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Late gadolinium enhancement identified with cardiac magnetic resonance imaging in sarcoidosis patients is associated with long-term ventricular arrhythmia and sudden cardiac death

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Aims Cardiac involvement with sarcoidosis is a major cause of morbidity and mortality in affected individuals. Cardiac magnetic resonance (CMR) imaging promises a new and more accurate assessment of cardiac sarcoidosis by identifying typical patterns of myocardial fibrosis. We assessed the utility of CMR in the prediction of adverse outcomes.

Methods and results One hundred and six CMR patients with biopsy-proven extracardiac and/or presumed cardiac sarcoidosis were enrolled. Late gadolinium enhancement (LGE) on CMR typical of sarcoidosis was used to determine the presence of cardiac involvement. Clinical endpoints and medical records were assessed and those with implantable cardioverter–defibrillators (ICDs) underwent device interrogation. Survival rates of patients with cardiac sarcoidosis were compared with those with only extracardiac disease. CMR identified 32 (30%) individuals as having cardiac sarcoidosis; the remaining 74 (70%) had only extracardiac disease. At a mean follow-up time of 36.8 $\pm$ 20.5 months, patients with cardiac sarcoidosis had a higher rate of the composite cardiac endpoint—comprising sudden cardiac death (SCD) and ventricular tachyarrhythmia—compared with those with only extracardiac disease ($P < 0.001$). There was a higher rate of SCD or ICD-aborted SCD in patients with cardiac sarcoidosis vs. those without ($P = 0.005$). In patients with cardiac sarcoidosis, the rate of SCD was lower in those with an ICD compared with those without ($P < 0.02$).

Conclusions Patients with evidence of cardiac sarcoidosis on CMR have higher rates of adverse cardiovascular events than those with only extracardiac disease. In patients with sarcoidosis detected on CMR, the presence of an ICD is associated with a lower rate of SCD.

Keywords Sarcoidosis • Magnetic resonance imaging • Late gadolinium enhancement • Sudden cardiac death • Arrhythmia • Defibrillation

Translational perspective

Prior studies have suggested that regional myocardial fibrosis identified by cardiac magnetic resonance (CMR) in patients with sarcoidosis is associated with a higher rate of adverse cardiac outcome. Despite only limited available evidence (AHA/ACC guidelines Class IIa Level C), this has led to the common practice of recommending implantable cardioverter–defibrillator (ICD) in sarcoidosis patients who have evidence of cardiac involvement. Nevertheless, few studies have demonstrated that the presence of sarcoidosis-related fibrosis on CMR is associated with a higher rate of adverse cardiac events, and no study has shown that ICD implantation mitigates this risk.

In this study, we present 3-year data demonstrating that sarcoidosis patients with regional myocardial fibrosis on CMR have a higher rate of malignant ventricular arrhythmia and/or sudden cardiac death (SCD) than those without fibrosis, and that the presence of an ICD is

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associated with a lower rate of SCD in sarcoidosis patients who have regional myocardial fibrosis. We believe that our data make a substantial contribution to the literature in this field, as they provide strong evidence for the use of both CMR and primary prevention ICD in the assessment and management of patients with sarcoidosis.

Introduction

Sarcoidosis is a multisystem granulomatous disease of unknown aetiology characterized by non-caseating granulomas in involved organs. Granulomas are often associated with pulmonary tissue and lymph node involvement, but can manifest in virtually any body tissue.[1] The incidence of sarcoidosis varies widely throughout the world, largely attributed to differences in environmental exposures, surveillance methods, predisposing HLA alleles, and other genetic factors.[2] The annual incidence is as high as 40 cases per 100 000 people in some Northern European countries, whereas in Australia the incidence ranges from 4.4 to 6.3 per 100 000.[3,4] Although much is known about the epidemiology and clinical course of non-cardiac sarcoidosis, less is understood about the manifestation, prognosis, and treatment of cardiac involvement.

Among the autopsies of patients with known extracardiac sarcoidosis, the incidence of myocardial granulomas diagnostic of cardiac involvement has been estimated to be between 20 and 30%.[1,5,6] Silverman *et al.*[6] found that less than half of the patients shown to have histological evidence of cardiac sarcoidosis at autopsy were diagnosed during their lifetime. Japanese studies have found that involvement of the myocardium may be as high as 58% in patients with extracardiac sarcoidosis and is responsible for up to 85% of deaths in patient with sarcoidosis.[7,8] Although ~40% of patients with cardiac involvement have no clinical signs or symptoms of the disease, the remainder suffer a range of complications determined by the profusion and location of cardiac granulomas.[9]

The major complications of cardiac sarcoidosis include sudden cardiac death (SCD), ventricular tachycardia or fibrillation (VT or VF), complete heart block (CHB), and congestive heart failure (CHF). Importantly, SCD resulting from ventricular tachyarrhythmia (VT) may be the first manifestation of the disease for a significant proportion of sufferers.[10]

A wide variety of diagnostic tools have been advocated in the detection of cardiac sarcoidosis, including electrocardiography (ECG), echocardiography (ECHO), radionucleotide studies (^{201}Tl or ^{99m}Tc scintigraphy), CMR, positron emission tomography (PET), and endomyocardial biopsy (EMB).[10] A significant drawback of CMR is that most patients with a pacemaker and/or implantable cardioverter–defibrillator (ICD) cannot undergo this test; however, the emergence of MR-compatible devices may overcome this in the future.[11] Nonetheless, compared with PET, CMR is cheaper and more widely available. PET also exposes patients to ionizing radiation, whereas CMR does not and this is of particular benefit if repeat imaging is anticipated.[10] EMB is highly specific and remains the only tool that can be used to make a definitive diagnosis of cardiac sarcoidosis. Nevertheless, it has sensitivities reported to be as low as 20%.[12]

In acute cases, sarcoidosis infiltrates on CMR might appear as zones of increased intramyocardial signal intensity on T_2-weighted images. Focal myocardial thickening is also often observed as a result of oedema on these images.[13] Variation of this presentation can occur, particularly in patients who are or have been treated with corticosteroid therapy. In these patients, increased signal intensity on T_2-weighted sequences without myocardial thickening and without gadolinium uptake can be observed.[14,15] CMR images can be enhanced with gadolinium diethylenetriamine pentaacetic acid (gad-DTPA) contrast. Late gadolinium enhancement (LGE) CMR is considered as a useful method for the early identification of cardiac sarcoidosis.[16,17] LGE has been associated with a reduction of regional wall motion as well as ^{201}Tl perfusion defects.[7] The potential importance of CMR in the assessment of cardiac sarcoidosis is great, as early diagnosis and treatment may improve prognosis.[18]

While corticosteroids have been advocated as first-line therapy to halt the progression of cardiac disease,[19] they do not seem to reduce the incidence of ventricular arrhythmias.[20] Definitive evidence is lacking regarding the role of ICD and pacemaker (PPM) devices in cardiac sarcoidosis.[9–11,21] Although it is widely accepted that device therapy is indicated for symptomatic patients with ventricular arrhythmias or CHB, no standardized treatment protocols for cardiac sarcoidosis exist.[22,23] The current 2008 American College of Cardiology/American Heart Association/Heart Rhythm Society guidelines present Class IIa; Level C evidence for prophylactic device implantation in cardiac sarcoidosis and as a result believe it to be a reasonable indication.[23] Thus, despite a paucity of randomized trial data and with evidence based on consensus opinions, case studies, or standards of care, it has been suggested that cardiac sarcoidosis may be an indication for prophylactic ICD implantation.[24,25]

Hence, to improve the outcomes for patients with cardiac sarcoidosis, two requirements need to be fulfilled: the diagnosis should be established early and accurately, and treatment should be effective.[26] We therefore set out to compare CMR findings and clinical endpoints in sarcoidosis patients in order to (i) appraise the utility of CMR in the prediction of adverse outcomes and (ii) explore the therapeutic role of ICD/PPM in the treatment of this insidious disease.

Methods

Patient selection

A retrospective single-centre observational study at the Alfred Heart Centre, Melbourne, was undertaken. A dedicated database of 3562 CMR scans performed between 1 January 2002 and 31 December 2012 was interrogated, yielding 242 patients in whom the term 'sarcoidosis' was used in either the indication for, or final report of their CMR.

Exclusion criteria included those who had no history of biopsy-proven extracardiac or cardiac sarcoidosis and no evidence of cardiac sarcoidosis on CMR ($n = 55$), a follow-up time of <6 months ($n = 30$), patients who were under the age of 18 at the time of follow-up ($n = 2$), those of non-English speaking background ($n = 7$), and individuals who were either non-contactable ($n = 23$) or refused consent ($n = 19$). This left a population of 106 patients who were recruited into the study (*Figure 1*).

The Human Research and Ethics Committees (HREC) of both the Alfred Hospital and the University of Notre Dame approved this study, and all patients provided informed consent regarding their participation.

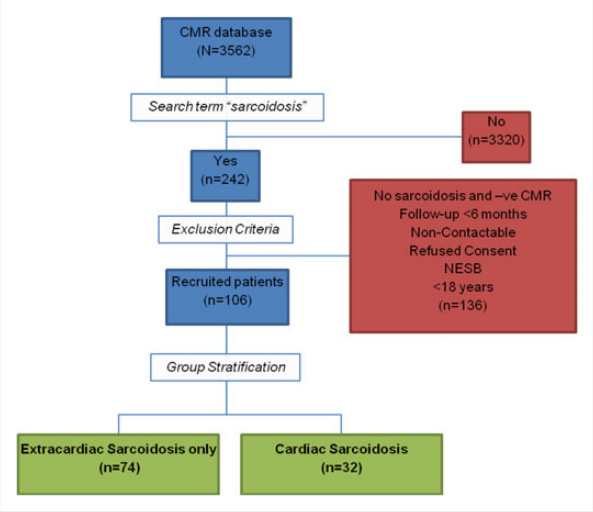

Figure 1 Patient selection.

CMR analysis

Two cardiologists experienced in CMR who were blinded to patient clinical history and sarcoidosis status assessed the CMR scans. Each CMR was appraised for ventricular scarring, morphology and function, as well as the location of scarring. The presence of LGE scarring on CMR in a non-vascular distribution typical for cardiac sarcoidosis was used to determine the presence of cardiac sarcoidosis. Specifically, cardiac sarcoidosis was deemed to be present if LGE was visible in two orthogonal views and the presence of another condition known to be associated with LGE, such as myocarditis or hypertrophic obstructive cardiomyopathy, could be excluded on clinical grounds. Only where consensus occurred between both assessors were patients deemed to have evidence of cardiac sarcoidosis on CMR.

Clinical endpoints and follow-up

The primary endpoint of the study was the composite cardiac event that included the occurrence of SCD, VT, or VF. The secondary endpoints of all-cause mortality and mortality due to SCD were also evaluated. As a number of patients with cardiac sarcoidosis had undergone ICD implantation for the primary prevention of SCD, the combined endpoint of SCD plus ICD-aborted SCD was also evaluated. Only instances where patients received an appropriate shock for VT or VF from their ICD were categorized as ICD-aborted SCD; anti-tachycardia pacing (ATP) was not included in this endpoint. Other secondary endpoints assessed included the occurrence of CHB, CHF, cardiomyopathy, pulmonary hypertension, pericardial effusion, and ventricular aneurysms. In addition, treatment with immunosuppressive therapies and ICD/PPM devices was explored.

A separate researcher, blinded to patient CMR results, assessed the sarcoidosis status and clinical endpoints experienced by the cohort. This consisted of a 10- to 15-min telephone survey, which was correlated with hospital medical records and the records of private treating physicians. Data of deceased patients were collected from medical records and death certificates. For those patients with an ICD, interrogations of these devices assessing for the registration of appropriate defibrillator therapies were undertaken according to the standard clinical practice.

Statistical analysis

All analyses were performed using the SPSS statistical software. Patients were divided into two groups: those with known extracardiac sarcoidosis and no cardiac involvement on CMR, and those with cardiac sarcoidosis on CMR (with or without a history of extracardiac disease; *Figure 1*). The specific clinical endpoints of patients with cardiac sarcoidosis on CMR vs. those with only extracardiac sarcoidosis were then compared.

Basic descriptive statistics were used to characterize the demographics and non-continuous variables of the cohort. For continuous variables, simple univariate statistics were used. One-way ANOVA ('analysis of variance') tests were used to compare continuous variables and Pearson's χ^2 ('chi-squared') tests were used for categorical variables.

Establishing dates for specific endpoints facilitated the use of Kaplan–Meier estimator plots for survival analyses. Log-rank (Mantel–Cox) tests were used to determine mean survival times and the degree of statistical significance between groups. Proportional hazards models (Cox multiple regression) were used to assess covariates for hazard rates.

Statistically significance was defined at $P < 0.05$. Confidence intervals (CIs) were reported at 95%.

Results

Study population

Demographic and clinical features of the cohort ($n = 106$) are presented in *Table 1*. Patients were predominantly middle-aged (51 ± 12.2 years) and male (60%). Seventy-four (70%) patients had only extracardiac sarcoidosis and the remaining 32 (30%) had cardiac sarcoidosis on CMR. The distribution of LGE scarring in the CMR-positive population is described in *Table 2*.

The most common extracardiac site for sarcoidosis involvement was the lung (70%). Patients generally had chronic sarcoidosis, with 61% of the study population having the disease for at least 5 years. Of the cardiac sarcoidosis group, 6 (19%) patients had no pre-existing diagnosis of extracardiac disease prior to CMR.

At the time of CMR, the left ventricular ejection fraction (LVEF) was lower in those with cardiac sarcoidosis than those with only extracardiac disease (60.36 ± 7.8 vs. 47.95 ± 11.07, $P < 0.01$). The mean time from CMR to follow-up was 36.8 ± 20.5 months and was not significantly different between the groups (36.7 ± 20 vs. 37.3 ± 23, $P =$ NS).

Clinical outcomes

At the time of follow-up, 16 patients had major adverse events; 12 patients were deceased and 8 had suffered from a VT or VF. Of the 12 deaths, 4 were due to SCD with respiratory arrest ($n = 5$), mantle cell lymphoma ($n = 1$), a motor vehicle accident ($n = 1$), and fatal haemoptysis ($n = 1$) making up the remaining non-SCD causes.

Composite cardiac endpoint, all-cause mortality, and sudden cardiac death

The rate of the composite cardiac endpoint was higher in cardiac sarcoidosis patients than those with only extracardiac disease (38 vs. 1.4%, $P < 0.001$; *Figure 2*). To determine the independence of the effect of cardiac sarcoidosis on the rate of the composite cardiac endpoint, the Cox proportional hazards model was utilized. In addition to the presence or absence of cardiac sarcoidosis on CMR, additional variables including age, sex, LVEF, and the number of organs affected with sarcoidosis were entered into the multivariate model. The presence of cardiac sarcoidosis on CMR was the only independent variable that was predictive of the composite cardiovascular outcome (hazard ratio 12.52, 95% C.I. 1.35–116.18, $P = 0.03$).

Table 1 Characteristics of the study cohort

Characteristics	Overall (*N* = 106)	Extracardiac sarcoidosis (*n* = 74)	Cardiac sarcoidosis (*n* = 32)	Significance (*P*-value)
Age, y	51 ± 12.2	50.3 ± 11.4	52.3 ± 14	NS (0.52)
Male sex, *n* (%)	60 (56.6)	39 (52.7)	21 (65.6)	NS (0.22)
Extracardiac sarcoidosis, *n* (%)				
Lung	74 (69.8)	62 (83.8)	12 (37.5)	<0.01
Lymph node	30 (28.3)	26 (35.1)	4 (12.5)	<0.02
Skin	8 (7.5)	7 (9.5)	1 (3.1)	NS (0.26)
Eye	6 (5.7)	5 (6.8)	1 (3.1)	NS (0.45)
Liver	5 (4.7)	4 (5.4)	1 (3.1)	NS (0.61)
Spleen	2 (1.9)	2 (2.7)	0 (0)	NS (0.35)
Kidney	1 (.9)	1 (1.4)	0 (0)	NS (0.51)
Brain	1 (.9)	1 (1.4)	0 (0)	NS (0.51)
Gall bladder	1 (.9)	1 (1.4)	0 (0)	NS (0.51)
Pancreas	1 (.9)	0 (0)	1 (3.1)	NS (0.13)
No. of organs involved, *n* (%)				
One site	62 (58.5)	45 (60.8)	17 (53.1)	NS (0.56)
Two sites	31 (29.2)	25 (33.8)	6 (18.8)	
Three sites	4 (3.8)	2 (2.7)	2 (6.3)	
Four sites	3 (2.8)	2 (2.7)	1 (3.1)	
Years since diagnosis, *n* (%)				
<1	6 (6)	4 (5.4)	2 (7.7)	NS (0.29)
1–4	33 (33)	24 (32.4)	9 (34.6)	
5–9	36 (36)	24 (32.4)	12 (46.2)	
≥10	25 (25)	22 (29.7)	3 (11.5)	
Time from CMR to follow-up, m	36.8 ± 20.5	36.7 ± 20	37.3 ± 23	NS (0.91)
Immunosuppressive therapy at any time since diagnosis, *n* (%)	61 (57.5)	48 (64.8)	13 (40.7)	NS (0.07)
LVEF at CMR	56.6 ± 10.5	60.36 ± 7.8	47.95 ± 11.07	*P* < 0.01

y, years; *n*, numbers; m, months; LVEF, left ventricular ejection fraction; NS, not significant.

Table 2 Distribution of LGE in patients with cardiac sarcoidosis

LGE location	Cardiac sarcoidosis (*n* = 32)
Epicardial/subepicardial, *n* (%)	19 (59.4)
Subendocardial, *n* (%)	0 (0)
Midwall, *n* (%)	8 (25)
Multiple discrete areas [≥2], *n* (%)	23 (71.9)
Left ventricle, *n* (%)	
Inferior/inferolateral wall	23 (71.9)
Anterior/anterolateral wall	19 (59.4)
Septal	18 (56.3)
All three left ventricular walls	8 (25)
Right ventricle, *n* (%)	2 (6.3)

There was a non-significant trend towards higher total mortality between the two groups, with 8 (5.4%) patients from the non-cardiac sarcoidosis group dying compared with 4 (12.5%) patients with cardiac involvement on CMR. There was a strong trend to a higher rate of SCD in those with cardiac sarcoidosis with 3 (9.4%) patients experiencing this outcome compared with only 1 (1.4%) in the non-cardiac sarcoidosis group ($P = 0.056$, log-rank test). For the endpoint of SCD or ICD-aborted SCD, event-free survival was significantly lower in patients with cardiac sarcoidosis compared with those with only extracardiac disease ($P = 0.005$; *Figure 3*). The rate of SCD or ICD-aborted SCD was 11-fold higher in the cardiac sarcoidosis group when compared with those with only extracardiac disease (15.6 $n = 5$, vs. 1.4%, $n = 1$).

Other morbidity

Fifteen (47%) of those with cardiac sarcoidosis had experienced CHF compared with 3 (4.1%) of those with only extracardiac disease ($P < 0.001$). When comparing those with cardiac involvement with those without, the incidence of cardiomyopathy, CHB, pulmonary hypertension, and ventricular aneurysm were all significantly higher. There was no difference in the incidence of pericardial effusion between the cardiac and non-cardiac sarcoidosis groups (*Table 3*).

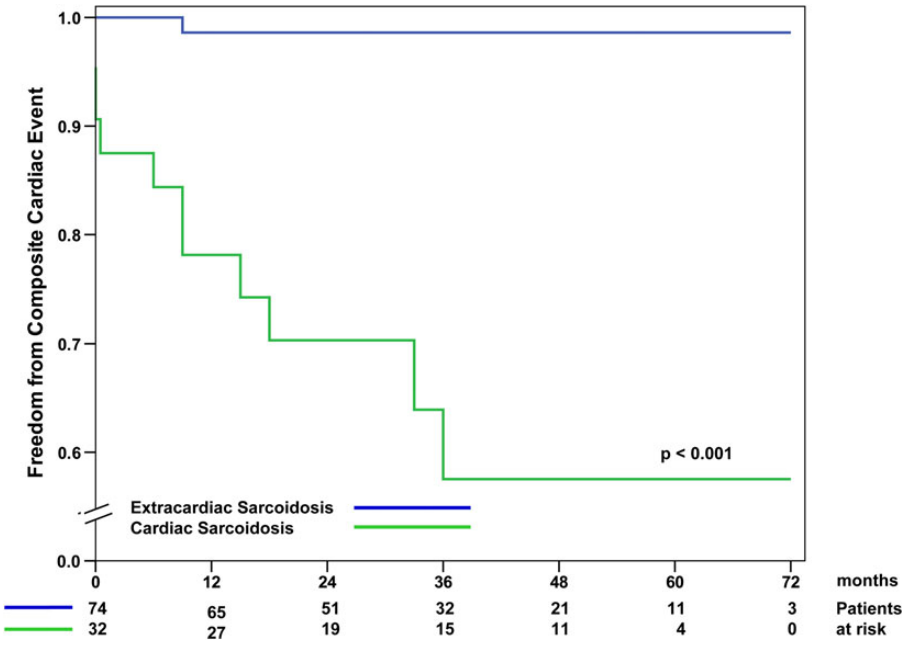

Figure 2 Kaplan–Meier plots for composite cardiac event (VT, VF, and SCD) according to sarcoidosis status. There was a higher rate of cardiac events in cardiac sarcoidosis groups compared with those with only extracardiac disease (mean time-to-event 47.9 ± 5.8 vs. 71.1 ± 0.9 months, $P < 0.001$).

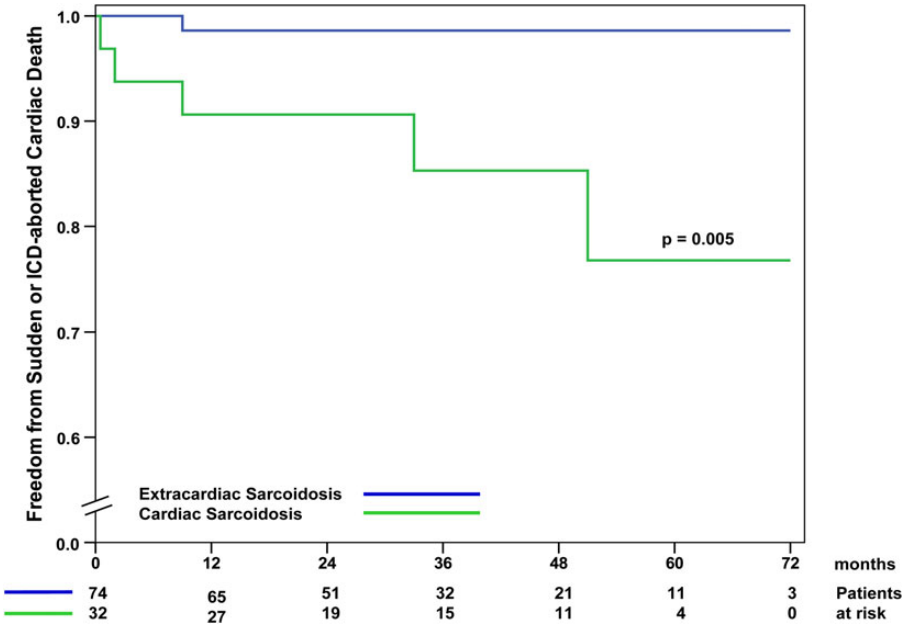

Figure 3 Kaplan–Meier plots for SCD or ICD-aborted SCD according to sarcoidosis status. There was a higher rate of SCD or ICD-aborted SCD in those with cardiac sarcoidosis compared with those with only extracardiac disease (mean time-to-event 61.7 ± 4.2 vs. 71.1 ± 0.9 months, $P = 0.005$).

Device implantation

Two (2.7%) patients in the extracardiac sarcoidosis only group had a PPM implanted and none had an ICD. In the cardiac sarcoidosis group, 2 (6.3%) patients had a PPM implanted and 19 (59.4%) had an ICD. In those patients with an ICD, 5 (26.3%) received appropriate ATP and 2 (10.5%) received appropriate ICD shocks. In those patients with

Table 3 Other morbidity

Other morbidity	Overall ($N = 106$)	Extracardiac sarcoidosis ($n = 74$)	Cardiac sarcoidosis ($n = 32$)	Significance (P-value)
Cardiomyopathy, *n* (%)	22 (20.8)	3 (4.1)	19 (59.4)	<0.001
CHF, *n* (%)	18 (17)	3 (4.1)	15 (46.9)	<0.001
Pulmonary hypertension, *n* (%)	14 (13.2)	6 (8.1)	8 (25)	<0.02
CHB, *n* (%)	5 (4.7)	1 (1.4)	4 (12.5)	<0.01
Pericardial effusion, *n* (%)	4 (3.8)	2 (2.7)	2 (6.3)	NS (0.38)
Ventricular aneurysm, *n* (%)	3 (2.8)	0 (0)	3 (9.4)	<0.01

cardiac sarcoidosis, those without ICD/PPM were more likely to die of SCD compared with those who had an ICD/PPM ($P < 0.02$; *Figure 4*). No patients in the cardiac sarcoidosis group with an ICD/PPM died of SCD compared with 3 (27.3%) of those with CMR evidence of sarcoidosis but no ICD/PPM. Importantly, the incidence of SCD in cardiac sarcoidosis patients with a device *in situ* was comparable with those who did not have cardiac involvement on CMR.

Immunosuppression

Among patients with cardiac sarcoidosis, 13 (47%) had received treatment with corticosteroids or another immunosuppressive medication. There was no significant effect of immunosuppression in patients with cardiac sarcoidosis in the occurrence of the composite cardiac endpoint ($P = 0.48$, log-rank test).

Discussion

The principal finding of this study was that, compared with patients with only extracardiac sarcoidosis, those with cardiac involvement on CMR were at an increased risk of the composite cardiac endpoint comprising SCD or VT. This risk was independent of patient age, sex, LVEF, and the extent of extracardiac sarcoidosis involvement. Although there was no significant difference in all-cause mortality between those with and without cardiac sarcoidosis, there was an increased rate of SCD or ICD-aborted SCD in those with cardiac involvement. Importantly, in patients with cardiac sarcoidosis, those with an ICD/PPM were less likely to die of SCD than those without, supporting the role of these devices in the management of cardiac sarcoidosis.

Our results are comparable with the recent findings of Staub and Biederman,[27] and Blankstein *et al.*,[28] who emphasized the prognostic utility of both CMR and PET, respectively, in predicting the occurrence of adverse events. The overall rate of CMR detected cardiac sarcoidosis in our study was 26%, which is consistent with autopsy series that have found myocardial lesions in 20–30% of patients with a known history of extracardiac sarcoidosis.[1,5,6] We also observed a rate of SCD comparable to the current literature, identifying the inherent risk for patients with cardiac sarcoidosis.[9,29] A prior study from Smedema *et al.*[16] highlighted the utility of the presence of LGE on CMR in the diagnosis of cardiac sarcoidosis in a large population of 101 patients, although the prognostic value of CMR was not assessed. More recently, Patel *et al.*[29] demonstrated an association of LGE with future adverse clinical events in patients with sarcoidosis, although due to a low overall number of adverse events survival analysis could not be performed. Our study supports the 2013 findings of Greulich *et al.*[30] who demonstrated the impact of cardiac sarcoidosis diagnosed on CMR with longer-term survival free of actual or aborted SCD, appropriate ICD discharge, and VT/VF. The clinical significance of these findings is notable as for a large proportion of patients with cardiac sarcoidosis initial presentation is SCD resulting from VT.[10] Nevertheless, our study is the first to emphasize the effect of ICD devices on SCD, thus supporting the advocacy of prophylactic device implantation in the CMR-positive population.

Previously, Schuller *et al.*[31] performed ICD interrogations of 112 patients with cardiac sarcoidosis, finding that appropriate therapies were administered in 32% of patients, with inappropriate therapies occurring in 12%. Kron *et al.*[32] have demonstrated comparable findings in a population of 235 patients across 13 institutions, with 36% of patients receiving appropriate therapy for VT/VF and 24% receiving inappropriate ICD therapies. The rate of appropriate ICD therapy in our study population is comparable with the findings of these prior studies; however, we found that the presence of an ICD was associated with a reduction of SCD in the cardiac sarcoidosis population. This finding provides further support for the use of CMR in the detection of myocardial involvement—while also highlighting its prognostic utility in predicting clinical outcomes—therefore strengthening the argument for prophylactic ICD implantation in those with positive CMR findings.

When comparing patients with cardiac sarcoidosis who had been treated with immunosuppressants with those who had not, we found no significant difference in the rate of the composite cardiac endpoint. In a study by Vignaux *et al.*,[33] the authors found that patients who had received immunosuppressant medications had improved CMR findings at 12-month follow-up compared with those who had received no treatment. Similarly, Osborne *et al.*[34] found with serial PET imaging that immunosuppressive therapy is associated with an improvement in LVEF in patient with cardiac sarcoidosis who demonstrated a reduction in myocardial inflammation. It has been suggested that such therapies may be of particular benefit if started before scar formation and irreversible ventricular dysfunction occurs.[35] However, in a study by Winters *et al.*,[20] it was found that the use of immunosuppressive medications had no effect on the rate of inducible VT. While we acknowledge that the lack of significance of immunosuppressive medications in reducing the occurrence of the composite cardiac endpoint may be due to low

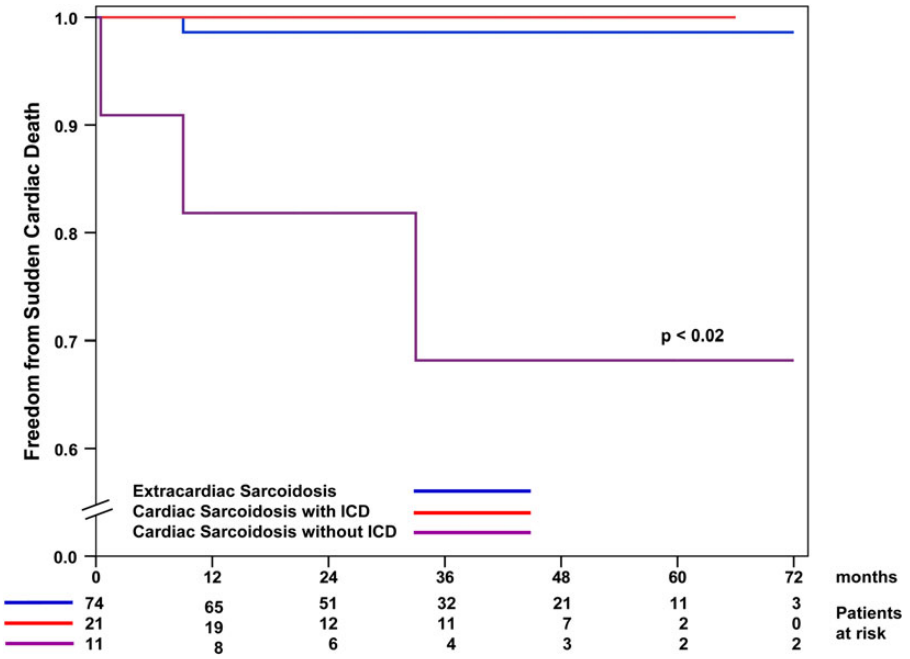

Figure 4 Kaplan–Meier plots for SCD in patients with cardiac sarcoidosis with and without ICD. There was a lower rate of SCD in those with an ICD to those without ICD (mean time-to-event 54.5 ± 8.6 vs. 66 months, $P < 0.02$).
Note: Since there were no SCD events in those with cardiac sarcoidosis and ICD, estimation is limited to longest survival time.

statistical power, it may also be attributed to evidence suggesting that such therapies do not reduce the risk of VT in affected populations.

When interpreting our findings, a number of limitations need to be considered. As our study was retrospective in design former exposures to risk variables prior to CMR, such as arrhythmias could not be accurately accounted for. This may have an impact on the event rate in the cardiac sarcoidosis group possibly skewing the presented data towards a higher rate of VT/VF and SCD. However, the rate of VT and SCD in our study was comparable with event rates in prior studies in sarcoidosis patients with an ICD in whom ICD interrogation could be carried out, suggesting that selection bias was not a major confounder to our results.[31,32,36] Furthermore, although the time to follow-up was not significantly different between those with and without evidence of cardiac sarcoidosis, the variability of the range (0.5–6.7 years) presents the potential for confounding as longer follow-up times may have allowed for the manifestation of more cardiovascular complications. Another limitation is that pertaining to the ability to differentiate sarcoidosis from acute myocarditis on CMR. It should be noted that although a combination of clinical findings along with additional CMR sequences, such as global relative enhancement, were implemented, acute myocarditis could not be definitively excluded in our dataset. Finally, the significant difference in LVEF between those with and without CMR evidence of cardiac sarcoidosis could potentially interact with the composite cardiac outcome. However, following Cox multiple regression modelling including LVEF along with other covariates that may have been associated with adverse outcomes, the presence of cardiac sarcoidosis was the only independent predictor of the composite cardiac event.

Our results demonstrate that individuals with evidence of cardiac sarcoidosis on CMR—regardless of previous sarcoidosis status—are at an increased risk of associated cardiac morbidity and mortality. Furthermore in those patients with cardiac sarcoidosis on CMR, the presence of an ICD is associated with a reduced incidence of SCD. These data highlight the prognostic utility of CMR in the assessment of cardiac sarcoidosis and also support the notion that patients with positive CMR findings be considered for a prophylactic ICD to reduce the incidence of associated mortality.

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Conflict of interest: none declared.

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