.7 years) met inclusion criteria. All included studies were of moderate-to-high quality (Newcastle-Ottawa Scale ≥ 6). In the pooled quantitative synthesis of three studies, patients with reduced GLS ($<15\%$) had a significantly higher risk of fatal VAs [hazard ratio/odds ratio (HR/OR): 1.10, 95% (confidence interval) CI 1.04–1.17]. On the other hand, 1% worsening of GLS was not associated with SCD and/or fatal VAs (HR/OR: 1.09, 95% CI 0.89–1.33). A combined meta-analysis using data from seven studies showed a significant association between GLS and SCD and/or fatal VAs in patients with HCM (HR/OR: 1.10, 95% CI 1.03–1.18).

Conclusions: GLS is associated with risk of fatal arrhythmic events in HCM and may help identify higher-risk patients, but evidence from observational studies does not prove causality and may be confounded. GLS could aid shared decision-making about ICDs in borderline cases when combined with established risk factors, but should not be used alone. Prospective multicenter studies with standardized imaging are needed to validate thresholds, confirm added prognostic value, and show impact on outcomes.

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Introduction

Sudden cardiac death (SCD) is the unexpected, sudden death from a heart issue, often associated with arrhythmia. Hypertrophic cardiomyopathy (HCM) is one of the leading causes of SCD, with an annual incidence of approximately 1% [1]. The identification of patients at

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increased risk of SCD is crucial in the management of HCM. For patients with high risk of SCD, besides lifestyle change and medication, implantable cardioverter-defibrillator (ICD) is a reliable and often essential treatment. However, ICD implantation is highly invasive, costly, and risky. Therefore, the accurate identification of SCD risk in patients with HCM is crucial for clinical decision-making. Many risk factors have been identified but individual risk stratification remains an unmet challenge [1].

Increased left ventricular wall thickness is a typical structural change of HCM, which can cause arrhythmia and SCD. Different echocardiographic markers have been examined for risk stratification purposes in patients with HCM [2,3]. Global longitudinal strain (GLS) is an echocardiographic marker that can identify subclinical left ventricular dysfunction [4]. It is derived from speckle-tracking echocardiography, which quantifies the percentage of myocardial deformation (shortening) in the longitudinal axis during systole. GLS has been proposed to predict an increased risk of ventricular arrhythmias in different clinical settings, including post-myocardial infarction patients [5], heart failure patients [6], and patients with non-ischemic cardiomyopathy [7]. It has been observed that GLS is associated with the outcome of HCM, including SCD [8]. It was suggested that GLS may provide additional information to established SCD risk stratification strategies in patients with HCM [9–11]. However, there is a lack of consensus on the threshold of GLS in predicting SCD. To address this unmet challenge, based on the studies in recent years, this meta-analysis aims to explore the association between GLS and SCD/fatal ventricular arrhythmias (VAs) in patients with HCM towards quantitative, individualized risk stratification of SCD.

Methods

Search strategy

A systematic literature review was performed to identify studies evaluating the association between GLS and the risk of SCD and/or fatal arrhythmic events. PubMed and the Cochrane Library were systematically searched from their inception until April 2025, using the following search algorithm: “global longitudinal strain AND (all-cause mortality OR sudden cardiac death OR ventricular arrhythmia OR ventricular tachycardia OR ventricular fibrillation).” The reference lists of the identified studies were manually checked to identify additional studies.

Outcomes of interest

Two investigators independently reviewed the search results. The outcome of interest was the association between left ventricular GLS and the risk of SCD and/or fatal VAs.

Study selection

Studies were included in the systematic review if they provided data about the association between GLS and the risk of SCD and/or fatal VAs in adult populations. For studies with overlapping populations, our inclusion criteria favored the most recently conducted study. Studies that reported data only about non-sustained ventricular tachycardia (VT) and studies written in languages other than English were excluded.

Data extraction and synthesis

Data were independently extracted by two authors. The following data were collected: first author names, journal of publication, year of publication, study design, study population, mean age, gender, type of studied outcome, number of patients with events, effect estimate of the studied outcome, and the vendor used for GLS measurement.

Quality assessment

The quality of the included studies was assessed using the Newcastle-Ottawa Scale. Each area of the scale was awarded one or two stars, contributing to a maximum total score of nine stars for each study. Studies with scores below six were categorized as low quality, those scoring between six and seven as moderate quality, and studies with scores ranging from eight to nine as high quality.

Statistical analysis

Heterogeneity was assessed using the I^2 statistic, with values $>50\%$ indicating significant statistical heterogeneity. The analyses were conducted with the Review Manager (RevMan, version 5.4; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2020).

Results

A total of 1050 studies were identified through the search strategy. Seven studies [9,12–17] were finally included in the systematic review. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram is presented in Fig. 1. The baseline characteristics and main findings of the included studies are summarized in Table 1. As shown in Table 1, the included studies used a similar definition for HCM diagnosis and primarily consisted of patients with preserved ejection fraction in the non-dilated phase of HCM. A total of 2167 patients were included (mean age: 54.7 years). In the quality assessment, all included studies scored above 5, and none was characterized as having poor quality (Online Table 1).

Association between GLS with SCD/fatal VAs in HCM patients

Haland et al. included 150 HCM patients, and VAs (non-sustained and sustained VT or aborted SCD) were documented in 37 patients [12]. Of these, 1 patient (3%) died of documented ventricular fibrillation (VF), 2 patients (5%) experienced VF with aborted cardiac arrest, 1 patient (3%) had sustained VT, and 33 patients (89%) had non-sustained VT. Patients with ventricular arrhythmias had significantly worse GLS compared to patients without arrhythmias. Another interesting finding was that a GLS worse than -14.9% optimally detected the presence of fibrosis [12]. Candan et al. examined the role of GLS in predicting

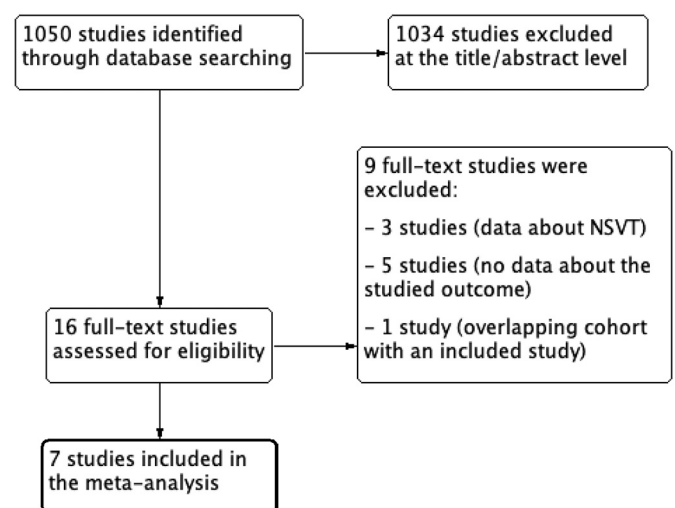


Fig. 1. Flow diagram of the search strategy. NSVT, non-sustained ventricular tachycardia.

Table 1
Baseline characteristics of the included studies.

Author	Year	Enrollment	Centers	Country/tries	Vendor	N	Age (years)	Males (%)	HCM definition	ICD (patients)
Haland TF	2016	n/a	Single	Norway	Vivid 7 or Vivid E9 machines (GE Healthcare, Horten, Norway) with offline data analyses (EchoPac® version 112 GE Healthcare).	150	54	61	definite diagnosis of HCM according to ESC guidelines	n/a
Candan O	2017	n/a	Single	Turkey	Vivid 7 machine (GE Vingmed Ultrasound AS, Horten, Norway)/(EchoPAC PC; GE Vingmed Ultrasound AS)	63	48.5	77.8	unexplained increase in wall thickness > 15 mm in the absence of abnormal load conditions	63
Nikoo MH	2024	March to June 2021	4-centers	Iran	GE Vivid E9, GE Healthcare, Horten, Norway). Image analysis was carried out on recorded data by EchoPAC, GE Medical Systems, Horten, Norway	34	62	64.7	maximal LVH > 15 mm in the absence of any other cardiac or systemic conditions that could generate a similar degree of LVH	19 had previous implantation of ICD and 15 were candidates for ICD therapy
Lee HJ	2022	2007–2019	Two-centers	Korea	Vendor-independent post-processing software (Imaging Arena, TomTec Imaging Systems, Munich, Germany)	835	56.3	73.3	HCM according to ESC guidelines	23
Hiemstra YL	2017	n/a	Single	Netherlands	Vivid 5, Vivid 7, and E9, GE-Vingmed, Milwaukee, WI). Images were digitally stored and analyzed offline (EchoPAC, version 112, GE Medical Systems, Horten, Norway)	427	52	66	maximal LVH ≥ 15 mm, in absence of any other cardiac or systemic disease that could cause a similar degree of LVH	150
Vergé MP	2018	2007–2014	single	France	Vivid 7 or E9 (General Electric Medical System®, Horten, Norway). Echopac® software version BT 11.3 (General Electric Medical System®, Horten, Norway).	217 (179 patients with strain data)	50.1	67	HCM based on LV hypertrophy on echocardiography (≥ 15 mm) unexplained by abnormal loading conditions	29
Debonnaire P	2014	2004–2014	single	Belgium	(Vivid-5, Vivid-7 and E9, GE-Vingmed, Milwaukee, WI), EchoPAC 110.0.0, GE Medical Systems, Horten, Norway.	92	50	69	non-dilated and hypertrophic LV with wall thickness ≥ 15 mm in the absence of any other cardiac or systemic disease that could account for the magnitude of LV hypertrophy	92

N, patient population; VT, ventricular tachycardia; ICD, implantable cardioverter-defibrillator; CA, cardiac arrest; GLS, global longitudinal strain; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; SCD, sudden cardiac death; HR, hazard ratio; OR, odds ratio; Exp (B), experimental estimation of group B; n/a, not applicable/not available.
[Author: Please define all abbreviations].

Table 1 (continued)

Author	GLS	LVEF	Numbers of patients with events	Types of arrhythmias	Estimate methods	Cut-off points	Estimate	p-value	Data type	Study design
Haland TF	−15.7	61.0	37	Ventricular arrhythmia (non-sustained and sustained VT and aborted CA)	OR	−15% CUT- OFF	1.22 (0.95–1.57)	0.120	Multivariate	Cross-sectional
Candan O	−12.1	n/a	17	Appropriate ICD shock	OR	n/a	1.285 (1.013–1.629)	0.039	Multivariate + crude data	Retrospective
Nikoo MH	−13.9	54.7	13	Ventricular arrhythmia	Exp (B)	−15.45% CUT- OFF	0.57 (0.007–176.783)	0.032	Univariate	n/a
Lee HJ	−15.2	64.6	20	SCD, aborted SCD, or appropriate ICD therapy	HR	15% CUT- OFF	1.14 (1.02–1.28)	0.004	Multivariate + crude data	Retrospective
Hiemstra YL	−15	65	63	SCD, aborted SCD, or appropriate ICD therapy	HR	−15% CUT- OFF	1.08 (1.01–1.16)	0.023	Multivariate	Retrospective
Vergé MP	−15.7	69.5	10	SCD, appropriate ICD therapy	HR	n/a	0.89 (0.74–1.06)	0.19	Univariate	Prospective
Debonnaire P	−13.3	70	21	Appropriate ICD therapy	HR	n/a	1.15 (1.02–1.30)	0.03	Multivariate	Retrospective

appropriate ICD shocks analyzing data from 63 HCM patients who received ICD implantation for primary or secondary prevention of SCD [14]. During follow-up, 17 (26.9%) patients were observed to have an appropriate ICD therapy. The study showed that GLS independently predicted appropriate ICD therapy while global longitudinal peak strain $> -10.7\%$ predicted appropriate ICD therapy with 70% sensitivity and 74% specificity [14]. Similarly, Debonnaire et al. examined the association of GLS with appropriate ICD therapies in 92 HCM patients [16]. Appropriate ICD therapy occurred in 21 patients (23%) during the follow-up period. GLS $<14\%$ was significantly associated with appropriate ICD therapies. Interestingly, the study showed that both left atrial volume index and GLS showed higher accuracy to predict appropriate ICD therapy compared to presence of ≥ 1 conventional SCD risk factors [16]. Another small cohort included 34 HCM patients, 19 with previous ICD implantation and 15 candidates for ICD therapy [13]. During follow-up, 13 patients received appropriate ICD therapy. GLS was significantly lower in patients who experienced appropriate therapy compared to those without fatal arrhythmias. Furthermore, a GLS cut-off value of -14.4% demonstrated a sensitivity of 92.3% and a specificity of 81% for the prediction of appropriate ICD therapy [13]. Lee et al. examined the role of GLS in predicting SCD in patients with HCM [9]. The cohort included 835 patients with HCM who were followed for a median of 6.4 years. Twenty patients (2.4%) experienced SCD, including those with appropriate ICD therapies. In multivariate analysis, GLS was a significant predictor of SCD, with a 14% higher risk for every 1% absolute decrease in GLS. The study also showed that GLS can help improve the sensitivity of the European Society of Cardiology risk score or the specificity of the 2011 American College of Cardiology/American Heart Association risk factor strategy [9]. Hiemstra et al. examined the role

of GLS in predicting the composite endpoint of SCD or appropriate ICD therapies in 427 HCM patients. GLS was significantly associated with the composite endpoint [15]. A prospective study evaluated 179 patients with adequate strain images to examine the association between global, regional, and multi-layer longitudinal strain with SCD or appropriate ICD therapy [17]. The study showed that only maximal wall thickness and mean left ventricular longitudinal strain in hypertrophic area were significantly predictive of SCD and appropriate ICD shock ($p < 0.05$). On the other hand, transmural, endocardial or epicardial GLS were not associated with fatal arrhythmic events [17].

Quantitative synthesis

We performed a pooled analysis by including studies that provided data on the impact of a 1% worsening of GLS on SCD and/or fatal VAs. Four studies [13,14,16,17] were included in this analysis. The results showed a non-significant association between GLS worsening (as a continuous variable) and SCD and/or fatal VAs [hazard ratio/odds ratio (HR/OR): 1.09, 95% confidence interval (CI) 0.89–1.33] (Fig. 2). On the other hand, a significant association was found between GLS and SCD and/or fatal VAs when using a cut-off of 15% for GLS. Specifically, three studies [9,12,15] were included in this analysis. GLS values less than 15% were significantly associated with a higher risk of SCD and/or fatal VAs in patients with HCM (HR/OR: 1.10, 95% CI 1.04–1.17) (Fig. 3). A combined meta-analysis using data from seven studies [9,12–17] was also performed. The results show a significant association between GLS and SCD and/or fatal VAs in patients with HCM (HR/OR: 1.10, 95% CI 1.03–1.18) (Fig. 4). The funnel plot is presented in Online Fig. 1.

Continuous GLS Meta-analysis

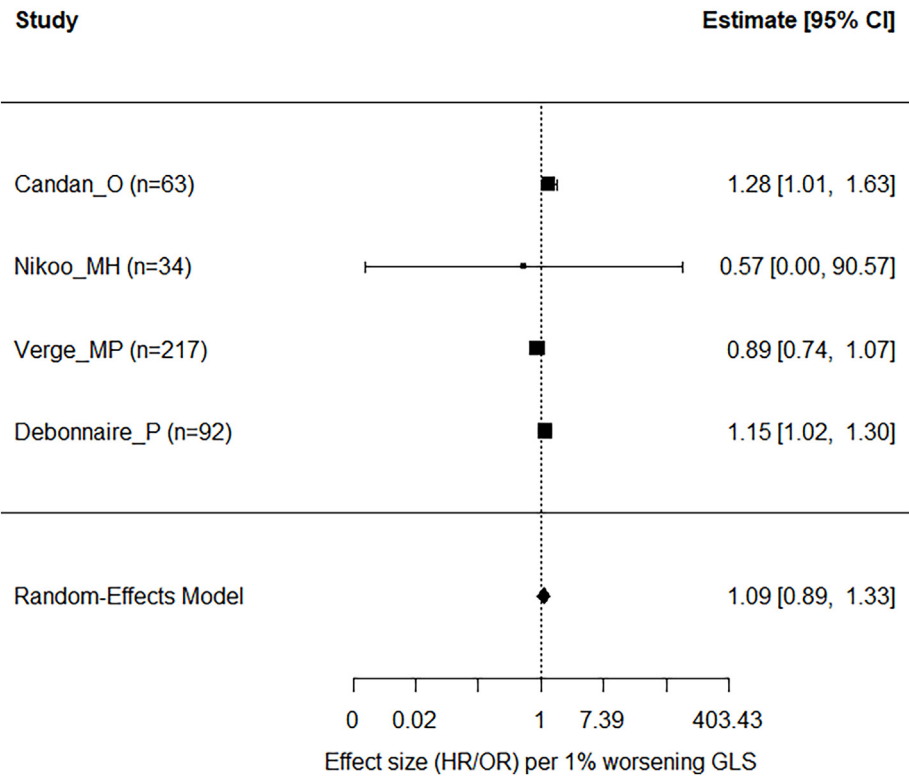


Fig. 2. Association between GLS (1% worsening) with SCD or fatal VAs
CI, confidence interval; GLS, global longitudinal strain; HR, hazard ratio; OR, odds ratio; SCD, sudden cardiac death; VA, ventricular arrhythmia.

GLS 15% Cutoff Meta-analysis

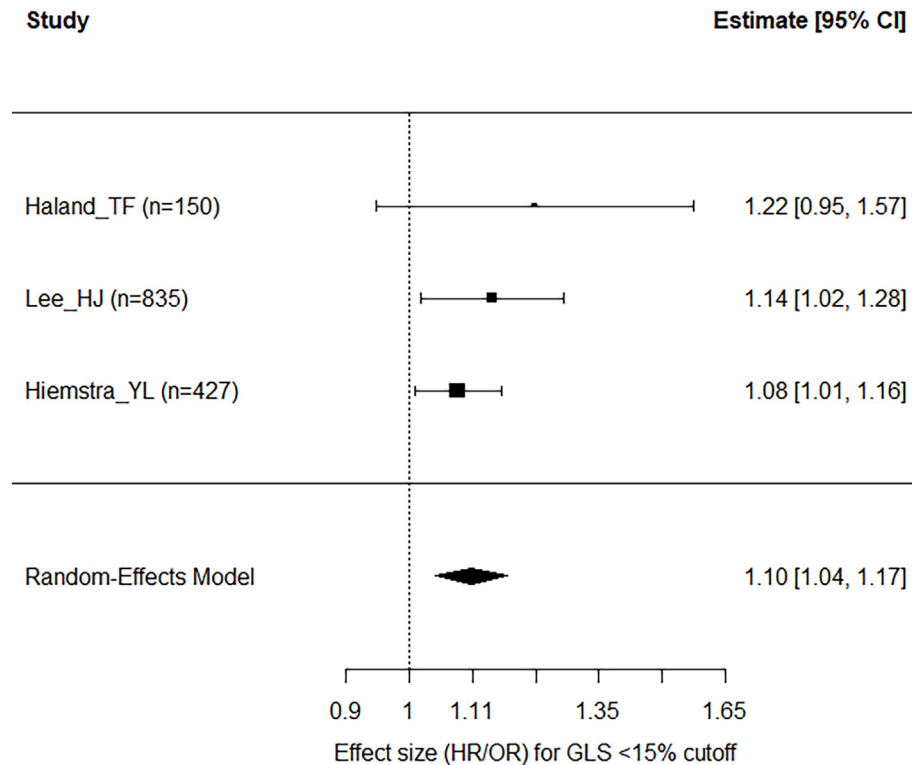


Fig. 3. Association between GLS (<15% cut-off) with SCD or fatal VAs
CI, confidence interval; GLS, global longitudinal strain; HR, hazard ratio; OR, odds ratio; SCD, sudden cardiac death; VA, ventricular arrhythmia.

Discussion

The results of this study show a positive association between GLS and SCD and/or fatal arrhythmic events in patients with HCM reinforcing the reliability of GLS as a prognostic marker.

Left ventricular ejection fraction (LVEF) has low sensitivity in detecting episodes of fatal VAs. Specifically, LVEF <35% has been found to be present in only 20% of those who died due to SCD [18]. GLS is an echocardiographic marker that provides a non-invasive evaluation of subclinical myocardial dysfunction. Two-dimensional strain is a simple, rapid, and reproducible method to measure different components of systolic strain in patients with HCM [19]. Impaired GLS has been associated with adverse outcomes in patients with HCM, including cardiac death, heart failure hospitalizations, heart transplantation, and all-cause mortality [8,20]. Across the studies summarized in Table 1, impaired GLS consistently predicted arrhythmic outcomes, whether expressed as ORs [Candan et al., 2017: OR = 1.29 (1.01–1.63)] or HRs [Debonnaire et al., 2014: HR = 1.15 (1.02–1.30); Hiemstra et al., 2017: HR = 1.08 (1.01–1.16); Lee et al., 2022: HR = 1.14 (1.02–1.28)]. The directionality of the association was uniform despite differences in patient characteristics and analysis models, highlighting GLS as an independent predictor of ventricular arrhythmic risk. The positive association between impaired GLS and fatal arrhythmic events suggests that GLS could be a useful tool for risk stratification in these patients when combined with other known risk factors. The relationship between GLS and non-sustained ventricular tachycardia (NSVT) further emphasizes its role as a risk stratification tool. Specifically, an observational study involving 59 HCM patients found that GLS was associated with the occurrence of NSVT [21]. GLS less than −11.9% predicted NSVT with 82% sensitivity and 60% specificity [21].

The pathophysiological mechanisms that may explain the association between impaired GLS and arrhythmic events include subclinical systolic dysfunction and its positive correlation with the extent of fibrosis in HCM patients [12,22]. Häland et al. (2016) showed that patients with ventricular arrhythmias had less negative GLS values ($-14.1 \pm 3.6\%$) than those without ($-16.3 \pm 3.4\%$), indicating that reduced strain parallels fibrosis and electrical instability [12]. This supports the concept that impaired myocardial deformation represents both contractile dysfunction and an arrhythmogenic substrate. In myectomized HCM patients, reduced longitudinal septal strain correlated better with fibrosis and arrhythmias compared to late gadolinium enhancement [23].

The role of GLS in risk stratification may be more significant in specific subgroups of HCM. Choi et al. examined the prognostic utility of GLS in patients with HCM and low-normal LVEF (50–60%) [24]. Patients with HCM and a low-normal LVEF have worse long-term outcomes than those with an LVEF $\geq 60\%$, including increased risks of hospitalizations for heart failure and cardiovascular death [25]. The authors demonstrated that impaired GLS was independently associated with a composite of cardiovascular death, including SCD and SCD-equivalent events [24]. As a result, GLS can serve as an additional tool for risk stratification in patients with low-normal LVEF.

Different cut-off values have been proposed for identifying high-risk patients. GLS below 8.35% was found to be an independent and definitive indicator for ICD implantation in HCM patients (specificity: 100%), while a GLS cut-off of −14.4% had a sensitivity of 92.3% and a specificity of 81% for this prediction [13]. Furthermore, the same study showed that GLS was a predictor of arrhythmic events independently of the demographic characteristics of HCM patients [13]. Another study demonstrated that a cut-off value of −14% for GLS could predict appropriate ICD therapy in a high-risk HCM population [15], while GLS > −15.6%

Combined Meta-analysis with Subgroups

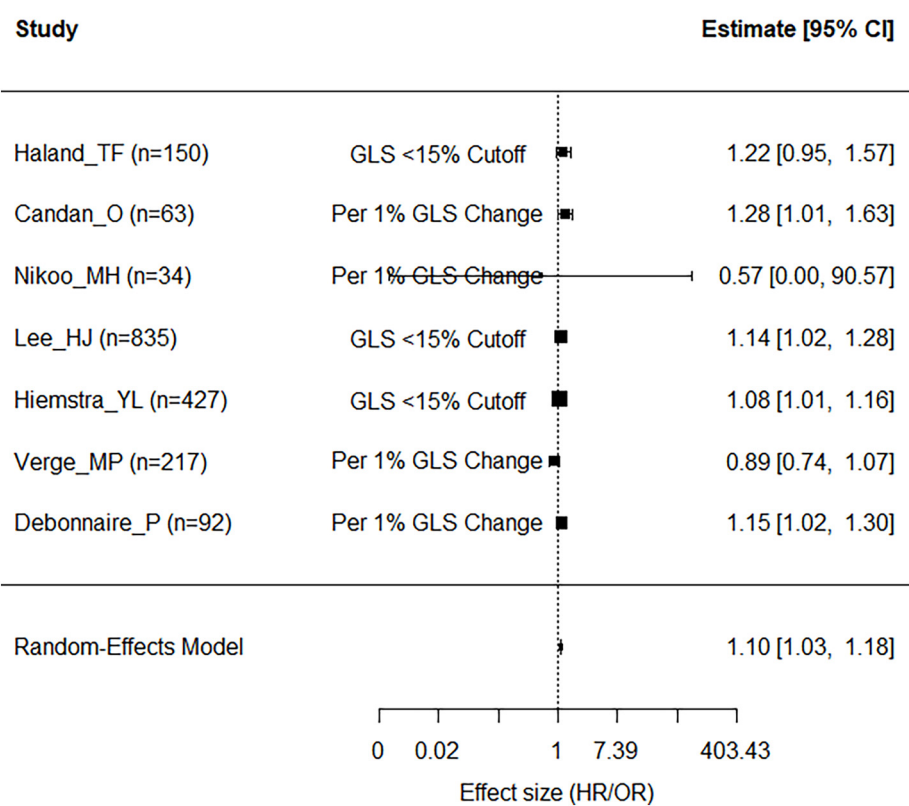


Fig. 4. Combined meta-analysis with subgroups for the association between GLS with SCD or fatal VAs. CI, confidence interval; GLS, global longitudinal strain; HR, hazard ratio; OR, odds ratio; SCD, sudden cardiac death; VA, ventricular arrhythmia.

was associated with an increased risk of cardiac death, heart failure hospitalization, and appropriate ICD therapy [8].

Most studies used GE EchoPAC systems (GE Vingmed Ultrasound AS, Horten, Norway), ensuring methodological consistency within this analysis, except for Lee et al. (2022) [9], who employed vendor-independent TomTec software (TOMTEC Imaging Systems GmbH, Munich, Germany). This enhanced internal comparability and supports the robustness of the observed associations across similar imaging platforms.

Limitations

Our study has several limitations. All the included studies were observational, which makes them susceptible to selection bias and residual confounding. Strain measurements are highly dependent on good image quality. The regions of interest in speckle-tracking software can be challenging to define in HCM patients, and these factors may influence the clinical implications of our results. An optimal GLS cut-off for identifying primary prevention HCM patients who would benefit from ICD implantation is not straightforward, as LV-GLS can vary with multiple conditions. For this reason, different cut-off values have been proposed in the literature for risk stratification purposes. Three studies used -15% as the threshold and provided effect estimates for the outcome of interest. As a result, we performed a pooled analysis using this threshold, since there were sufficient data for quantitative synthesis. However, the results of this analysis should be interpreted with caution due to the small number of studies and the different vendors used for GLS measurements. Differences in vendor algorithms and post-processing can produce clinically meaningful variation in GLS and can influence the results [26]. Although most studies used GE EchoPAC systems, one (Lee et al., 2022) [9] employed vendor-independent TomTec

software. This methodological variability, while limited, may influence absolute GLS values and thus limits generalizability. Inter-vendor differences in GLS measurement highlight the need for broader standardization across imaging platforms before GLS thresholds can be universally applied. In addition, GLS reference values are age-dependent [27], so these results may not generalize to markedly different age groups. Finally, most studies were also conducted in tertiary referral centers, potentially overestimating event prevalence compared with the general HCM population.

Conclusions

GLS is associated with risk of fatal arrhythmic events and may help identify patients with HCM at higher risk. Because the available evidence is derived from observational studies, these findings do not establish causality and may be influenced by residual confounding and bias. GLS could inform shared decision-making about ICD implantation in borderline cases when considered alongside established risk factors but should not be used alone to dictate therapy. Prospective, multicenter studies with standardized imaging protocols are needed to validate consistent GLS thresholds, determine incremental prognostic value beyond current risk models, and assess impact on clinical outcomes before routine adoption in decision pathways.

Funding

Not received.

Declaration of competing interest

Nothing to declare.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jcc.2026.04.006>.

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