

Cardiac Sarcoidosis Detected by Late Gadolinium Enhancement and Prevalence of Atrial Arrhythmias

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Cardiovascular magnetic resonance (CMR) imaging is being increasingly used to help identify patients with cardiac sarcoidosis (CS). Whereas ventricular arrhythmias have been well studied in this population, atrial arrhythmias have not been thoroughly investigated. We sought to better characterize the arrhythmia burden of a cohort of patients diagnosed with CS by CMR imaging. Patients with biopsy-proven extracardiac sarcoidosis were referred to the University of Chicago for evaluation of the presence of CS. CMR imaging was used to categorize the patients into 2 groups; those with and those without late gadolinium enhancement (LGE) for comparison of arrhythmic events. Arrhythmic evaluation included Holter monitor, event recorder, electrophysiology testing, or implantable cardioverter-defibrillator (ICD) interrogation; 192 consecutive patients were evaluated with CMR imaging, 57 of whom did not have ambulatory monitoring results and thus were excluded. LGE was present in 44 patients. Atrial arrhythmias were documented in 16 patients (36%) with myocardial LGE and in 11 patients (12%) without myocardial LGE ($p = 0.002$). Ventricular arrhythmias were documented in 27% of patients with myocardial LGE and 2.2% of LGE-negative patients ($p = 0.00076$). Of 26 LGE-positive patients with ICDs, 8 (30.8%) received therapies, 3 (11.5%) of which were inappropriate for atrial arrhythmias. In conclusion, atrial arrhythmias were documented more frequently than ventricular arrhythmias in patients with sarcoidosis with cardiac involvement and were 3 times more prevalent than in patients with sarcoidosis without cardiac involvement. Risk-benefit assessment of anticoagulation for primary prevention of stroke should be performed for patients with CS. In patients receiving implantable defibrillators, programming to minimize inappropriate ICD shocks for atrial arrhythmias must be considered. © 2014 Elsevier Inc. All rights reserved. (Am J Cardiol 2014;113:1556–1560)

Patients with cardiac sarcoidosis (CS) are becoming increasingly identifiable with the emergence of cardiovascular magnetic resonance (CMR) imaging as a reliable diagnostic tool for detecting myocardial involvement based on the presence of late gadolinium enhancement (LGE).^{1–3} Because of the risk for ventricular arrhythmias in this population, attention has focused on patient selection for implantable cardioverter-defibrillator (ICD) therapy.^{4–6} Data regarding atrial arrhythmias are scant, indicating a prevalence of 19% to 32%^{7,8} in patients with cardiac sarcoidosis and 15.5% in patients with cardiac amyloidosis.⁹ In this investigation, we examined the burden of atrial arrhythmias in patients with evidence of CS on CMR imaging.

Methods

We performed a retrospective analysis on a select cohort of consecutive patients with biopsy-proven extracardiac sarcoidosis who were referred to the University of Chicago

for evaluation of the presence of CS. Patients who were diagnosed with biopsy-proven sarcoidosis were referred for cardiac evaluation regardless of symptoms. CMR imaging was used to categorize the patients into 2 groups: those with LGE (LGE+) and those without LGE (LGE–) for comparison of arrhythmic events. The patients without LGE on CMR imaging effectively served as the control population.

All CMR imaging procedures were performed at the University of Chicago from January 2007 to July 2011 (1.5-T Achieva; Philips Healthcare, Cleveland, Ohio). Cine and LGE imaging were performed according to standard protocols published by the Society of Cardiovascular Magnetic Resonance.¹⁰ Left ventricular (LV) end-diastolic and end-systolic volumes, mass, and ejection fraction were measured from the LV short-axis cine images using the method of discs. The diagnosis of CS was made when any amount of LGE was present anywhere in the LV myocardium. LGE was considered to be present if seen in 2 different views and if the mean signal intensity was >4 SDs higher than the noise of remote normal myocardium. The extent of LV LGE was semi-quantitatively determined as the number of myocardial segments that had any LGE expressed as a percentage.

Comprehensive transthoracic echocardiography (iE33 imaging system, Philips Healthcare) that included 2-dimensional, Doppler, and tissue Doppler echocardiography was performed to assess diastolic function. Pulsed wave mitral inflow, tissue Doppler of the septal and lateral mitral annulus,

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Table 1
Patient characteristics

Variable	LGE+ Group (n = 44)	LGE- Group (n = 91)	p Value
Age, yrs (range)	52 ± 12.94 (23–84)	50 ± 10.74 (27–77)	0.23
Men	14 (32)	21 (23)	0.57
African-American	25 (57)	50 (55)	0.84
Caucasian	15 (34)	36 (40)	0.54
Hispanic	1 (2)	3 (3)	0.73
Unknown/other	3 (7)	2 (2)	0.27
ACE-I/ARB	21 (48)	37 (41)	0.61
β Blocker	13 (30)	20 (22)	0.29
Statin	9 (21)	19 (21)	0.94
Percent LGE present	11.96 (5.9–38.3)	0	<0.001
Abnormal electrocardiogram	29 (66)	22 (24)	<0.001
LV ejection fraction (%)	57.9 ± 6.2	60.6 ± 6.6	0.68
LV diastolic dysfunction present (%)	33	64	0.36
LA volume (cm ³)	57.9 ± 21.7	51.8 ± 19.2	0.22
E/A ratio	1.05 ± 0.37	1.15 ± 0.38	0.28
E/e' ratio	10.48 ± 4.59	9.69 ± 3.15	0.36
Pulmonary sarcoid	33 (75)	75 (82)	0.22

Data are presented as mean ± SD, median (interquartile range), or n (%), unless otherwise specified.
ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker.

and left atrium volumes were used to determine the presence of diastolic dysfunction and abnormal LV filling pressures based on clinical criteria.

Techniques for investigation of arrhythmias included 24- or 48-hour Holter monitor, 30-day event recorder, electrophysiology testing, and ICD interrogation. Both ventricular and atrial arrhythmias were reviewed and classified by an electrophysiologist. Atrial arrhythmias were subclassified as atrial fibrillation, atrial tachycardia, atrial flutter, or supraventricular tachycardia. All ICD detections and therapies were reviewed and classified based on stored device electrograms. Atrial and ventricular arrhythmias lasting >30 seconds were included in the analysis. Patients with nonsustained arrhythmias lasting <30 seconds were excluded from the analysis. Baseline electrocardiograms were evaluated and defined as abnormal if they demonstrated atrioventricular delay (PR interval >200 ms) or block, QRS duration >120 ms, abnormal axis, or any rhythm abnormality not consistent with normal sinus rhythm.

Continuous variables are compared as mean ± SD, and categorical data are compared as percentages. Comparisons within and between groups were performed using a 2-tailed paired Student *t* test, Fisher's exact test or chi-square test, as applicable. All reported p values were 2-tailed, and statistical significance was defined as a 2-sided p value <0.05.

Results

One hundred ninety-two consecutive patients with CS were evaluated by CMR imaging from January 2007 to July 2011; 57 of them did not have ambulatory monitoring results and thus excluded from the analysis. The median time of follow-up was 25 months from the time the CMR imaging was performed until study completion. Forty-four patients demonstrated LGE on CMR imaging consistent with CS and 91 lacked LGE. Clinical characteristics of the study cohort appear in Table 1.

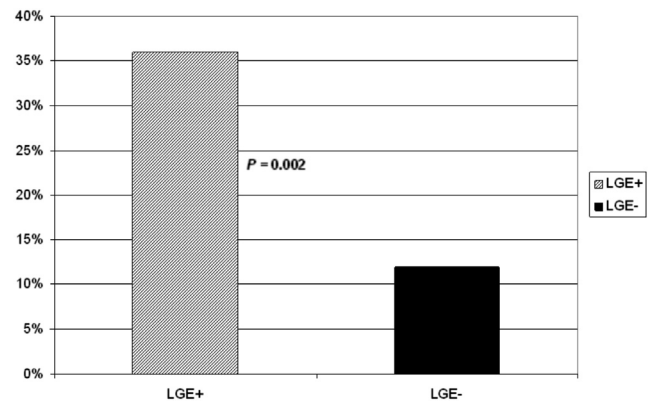


Figure 1. Incidence of atrial arrhythmias was 3 times more common in the LGE-positive group than the LGE-negative group (36% vs 12%, $p = 0.002$).

Table 2
Means of arrhythmic evaluation

Arrhythmic Evaluation	LGE+ Group (n = 44)	LGE- Group (n = 91)
30-Day event recorder	11 (25)	43 (47)
48-H Holter monitor	7 (16)	40 (44)
Electrophysiological study	17 (39)	9 (10)
ICD interrogation	26 (59)	3 (3)

Data are presented as n (%).

Atrial arrhythmias were documented in 16 LGE+ patients (36%) and in 11 LGE- patients (12%; $p = 0.002$; Figure 1). All patients with atrial arrhythmias in both groups were symptomatic. Twenty-two unique arrhythmias were observed in the 16 LGE+ patients: 7 were atrial fibrillation, 4 atrial flutter, 8 atrial tachycardia, and 3 supraventricular tachycardia. Means of arrhythmia diagnosis are detailed in Table 2. The median length of time for ICD arrhythmia

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