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CMR Imaging Predicts Death and Other Adverse Events in Suspected Cardiac Sarcoidosis

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OBJECTIVES This study aimed to demonstrate that the presence of late gadolinium enhancement (LGE) is a predictor of death and other adverse events in patients with suspected cardiac sarcoidosis.

BACKGROUND Cardiac sarcoidosis is the most important cause of patient mortality in systemic sarcoidosis, yielding a 5-year mortality rate between 25% and 66% despite immunosuppressive treatment. Other groups have shown that LGE may hold promise in predicting future adverse events in this patient group.

METHODS We included 155 consecutive patients with systemic sarcoidosis who underwent cardiac magnetic resonance (CMR) for workup of suspected cardiac sarcoid involvement. The median follow-up time was 2.6 years. Primary endpoints were death, aborted sudden cardiac death, and appropriate implantable cardioverter-defibrillator (ICD) discharge. Secondary endpoints were ventricular tachycardia (VT) and nonsustained VT.

RESULTS LGE was present in 39 patients (25.5%). The presence of LGE yields a Cox hazard ratio (HR) of 31.6 for death, aborted sudden cardiac death, or appropriate ICD discharge, and of 33.9 for any event. This is superior to functional or clinical parameters such as left ventricular (LV) ejection fraction (EF), LV end-diastolic volume, or presentation as heart failure, yielding HRs between 0.99 (per % increase LVEF) and 1.004 (presentation as heart failure), and between 0.94 and 1.2 for potentially lethal or other adverse events, respectively. Except for 1 patient dying from pulmonary infection, no patient without LGE died or experienced any event during follow-up, even if the LV was enlarged and the LVEF severely impaired.

CONCLUSIONS Among our population of sarcoid patients with nonspecific symptoms, the presence of myocardial scar indicated by LGE was the best independent predictor of potentially lethal events, as well as other adverse events, yielding a Cox HR of 31.6 and of 33.9, respectively. These data support the necessity for future large, longitudinal follow-up studies to definitely establish LGE as an independent predictor of cardiac death in sarcoidosis, as well as to evaluate the incremental prognostic value of additional parameters. (J Am Coll Cardiol Img 2013;6:501–11) © 2013 by the American College of Cardiology Foundation

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Cardiac involvement is the most important cause of death in sarcoidosis patients, yielding a 5-year mortality rate between 25% and 66% despite immunosuppressive treatment (1–3). Because ventricular tachyarrhythmias resulting from myocardial granulomas causing electric instability have been identified as the underlying mechanism of death (2,3), some patients may benefit from implantable cardioverter-defibrillator (ICD) placement (4), yet risk stratification and clinical management remain difficult (5).

Several groups recently determined that cardiac magnetic resonance (CMR) using late gadolinium enhancement (LGE), not only can improve the detection of cardiac sarcoidosis in comparison to standard clinical evaluation with the use of consensus criteria (6,7), but furthermore may hold promise in predicting future adverse events, including cardiac death, in this patient group.

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

ECG = electrocardiogram

HR = hazard ratio

ICD = implantable cardioverter-defibrillator

LGE = late gadolinium enhancement

LV = left ventricle/ventricular

LVEDV = left ventricular end-diastolic volume

LVEF = left ventricular ejection fraction

nsVT = nonsustained ventricular tachycardia

RV = right ventricle/ventricular

SCD = sudden cardiac death

VT = ventricular tachycardia

Consequently, the primary objective of this study was to establish the prognostic value of a comprehensive CMR examination in risk stratification of patients with suspected cardiac sarcoidosis. Specifically, we sought to demonstrate that the presence of LGE visualized by CMR predicts future lethal and other adverse events. In addition, we aimed at identifying additional predictors for adverse events in this patient group during long-term follow-up.

METHODS

Patient population. One-hundred fifty-five consecutive patients presenting at one of the participating institutions between January 2002 and December 2011 for workup of suspected cardiac sarcoidosis (all comers) were prospectively enrolled in the long-term follow-up if they fulfilled the following criteria: 1) systemic sarcoidosis diagnosed by biopsy and/or clinical criteria; *and* 2) no history of coronary artery disease or myocardial infarction; *and* 3) successfully underwent CMR imaging (Table 1). Patients with valvular or congenital heart disease demonstrated by CMR were not included. All patients gave informed consent.

CMR protocol. Electrocardiogram (ECG)-gated CMR imaging was performed in breath-hold using a 1.5-T Magnetom Symphony, Magnetom Sonata, Magnetom Espree, Magnetom Avanto, or Magnetom Aera magnetic resonance imaging scanner (Siemens Healthcare, Erlangen, Germany) in line with Society for Cardiovascular Magnetic Resonance/European Cardiovascular Magnetic Resonance recommendations (8). Both cine and LGE short-axis CMR images were prescribed every 10 mm (slice thickness 6 mm) from base to apex. In-plane resolution was typically 1.2 × 1.8 mm. Cine CMR was performed using a steady-state free-precession sequence. LGE images were acquired on average 5 to 10 min after contrast administration using segmented inversion recovery fast gradient echo (9), constantly adjusting inversion time (10). The contrast dose (gadodiamide or gadopentetate dimeglumine) was 0.15 mmol/kg.

CMR analysis. Cine and contrast images were evaluated by 2 experienced observers as described elsewhere (11,12). In brief, endocardial and epicardial borders were outlined on the short-axis cine images. Volumes and left ventricular (LV) ejection fraction (EF) were derived by summation of epicardial and endocardial contours. The LV mass was calculated by subtracting endocardial from epicardial volume at end-diastole and multiplying by 1.05 g/cm^3 (13). Extent of LGE was assessed using the Siemens Argus analysis software package, and the results were expressed as percentage of myocardial mass. There was good interobserver agreement when analyzing LVEF (kappa = 0.92; $p < 0.001$) and LGE extent (kappa = 0.88; $p < 0.001$).

Clinical follow-up. Clinical follow-up was performed using a standardized questionnaire at least 3 months after initial presentation. In case of a suspected event, all necessary medical records were obtained and reviewed by the authors acting as an endpoint committee.

Variables, endpoints, and definitions. All variables were collected directly from patients and/or medical records, except the CMR parameters, which were evaluated as described in the previous text. Vari-

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