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Predictive value of cardiac magnetic resonance imaging for fatal arrhythmias in structural and nonstructural heart diseases

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ABSTRACT

Background: The risk stratification for fatal arrhythmias remains inadequate. Cardiac magnetic resonance (CMR) imaging provides a detailed evaluation of arrhythmogenic substrates. This study investigated the predictive capacity of multiparametric CMR for fatal ventricular arrhythmias (VAs) in a heterogeneous disease cohort.

Methods: The study included 396 consecutive patients with structural heart disease (SHD, n = 248) and non-apparent SHD (n = 148) who underwent CMR scans between 2018 and 2022. The primary endpoint was fatal composite arrhythmias.

Results: Thirty-three patients (8.3 %) experienced fatal arrhythmias (25 with SHD, 8 with non-apparent SHD) over a median follow-up of 24 months. The independent risk factors for patients with SHD included syncope (hazard ratio [HR] = 5.347; $P < 0.001$), VA history (HR = 3.705; P = 0.004), right ventricular ejection fraction (RVEF) ≤ 45 % (HR = 2.587; $P = 0.039$), and the presence of late gadolinium enhancement (LGE) (HR = 4.767; $P = 0.040$). In the non-apparent SHD group, fatal arrhythmias were independently correlated with VA history (HR = 10.23; $P = 0.005$), RVEF ≤ 45 % (HR = 8.307; $P = 0.015$), and CMR myocardial abnormalities (HR = 5.203; $P = 0.033$). Patients at high risk of fatal arrhythmia in the SHD and non-apparent SHD groups exhibited 3-year event-free survival rates of 69.4 % and 83.5 %, respectively.

Conclusion: CMR provides effective prognostic information for patients with and without apparent SHD. The presence of LGE, CMR myocardial abnormalities, and right ventricular dysfunction are strong risk markers for fatal arrhythmias.

1. Introduction

Sudden cardiac death (SCD) is caused primarily by fatal ventricular arrhythmias (VAs), which predominantly occur in structural heart disease (SHD) but can manifest in structurally normal hearts. Sudden cardiac arrest exhibits low survival rates; predicting its risk factors warrants further investigation.

Identifying early warning signs of fatal arrhythmias can be challenging. The prevalent "gold standard", roughly dichotomizing potential risk populations based on a left ventricular ejection fraction (LVEF) of ≤35 %, falls short of providing precise, individualized risk stratification [1]. Nearly 90 % of SCD cases in SHD have an LVEF of >35 %, while half of SCD cases occur in individuals without known heart disease [2]. Thus, developing validated predictive tools beyond LVEF is necessary for identifying most at-risk individuals.

Cardiac magnetic resonance (CMR) offers advantages in evaluating cardiac morphology, function, and tissue characteristics. It has emerged as a promising and novel approach for identifying arrhythmogenic substrates and providing prognostic implications [1]. Various studies have explored the predictive ability of CMR for SCD and VAs. CMR-detected myocardial fibrosis, particularly midwall fibrosis, has been shown to be significantly associated with increased risk of SCD, while structural myocardial abnormalities detected in non-apparent SHD (naSHD) may correlate with arrhythmic events [3–7]. However, most of these studies focused on SHD, paid limited attention to structurally normal hearts, and lacked comparisons between the two groups.

Abbreviations: ARVC, arrhythmogenic right ventricular cardiomyopathy; CMR, cardiac magnetic resonance; ICD, implantable cardioverter defibrillator; LGE, late gadolinium enhancement; LV, left ventricle; LVEF, left ventricular ejection fraction; naSHD, non-apparent SHD; RV, right ventricular; RVEF, right ventricular ejection fraction; SCD, sudden cardiac death; SHD, structural heart disease; VA, ventricular arrhythmia; VT, ventricular tachycardia; WMA, wall motion abnormalities.

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Therefore, we conducted a study that combined clinical data and multiparametric CMR to identify prognostic biomarkers of fatal VAs in patients with SHD and naSHD, aiming to use these CMR-derived markers to enhance risk stratification in these populations. By including both populations, this study provides a comprehensive evaluation of CMR's prognostic value across a broader spectrum of cardiac conditions.

2. Methods

2.1. Patient selection and grouping

Consecutive patients with SHD or naSHD who underwent CMR scans between April 2018 and April 2022 were prospectively enrolled. All participants were aged 18–80 years. Individuals who recently experienced an acute myocardial infarction, acute myocarditis, or any other conditions that might have contributed to greater mortality were excluded. SHD refers to cardiac structural abnormalities resulting from various cardiovascular or systemic disorders, including: 1) coronary artery disease; 2) primary cardiomyopathies, such as hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy (ARVC), restrictive cardiomyopathy, and LV hypertrabeculation; 3) secondary cardiomyopathies arising from an extracardiovascular cause, such as amyloidosis and alcohol [8]; 4) hypertensive heart disease; 5) valvular heart disease; 6) congenital heart disease. NaSHD is characterized by the absence of apparent structural cardiac abnormalities on imaging examinations such as CMR, echocardiography, and coronary artery imaging, specifically excluding myocardial hypertrophy, valvular abnormalities, and cardiac chamber dilation, as well as previously described SHD conditions.

All participants gave written informed consent. This study adhered to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Shanghai General Hospital.

2.2. CMR protocol and analysis

Scans were performed on a 3.0-Tesla system (Ingenia, Philips; Vida Siemens). Images were obtained during multiple breath-holding sessions at the final expiration. Cine imaging, characterized by a slice thickness of 8 mm, repetition time of 2.8–3.2 ms, and echo time of 1.4–1.5 ms, utilized steady-state free precession in both long- and short-axis planes. T1-weighted imaging employed a fast-spin echo pulse sequence executed in consecutive short-axis planes. For T2-weighted imaging in short-axis planes, a triple-inversion recovery fast-spin echo pulse sequence was utilized. Late gadolinium enhancement (LGE) imaging occurred 10 min after intravenous administration of a gadolinium-based contrast agent (0.2 mmol/kg). LGE imaging was conducted using a phase-sensitive inversion recovery sequence in both short-axis and four-chamber views with a slice thickness of 8 mm, repetition time of 2.4 ms, and echo time of 1.1 ms.

Image analysis was conducted using Cvi42 version 5.17 (Circle Cardiovascular Imaging Inc., Calgary, Canada) by an experienced radiologist who was blinded to patient outcomes. Manual contouring of the endocardium and epicardium was performed in short-axis planes during end-diastolic and end-systolic phases (Fig. 1). Indexing of myocardial mass and volumes was performed relative to the body surface area. LV wall motion abnormalities (WMAs) were visually assessed using a 17-segment model; right ventricular (RV) WMAs underwent evaluation in short-axis and four-chamber planes. Fatty replacement or edema was visually assessed with T1- and T2-weighted images.

LGE presence was confirmed only if it appeared in two spatial orientations. When no enhancement was detected, LGE mass was recognized as zero [6]. The LGE extent, indicative of the scar burden, was quantified as the percentage ratio of LGE mass to LV mass. Fig. 1 shows a variety of CMR abnormalities.

2.3. Risk factor candidates

Candidate predictors encompassed demographic characteristics and clinical data, established SCD risk markers, and CMR parameters. Established predictors under consideration included familial SCD, syncope, and VA history (non-sustained ventricular tachycardia [VT] or ventricular premature complexes $\geq$ 10/h) [1,9,10]. The electrocardiographic diastolic index, which reflects diastolic dysfunction, was also included as a candidate predictor [11]. Thresholds of LVEF $\leq$ 35 % for LV dysfunction and RV ejection fraction (RVEF) $\leq$ 45 % for RV dysfunction were established [12]. Moderate structural abnormalities on CMR were set as thresholds since mild changes are presumed consequential rather than causative of arrhythmias, especially in naSHD (details in Supplemental Table S1) [13]. CMR myocardial abnormalities were defined as abnormal tissue characteristics (fatty replacement, edema, and LGE presence) or WMA.

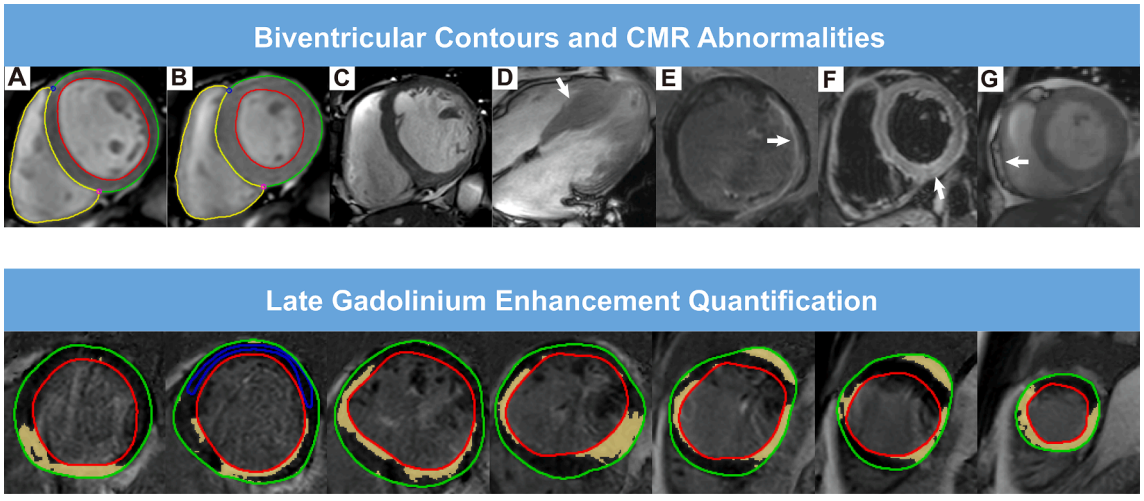

Fig. 1. Cardiovascular Magnetic Resonance Imaging. Manual contouring is performed on the left ventricular (LV) endocardium (red line), LV epicardium (green line), and right ventricular endocardium (yellow line) at the (A) end-diastolic and (B) end-systolic phases. The upper images also depict (C) biventricular dilatation, (D) myocardial hypertrophy, (E) late gadolinium enhancement (LGE), (F) myocardial edema, and (G) fatty replacement. Below, graphs showcase the quantification of LGE. A signal intensity > 5 standard deviations above the reference myocardium (blue line) is considered a myocardial scar (yellow area). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

2.4. Follow-up and endpoints

Follow-up assessments were performed biannually, commencing from the date of the initial CMR scan and concluding in July 2023. Data regarding arrhythmic events and mortality status were sourced from medical records using the International Classification of Diseases codes for death certificates. Therapies involving implantable cardioverter-defibrillators (ICD) were evaluated by a cardiovascular specialist and deemed appropriate for conditions such as ventricular fibrillation or sustained VT.

The primary outcome was fatal arrhythmias, including SCD, ventricular fibrillation, hemodynamically unstable sustained VT, and appropriate ICD therapies. SCD was characterized as "unexpected death occurring within 1 h of symptom onset and was presumed to have a cardiac cause" [1].

2.5. Statistical analyses

Candidate predictors with more than 20 % missing values were excluded. For the retained variables, missing values in continuous variables were imputed using the mean, and those in categorical variables were imputed using the mode. Continuous and categorical variables underwent comparison using Student's *t*-test or the Mann–Whitney *U* test and chi-squared test. Univariate analysis was conducted using Cox proportional hazards regression. Variables with $P < 0.05$ were subsequently included in the multivariate analysis, which was performed using forward stepwise Cox regression to identify independent risk factors for the endpoint. The nonlinear relationship between scar burden and the outcome was fitted utilizing a logarithmic curve. The optimal threshold for the nomogram score was determined utilizing X-tile version 3.4.7 (Yale University, New Haven, CT, USA). Kaplan–Meier analysis was performed to determine event-free survival rates. Survival differences were assessed using the log-rank test. Statistical significance was set at $P < 0.05$. R version 4.2.2 (R Foundation, Vienna, Austria) was used for all statistical analyses.

3. Results

3.1. Patient demographics

The entire cohort included 396 patients: 248 (63 %) diagnosed with SHD and 148 (37 %) with naSHD. The cohort's mean age was 49.2 ± 14.7 years, with females constituting 36 % of the population. Table 1 presents the patients' baseline characteristics. Dilated cardiomyopathy (40 %) predominated in the SHD group; idiopathic VA (35 %) accounted for the highest proportion in the naSHD group. Detailed etiologic distributions are presented in Supplemental Figure S1. The naSHD group comprised younger patients with a balanced sex ratio. The SHD group was more likely to show typical electrocardiographic abnormalities.

3.2. CMR characteristics

Within the SHD group, the average LVEF was 46 %, with 40 % having an LVEF ≤ 35 %. The average RVEF was 48 %; 44 % of these patients had an RVEF ≤ 45 %. Most patients (82 %) exhibited CMR myocardial abnormalities; 157 (63 %) showed LGE, with a median extent of 2.45 %. Detailed CMR findings can be find in Table 1.

The naSHD group had an average LVEF of 60 % and an average RVEF of 55 %. In total, 18 (12 %) patients showed concealed abnormalities on CMR, including RV dysfunction (n = 5), myocardial abnormalities (n = 11), and both (n = 2). Three patients diagnosed with idiopathic VA showed LGE.

3.3. Primary outcome

In a median follow-up period of 24 (interquartile range, 16–40)

Table 1
Baseline characteristics.

	Total (n = 396)	SHD (n = 248)	naSHD (n = 148)	*P*-value
Age, y	49.2 ± 14.7	51.7 ± 13.9	45.0 ± 15.1	<0.001
Female, n (%)	144 (36.4)	69 (27.8)	75 (50.7)	<0.001
Body mass index, kg/m^2	24.6 ± 4.1	25.3 ± 4.4	23.5 ± 3.3	<0.001
Systolic blood pressure, mm Hg	127 ± 19	127 ± 20	127 ± 16	0.680
Diastolic blood pressure, mm Hg	78 ± 13	78 ± 14	76 ± 12	0.188
Endpoint events, n (%)	33 (8.3)	25 (10)	8 (5.4)	0.103
Familial SCD, n (%)	11 (2.8)	10 (4)	1 (0.7)	0.049
Syncope history, n (%)	33 (8.3)	21 (8.5)	12 (8.1)	0.900
VA history, n (%)	114 (28.8)	82 (33.1)	32 (21.6)	0.015
Comorbidities, n (%)				
Diabetes mellitus	50 (12.6)	39 (15.7)	11 (7.4)	0.016
Hypertension	151 (38.1)	112 (45.2)	39 (26.4)	<0.001
Chronic kidney disease	16 (4)	13 (5.2)	3 (2)	0.116
Medications, n (%)				
ACEI/ARB/ARNI	186 (47)	163 (65.7)	23 (15.5)	<0.001
Aspirin	101 (25.5)	76 (30.6)	25 (16.9)	0.002
β-blocker	243 (61.5)	202 (81.5)	41 (27.9)	<0.001
Statin	142 (35.9)	114 (46)	28 (18.9)	< 0.001
MRA	107 (27)	104 (41.9)	3 (2)	< 0.001
ICD implantation, n (%)	26 (6.6)	24 (9.7)	2 (1.4)	0.001
Ablation, n (%)	34 (8.6)	13 (5.2)	21 (14.2)	0.002
Laboratory studies				
eGFR, ml/min/1.73 m^2	102 (86–123)	96 (77–116)	111 (97–131)	<0.001
Brain natriuretic peptide, pg/ml	85 (34–368)	222 (78–630)	32 (23–58)	<0.001
ECG parameters				
CLBBB, n (%)	18 (4.6)	16 (6.5)	2 (1.4)	0.020
CRBBB, n (%)	16 (4.1)	15 (6)	1 (0.7)	0.009
Q wave/fragment QRS, n (%)	129 (32.8)	103 (41.7)	26 (17.8)	<0.001
T wave inversion, n (%)	79 (20.1)	69 (27.8)	10 (6.8)	<0.001
QTc interval, ms	428 (407–453)	438 (411–465)	417 (400–439)	<0.001
QRS duration, ms	92 (84–102)	96 (88–106)	88 (81–96)	<0.001
EDI	12.1 ± 9.7	12.5 ± 10.2	11.6 ± 8.9	0.276
CMR parameters				
LVEF, %	56 (35–61)	46 (26–59)	60 (57–66)	<0.001
LVEF ≤ 35 %, n (%)	98 (24.7)	98 (39.5)	0 (0)	<0.001
LVEDVi, mL/m^2	80.6 (67.5–106.4)	94.7 (71.8–130)	71.1 (62.4–81.1)	<0.001
LVESVi, mL/m^2	34 (26.6–66.2)	48.5 (30.1–95.1)	28.2 (23.2–32.8)	<0.001
LVMi, g/m^2	53.5 (44.4–70.7)	62.5 (50.6–80.8)	43.4 (36.9–50.8)	<0.001
LV dilatation, n (%)	82 (20.7)	82 (33.1)	0 (0)	<0.001
Myocardial hypertrophy, n (%)	71 (17.9)	70 (28.2)	1 (0.7)	<0.001
RVEF, %	52 (40–56)	48 (31–54)	55 (52–58)	<0.001
RVEF ≤45%, n (%)	117 (29.5)	110 (44.4)	7 (4.7)	<0.001
RVEDVi, mL/m^2	82.6 (69.5–99.6)	84.9 (70.3–104.3)	79.1 (68.5–93.7)	0.006
RVESVi, mL/m^2	40.4 (31.1–55.1)	45.9 (32–65.9)	36.5 (29.8–44)	<0.001
RV dilatation, n (%)	16 (4)	16 (6.5)	0 (0)	0.002
Presence of LGE, n (%)	160 (40)	157 (63)	3 (2)	<0.001
LGE extent, %	0 (0–1.6)	1.2 (0–4)	0 (0–0)	<0.001
Myocardial abnormalities, n (%)	217 (54.8)	204 (82.3)	13 (8.8)	<0.001

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; CLBBB, complete left bundle branch block; CRBBB, complete right bundle branch block; EDI, electrocardiographic diastolic index; eGFR, estimate glomerular filtration rate; ICD, implantable cardioverter–defibrillator; LGE, late gadolinium enhancement; LV, left ventricular; LVEDVi, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume index; LVMi: left ventricular mass index; MRA, mineralocorticoid receptor antagonist; naSHD, non-apparent structural heart disease; RV, right ventricular; RVEDVi, right ventricular end-diastolic volume index; RVEF, right ventricular ejection fraction; RVESVi, right ventricular end-systolic volume index; SCD, sudden cardiac death; SHD, structural heart disease; VA, ventricular arrhythmia.

months, 33 patients (8.3 %) experienced fatal arrhythmic events, including 4 cases (1 %) of SCD (3 in the SHD group, 1 in the naSHD group), 7 (1.8 %) of ventricular fibrillation, and 22 (5.5 %) of VT. ICD implantation was performed in 2 patients from the naSHD group and 24 patients from the SHD group during follow-up; 41 % of patients received appropriate ICD therapies. More patients in the naSHD group underwent radiofrequency ablation for VA compared to the SHD group (14.1 % vs. 5.2 %, $P = 0.002$).

3.4. Predictors in the SHD group

The unadjusted risk factors are provided in Table 2 and elaborated upon in Supplemental Table S3. Multivariate model delineated four independent risk factors: syncope (hazard ratio [HR] = 5.347; 95 % confidence interval [CI], 2.230–12.822; $P < 0.001$), VA history (HR = 3.705; 95 % CI, 1.506–9.110; $P = 0.004$), RVEF ≤ 45 % (HR = 2.587; 95 % CI, 2.587; $P = 0.039$), and LGE presence (HR = 4.767; 95 % CI, 1.072–21.206; $P = 0.040$) (Table 2).

C-statistics for each independent risk factor in the univariate model ranged from 0.555 to 0.684; this metric increased to 0.760 when combining CMR-based predictors. The multivariate model showed an overall C-statistic of 0.841 (Supplemental Table S4).

Significant differences in survival were noted among individuals with and without each CMR risk marker (Fig. 2A and B). Patients at high risk, stratified based on the nomogram score (Supplemental Figure S2A), exhibited significantly worse prognoses than their low-risk counterparts ($P < 0.0001$) (Fig. 2C). The 3-year cumulative event-free survival rate for the low-risk subset was 92.4 %, in contrast to 69.4 % for the high-risk subset.

Table 2
Univariate and multivariate analyses.

	Univariate		Multivariate	
	Hazard ratio (95 % CI)	*P*-value	Hazard ratio (95 % CI)	*P*-value
SHD				
Familial SCD	4.3 (1.5–12.8)	0.007		
Syncope history	7.5 (3.2–17.7)	<0.001	5.3 (2.2–12.8)	<0.001
VA history	5.9 (2.4–14.2)	<0.001	3.7 (1.5–9.1)	0.004
RVEF ≤ 45 %	4.2 (1.7–10.1)	0.001	2.5 (1.0–6.3)	0.039
Presence of LGE	9.6 (2.2–41.3)	0.002	4.7 (1.1–21.2)	0.040
CMR abnormalities	7.7 (1.0–58.0)	0.046		
Non-apparent SHD				
VA history	11.9 (2.4–59.1)	0.002	10.2 (2.0–52.2)	0.005
RVEF ≤ 45 %	8.1 (1.6–40.2)	0.011	8.3 (1.5–45.5)	0.015
Presence of LGE	8.6 (1.1–70.2)	0.044		
CMR abnormalities	7.9 (1.8–33.5)	0.005	5.2 (1.1–23.6)	0.033

CMR, cardiovascular magnetic resonance; LGE, late gadolinium enhancement; RVEF, right ventricular ejection fraction; SCD, sudden cardiac death; SHD, structural heart disease; VA, ventricular arrhythmias.

3.5. Predictors in the naSHD group

Unadjusted correlation with fatal arrhythmias was confirmed in four covariates (Table 2; details in Supplemental Table S3). The multivariate model identified that the primary outcome was predicted independently by VA history (HR = 10.23; 95 % CI, 2.001–52.258; $P = 0.005$), RVEF ≤ 45 % (HR = 8.307; 95 % CI, 1.515–45.542; $P = 0.015$), and CMR myocardial abnormalities (HR = 5.203; 95 % CI, 1.145–23.649; $P = 0.033$). C-statistics varied from 0.610 to 0.711 for CMR risk markers considered individually or in combination. The multivariate Cox regression model demonstrated a C-statistic of 0.722 (0.623–0.820) (Supplemental Table S4).

The patients in the naSHD group were stratified depending on their nomogram score (Supplemental Figure S2B). Those with ≥ 1 CMR risk factor had significantly worse event-free survival (Fig. 2D–F). For the low- and high-risk subsets, the 3-year event-free survival rates were 97.8 % and 83.5 %, respectively.

4. Discussion

Our study had three main findings. First, CMR exhibited outstanding prognostic ability across a diverse spectrum of cardiac disorders. Presence of LGE and CMR abnormalities were significant risk markers for SHD and naSHD, respectively. Second, a moderate reduction in RV function emerged as an independent risk marker for both SHD and naSHD.

In our study cohort, cardiac abnormalities missed on routine imaging workup were identified on CMR. In the naSHD group, 12 % of the patients presented with concealed CMR abnormalities. These abnormalities might be secondary to the primary disease, such as idiopathic VT-induced cardiomyopathy, or early indicators for underlying SHD, exemplified by mild RV dilatation and dysfunction rating in the diagnostic "gray zone" of ARVC [14].

Myocardial scar-related reentry is the primary cause of VAs in SHD [15]. The surviving myocardial tissue within the scar area forms the "central isthmus" of the reentry loop, where wavefronts conduct slowly and create a reentrant circuit with the surrounding normal myocardium [16]. Therefore, myocardial scarring is considered the substrate for SCD. LGE-CMR uniquely excels in identifying and characterizing arrhythmogenic substrates. LGE was identified as a robust risk marker of fatal arrhythmia in the SHD cohort, showing a nearly 5-fold increased risk post-adjustment for other predictors. Similar results have been reported; Gulati et al. [3] and Perazzolo et al. [17] discovered that LGE was linked to a 4- to 5-fold elevated arrhythmic risk in dilated cardiomyopathy. Chan et al. [4] and Weng et al. [18] observed a similar association in hypertrophic cardiomyopathy. In addition, the prognostic significance of myocardial scarring conditions, including coronary artery disease, mitral valve prolapse, and cardiac sarcoidosis, has been validated [6,19–22]. These findings suggest that LGE is a strong indicator of heightened susceptibility to fatal arrhythmias across various SHD etiologies.

Unlike patients with SHD, those with structurally normal hearts usually do not manifest myocardial impairment. Rather, arrhythmias in these individuals are attributed primarily to enhanced automaticity or activities triggered by electrical defects [23,24]. Such subtle cellular alterations are scarcely detectable with conventional noninvasive imaging techniques. Several studies have reported the capacity of CMR to identify concealed cardiac abnormalities in primary electrical diseases and apparently normal hearts [7,25,26], suggesting its promising utility in risk stratification for patients without apparent SHD.

Our data revealed that CMR myocardial abnormalities, including abnormal tissue characterization and WMA, indicated a 5-fold greater risk of fatal arrhythmias in the naSHD group. Prior studies substantiate our observation. Nucifora et al. [7] observed a pronounced association between CMR-detected myocardial structural abnormalities and arrhythmic composite events, noting an HR as high as 41.6. Zorzi et al.

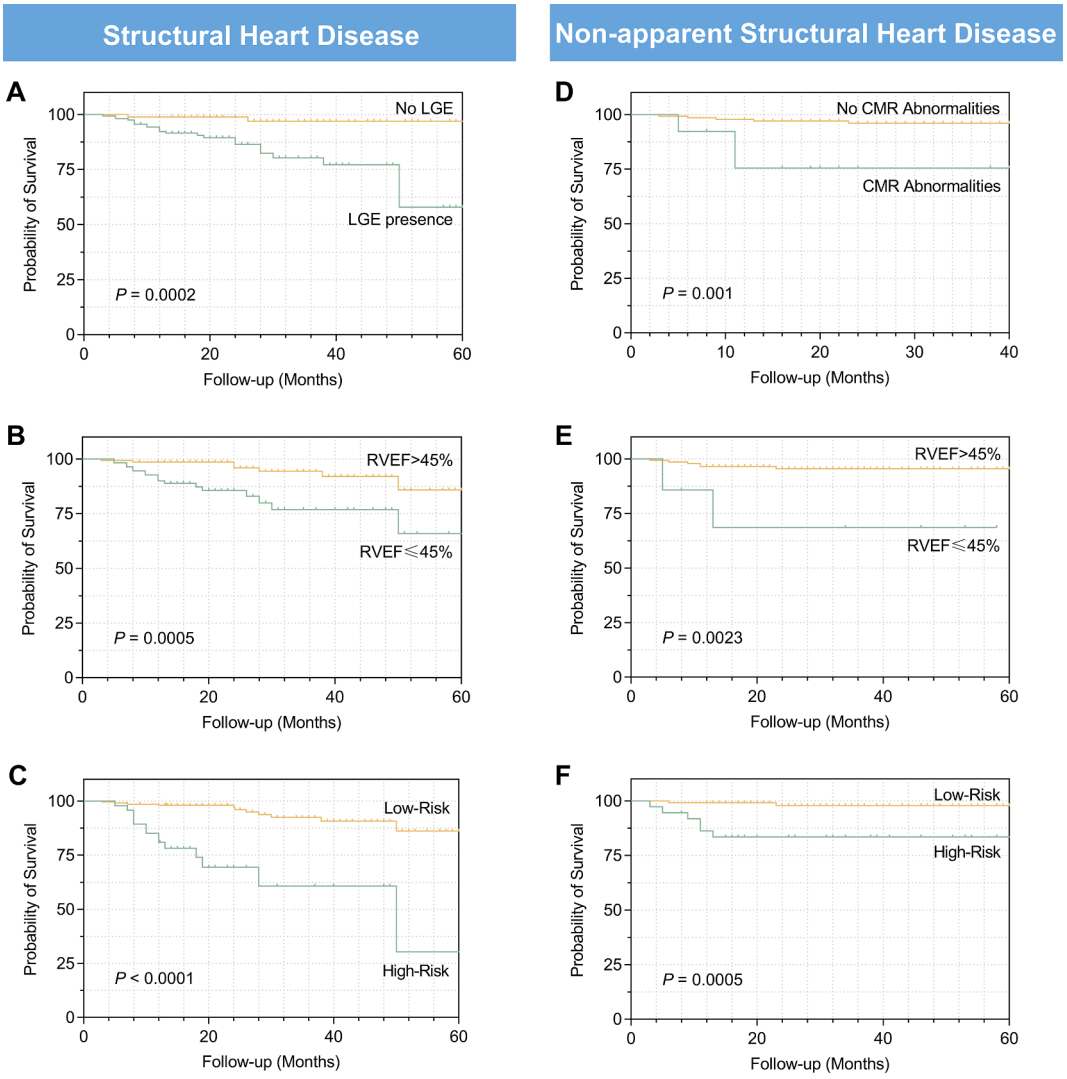

Fig. 2. Kaplan–Meier Analyses. Survival analyses, based on the presence or absence of CMR-based risk factors and risk stratification, reveal significant disparities **(A)** LGE, **(B)** RVEF ≤ 45 % in the structural heart disease **(**SHD) group, **(C)** low-risk versus high-risk classification in the SHD group, **(D).** CMR myocardial abnormalities, **(E)** RVEF ≤ 45 % in the non-apparent SHD group, **(F)** low-risk versus high-risk classification in the non-apparent SHD group).

[27] observed a stria-pattern LGE in athletes without SHD who experienced life-threatening arrhythmias. Likewise, a recent study on VA with diverse etiologies (predominantly idiopathic) demonstrated that abnormal CMR features, including LGE, WMA, and LVEF < 50 %, effectively predicted major adverse cardiac events [28]. CMR myocardial abnormalities reflect pathological changes such as localized myocardial fibrosis, fat replacement, or chronic inflammatory infiltrates. It is possible that these concealed myocardial structural abnormalities are associated with rare phenotypes of ARVC, including left dominant and biventricular patterns of disease expression, which exhibit the same SCD risk as the classic pattern [7,29].

CMR myocardial abnormalities demonstrated limited discriminative ability in SHD; LGE proved ineffective for prognostic prediction in naSHD. These results may be attributed to the high prevalence (82 %) of myocardial abnormalities in SHD and the minimal occurrence (2 %) of LGE in naSHD.

This study identified RVEF ≤ 45 % as a potential indicator for fatal arrhythmias. Approximately 44 % of patients with SHD and nearly 5 % of those with naSHD showed a moderate decrease in RV function, correlating with a 2.5-fold and 8-fold greater risk of arrhythmic events, respectively. RV dysfunction and increased pressure are often associated with atrial arrhythmias, whereas their association with VAs is less frequently reported [30]. However, emerging evidence suggests that RV dysfunction holds promise as a novel indicator of SCD risk. Studies have shown that chronic obstructive pulmonary disease and obstructive sleep apnoea, characterized by their propensity to cause RV remodeling, are associated with an increased risk of SCD [31,32]. Pandat et al. [33] compared SCD patients with controls and found that for every 5 % decrease in RV fractional area change, there was a 1.14-fold increase in the risk of SCD. Wang et al. [22] reported a tripling of SCD risk in cardiac sarcoidosis with RV abnormalities on CMR. Mikami et al. [12] mixed-cohort study showed that an RVEF ≤ 45 % independently forecasted a 2.98-times greater risk of SCD and appropriate ICD therapies. Similarly, Aktas et al. [34] found that severely impaired RV function was independently associated with a twofold increased risk of the combined endpoint of ICD therapy or death.

RVEF is explicitly included in the risk calculator for ARVC, wherein each percentage reduction in RVEF increases the risk of fast sustained VAs by 1.03-fold [35]. An idiopathic premature ventricular complexes cohort study revealed increased susceptibility to severe arrhythmic events in patients with RV structural abnormalities ascertained by CMR [14]. Isbister et al. [25] observed reduced RVEF and increased RV volume during the disease progression of Brugada syndrome.

A plausible explanation could be that reduced RV function and

increased volume may induce changes in the cardiomyocyte membrane potential and sympathetic overactivation, ultimately leading to increased autoregulation and triggered activity. Moreover, RV failure often indicates the presence of chronic hypoxic conditions, which may mediate the development of fatal arrhythmias through cardiac autonomic dysfunction, prolonged ventricular repolarization, increased transmural action potential duration, and upregulated endocardial calcium channel expression [36].

4.1. Clinical implications

This study showed that the presence of LGE and CMR abnormalities has prognostic value for SHD and naSHD, respectively. This difference indicates the importance of tailored risk assessment and management strategies for each group. RV dysfunction is a strong risk indicator for patients with both SHD and naSHD, highlighting the necessity of RV assessment in routine clinical practice, including monitoring RV function, structure, and pressure; as well as enhancing treatment strategies for RV management, such as volume control and improving RV remodeling. Additionally, this study demonstrates the ability of CMR to identify subtle cardiac abnormalities that might be missed by conventional imaging techniques, thereby providing a basis for risk stratification of fatal VAs, which is particularly important for patients with naSHD who lack risk assessment tools. Further genetic and electrophysiological testing is necessary for individuals identified as high-risk based on these markers.

4.2. Study limitations

This single-center investigation encompassed patients with a broad spectrum of heart disorders instead of concentrating on a singular disease. Furthermore, the limited sample size may affect the generalizability of the findings. Verification across each disease category necessitates larger-scale multicenter studies with a larger sample size, as well as the inclusion of competing mortality risks and the benefits of ICD therapy in the analysis to assist in guiding clinical decisions. Moreover, the study excluded patients over the age of 80, which could limit the applicability of our findings among older adults. Future studies should consider strategies to focus on older patients, potentially adjusting for their unique risk profiles and medical needs to better understand the predictive power of CMR across all age groups.

5. Conclusions

CMR can be applied for risk stratification of fatal arrhythmias in individuals with SHD or naSHD. RV dysfunction and LGE are closely correlated with fatal arrhythmias in patients with SHD. RV dysfunction and CMR myocardial abnormalities are independent predictors for patients with naSHD.

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CRediT authorship contribution statement

Xing Xing: Writing – original draft, Investigation, Formal analysis, Data curation. **Xiaoqiang Liu:** Writing – review & editing, Methodology, Conceptualization. **Yi Zhang:** Writing – review & editing, Resources, Formal analysis. **Lei Zhang:** Writing – review & editing, Resources, Formal analysis. **Gu Shen:** Writing – review & editing, Investigation. **Yulong Ge:** Writing – review & editing, Investigation. **Fang Wang:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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