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Cardiac Sarcoidosis:

Remembering the Forgotten Right Ventricle*

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Keywords

cardiovascular magnetic resonance; late gadolinium enhancement; outcomes; right ventricle; sarcoidosis; systolic dysfunction

Sarcoidosis is a multisystem, granulomatous disorder of unclear cause. Although the lungs are most commonly involved, other susceptible sites include the skin, eyes, kidneys, heart, reticuloendothelial system, and central nervous systems (1). Cardiac involvement has been reported in approximately 25% of patients with systemic sarcoidosis, although isolated cardiac involvement can occur in the absence of systemic disease. Cardiac sarcoidosis predominantly involves the left ventricle and can present with high-grade atrioventricular block, myopericarditis, heart failure, or life-threatening arrhythmias. Cardiac involvement is a leading cause of death in patients with sarcoidosis, thus early recognition and initiation of therapy is important (1,2). Unfortunately, because of the patchy nature of the disease, many cardiac tests, including electrocardiography, echocardiography, myocardial perfusion imaging, and endomyocardial biopsy, have poor diagnostic sensitivity (3). Cardiac magnetic resonance (CMR) with late gadolinium enhancement (LGE) imaging can accurately detect even small areas of myocardial damage, thus making it a reliable diagnostic tool (4). In addition, LGE-CMR is also a useful instrument for risk stratification. Studies have demonstrated that patients with myocardial damage detected by LGE-CMR have significantly higher rates of adverse events and cardiac death in comparison with patients without LGE (5,6). In addition to LGE, there are also other factors that are important predictors of adverse outcomes in cardiac sarcoidosis, including left ventricular (LV) ejection fraction (7), a multifocal pattern of LGE (8), and the burden of LGE (9).

Whereas LV involvement in cardiac sarcoidosis has been well characterized using LGE-CMR imaging (10), right ventricular (RV) involvement has been less clearly studied. CMR imaging is the preferred imaging modality to assess the right ventricle (11), and similar to reduced LV systolic function, the presence of RV dysfunction and RV LGE also portends a poor prognosis with cardiac sarcoidosis (2,9,10,12). Consequently, assessment of RV

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involvement has become increasingly important in its role in cardiac sarcoidosis. RV dysfunction is common in sarcoidosis and is typically associated with lung disease, pulmonary hypertension, or direct LV involvement but can also be an isolated finding (2). Recent CMR studies showed that RV LGE in patients with cardiac sarcoidosis and preserved LV systolic function was predictive of arrhythmias and adverse events (9). However, the added value of RV involvement in the setting of LV involvement has not yet been thoroughly studied.

Against this background, Velangi et al. () aim to define the prevalence of RV dysfunction and RV LGE in patients with sarcoidosis in this issue of *iJACC*. The investigators present findings from 290 patients with biopsy-proven sarcoidosis who were referred for CMR imaging to screen for cardiac involvement according to the expert consensus statement issued by the Heart Rhythm Society (13). Twelve percent of the cohort had RV dysfunction and 5.5% had RV LGE, defined as any presence of RV free wall LGE (14). The investigators are commended on evaluating RV LGE, which can be technically challenging because of the partial volume effect, making it difficult to differentiate epicardial fat from RV LGE. The partial volume effect also limits the ability to accurately quantify the extent of RV LGE. It remains to be seen how reliably RV LGE can be identified at less experienced CMR centers.

The cohort was followed for a median of 3.2 years for an endpoint of all-cause death or ventricular arrhythmias (14). Similar to previously described cohorts, the presence of RV systolic dysfunction was independently associated with all-cause mortality. However, it was not associated with arrhythmia. Conversely, RV LGE was associated with the arrhythmic endpoint but not death. Consistent with prior CMR studies, all patients with RV LGE also had LV LGE (8).

Despite these results, the study had several limitations. First, the study follow-up period was short. Although low RV ejection fraction was not associated with arrhythmic outcomes, it is worrisome that the Kaplan-Meier curves flattened after the second year, when the sample size falls to half of where it started. Perhaps the conclusion would differ with more patients and a longer follow-up.

Second, the overall number of arrhythmic events is small because only 18 patients (6%) died or had ventricular tachycardia or sudden cardiac death during follow-up. The investigators propose that that the presence of RV LGE may be used as a marker of extensive LGE to warrant implantable cardioverter-defibrillator placement. Although RV involvement may suggest the presence of more arrhythmogenic tissue, it is unclear if there are enough complementary data available from other centers to recommend implantable cardioverter-defibrillator placement on the basis of RV LGE at this time. Identifying a critical threshold of RV LGE burden may provide further improvements in risk stratification and facilitate decision making about patient management (15), but RV LGE burden is likely to be difficult to measure reliably as discussed earlier.

Lastly, it is also worth noting that 80 percent of patients included in the cohort were white, and it is unknown how applicable the findings from the study would be to other ethnicities.

Limitations notwithstanding, this is an important study that provides insight into the added prognostic value of LGE-CMR imaging of the right ventricle in cardiac sarcoidosis. To use these results in clinical practice, several questions must be answered: What threshold of RV LGE burden should prompt implantable cardioverter-defibrillator placement? How should patients with RV involvement be monitored? What is the role for immunosuppressive therapy for isolated RV involvement?

Although cardiac sarcoidosis is a rare disorder, the disease has been easier to diagnose through the use of imaging modalities such as CMR and positron emission tomography. The increased use of CMR and positron emission tomography to evaluate patients with suspected cardiac sarcoidosis has clearly helped improve our understanding of the natural history of the condition and has led to new insights into how we might treat it. However, the body of evidence related to the treatment and management of cardiac sarcoidosis remains nearly void of the prospective, randomized controlled trials that are needed to truly understand how to best treat cardiac sarcoidosis.

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