JACC: CARDIOVASCULAR IMAGING VOL. 18, NO. 7, 2025


ORIGINAL RESEARCH

# Extent and Features of Late Gadolinium Enhancement Stratify Arrhythmic Risk in Patients With Biopsy-Proven Sarcoidosis

Alessia Azzu, MD, PhD,[a,b] Alexios S. Antonopoulos, MD, PhD,[a] Joseph Okafor, MD,[b,c] Marco Morosin, MD,[d] Emmanuel Androulakis, MD, PhD,[a] Suzan Hatipoglu, MD,[a] Batool Almogheer, MD,[a] Raheel Ahmed, MD,[b,e] Raad Mohiaddin, MD, PhD,[a,b] Francisco Alpendurada, MD, PhD,[a,b] Cemil Izgi, MD,[a,b] Amrit Lota, MD, PhD,[a,b] Kshama Wechalekar, MD,[b,f] Rajdeep Khattar, MD, PhD,[b,c] Athol Wells, MD, PhD,[b,g] John Baksi, MD, PhD,[a,b] Rakesh Sharma, MD, PhD,[b,e] Vasileios Kouranos, MD, PhD,[b,e] Dudley J. Pennell, MD[a,b]

## ABSTRACT

**BACKGROUND** Risk assessment in cardiac sarcoidosis remains challenging.

**OBJECTIVES** This study explored the prognostic value of myocardial late gadolinium enhancement (LGE) in sarcoidosis patients.

**METHODS** The study cohort included 324 patients with biopsy-proven sarcoidosis. LGE extent, pattern, and location were analyzed. The primary endpoint was ventricular tachycardia (VT) or ventricular fibrillation (VF) or appropriate device therapy. Secondary endpoints were hospitalization for heart failure (HF) or heart transplantation (HTx) and all-cause mortality.

**RESULTS** Over a 4.6-year follow-up, 30 patients (9.3%) reached the primary endpoint. HF/HTx occurred in 15 patients (4.6%) and all-cause mortality in 41 (12.7%). LGE extent was independently predictive of the primary endpoint (per SD change: HR: 1.03 [95% CI: 1.00-1.06]; $P = 0.047$), but not of HF/HTx ($P = 0.30$) or all-cause mortality ($P = 0.50$). Further to LGE extent, LGE on the right ventricular (RV) septum (HR: 5.43 [95% CI: 2.61-11.30]; $P < 0.001$), RV free wall (HR: 4.30 [95% CI: 1.99-9.27]; $P < 0.001$), and multifocal LGE (HR: 4.62 [95% CI: 2.19-9.72]; $P < 0.001$) were strongly predictive of the arrhythmia endpoint. Based on these findings, we propose an algorithm that identifies 4 patient subgroups and stratifies well the arrhythmia risk in biopsy-proven sarcoidosis patients (cumulative event rates: 1%, 11%, 23%, and 44%, respectively; chi-square = 44.7; $P = 1.084 \times 10^{-9}$). Compared with the Heart Rhythm Society classification system, this approach significantly enhanced model performance (chi-square = 8.02; $P = 0.046$) and risk discrimination ($\Delta$AUC = 0.082; $P = 0.019$), and reclassified 43% of the population (9% to higher and 34% to lower risk categories).

**CONCLUSIONS** The authors propose a new risk stratification approach based on LGE features for assessing the risk of life-threatening ventricular arrhythmias in patients with biopsy-proven sarcoidosis. (JACC Cardiovasc Imaging. 2025;18:768-780) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

From the [a]Cardiovascular Magnetic Resonance Unit, Royal Brompton Hospital, London, United Kingdom; [b]National Heart and Lung Institute, Imperial College London, London, United Kingdom; [c]Department of Echocardiography, Royal Brompton Hospital, London, United Kingdom; [d]Adult Intensive Care Unit, Royal Brompton Hospital, London, United Kingdom; [e]Department of Cardiology, Royal Brompton Hospital, London, United Kingdom; [f]Nuclear Medicine Department, Royal Brompton Hospital, London, United Kingdom; and the [g]Interstitial Lung Disease Unit, Royal Brompton Hospital, London, United Kingdom.



Manuscript received May 16, 2024; revised manuscript received January 2, 2025, accepted February 14, 2025.

ISSN 1936-878X https://doi.org/10.1016/j.jcmg.2025.02.012

Cardiac sarcoidosis (CS) is an inflammatory condition of unknown etiology associated with life-threatening ventricular arrhythmias, conduction abnormalities, heart failure, and sudden cardiac death (SCD).[1] Non-necrotizing granulomatous inflammation is the histologic hallmark in CS, but the diagnosis can sometimes be challenging in the absence of biopsy confirmation.[2] Furthermore, the prognosis is not well defined clinically, and significant uncertainties remain in the clinical management of patients with CS.

Previous studies have demonstrated that cardiac magnetic resonance (CMR) is the most valuable modality not only for diagnosis, but also for risk assessment in CS.[3] The presence of myocardial fibrosis, as detected by late gadolinium enhancement (LGE) has been associated with adverse cardiac events in several CS studies.[4-6] Joint AHA (American Heart Association)/ACC (American College of Cardiology)/HRS(Heart Rhythm Society) guidelines and the most recent ESC (European Society of Cardiology) guidelines recognize the prognostic value of left ventricular (LV) function and recommend an implantable cardioverter-defibrillator (ICD) in all patients with CS and left ventricular ejection fraction (LVEF) ≤35% (Class I recommendation).[7,8] However, both sets of guidelines have not yet defined the high-risk population that would benefit from primary-prevention ICD placement when LVEF is >35%. The AHA/ACC/HRS guidelines suggest ICD placement in CS patients with LVEF >35% if they have myocardial scar on CMR or positron emission tomography (PET), syncope, or an indication for a permanent pacemaker (Class IIa recommendation).[7] Were these guidelines to be applied, then most patients with a diagnosis of CS would also fulfill the criteria for ICD placement, because the presence of fibrosis is one of the key criteria to diagnose the condition.[9]

The most recent ESC guidelines recognized the importance of LGE extent as prognostic factor and suggested an ICD as primary prevention for patients with CS with LVEF >35% and evidence of "significant" LGE on CMR (after the resolution of acute inflammation). In contrast, in patients with only "minor" LGE and an LVEF of 35% to 50%, it is suggested that risk stratification should be based on an electrophysiologic study (Class IIa recommendation).[8] However, definitions of "significant" and "minor" LGE are not provided by the guidelines. Only a few studies suggest that using a threshold of myocardial fibrosis extent can aid the decision for ICD placement, but such cutoffs have not been validated and are not in the guidelines.[10-12]

In the present study, we explored the prognostic significance of the extent, pattern, and location of myocardial LGE in patients with biopsy-proven sarcoidosis. We aimed to identify LGE features that might be associated with a higher risk of adverse cardiac events and provide a novel algorithm for risk stratification in CS.

**ABBREVIATIONS AND ACRONYMS**

**CMR** = cardiac magnetic resonance

**CS** = cardiac sarcoidosis

**LGE** = late gadolinium enhancement

**HF** = heart failure

**HTx** = heart transplantation

**ICD** = implantable cardioverter-defibrillator

**LV** = left ventricular

**LVEF** = left ventricular ejection fraction

**PET** = positron emission tomography

**RV** = right ventricular

**SCD** = sudden cardiac death

**VF** = ventricular fibrillation

**VT** = ventricular tachycardia

## METHODS

**STUDY DESIGN AND PARTICIPANTS.** We identified patients with biopsy-proven sarcoidosis who were investigated at the Royal Brompton Hospital from 2004 to 2023. Only patients with biopsy-proven sarcoidosis and good-quality CMR images were included. Patients with significant obstructive coronary artery disease, significant valvular heart disease, or suspicion of an alternative diagnosis of cardiomyopathy were excluded. Significant coronary artery disease was defined as previous percutaneous coronary intervention, coronary artery bypass graft, or known obstructive coronary artery disease. Significant valvular artery disease was defined as severe valvular stenosis or regurgitation or previous valve replacement or repair. An alternative diagnosis of cardiomyopathy was established by a multidisciplinary team based on clinical and imaging findings as well as genetic testing when appropriate.

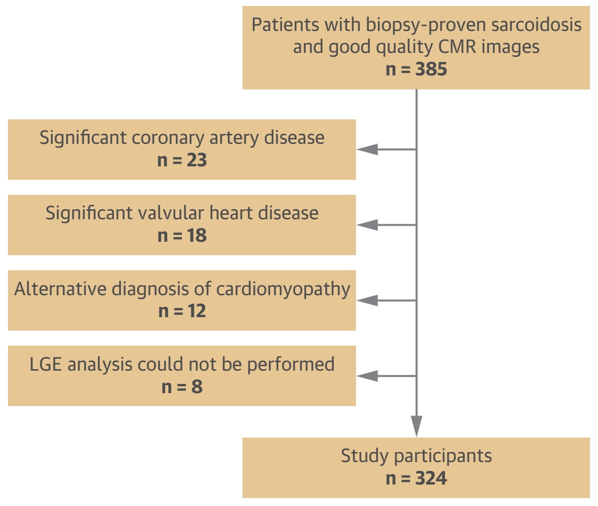
Patients' medical records were searched for all clinical information. Medical imaging data sets of CMR studies were retrieved for independent review and analysis. Follow-up event data were collected from electronic hospital records. Time to first clinical event was defined as the time from the date of the index CMR scan to the date of the first event. Follow-up duration was calculated from the date of the index CMR scan until death or last clinical contact with the patient.

The primary endpoint was a life-threatening ventricular arrhythmic event, including sustained ventricular tachycardia (VT) (>100 beats/min lasting >30 s or requiring earlier termination), ventricular fibrillation (VF), appropriate ICD shock, or appropriate antitachycardia pacing. The secondary endpoints of the study were hospitalization for heart failure or heart transplantation, and all-cause mortality. The study was approved by the Research Ethics Committee of the Health Research Authority, United Kingdom.

**CMR STUDIES.** Digitally archived multiscanner multicenter CMR studies, performed in our institution or imported from referring UK hospitals, were

JACC: CARDIOVASCULAR IMAGING, VOL. 18, NO. 7, 2025
JULY 2025:768-780

**FIGURE 1 Flowchart Showing Exclusion of Patients From the Study**




CMR = cardiac magnetic resonance; LGE = late gadolinium enhancement.

retrospectively reviewed. All imaging protocols included steady-state free precession breath-hold cine imaging for the assessment of ventricular volumes and function, and standard LGE sequences with magnitude inversion recovery and phase-sensitive inversion recovery reconstructions, according to standard recommendations. In patients with a cardiac implantable electronic device, gradient echocardiography sequences for cine imaging and wide-band LGE acquisitions were used to improve image quality.

**CMR ANALYSES.** All studies were analyzed with the use of CVI42 software (version 5.13.4, Circle Cardiovascular Imaging) by 3 CMR-experienced operators blinded to clinical information. Patients were classified into 3 categories based on LV systolic function: LVEF ≤35%, LVEF 36%-50%, and LVEF >50%. LGE location in the left ventricle was described according to both the AHA 17 myocardial segments model[13] and a wall segmentation model (anterior, septal, inferior, and lateral). Multifocal LGE was defined as the presence of enhancement in at least 2 nonconsecutive and nonadjacent AHA myocardial segments. The LGE pattern was described according to the type of involvement of myocardial layers as mid-wall, subepicardial, subendocardial, transmural, or mixed. In the presence of at least 1 segment of transmural LGE, patients were classified as having transmural LGE. Mixed pattern included a combination of at least 2 different patterns between mid-wall, subepicardial, and subendocardial LGE. Patients with only focal prominent LGE in the ventricular insertion points were identified. The presence of LGE in the right ventricular (RV) free wall or on the right side of the interventricular septum also was recorded.

LGE extent was expressed as the number of LV segments involved (17-segment model) and as a percentage of the overall LV myocardial mass. Quantification of LGE extent was assessed using the signal threshold vs reference myocardium method, which analyses the signal intensity of enhanced myocardial areas compared with a reference region of interest placed over normal nulled myocardium. A signal threshold of >5 SDs above the mean signal of the reference myocardium was applied to calculate the total LGE mass. LGE extent, as a percentage, was automatically calculated by dividing the LGE mass by the total LV mass. The >5-SD threshold was chosen because it was the most used in previous CS cohorts[10,14-17] and provided the best agreement with visual assessment. In case of inaccurate tracking, manual adjustment was performed. Interobserver variability was assessed by a fourth independent CMR operator, who analyzed LGE mass and extent in 27 CMR studies. Coefficient of variation was 6.1% for LGE mass and 6.3% for LGE extent.

**STATISTICAL ANALYSIS.** We present continuous variables as mean ± SD or median (Q1-Q3) as appropriate. We compared categoric variables between 2 or more groups with the chi-square test, and we compared continuous variables between groups with either Student's *t*-test or Mann-Whitney *U*-test (for 2 groups, as appropriate) or by analysis of variance (for 3 groups). We tested correlations between continuous variables with either Pearson's *r* or Spearman's rank correlation coefficient, as appropriate. The prognostic value of LGE extent, LGE mass, and number of myocardial segments for the various study endpoints of ventricular arrhythmia, heart failure or heart transplantation, and all-cause mortality was explored in unadjusted Cox regression models and after adjustment for age, sex, and presence of LV systolic dysfunction (ie, LVEF <50%). The different LGE patterns for the arrhythmia endpoint were assessed in the overall population and in specific population subgroups, ie, without ventricular arrhythmia events at presentation, LVEF >35%, and LVEF >50%. The optimum cutoff for LGE extent was selected by identifying the value that maximized Youden's J statistic (sum of sensitivity and specificity) on logistic regression analysis for the primary endpoint to ensure an optimum balance between sensitivity and specificity in our models. Cox proportional hazard regression models were fitted to test the association of each variable with the outcome of interest. The assumption of proportional hazards was checked with the use of the Schoenfeld residuals test. Kaplan-Meier survival curves for the study subgroups, ie, with high vs low LGE extent and presence or absence of high-risk LGE features, were plotted with numbers at risk shown below each graph. In the subgroup of patients who did not show arrhythmia at presentation, we fitted a Cox proportional hazards regression model with as an independent variable the HRS indication for an ICD (ie, no indication for ICD, Class IIa, or Class I). On top of this model, we added, as a second covariate, the proposed risk classification system (ie, low, intermediate, high, or very high risk category). The 2 nested models were compared by means of the change in the likelihood ratio test (chi-square). The C-index of the model was derived from time-dependent ROC curve analysis, and the improvement in risk discrimination was assessed by the change in the c-index (ΔAUC) of the nested models (from time-dependent ROC analysis). The improvement in risk reclassification was assessed in a risk classification table. Statistical analyses were performed with the use of R version 4.2.0. All tests were 2-sided and alpha was set at 0.05.

## RESULTS

**PATIENT DEMOGRAPHICS.** Of the initial 385 patients with biopsy-proven sarcoidosis and available good-quality CMR images who were screened for eligibility, we excluded 23 patients with known significant coronary artery disease, 18 with significant valvular heart disease, and 12 with an alternative diagnosis of cardiomyopathy. In addition, we excluded 8 patients in whom LGE extent could not be quantified due to technical issues during acquisition. In total, 324 patients with biopsy-proven sarcoidosis were included in this study (Figure 1). The study cohort included 212 (65.4%) men and 112 (34.6%) women. Mean age at the time of the baseline CMR scan was 53.6 years. Demographics and clinical characteristics of the study population are reported in Table 1. Baseline CMR findings are presented in Table 2.

**ADVERSE CARDIAC EVENTS DURING FOLLOW-UP.** During a median follow-up period of 4.6 years (Q1-Q3: 2.3-7.5 years), 30 patients (9.3%) reached the primary endpoint including sustained VT (n = 22) or VF (n = 8). Among them, appropriate ICD therapy occurred for VT in 14 patients and for VF in 6 patients. Hospitalization for heart failure was recorded in 15 patients (4.6%), and 3 (0.9%) underwent heart transplantation. Overall, 41 patients (12.7%) died of any cause. In total, 61 patients reached at least 1 study

**TABLE 1 Demographics of the Study Population (N = 324)**

| | |
|---|---|
| Age, y | 53.6 ± 11.6 |
| Male | 212 (65.4) |
| Comorbidities | |
| Hypertension | 134 (41.4) |
| Dyslipidemia | 73 (22.5) |
| Diabetes | 61 (18.8) |
| Smoking history | 104 (32.1) |
| Ethnicity | |
| Caucasian | 236 (73.1) |
| Asian | 44 (13.6) |
| Black | 33 (10.2) |
| Other | 11 (3.4) |
| Organ involvement with sarcoidosis | |
| Lung | 305 (94.1) |
| Liver | 23 (7.1) |
| Spleen | 10 (3.1) |
| Kidney | 6 (1.9) |
| Skin | 43 (13.3) |
| Skeleton | 6 (1.9) |
| Eye | 19 (5.9) |
| Nervous system | 14 (4.3) |
| Other | 4 (1.2) |
| Endomyocardial biopsy | 4 (1.2) |
| Clinical presentation before CMR | |
| VF | 4 (1.2) |
| Sustained VT | 27 (8.3) |
| High-degree AV block[a] | 41 (12.7) |
| LVEF <40% | 31 (9.6) |
| Syncope or pre-syncope | 21 (6.5) |
| Disproportionate dyspnea | 62 (19.1) |
| Chest pain | 37 (11.4) |
| Palpitations | 82 (25.3) |
| Asymptomatic screening | 110 (33.6) |
| Cardiac implantable electronic device | |
| Any device | 110 (33.6) |
| Dual-chamber PPM | 36 (11.1) |
| ICD | 69 (21.3) |
| CRT-D | 43 (13.3) |
| Medications | |
| Steroids | 246 (75.9) |
| Nonsteroidal agents | 181 (55.9) |
| Heart failure medication | 117 (36.1) |
| Clinical outcomes | |
| Death | 41 (12.7) |
| Sustained VT | 22 (6.8) |
| VF | 8 (2.5) |
| Appropriate ICD therapy | 20 (6.2) |
| Hospitalization for heart failure | 15 (4.6) |
| Heart transplantation | 3 (0.9) |
| FDG-PET | |
| FDG-PET positive anytime | 194 (59.9) |

Values are mean ± SD or n (%). [a]High-degree AV block was defined as Mobitz type II 2nd or 3rd degree AV block.

AV = atrioventricular; CMR = cardiac magnetic resonance; CRT-D = cardiac resynchronization therapy defibrillator; FDG-PET = $^{18}$F-fluorodeoxyglucose positron emission tomography; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; PPM = permanent pacemaker; VF = ventricular fibrillation; VT = ventricular tachycardia.

JACC: CARDIOVASCULAR IMAGING, VOL. 18, NO. 7, 2025
JULY 2025:768-780

**TABLE 2 CMR Findings in the Study Population and Subgroups for the Arrhythmic Endpoint**

| | Whole Cohort (N = 324[a]) | Arrhythmia Endpoint No (n = 294) | Arrhythmia Endpoint Yes (n = 30) | P Value |
|---|---|---|---|---|
| LVEDV, mL | 159.9 ± 53.7 | 156.6 ± 50.2 | 192.2 ± 74.1 | 0.001 |
| LVESV, mL | 69.6 ± 47.3 | 65.1 ± 40.3 | 115.0 ± 79.6 | <0.001 |
| LVSV, mL | 90.1 ± 23.8 | 91.5 ± 23.9 | 76.6 ± 18.2 | 0.001 |
| LVEF, % | 59.2 ± 13.1 | 60.7 ± 11.7 | 44.7 ± 16.5 | <0.001 |
| LVMWT, mm | 11.1 ± 2.5 | 11.0 ± 2.3 | 11.6 ± 3.6 | 0.27 |
| RVEDV, mL | 166.5 ± 48.6 | 165.1 ± 48.4 | 180.0 ± 49.4 | 0.119 |
| RVESV, mL | 77.3 ± 37.3 | 74.8 ± 36.0 | 100.9 ± 41.5 | <0.001 |
| RVSV, mL | 89.2 ± 24.3 | 90.2 ± 24.4 | 78.6 ± 21.0 | 0.013 |
| RVEF, % | 55.0 ± 10.6 | 56.0 ± 10.1 | 45.6 ± 11.1 | <0.001 |
| LVEF category, % | | | | <0.001 |
| >50 | 260 (80.2) | 247 (84.0) | 13 (43.3) | |
| 36-50 | 43.0 (13.3) | 36 (12.2) | 7 (23.3) | |
| ≤35 | 21.0 (6.5) | 11 (3.7) | 10 (33.3) | |
| LGE extent | | | | |
| LGE extent, % | 6.6 (2.7-13.7) | 6.2 (2.3-11.7) | 16.8 (7.9-38.6) | <0.001 |
| LGE mass, g | 6.3 (2.7-12.6) | 5.9 (2.4-11.1) | 15.0 (10.2-30.1) | <0.001 |
| Number of LGE segments | 3.5 ± 3.8 | 3.2 ± 3.7 | 6.7 ± 3.8 | <0.001 |
| LGE pattern | | | | 0.003 |
| Mid-wall | 147 (45.4) | 137 (46.6) | 10 (33.3) | |
| Subepicardial | 29 (9.0) | 28 (9.5) | 1 (3.3) | |
| Subendocardial | 6 (1.9) | 5 (1.7) | 1 (3.3) | |
| Transmural | 48 (14.8) | 38 (12.9) | 10 (33.3) | |
| Mixed pattern | 44 (13.6) | 36 (12.2) | 8 (26.7) | |
| Insertion point fibrosis only | 22 (6.8) | 22 (7.5) | 0 (0.0) | |
| No LGE | 28 (8.6) | 28 (9.5) | 0 (0.0) | |
| LGE location | | | | |
| Anterior | 68 (21.0) | 53 (18.0) | 15 (50.0) | <0.001 |
| Septal | 167 (51.5) | 143 (48.6) | 24 (80.0) | 0.002 |
| Inferior | 112 (34.6) | 96 (32.7) | 16 (53.3) | 0.039 |
| Lateral | 184 (56.8) | 164 (55.8) | 20 (66.7) | 0.341 |
| Multifocal | 59 (18.2) | 46 (15.6) | 13 (43.3) | <0.001 |
| RV free wall | 36 (11.1) | 25 (8.5) | 11 (36.7) | <0.001 |
| RV side of the septum | 41 (12.7) | 28 (9.5) | 13 (43.3) | <0.001 |

Values are mean ± SD, n (%), or median (Q1-Q3), unless otherwise indicated. [a]27 patients (8.3%) had a cardiac implantable electronic device at the time of CMR.

LGE = late gadolinium enhancement; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; LVMWT = left ventricular maximum wall thickness; RV = right ventricular; RVEDV = right ventricular end-diastolic volume; RVEF = right ventricular ejection fraction; RVESV = right ventricular end-systolic volume; other abbreviations as in Table 1.

endpoint; and among them, 7 reached both the primary endpoint and 1 of the secondary endpoints. Survival curves for the study endpoints are shown in Figure 2.

**LGE EXTENT AND PREDICTION OF MAJOR ADVERSE CARDIAC EVENTS IN PATIENTS WITH BIOPSY-PROVEN SARCOIDOSIS.** There were no differences in patient demographics (age, sex) or prevalence of traditional risk factors (arterial hypertension, diabetes mellitus, dyslipidemia, or smoking history) among subgroups of patients based on the presence or absence of primary endpoint. In the whole study population, LGE extent (as % of LV mass) was significantly higher among patients who reached the primary endpoint during follow-up (16.8% [Q1-Q3: 7.9%-38.6%] vs 6.2% [Q1-Q3: 2.3%-11.7%]; $P < 0.001$) (Table 2). In univariate cox regression analysis, LGE extent was significantly associated with the primary endpoint (ie, the composite of sustained VT, VF, and appropriate ICD therapy; $P < 0.001$) and with the secondary endpoints of heart failure and heart transplant ($P = 0.014$), but not with all-cause mortality ($P$ = NS). After adjustment for age, sex, and presence of LV systolic dysfunction (ie, LVEF <50%), LGE extent was still significantly associated with the arrhythmia endpoint ($P = 0.047$) but not with any of the other study endpoints (Table 3). ROC analysis showed that the optimum cutoff of LGE extent for the prediction of the arrhythmic endpoint in the whole cohort was 7.4%, providing a sensitivity of 83% and specificity of 70%

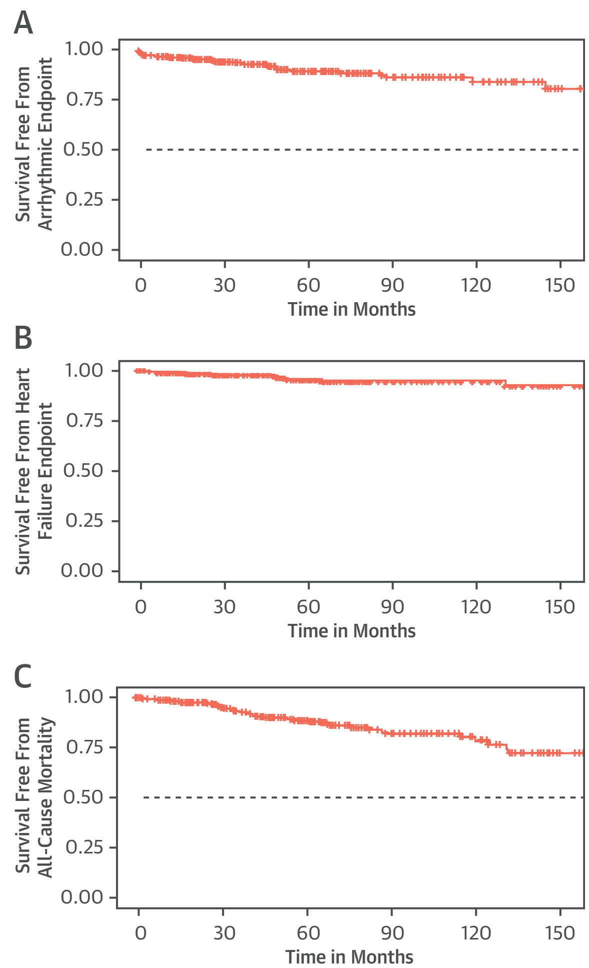
(AUC: 0.795) (Supplemental Figure 1). In leave-one-out cross-validation, we obtained an average C-index of 0.792 across all iterations.

**PREDICTORS OF VENTRICULAR ARRHYTHMIC EVENTS IN PATIENTS WITH BIOPSY-PROVEN SARCOIDOSIS.** In our cohort, 260 patients (80.2%) had LVEFs >50% in their index CMR scan, 43 (13.3%) showed LVEFs from 36% to 50%, and the remaining 21 subjects (6.5%) had LVEFs ≤35%. The subgroup of patients with LVEF ≤35% was significantly more likely to develop a ventricular arrhythmic event during follow-up (HR: 5.24 [95% CI: 2.16-12.7]; $P < 0.001$), although most arrhythmic events occurred in patients with LVEF >35% (n = 20 out of 30 arrhythmic events). Survival curves per LVEF subgroups are shown in Figure 3A.

Next to LVEF, high LGE extent (≥7.4% of LV mass) was significantly associated with the primary endpoint during follow-up (HR: 6.24 [95% CI: 2.38-16.40]; $P < 0.001$) in the whole cohort. Survival curves are shown in Figure 3B. LGE on the right side of the interventricular septum, LGE in the RV free wall, multifocal LGE in the LV, and transmural LGE were all more frequent among patients who reached the arrhythmia endpoint (Table 2) and all associated with multifold increased risk for the arrhythmic endpoint, even in subgroup analyses for primary prevention of SCD (ie, after excluding from the whole cohort those patients who experienced sustained VT, VF, or aborted SCD at presentation) (Table 4). Among patients with LVEF >35% and those with LVEF >50%, LGE extent ≥7.4%, LGE on the right side of the septum, and multifocal LGE were still predictive of arrhythmia events (Table 4). Kaplan-Meier survival curves for the whole cohort for the presence and absence of each of these LGE locations and patterns are shown in Figures 3C to 3F. The same analyses in the subgroup of patients without sustained VT, VF, or aborted SCD at presentation are shown in Supplemental Figures 2 and 3. Illustrations of different types of LGE involvement within study participants are shown in Figure 4.

**PROPOSED ALGORITHM FOR ARRHYTHMIC RISK STRATIFICATION IN PATIENTS WITH BIOPSY-PROVEN SARCOIDOSIS BASED ON LVEF, LGE EXTENT, AND HIGH-RISK LGE FEATURES.** Based on our observations, we defined high-risk LGE as the presence of at least 1 high-risk LGE feature, defined as LGE on the right side of the septum, LGE in the RV free wall, or multifocal LGE in the LV. Among the 324 study patients, we identified 4 risk group categories based on LVEF, LGE extent, and the presence of high-risk LGE features (Central Illustration A). Patients at very high risk of developing life-threatening ventricular arrhythmias were all those with LVEF ≤35% and LGE extent ≥7.4%. The high risk category included patients with LVEF ≤35% and LGE extent <7.4% with high-risk LGE features, and patients with LVEF 36%-50% and high-risk LGE features, independently from LGE extent. In the intermediate risk category were subjects with either LVEF ≤35% or LVEF 36%-50% and LGE <7.4% in the absence of high-risk LGE, and those with LVEF >50% and LGE ≥7.4%, or LGE <7.4% and high-risk LGE. Finally, the low risk category included only patients with LVEF >50% and LGE <7.4% in the absence of high-risk LGE. Based on this risk classification system, a total of 16 patients

**FIGURE 2 Kaplan-Meier Curves for Study Endpoints**




Kaplan-Meier curves for the arrhythmic endpoint (sustained ventricular tachycardia, ventricular fibrillation, appropriate implantable cardioverter-defibrillator therapy) (A), heart failure endpoint (hospitalization for heart failure, heart transplantation) (B), and all-cause mortality, in the whole cohort of patients with biopsy-proven sarcoidosis (C).

**TABLE 3 Cox Proportional Hazard Regression Analyses for the Study Endpoints**

| | Unadjusted | | Model 1 | | Model 2 | |
|---|---|---|---|---|---|---|
| | HR (95% CI) | *P* Value | HR (95% CI) | *P* Value | HR (95% CI) | *P* Value |
| Arrhythmic endpoint | | | | | | |
| LGE mass, g, per SD | 1.03 (1.01-1.04) | <0.001 | 1.03 (1.01-1.04) | <0.001 | 1.01 (1.00-1.03) | 0.140 |
| LGE extent, %, per SD | 1.06 (1.03-1.08) | <0.001 | 1.06 (1.03-1.08) | <0.001 | 1.03 (1.00-1.06) | 0.047 |
| Number of segments with LGE | 1.17 (1.09-1.26) | <0.001 | 1.18 (1.10-1.28) | <0.001 | 1.09 (0.99-1.20) | 0.068 |
| Hospitalization for heart failure or heart transplantation | | | | | | |
| LGE mass, g, per SD | 1.02 (1.00-1.03) | 0.046 | 1.02 (1.00-1.03) | 0.042 | 1.00 (0.98-1.03) | 0.700 |
| LGE extent, %, per SD | 1.04 (1.01-1.07) | 0.014 | 1.04 (1.01-1.07) | 0.011 | 1.02 (0.98-1.09) | 0.300 |
| Number of segments with LGE | 1.16 (1.06-1.28) | 0.002 | 1.16 (1.05-1.28) | 0.002 | 1.11 (0.98-1.25) | 0.110 |
| All-cause mortality | | | | | | |
| LGE mass, g, per SD | 1.00 (0.99-1.02) | 0.800 | 1.02 (1.00-1.03) | >0.900 | 1.00 (0.97-1.02) | 0.700 |
| LGE extent, %, per SD | 0.99 (0.97-1.03) | >0.900 | 0.99 (0.97-1.02) | >0.900 | 0.99 (0.95-1.03) | 0.500 |
| Number of segments with LGE | 1.01 (0.93-1.09) | 0.800 | 0.99 (0.91-1.07) | >0.900 | 0.97 (0.87-1.07) | 0.500 |

Model 1: after adjustment for age and sex. Model 2: after adjustment for age, sex, and presence of left ventricular impairment (ie, LVEF <50%). Abbreviations as in Tables 1 and 2.

(5%) were in the very high risk, 39 (12%) in the high risk, 122 (38%) in the intermediate risk, and 147 (45%) in the low risk category of developing a life-threatening ventricular arrhythmia during follow-up. The respective survival curves of the risk subgroups are shown in Central Illustration B. The event rate was 44% (10.8% per year) in the very high risk group, 23% (or 5.6% per year) among high risk patients, and 11% (or 2.7% per year) in the intermediate risk group. Only 1% (0.2% per year) of patients in the low risk category reached the arrhythmic endpoint during the follow-up period (Central Illustration C).

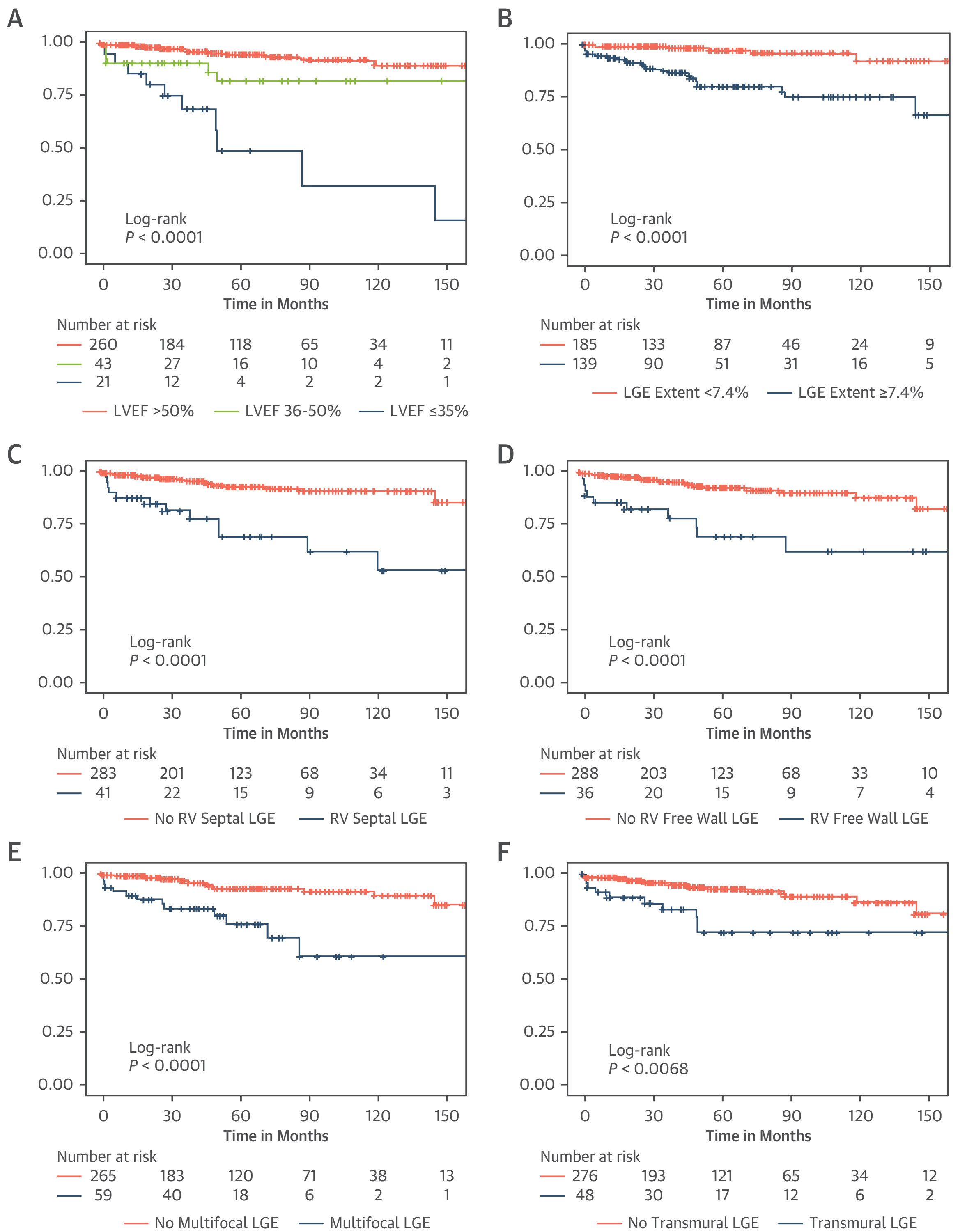
**COMPARISON OF PROPOSED ALGORITHM FOR ARRHYTHMIC RISK STRATIFICATION WITH HRS RECOMMENDATIONS.** This risk stratification approach based on LVEF, LGE extent, and presence of high-risk LGE features was compared with the HRS recommendations for ICD placement for primary prevention of SCD in CS.[7] Among the overall cohort of 324 patients, 27 presented with ventricular arrhythmias (23 with sustained VT and 4 with VF) and received an ICD for secondary prevention of SCD. In the subgroup of patients who were assessed for ICD placement for primary prevention of SCD (n = 297), compared with the HRS criteria, the proposed risk stratification algorithm based on LVEF and LGE features significantly enhanced the model's prognostic performance (chi-square = 8.02; $P$ = 0.046), risk discrimination (ΔAUC = 0.082; $P$ = 0.019), and reclassification for the primary endpoint (Table 5). More specifically, a significant proportion of HRS Class IIa patients (43%) were reclassified to a lower risk category, and a smaller proportion to a higher risk category (11%).

## DISCUSSION

This study investigated the prognostic significance of comprehensively acquired CMR features including LGE extent, pattern, and location in a large cohort of patients suspected of cardiac involvement in the presence of biopsy-proven sarcoidosis. The burden of LGE was associated with the risk of life-threatening ventricular arrhythmic events, but not heart failure or all-cause mortality. High LGE extent (ie, ≥7.4% of LV mass) as well as specific high-risk LGE features (ie, LGE on the right side of the septum, LGE in the RV free wall, or multifocal LGE) are markers of increased arrhythmic risk even in patients with preserved LVEF and can be used to improve risk stratification in CS. Conversely, CS patients with preserved LVEF, limited LGE extent, and no high-risk LGE features may be at low risk of arrhythmic events. We propose the combination of LVEF, LGE extent as defined by % LGE mass, and high-risk LGE features to assist in the clinical decision making for ICD placement in patients with CS.

Multiple previous studies have demonstrated that in patients with CS, the presence of myocardial LGE is a strong predictor of cardiac events such as SCD, ventricular arrhythmias, ICD discharge, and hospital admission for heart failure. Hulten et al,[4] in a meta-analysis, showed that the annualized incidence of death or ventricular arrhythmias was 8.8% in LGE-positive patients vs 0.6% in LGE-negative subjects. Another meta-analysis showed that patients with known or suspected CS and positive LGE have higher odds for both all-cause mortality and arrhythmic events than those without LGE, even if the presence of normal or near normal cardiac function.[5] More

**FIGURE 3 Kaplan-Meier Curves Showing Survival Free From the Arrhythmia Endpoint**




Kaplan-Meier curves showing survival free from the arrhythmic endpoint (sustained ventricular tachycardia, ventricular fibrillation, appropriate implantable cardioverter-defibrillator therapy) for patients stratified by LVEF (A), LGE extent (B), presence of LGE on the right side of the interventricular septum (C), presence of LGE in the RV free wall (D), presence of multifocal LGE in the left ventricle (E), and presence of transmural LGE in the left ventricle (F). ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; RV = right ventricular; VF = ventricular fibrillation; VT = ventricular tachycardia; other abbreviation as in Figure 1.

JACC: CARDIOVASCULAR IMAGING, VOL. 18, NO. 7, 2025
JULY 2025:768-780

**TABLE 4 Subgroup Analyses for the Arrhythmia Endpoint by Clinical Presentation and LVEF**

| | Whole Cohort | | No VT/VF at Presentation | | LVEF >35% | | LVEF >50% | |
|---|---|---|---|---|---|---|---|---|
| | HR (95% CI) | *P* Value | HR (95% CI) | *P* Value | HR (95% CI) | *P* Value | HR (95% CI) | *P* Value |
| LGE extent ≥7.4% | 6.24 (2.38-16.40) | <0.001 | 11.60 (2.66-50.40) | 0.001 | 4.09 (1.47-11.40) | 0.007 | 3.06 (1.00-9.38) | 0.050 |
| LGE at RV side of the septum | 5.43 (2.61-11.30) | <0.001 | 8.82 (3.47-22.40) | <0.001 | 6.19 (2.48-15.4) | <0.001 | 4.81 (1.48-15.70) | 0.009 |
| LGE at RV free wall | 4.30 (1.99-9.27) | <0.001 | 7.56 (2.92-19.6) | <0.001 | 5.80 (2.28-14.80) | <0.001 | 3.93 (1.08-14.30) | 0.038 |
| Multifocal LGE | 4.62 (2.19-9.72) | <0.001 | 2.88 (1.08-7.74) | 0.035 | 2.09 (0.69-6.29) | 0.200 | 4.63 (1.46-14.70) | 0.009 |
| Transmural LGE | 2.87 (1.33-6.21) | 0.007 | 4.28 (1.66-11.10) | 0.003 | 4.99 (2.00-12.50) | <0.001 | – | – |

Abbreviations as in Tables 1 and 2.

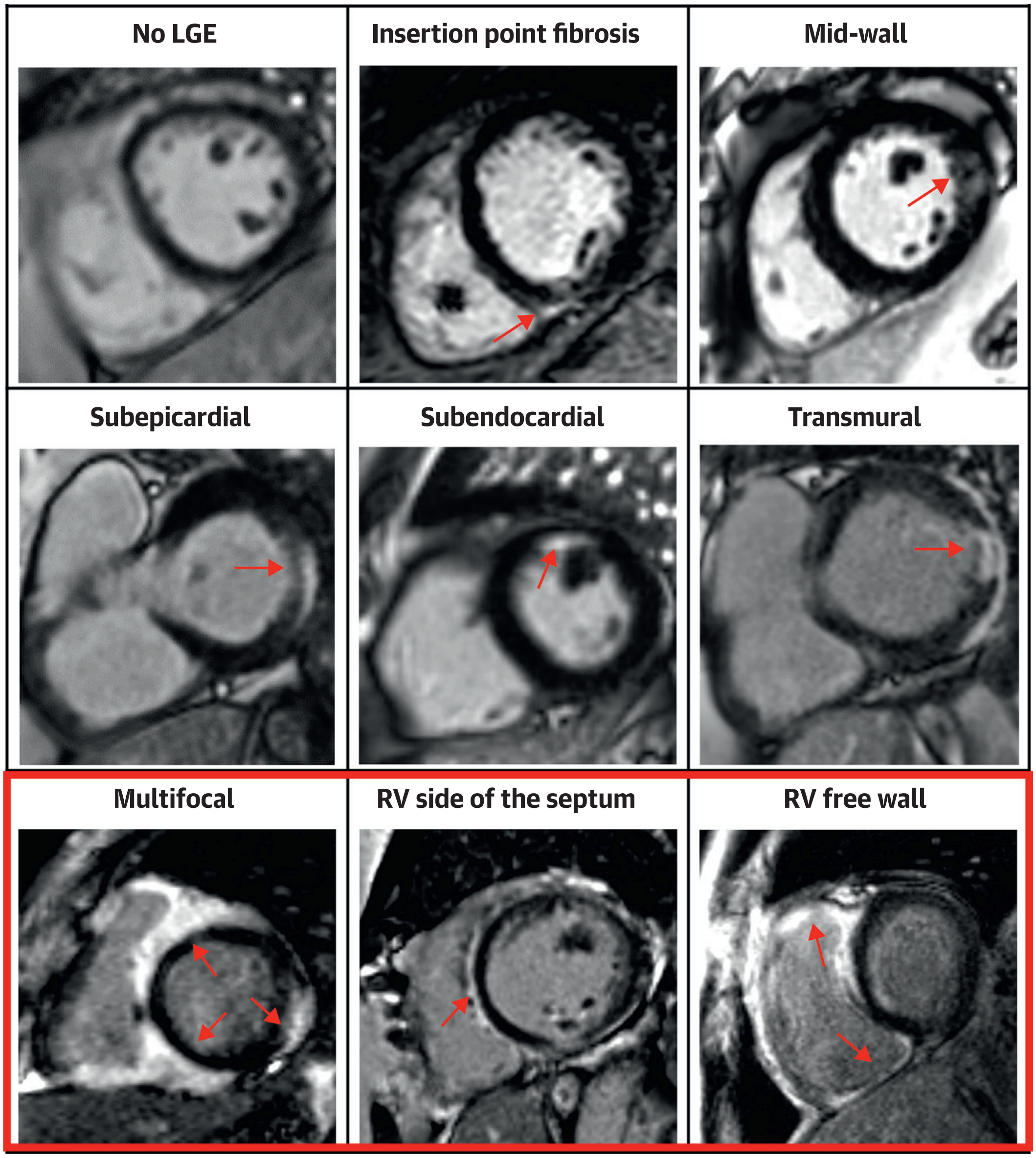
recently, a large meta-analysis demonstrated a 20-fold risk of ventricular arrhythmias in patients with LGE compared with those without and a markedly elevated risk in those with biventricular LGE.[6]

A number of studies have assessed the prognostic value of LGE burden to identify an optimal cutoff that could predict adverse cardiac events with the use of different combinations of composite endpoints that included ventricular arrhythmias, hospitalization for heart failure, all-cause death, nonsustained VT, and atrioventricular block.[10,12,14-20] Only a few studies have focused on finding the LGE threshold that could predict life-threatening arrhythmic events in CS. Detecting a critical cutoff of LGE extent is thought to be crucial for identifying those patients who might benefit from an ICD for primary prevention of SCD. Kazmirczak et al,[10] in a cohort of 290 patients with known or suspected CS with biopsy-proven extracardiac sarcoidosis and LGE present in 30% of the cohort, identified an LGE cutoff of 5.7% to be predictive of SCD and arrhythmic events in patients with LVEF >35% and Class IIa recommendations for ICD placement. Similarly, Crawford et al[11] found that 6% was the optimal LGE cutoff to predict VT/VF among their 51 patients with LVEF >35%. A large Finnish study, which included 201 CS patients with LV LGE, also used an LGE mass >6% as the best risk discriminator for life-threatening arrhythmias.[12] In our cohort, including 324 patients with biopsy-proven sarcoidosis, 296 of which with myocardial LGE, a cutoff of 7.4% of LGE extent provided the best balance between sensitivity and specificity. However, we observed that beyond LVEF and LGE presence or extent, LGE location and pattern were additional prognostic markers for malignant arrhythmias.

Okasha et al,[21] in a systematic review and meta-analysis of gross pathology images from 49 CS patients who underwent autopsy or heart transplantation, observed that in >90% of cases myocardial involvement was subepicardial, multifocal, septal, or in the RV free wall. Athwal et al[22] reported a higher risk of ventricular arrhythmias and heart failure, independent from LVEF and LGE extent, in patients with "pathology-frequent LGE," defined as the presence of LGE in at least 1 of the locations or patterns defined by Okasha et al.[21] Crawford et al[11] reported positive predictive values for death or VT/VF of 100% for RV LGE and 48% for multifocal LGE. In a recent study from our group, patients with CS who presented with cardiac arrest or life-threatening arrhythmias were more likely to have LGE on the right side of the septum or in the basal anteroseptum.[23] In the present cohort, 43% of patients who developed an arrhythmic event during follow-up had LGE on the right side of the septum on the baseline CMR, and 37% showed LGE in the RV free wall. LGE on the right side of the septum was associated with a 6-fold increased risk of developing a life-threatening arrhythmia in all patients with LVEF >35% and almost 5 times higher risk in patients with LVEF >50%.

Our observations are important because, to our knowledge, this study included the largest number of patients with biopsy-proven sarcoidosis and myocardial LGE. In addition, compared with previously published studies,[12,22] our cohort did not include patients with concomitant significant coronary artery disease or significant valvular heart disease, which has the potential to confound survival analysis. We consolidate the need to move beyond LVEF for arrhythmic risk stratification, because most events occurred in patients with LVEF >35%. In addition, we demonstrate that LGE presence is not invariably associated with high arrhythmic risk in CS, and we provide a definition for high-risk LGE, that could be incorporated in clinical management guidelines for refined arrhythmic risk stratification in CS. Comparing our proposed risk algorithm with the HRS recommendations for ICD implantation in CS, we demonstrate that a large proportion (43%) of patients meeting Class IIa recommendations would be reclassified to a low-risk group based on their LVEF, LGE

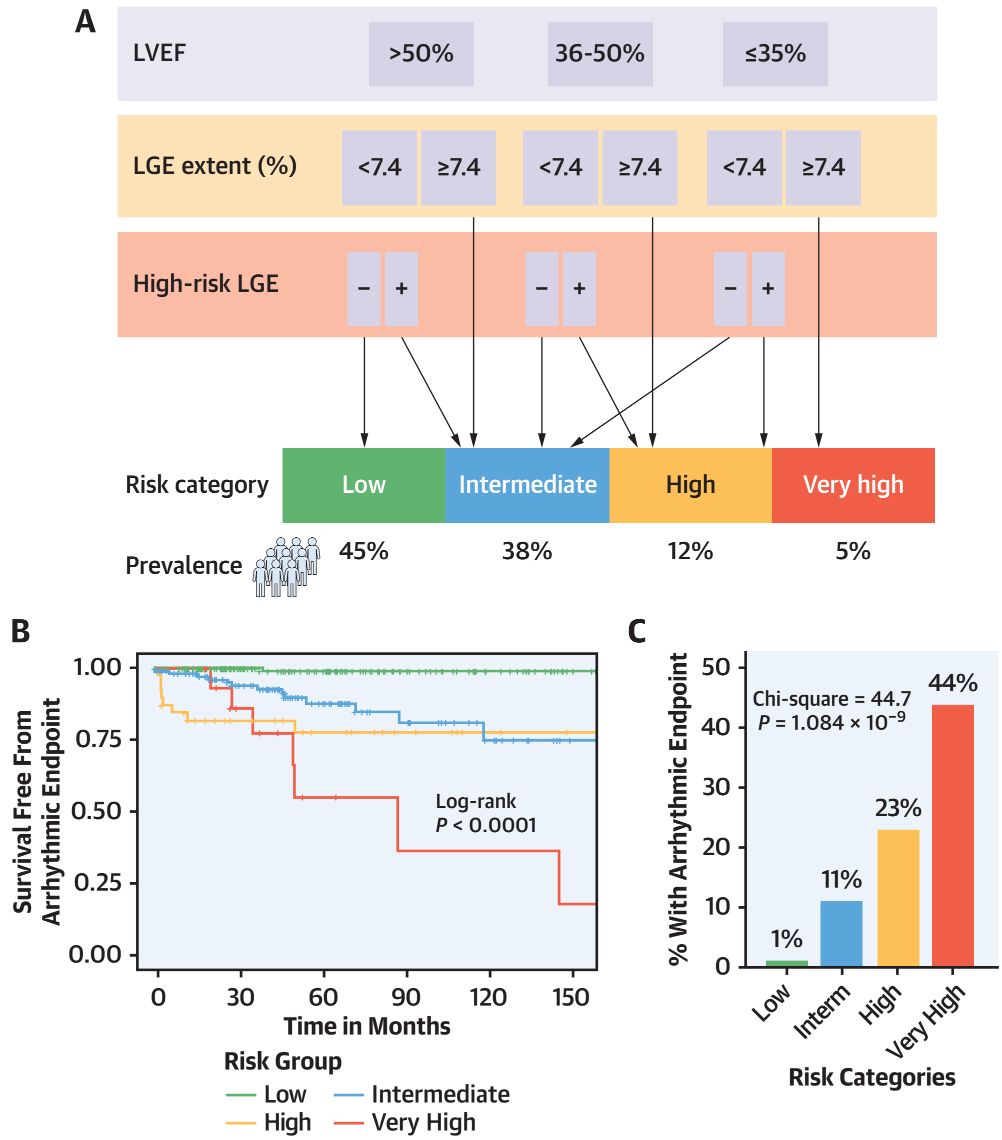
**FIGURE 4** LGE Features in Patients With Biopsy-Proven Cardiac Sarcoidosis




Examples of different LGE features in patients with biopsy-proven sarcoidosis. Bottom panels highlighted in red show the "high-risk" LGE features. Red arrows indicate areas of LGE. Abbreviations as in Figures 1 and 3.

extent, and LGE features (event rate 0.2% per year). Even within patients meeting Class I recommendations, our algorithm identified some (11%) at lower risk. Conversely, 11% of HRS Class IIa patients would be considered as having a high risk of developing ventricular arrhythmias and should be prioritized for ICD placement. Patients with CS with LVEF >50%, limited LGE extent and no high-risk LGE features have an overall low risk of developing life-threatening ventricular arrhythmias, and despite HRS recommendations,[7] ICD implantation could be withheld in these patients. An electrophysiologic study should be considered for further risk stratification according to current guidelines,[7,8] as well as regular clinical and imaging monitoring during surveillance. Based on our findings, those with

**CENTRAL ILLUSTRATION** **Proposed Algorithm for Arrhythmic Risk Stratification in Patients With Biopsy-Proven Sarcoidosis[a]**




Azzu A, et al. JACC Cardiovasc Imaging. 2025;18(7):768-780.

(A) Proposed algorithm for arrhythmia risk stratification in patients with biopsy-proven sarcoidosis based on LVEF, LGE extent (%), and high-risk LGE features (ie, LGE on the right side of the septum, LGE in the right ventricular free wall, and left ventricular multifocal LGE). (B) Survival curves based on the proposed algorithm. (C) Observed event rate based on the proposed risk group categories. [a]In the absence of significant coronary artery disease (ie, previous percutaneous coronary intervention, coronary artery bypass graft, or known obstructive coronary artery disease), significant valvular artery disease (ie, severe valvular stenosis or regurgitation or previous valve replacement or repair) or alternative diagnosis of cardiomyopathy. Interm = intermediate; LGE = late gadolinium enhancement; LVEF = left ventricular ejection fraction.

LVEF ≤50% in the presence of high-risk LGE features have a high arrhythmic risk independently from LGE extent and should be considered for ICD placement for primary prevention of SCD. If results are confirmed in prospective multicenter validation studies, such an algorithm may be incorporated in international guidelines focusing on risk stratification of CS patients against SCD.

**TABLE 5 Comparison of the Added Prognostic Value of a Model Based on LVEF, LGE Extent, and High-Risk LGE Features vs HRS Classes for Arrhythmic Risk Stratification and Decision for ICD Placement for Primary Prevention of Sudden Cardiac Death**

| HRS Class | Risk Group Category | | | | Total | Risk Reclassification | |
|---|---|---|---|---|---|---|---|
| | Low | Intermediate | High | Very High | | Risk Up | Risk Down |
| No ICD indication[a] | 48 (0) | 2 (0) | – | – | 50 (0) | – | – |
| Class IIa | 98 (1) | 105 (6) | 26 (2) | – | 229 (9) | 26 (11%) | 98 (43%) |
| Class I | – | 1 (0) | 2 (2) | 15 (7) | 18 (9) | – | 2 (11%) |
| Total | 146 (1) | 108 (6) | 28 (4) | 15 (7) | 297 (18) | 26 (9%) | 100 (34%) |

Patients who presented with ventricular arrhythmias and received an ICD for secondary prevention of sudden cardiac death (n = 27) were excluded from the whole cohort. Numbers in parentheses not designated as % represent the numbers of ventricular arrhythmic events. [a]Patients with no LGE (n = 28) or insertion point fibrosis only (n = 22).
HRS = Heart Rhythm Society; other abbreviations as in Tables 1 and 2.

**STUDY LIMITATIONS.** This was a retrospective observational study performed in a single tertiary center and as such is subject to selection and referral bias. The cohort is predominantly Caucasian, with a smaller percentage of Asian and Black patients. Although patients with poor-quality CMR studies were appropriately excluded from this study, the accuracy of LGE extent quantification might have been affected in patients who had a cardiac implantable electronic device at the time of CMR. The effect of immunosuppressive, antiarrhythmic, or heart failure medications on clinical outcomes was beyond the scope of this study. Finally, cardiovascular mortality was not assessed independently as the cause of death was not available for most patients. Given the relatively small number of arrhythmic events, external validation of the findings in other cohorts is desirable.

## CONCLUSIONS

We present data from one of the largest available cohorts of patients with biopsy-proven sarcoidosis and myocardial LGE. We propose an algorithm for arrhythmic risk stratification based on LVEF, LGE extent, and the presence of high-risk LGE features. Patients with biopsy-proven sarcoidosis who show LVEF >50% and LGE extent <7.4% in the absence of high-risk LGE features have a low risk of developing life-threatening ventricular arrhythmias. All patients with LVEF ≤50% and high-risk LGE features have a high arrhythmic risk independently from LGE extent and should be considered for ICD placement for primary prevention of SCD.

## FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Wells has received consulting or speaker fees from Boehringer Ingelheim, Roche, Veracyte, Chiesi, and CSL Behring. Dr Pennell has received research support from Siemens. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

**ADDRESS FOR CORRESPONDENCE:** Dr Alessia Azzu, National Heart and Lung Institute, Imperial College London, Royal Brompton and Harefield Hospitals, Guy's and St Thomas' NHS Foundation Trust, Sydney Street, SW3 6NP Chelsea, London, United Kingdom. E-mail: a.azzu@rbht.nhs.uk.

### PERSPECTIVES

**COMPETENCY IN MEDICAL KNOWLEDGE:** This study proposes a novel risk stratification approach based on LVEF and LGE features for identifying elevated risk of developing life-threatening ventricular arrhythmias in patients with biopsy-proven sarcoidosis.

**TRANSLATIONAL OUTLOOK:** Large multicenter studies are required to confirm the need of an ICD for primary prevention of SCD in patients with biopsy-proven sarcoidosis who show high-risk features of myocardial LGE.

## REFERENCES

**1.** Kouranos V, Khattar RS, Okafor J, et al. Predictors of outcome in a contemporary cardiac sarcoidosis population: role of brain natriuretic peptide, left ventricular function and myocardial inflammation. *Eur J Heart Fail*. 2023.

**2.** Uemura A, Morimoto S, Hiramitsu S, Kato Y, Ito T, Hishida H. Histologic diagnostic rate of cardiac sarcoidosis: evaluation of endomyocardial biopsies. *Am Heart J*. 1999;138(2 Pt 1):299–302.

**3.** Kouranos V, Tzelepis GE, Rapti A, et al. Complementary role of CMR to conventional screening in the diagnosis and prognosis of cardiac sarcoidosis. *JACC Cardiovasc Imaging*. 2017;10(12):1437–1447.

**4.** Hulten E, Agarwal V, Cahill M, et al. Presence of late gadolinium enhancement by cardiac magnetic resonance among patients with suspected cardiac sarcoidosis is associated with adverse cardiovascular prognosis: a systematic review and meta-analysis. *Circ Cardiovasc Imaging*. 2016;9(9):e005001.

**5.** Coleman GC, Shaw PW, Balfour PC Jr, et al. Prognostic value of myocardial scarring on CMR in patients with cardiac sarcoidosis. *JACC Cardiovasc Imaging*. 2017;10(4):411–420.

**6.** Stevenson A, Bray JJH, Tregidgo L, et al. Prognostic value of late gadolinium enhancement detected on cardiac magnetic resonance in cardiac sarcoidosis. *JACC Cardiovasc Imaging*. 2023;16(3):345–357.

**7.** Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2018;72(14):1677–1749.

**8.** Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur Heart J*. 2022;43(40):3997–4126.

**9.** Birnie DH, Sauer WH, Bogun F, et al. HRS expert consensus statement on the diagnosis and management of arrhythmias associated with cardiac sarcoidosis. *Heart Rhythm*. 2014;11(7):1305–1323.

**10.** Kazmirczak F, Chen KA, Adabag S, et al. Assessment of the 2017 AHA/ACC/HRS guideline recommendations for implantable cardioverter-defibrillator implantation in cardiac sarcoidosis. *Circ Arrhythm Electrophysiol*. 2019;12(9):e007488.

**11.** Crawford T, Mueller G, Sarsam S, et al. Magnetic resonance imaging for identifying patients with cardiac sarcoidosis and preserved or mildly reduced left ventricular function at risk of ventricular arrhythmias. *Circ Arrhythm Electrophysiol*. 2014;7(6):1109–1115.

**12.** Nordenswan HK, Poyhonen P, Lehtonen J, et al. Incidence of sudden cardiac death and life-threatening arrhythmias in clinically manifest cardiac sarcoidosis with and without current indications for an implantable cardioverter defibrillator. *Circulation*. 2022;146(13):964–975.

**13.** Cerqueira MD, Weissman NJ, Dilsizian V, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. *Circulation*. 2002;105(4):539–542.

**14.** Ise T, Hasegawa T, Morita Y, et al. Extensive late gadolinium enhancement on cardiovascular magnetic resonance predicts adverse outcomes and lack of improvement in LV function after steroid therapy in cardiac sarcoidosis. *Heart*. 2014;100(15):1165–1172.

**15.** Agoston-Coldea L, Kouaho S, Sacre K, et al. High mass (>18g) of late gadolinium enhancement on CMR imaging is associated with major cardiac events on long-term outcome in patients with biopsy-proven extracardiac sarcoidosis. *Int J Cardiol*. 2016;222:950–956.

**16.** Flamee L, Symons R, Degtiarova G, et al. Prognostic value of cardiovascular magnetic resonance in patients with biopsy-proven systemic sarcoidosis. *Eur Radiol*. 2020;30(7):3702–3710.

**17.** Murtagh G, Laffin LJ, Beshai JF, et al. Prognosis of myocardial damage in sarcoidosis patients with preserved left ventricular ejection fraction: risk stratification using cardiovascular magnetic resonance. *Circ Cardiovasc Imaging*. 2016;9(1):e003738.

**18.** Smedema JP, van Geuns RJ, Ector J, Heidbuchel H, Ainslie G, Crijns H. Right ventricular involvement and the extent of left ventricular enhancement with magnetic resonance predict adverse outcome in pulmonary sarcoidosis. *ESC Heart Fail*. 2018;5(1):157–171.

**19.** Ekstrom K, Lehtonen J, Hanninen H, Kandolin R, Kivisto S, Kupari M. Magnetic resonance imaging as a predictor of survival free of life-threatening arrhythmias and transplantation in cardiac sarcoidosis. *J Am Heart Assoc*. 2016;5(5):e003040.

**20.** Yasuda M, Iwanaga Y, Kato T, et al. Risk stratification for major adverse cardiac events and ventricular tachyarrhythmias by cardiac MRI in patients with cardiac sarcoidosis. *Open Heart*. 2016;3(2):e000437.

**21.** Okasha O, Kazmirczak F, Chen KA, Farzaneh-Far A, Shenoy C. Myocardial involvement in patients with histologically diagnosed cardiac sarcoidosis: a systematic review and meta-analysis of gross pathological images from autopsy or cardiac transplantation cases. *J Am Heart Assoc*. 2019;8(10):e011253.

**22.** Athwal PSS, Chhikara S, Ismail MF, et al. Cardiovascular magnetic resonance imaging phenotypes and long-term outcomes in patients with suspected cardiac sarcoidosis. *JAMA Cardiol*. 2022;7(10):1057–1066.

**23.** Hatipoglu S, Gardezi SKM, Azzu A, et al. Diagnosis of cardiac sarcoidosis in patients presenting with cardiac arrest or life-threatening arrhythmias. *Heart*. 2023;109(10):748–755.

**KEY WORDS** biopsy-proven sarcoidosis, cardiac sarcoidosis, cardiac magnetic resonance, myocardial fibrosis

**APPENDIX** For supplemental figures, please see the online version of this paper.