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Late Gadolinium Enhancement Among Survivors of Sudden Cardiac Arrest

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ABSTRACT

OBJECTIVES The aim of this study was to describe the role of contrast-enhanced cardiac magnetic resonance (CMR) in the workup of patients with aborted sudden cardiac arrest (SCA) and in the prediction of long-term outcomes.

BACKGROUND Myocardial fibrosis is a key substrate for SCA, and late gadolinium enhancement (LGE) on a CMR study is a robust technique for imaging of myocardial fibrosis.

METHODS We performed a retrospective review of all survivors of SCA who were referred for CMR studies and performed follow-up for the subsequent occurrence of an adverse event (death and appropriate defibrillator therapy).

RESULTS After a workup that included a clinical history, electrocardiogram, echocardiography, and coronary angiogram, 137 patients underwent CMR for workup of aborted SCA (66% male; mean age 56 ± 11 years; left ventricular ejection fraction 43 ± 12%). The presenting arrhythmias were ventricular fibrillation (n = 105 [77%]) and ventricular tachycardia (n = 32 [23%]). Overall, LGE was found in 98 patients (71%), with an average extent of 9.9 ± 5% of the left ventricular myocardium. CMR imaging provided a diagnosis or an arrhythmic substrate in 104 patients (76%), including the presence of an infarct-pattern LGE in 60 patients (44%), noninfarct LGE in 21 (15%), active myocarditis in 14 (10%), hypertrophic cardiomyopathy in 3 (2%), sarcoidosis in 3, and arrhythmogenic cardiomyopathy in 3. In a median follow-up of 29 months (range 18 to 43 months), there were 63 events. In a multivariable analysis, the strongest predictors of recurrent events were the presence of LGE (adjusted hazard ratio: 6.7; 95% CI: 2.38 to 18.85; $p < 0.001$) and the extent of LGE (hazard ratio: 1.15; 95% CI: 1.11 to 1.19; $p < 0.001$).

CONCLUSIONS Among patients with SCA, CMR with contrast identified LGE in 71% and provided a potential arrhythmic substrate in 76%. In follow-up, both the presence and extent of LGE identified a group at markedly increased risk of future adverse events. (J Am Coll Cardiol Img 2015;8:414–23) © 2015 by the American College of Cardiology Foundation.

Among survivors of sudden cardiac arrest (SCA), the recommended workup includes the routine performance of an echocardiogram and coronary angiography (1–3). However, after clinical review, electrocardiogram (ECG), echocardiography, and coronary angiography, the cause of the arrest is unclear in up to 50% of patients (4). Ventricular fibrillation (VF) and ventricular tachycardia (VT)

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are the 2 most common arrhythmias detected among survivors of SCA (5-7). Myocardial scar is a key substrate for the generation and maintenance of malignant ventricular arrhythmias (8-10). Tissue

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characterization and the identification of myocardial scar using late gadolinium enhancement (LGE) are key strengths of cardiac magnetic resonance (CMR) (11,12). There are limited data testing the role of CMR in the workup of survivors of SCA (4). Therefore, our first goal was to add to this limited data set and test the role of the unique tissue characterization provided by CMR in the workup of survivors of SCA. Furthermore, myocardial scar by LGE has been shown to identify the origin of ventricular arrhythmias (10,13), and LGE has been shown to be a key predictor of subsequent adverse events in patients with implantable cardioverter-defibrillators (ICDs) placed for primary prevention of sudden cardiac death (14-16). Survivors of SCA are at significantly increased risk of subsequent adverse cardiac events, with a mortality rate approaching 10% per year despite ICD insertion (5,6,17). However, there are no data testing the role of the presence and extent of LGE for prediction of subsequent adverse events among survivors of SCA. Therefore, in a second aim, we wanted to test the role of the presence and extent of LGE for the prediction of subsequent adverse events among survivors of SCA. Our hypothesis was that a CMR study through detection of LGE would identify a potential arrhythmic substrate among survivors of SCA and that the presence and extent of LGE would be a discriminator of subsequent adverse events after ICD insertion.

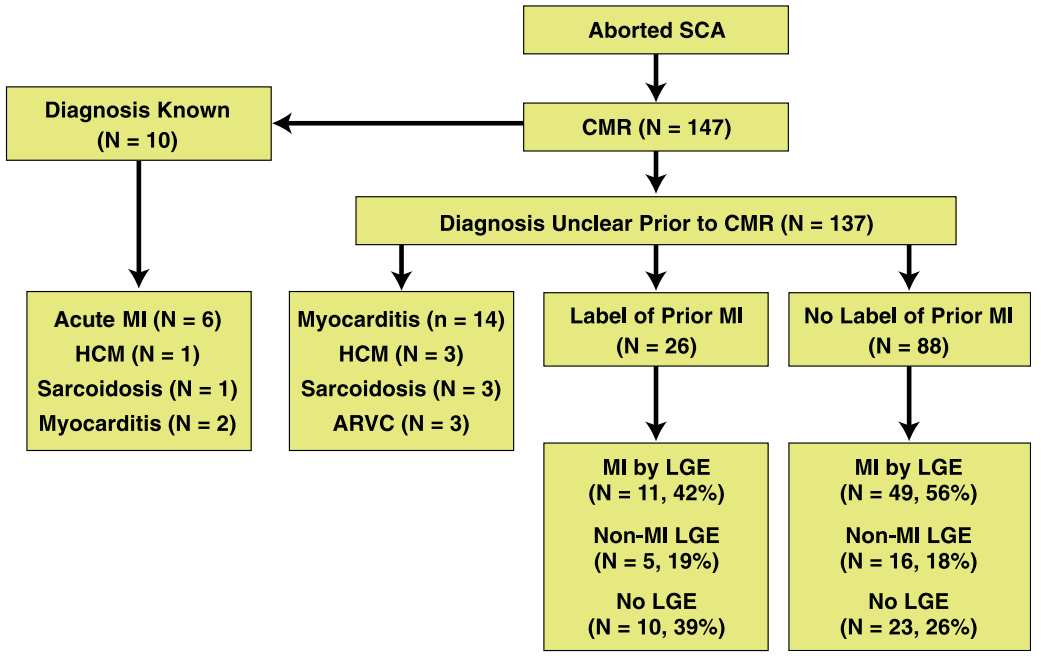
ABBREVIATIONS AND ACRONYMS

ATP = antitachycardia pacing
CMR = cardiac magnetic resonance
ECG = electrocardiogram
ICD = implantable cardioverter-defibrillator
LGE = late gadolinium enhancement
LVEF = left ventricular ejection fraction
MACE = major adverse cardiac events
MI = myocardial infarction
RV = right ventricle/ventricular
SCA = sudden cardiac arrest
VF = ventricular fibrillation
VT = ventricular tachycardia

METHODS

STUDY POPULATION. We conducted a combination prospective and retrospective study. We prospectively collected data on consecutive patients resuscitated from SCA who underwent a CMR study and performed a retrospective follow-up for adverse events. SCA was defined as the sudden cessation of effective cardiac mechanical activity, resulting in unresponsiveness without normal breathing or signs of circulation (18). Studies were performed between 2005 and 2011 at the Brigham and Women's Hospital and Massachusetts General Hospital. The CMR study was requested after a workup that included clinical

FIGURE 1 Groups Separated According to Final Diagnosis



A flow diagram of all 147 patients categorized into each of the major diagnostic groups. CMR = cardiac magnetic resonance; HCM = hypertrophic cardiomyopathy; LGE = late gadolinium enhancement; MI = myocardial infarction; SCA = sudden cardiac arrest.

assessment, ECG, echocardiogram, and coronary angiogram that did not reveal a clear etiology for the SCA. We excluded patients diagnosed with acute myocardial infarction (MI) or who underwent revascularization at the time of admission. A prior MI was defined as either clinical evidence of an MI per electronic medical records or ECG evidence defined by Minnesota codes 1.1.1 to 1.2.8 (19). Medications were recorded at the time of discharge from the hospital. The protocol was approved by the Human Subjects Review Committee of both hospitals.

CMR PROTOCOL. All images were acquired with ECG gating, breath-holding, and the patient in a supine position, as previously described (16). Subjects were imaged on either a 1.5-T or 3.0-T CMR system (Signa CV/I HDXt platform, General Electric Healthcare, Waukesha, Wisconsin, or Tim Trio, Siemens, Erlangen, Germany, respectively). Both CMR protocols consisted of cine steady-state free precession imaging for cardiac function and LGE imaging for myocardial fibrosis (16,20–22). All images were analyzed with specialized software (Mass Research, University Medical Centre, Leiden, the Netherlands) by researchers blinded to clinical outcomes (16).

LATE GADOLINIUM ENHANCEMENT. LGE was considered present only if confirmed on both short-axis and matching long-axis myocardial locations. The presence and pattern of LGE was confirmed by 2 level 3 CMR experts blinded to all other clinical data. LGE was quantified by using regions defined as more than 50% of maximal signal intensity of the enhanced area (full width at half maximum [FWHM]) (16). The extent of LGE was not quantified at the time of the original CMR study and was quantified retrospectively by investigators blinded to all other clinical details. The distribution of LGE was characterized as subendocardial, transmural, mid-wall, epicardial, or focal/involving the right ventricular (RV) insertion points. If more than 1 pattern was present, the distribution was characterized on the basis of the predominant pattern.

METHODS OF CLINICAL FOLLOW-UP. Major adverse cardiac events (MACE) were defined as a composite of

TABLE 1 Baseline Patient Characteristics According to the Presence or Absence of LGE

	Cohort (n = 137)	LGE Negative (n = 39)	LGE Positive (n = 98)	p Value
Age, yrs	56 ± 12	56 ± 12	56 ± 13	0.88
Male	90 (66)	32 (82)	58 (59)	0.05
Diabetes	28 (20)	6 (15)	22 (22)	0.36
Hypertension	31 (23)	10 (25)	21 (21)	0.82
Atrial fibrillation	40 (29)	10 (25)	30 (31)	0.54
History of myocardial infarction	28 (20)	11 (28)	17 (17)	0.79
Ventricular fibrillation	105 (77)	36 (92)	69 (70)	0.05
Ventricular tachycardia	32 (23)	5 (13)	27 (27)	0.05
SCA to CMR, months	0.10 (0.05–0.25)	0.10 (0.05–0.25)	0.13 (0.05–0.25)	0.42
CMR to ICD, months	0.10 (0.05–0.25)	0.15 (0.05–0.25)	0.07 (0.05–0.25)	0.08
BMI, kg/m^2	29 ± 7	30 ± 5	29 ± 7	0.69
Systolic blood pressure, mm Hg	115 ± 16	114 ± 15	116 ± 17	0.36
Diastolic blood pressure, mm Hg	70 ± 10	69 ± 12	71 ± 10	0.54
Heart rate, beats/min	71 ± 13	72 ± 16	71 ± 11	0.80
Medications				
ACEI/ARB	107 (78)	29 (74)	78 (80)	0.18
Beta-blocker	128 (93)	38 (97)	90 (92)	1.00
Spironolactone	20 (15)	7 (18)	13 (13)	0.60
Diuretic	30 (22)	9 (23)	21 (21)	1.00
Antiarrhythmic	19 (14)	4 (10)	15 (15)	0.43
Warfarin	18 (13)	4 (10)	14 (14)	0.59
Aspirin	40 (29)	12 (31)	28 (28)	1.00
Statin	44 (62)	14 (36)	30 (31)	0.67
QRS duration, ms	113 ± 30	110 ± 28	118 ± 33	0.19
QTc duration, ms	448 ± 30	447 ± 31	451 ± 26	0.42
GFR, ml/min/1.73 m^2	71 ± 18	73 ± 16	71 ± 19	0.44

Values are mean ± SD, n (%), or median (interquartile range).

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BMI = body mass index; CMR = cardiac magnetic resonance; GFR = glomerular filtration rate; ICD = implantable cardioverter-defibrillator; LGE = late gadolinium enhancement; SCA = sudden cardiac arrest.

all-cause mortality and appropriate ICD intervention. An appropriate ICD intervention was defined as either antitachycardia pacing (ATP) or an ICD shock and was classified as appropriate if the intervention was a result of ventricular tachyarrhythmia according to established criteria (23). Adjudication of ICD events were performed by 2 cardiac electrophysiologists (S.B.D. and M.T.) blinded to all other clinical data. Mortality was ascertained using the Social Security Death Index and confirmed using electronic chart review and, if necessary, contact with the primary provider. Patients were followed at 3- to 6-month intervals via clinic visits or, if appropriate, transmitted ICD data. Survival analyses were performed for the composite endpoint. The duration of follow-up was determined from the CMR study date to the occurrence of an endpoint or the date of the last clinical follow-up. Patients were censored at the date of the last clinical follow-up.

STATISTICAL ANALYSIS. Continuous data are presented as mean ± SD or median (interquartile range). Categorical data are presented as number and percentages. Continuous data were compared with the use of unpaired Student *t* tests or Wilcoxon rank-sum tests when appropriate. Categorical data were compared using the Fisher exact test. The hazard ratio for the prediction of the events was calculated for MACE using Cox regression models. We used 2 Cox regression models, and each model contained risk markers associated with adverse outcomes; these included age, sex, history of diabetes, left ventricular ejection fraction (LVEF) and LV end-diastolic volume. In the first model, we included the presence of LGE; in the second, we included the extent of LGE. To find the best overall multivariable model for the composite endpoint, we used a stepwise-backward selection with a probability to remove the effect from the regression at $p > 0.05$. The proportional-hazards assumption was met in all models, and all models fit the data well. Event curves were determined according to the Kaplan-Meier method, and comparisons of cumulative event rates were performed by the log-rank test. A receiver-operating characteristic (ROC) curve was constructed to determine the optimal value with the maximum sensitivity and specificity of LGE extent to predict adverse cardiovascular events. Stata/SE 10.0 was used for the statistical analysis (version 10.0, StataCorp LP, College Station, Texas).

RESULTS

The number of patients referred for a CMR study for workup of SCA was 147 (Figure 1). From these 147 patients, there were 137 with a diagnosis that was not clear before the CMR study (Table 1). The presenting arrhythmias were VF (n = 105 [77%]) and VT (n = 32 [23%]). The average LVEF was 43 ± 12% and RVEF was 45 ± 12% (Table 2). Of the entire cohort, 96 patients (70%) had an LVEF of <50% at the time of CMR.

TABLE 2 CMR Measurements of Entire Cohort Stratified According to the Presence or Absence of LGE

	Cohort (n = 137)	LGE Negative (n = 39)	LGE Positive (n = 98)	p Value
CMR				
LVEDV, ml	189 ± 44	188 ± 41	190 ± 45	0.88
LVEDV index, ml/m^2	98 ± 25	97 ± 25	98 ± 26	0.89
LVESV, ml	111 ± 42	108 ± 42	112 ± 41	0.60
LVESV index, ml/m^2	57 ± 22	56 ± 24	58 ± 22	0.66
LVEF, %	43 ± 12	44 ± 14	42 ± 11	0.35
LV mass, g	151 ± 48	148 ± 50	157 ± 44	0.30
LV mass index, g/m^2	77 ± 26	76 ± 27	81 ± 24	0.34
RVEDV, ml	151 ± 53	151 ± 53	151 ± 53	0.96
RVEDV index, ml/m^2	77 ± 27	75 ± 27	78 ± 27	0.61
RVESV, ml	85 ± 43	81 ± 36	87 ± 45	0.40
RVESV index, ml/m^2	44 ± 21	40 ± 18	45 ± 23	0.18
RVEF, %	45 ± 12	47 ± 11	45 ± 12	0.35
LGE				
LGE	96 (70)	0 (0)	98 (100)	
LGE FWHM (% of LV mass)			9.9 ± 5.0	
LGE location				
Subendocardial			46 (47)	
Transmural			20 (20)	
Epicardial			8 (8)	
Mid-myocardial			23 (23)	
Focal/insertion points			1 (1)	

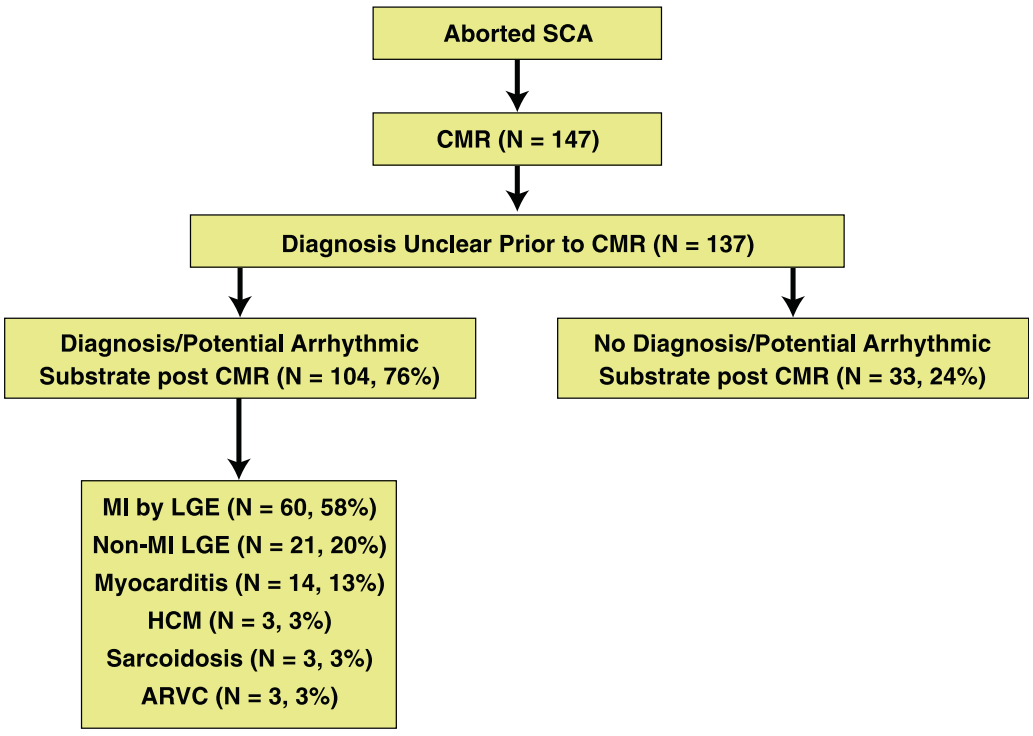
Values are mean ± SD or n (%).

FWHM = full width at half maximum; LV = left ventricular; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; 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.

LATE GADOLINIUM ENHANCEMENT. LGE was present in 98 patients (71%) (Table 2). The LGE pattern was subendocardial in 46 (47%), transmural in 20 (21%), mid-myocardial in 23 (23%), epicardial in 8 (8%), and at the insertion point of the RV in 1 of the patients (1%). The average extent of LGE was 9.9 ± 5% of the LV myocardium. Patients were grouped according to the presence or absence of LGE (Tables 1 and 2). VT was more commonly the presenting arrhythmia in patients with LGE, and VF was more common in those without LGE. There was a higher percentage of men in the LGE-negative group; otherwise, there were no significant differences between patients with and without LGE.

IDENTIFICATION OF AN ARRHYTHMIC SUBSTRATE. Among the 137 patients who were referred for a contrast CMR study for workup of SCA, a diagnosis or

FIGURE 2 CMR Provides a Diagnosis or Potential Arrhythmic Source



A flow diagram showing how the information from a contrast CMR study can provide a key finding or diagnosis. ARVC = arrhythmogenic right ventricular cardiomyopathy; other abbreviations as in Figure 1.

potential arrhythmic substrate was identified in 104 patients (76%). The abnormalities included the presence of an infarct-pattern LGE in 60 patients (44%), noninfarct LGE in 21 (19%), active myocarditis in 14 (10%), hypertrophic cardiomyopathy in 3 (2%), sarcoidosis in 3, and arrhythmogenic cardiomyopathy in 3. There were 26 patients with a prior clinical or ECG diagnosis of a remote MI. Among these 26 patients, a non-MI pattern of LGE was identified in 19%, an MI pattern of LGE was identified in 42%, and no LGE was identified in 39% (Figure 2).

CLINICAL FOLLOW-UP. All patients underwent ICD placement. The median follow-up was 29 months (interquartile range: 18 to 43 months). There were 63 subsequent adverse events among the 137 patients. These events included death in 16 patients and an appropriate ICD intervention in 47 patients. The appropriate ICD interventions included ICD discharge in 26 patients and 21 pace-terminated events. There were 7 events among the 41 patients without LGE (event rate of 7% per year) and 56 events among the 96 patients with LGE (event rate of 23% per year) (Tables 3 and 4). The 7 adverse events in LGE-negative patients consisted of 2 deaths (LVEF 15% and 45% at time of CMR), 2 appropriate ICD discharges (LVEF 31% and 62% at the time of CMR), and 3 ATP discharges (LVEF 28%, 38%, and 25%). The initial event in an LGE-negative patient was an ATP event after 13 months, and the 2 deaths occurred at 53 and 68 months of follow-up. During follow-up of the patients with LGE, there were 34 VT events and 8 VF events compared with 4 VT events and 1 VF event among the LGE-negative patients. There were 23 inappropriate ICD discharges overall, and this included 13 among the 41 patients without LGE and 10 among the 96 patients with LGE. The study cohort also consisted of 10 patients with angiographically significant coronary artery disease (>50% narrowing in the distribution of a major epicardial vessel). Among these 10 patients, 6 had LGE and 4 did not have LGE. We repeated the event analysis after stratifying based on the LVEF by CMR. There were 48 events among the 96 patients with an LVEF <50%

(event rate 20%/year); in comparison, there were 15 events among the 41 patients with an LVEF >50% (event rate 15%/year).

UNIVARIABLE AND MULTIVARIABLE ASSOCIATIONS WITH MACE. In the initial Cox model, which contained variables associated with adverse outcomes and the presence of LGE, we found that the presence of LGE provided the strongest association with adverse outcomes (Tables 5 and 6). In a second model, which contained variables associated with adverse outcomes and the extent of LGE, we found that the extent of LGE provided the strongest association with adverse outcomes (Tables 7 and 8). A ROC curve among patients with LGE was generated to determine what extent of LGE could help identify a group at further increased risk of MACE (Figure 3). Analysis of the ROC curve revealed that a percentage of LGE by volume of ≥8.1% using the FWHM method (area under the curve 0.89; sensitivity 90%; specificity 80%) maximized the sum of sensitivity and specificity for prediction of events. Kaplan-Meier curves generated for event-free survival among patients by both the binary presence or absence of LGE and the extent of LGE are presented (Figure 4). Patients with an LGE extent ≥8.1% represented a subgroup at very high risk of subsequent adverse events. In this subgroup with an LGE extent of ≥8.1%, there were 45 events, or a cumulative event rate of more than 78%. In comparison, among patients with an LGE extent of <6.8%, there were 5 events, or a cumulative event rate of 9%.

DISCUSSION

In this study, we showed the additive value of a contrast CMR study in survivors of SCA, especially when an initial workup was unrevealing. Specifically, we showed how the presence and pattern of LGE was valuable in the diagnostic workup of patients who survive a cardiac arrest. The presence of LGE identified a potential arrhythmic substrate among 76% of patients among whom a workup involving clinical assessment, ECG, echocardiogram, and coronary angiogram did not show a clear cause of arrest. Among these, most had an unrecognized infarct, followed by scar related to prior or active myocarditis, scar related to dilated cardiomyopathy, or unrecognized hypertrophic cardiomyopathy, sarcoidosis, or arrhythmogenic cardiomyopathy. The study also tested the predictors of subsequent adverse events among patients who survived SCA and found that almost 45% of patients either died or had appropriate ICD therapy in follow-up and that the presence and the extent of

TABLE 3 Characteristics of Patients With and Without Subsequent MACE

	No MACE (N = 74)	MACE (N = 63)	p Value
Age, yrs	56 ± 12	56 ± 12	0.72
Male	48 (65)	42 (67)	0.86
Diabetes	13 (18)	15 (24)	0.40
Hypertension	18 (24)	13 (21)	0.68
Prior myocardial infarction	14 (19)	14 (22)	0.68
Atrial fibrillation	18 (24)	22 (35)	0.19
Medications			
Aspirin	21 (28)	19 (30)	0.85
Beta-blocker	67 (91)	61 (97)	0.18
ACEI/ARB	57 (77)	50 (79)	0.84
Spironolactone	10 (14)	10 (16)	0.81
Diuretic	13 (18)	17 (27)	0.22
Statin	26 (35)	18 (29)	0.47
Anticoagulant	8 (11)	10 (16)	0.45
BMI, kg/m^2	30 ± 5	28 ± 8	0.12
Systolic blood pressure, mm Hg	116 ± 15	115 ± 18	0.76
Diastolic blood pressure, mm Hg	70 ± 11	70 ± 10	0.87
Heart rate, beats/min	73 ± 13	70 ± 12	0.27
QRS duration, ms	112 ± 32	114 ± 29	0.67
QTc duration, ms	446 ± 29	451 ± 30	0.31
GFR, ml/min/1.73 m^2	74 ± 16	68 ± 20	0.06

Values are mean ± SD or n (%).
MACE = major adverse cardiac events; other abbreviations as in Table 1.

TABLE 4 Characteristics of Patients With and Without Subsequent MACE

	No MACE (n = 74)	MACE (n = 63)	p Value
CMR			
LVEDV, ml	189 ± 43	190 ± 46	0.89
LVEDV index, ml/m^2	96 ± 24	100 ± 26	0.39
LVESV, ml	111 ± 43	111 ± 41	0.96
LVESV index, ml/m^2	57 ± 22	58 ± 23	0.65
LVEF, %	43 ± 13	43 ± 11	0.98
LV mass, g	145 ± 46	156 ± 50	0.18
LV mass index, g/m^2	76 ± 25	79 ± 27	0.42
RVEDV, ml	150 ± 54	152 ± 52	0.82
RVEDV index, ml/m^2	75 ± 29	79 ± 25	0.37
RVESV, ml	83 ± 41	88 ± 45	0.46
RVESV index, ml/m^2	42 ± 21	46 ± 21	0.23
RVEF, %	46 ± 11	45 ± 12	0.62
LGE	40 (54)	56 (89)	<0.001
LGE extent (FWHM)	5.7 ± 2.3	12.8 ± 4.2	<0.001
LGE location			
Subendocardial	28 (70)	18 (32)	<0.001
Transmural	7 (18)	13 (23)	0.61
Epicardial	1 (2)	7 (13)	0.13
Mid-myocardial	4 (8)	19 (32)	<0.01
Insertion point	1 (2)	0 (0)	0.42

Values are mean ± SD or n (%).
Abbreviations as in Tables 1 and 2.

TABLE 5 Multivariable Model for MACE

	Hazard Ratio	SE	p Value	95% CI
LGE	6.70	3.54	<0.001	2.38-18.85
Age	0.99	0.02	0.66	0.96-1.02
Male	1.70	0.57	0.11	0.89-3.28
LVEF	1.00	0.02	0.77	0.97-1.04
Diabetes	1.02	0.36	0.95	0.52-2.03
LVEDV	1.00	0.00	0.43	1.00-1.01

CI = confidence interval; other abbreviations as in Tables 1 and 2.

TABLE 7 Multivariable Model for MACE

	Hazard Ratio	SE	p Value	95% CI
LGE extent (FWHM)	1.15	0.02	<0.001	1.11-1.19
Age	1.01	0.01	0.25	0.99-1.04
Male	1.17	0.34	0.59	0.66-2.09
LVEF	1.01	0.01	0.63	0.98-1.04
Diabetes	0.91	0.29	0.78	0.48-1.72
LVEDV	1.00	0.00	0.51	1.00-1.01

Abbreviations as in Tables 1, 2, 3, 5 and 6.

LGE provided strong and independent prognostic information among this high-risk cohort.

White et al. (4) tested the diagnostic yield of CMR among 30 patients with resuscitated SCA. The study structure was different in that all patients with resuscitated SCA underwent CMR in comparison with our study in which CMR was not protocol based and patients were referred for CMR only after the initial workup did not reveal a clear etiology. In the study by White et al. (4) they performed a clinical assessment, ECG, echocardiogram, and assessment of coronary anatomy in a consecutive series of patients with an SCA. After this assessment, the cause of SCA was unclear in 50%. They next performed a contrast CMR study and in the 50% of patients in whom the etiology of the SCA was unclear, CMR provided a diagnosis in 74%. That diagnosis varied but included an MI in over one-third of patients. We extended the findings of White et al. (4) and tested the role of CMR in a large cohort of survivors of SCA. In our study containing 137 patients with resuscitated SCA without a clear diagnosis before CMR, we found that CMR provided an arrhythmic substrate in more than 75% of patients. Indeed, a large percentage of the diagnosis involved unrecognized myocardial infarcts. This finding of an unrecognized myocardial infarct is in keeping with prior work among "healthy subjects" (24), patients with known coronary disease free of recognized MI (25), patients with diabetes (26), and patients with atrial fibrillation (22), showing that unrecognized MIs are a relatively frequent occurrence with a clear prognostic effect. The finding of an unrecognized MI in patients free of significant coronary disease and presenting with SCA is new. In patients with a similar mean LVEF and presumed ischemic cardiomyopathy, LGE is found in close to 100% (27). However, in patients with presumed nonischemic cardiomyopathy, LGE is found in an ischemic distribution in 20% (27), leading to the hypothesis that the presence of LGE in angiographically normal coronary arteries may be a marker for increased risk of SCA.

The implantation of an ICD is warranted in all, and ICDs improve survival among patients resuscitated from SCA (5–7,17). In the AVID (Antiarrhythmics Versus Implantable Defibrillators) study, 68% of patients either died or had secondary therapy at 2 years (28). Similarly, among a large population of patients who survived SCA, approximately 40% either died or required appropriate ICD therapy at 2 to 3 years (29). In our study, the cumulative event rate was 45% among all patients resuscitated from SCA. However, there are no prior data testing the role of LGE on future outcomes among patients resuscitated from SCA. In a complementary study, Dawson et al. (30) tested the role of LGE among a cohort of patients with nonsustained and sustained VT. In that study, the mean LVEF was 60%, one-third underwent ICD insertion, and one-third had LGE. The pattern of LGE was nonischemic in two-third and ischemic in one-third. They found that the presence of LGE provided stronger prognostic information than LVEF. Among patients with resuscitated SCA, we found that both the presence and the extent of LGE were associated with a markedly increased rate of subsequent adverse events. There

TABLE 6 Multivariable Model for MACE: Stepwise Cox Regression (Exclusion Criteria p > 0.05)

	Hazard Ratio	SE	p Value	95% CI
LGE	6.25	3.28	<0.001	2.24-17.47

SE = standard error; other abbreviations as in Tables 1, 3, and 5.

TABLE 8 Multivariable Model for MACE: Stepwise Cox Regression (Exclusion Criteria p > 0.05)

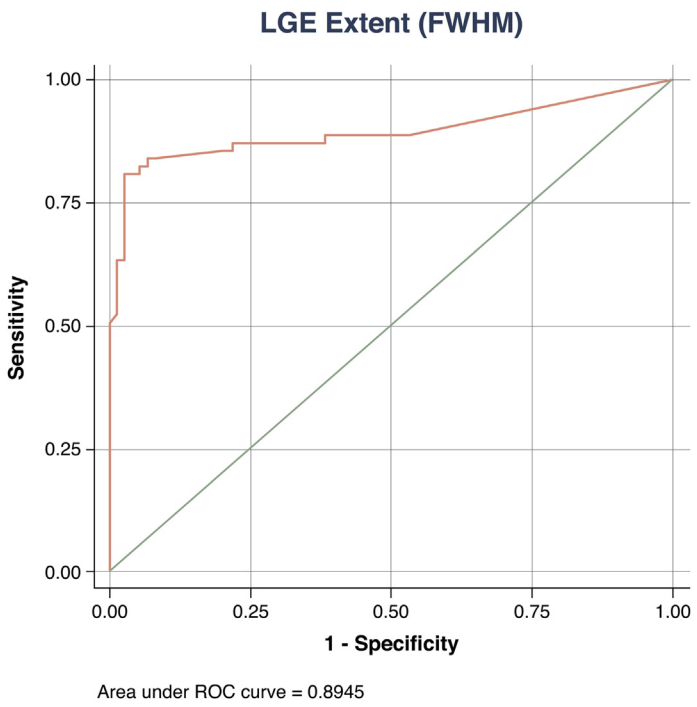
	Hazard Ratio	SE	p Value	95% CI
LGE extent (FWHM)	1.14	0.02	<0.001	1.10-1.19

Abbreviations as in Tables 1, 2, 3, 5 and 6.

are no randomized data among any cohort showing that an intervention based on LGE can improve outcomes. Therefore, an extension of this work would test whether intervention based on the presence or extent of LGE, either via medications, ICD programming (31), or advance electrophysiological (32) techniques, can reduce the frequency of ICD discharge or death. For example, in this study, a small number of patients were prescribed pharmacological antiarrhythmic therapy on discharge, and future studies could test whether antiarrhythmic therapy at discharge could reduce the rate of recurrent events.

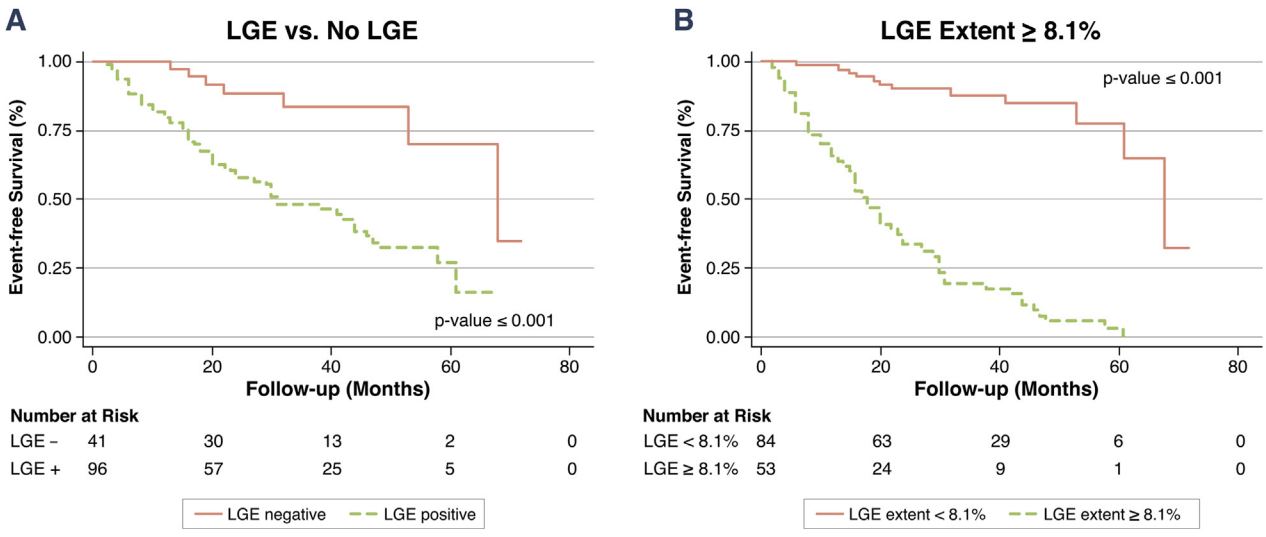
STUDY LIMITATIONS. This study should be interpreted within the context of the design format. This was a cohort of patients resuscitated from SCA who were referred for a CMR study as a workup for structural causes of arrhythmias. We did not include all patients successfully resuscitated from SCA, and the decision to perform a CMR study was at the discretion of the primary physician and not part of an institutional protocol. We agree that this lack of a standardized and protocol-driven approach leads to a significant selection bias. Furthermore, CMR protocols, magnet strength, and ICD programming varied across institutions and across time and were not identical for all patients. This was not a multicenter study and only involved 2 centers. However, we believe that our cohort is representative of prior

FIGURE 3 ROC Curve for LGE Extent and the Prediction of MACE



Receiver-operating curve (ROC) testing LGE extent as a predictor of major adverse cardiac events (MACE). Analysis revealed that the percentage of LGE by volume of ≥8.1% provided the maximal combination of sensitivity and specificity. FWHM = full width at half maximum; other abbreviation as in Figure 1.

FIGURE 4 Event-Free Survival Separated According to the Presence and Extent of LGE



Kaplan-Meier curves displaying event-free survival in cohorts according to **(A)** the dichotomous presence or absence of LGE and **(B)** an extent of LGE of ≥8.1% or <8.1% of the volume of the left ventricle. Abbreviation as in Figure 1.

studies among patients resuscitated from SCA. Specifically, 3 secondary prevention randomized controlled trials have reported cardiac function in survivors of SCA randomized to ICD versus medical therapy. In the AVID study, the mean LVEF was 32% (7), whereas, in the CIDS (Canadian Implantable Defibrillator Study) trial, which enrolled a similar study cohort, the mean LVEF was 34% (5). In the CASH (Cardiac Arrest Study Hamburg) study, the mean LVEF was 45% (6), similar to that reported in an observational population study of survivors of SCA (33). Our study cohort consisted of patients who were broadly similar. We found a mean LVEF of 41% and a similar presenting arrhythmia. This study does not provide mechanistic insight into the cause of the ischemic pattern of LGE, but possibilities include vasospasm, embolism, myocarditis, and occult plaque rupture (34). We also recorded the medical therapy at the time of discharge; therefore, how therapy was modified over time was not captured and how the presence of LGE influenced therapy is unknown.

CONCLUSIONS

Among patients resuscitated from SCA who were referred for CMR study, we found that a contrast CMR study provided added value, especially among patients in whom the diagnosis was unclear after an initial standard workup.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Among patients with SCA, a CMR study of the heart with contrast identifies scar in the heart in 71% and provides a potential arrhythmic substrate in 76% of patients. Furthermore, both the presence and extent of scar are markers that identify survivors of SCA who are markedly increased risk of future adverse events.

TRANSLATIONAL OUTLOOK: Additional studies are needed to validate the findings and test whether the routine performance of CMR in survivors of SCA may be of diagnostic use in broad populations and test whether the information provided by CMR can help guide therapies to prevent subsequent adverse outcomes in survivors of SCA.

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