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EDITORIAL COMMENT

Management of Cardiac Sarcoidosis With Mildly Impaired Cardiac Function*

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Sarcoidosis is an inflammatory disease of unknown etiology characterized by the noncaseating granulomas in several organs.[1] Cardiac involvement occurs in approximately 5% of patients with sarcoidosis, but it is responsible for significant morbidity and mortality.[2] Lethal arrhythmia, such as sustained ventricular tachycardia (VT) or ventricular fibrillation, is one of the common manifestations in cardiac sarcoidosis (CS). Identification of patients who are at risk for lethal arrhythmia is crucial but often difficult in clinical settings.

The incidence of lethal arrhythmias is reported to be high among patients with reduced left ventricular ejection fraction (LVEF).[3,4] According to the 2016 Japanese Circulation Society

guidelines, an implantable cardioverter-defibrillator is a Class IIa indication in patients with an LVEF of ≤35% even with optimal pharmacotherapy, including immunosuppressive therapy.[5]

However, the management of CS patients with mildly impaired cardiac function (LVEF of >35%) remains controversial. The current guideline recommends ICD insertion in patients with an LVEF of <50%; either: 1) late enhancement on cardiac magnetic resonance (CMR); 2) positive findings on ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET); or 3) positive findings on gallium-67 (^{67}Ga) scintigraphy; and in whom sustained VT or ventricular fibrillation was induced during electrophysiologic testing.[5]

In this issue of *JACC: Asia*, Kamada et al[6] evaluated the prognosis and arrhythmic events in 322 patients with CS and mildly impaired cardiac function. They found that sudden cardiac death occurred in 3 patients and that 31 patients had appropriate ICD discharges. Concomitant nonsustained ventricular tachycardia (NSVT) with atrioventricular block (AVB) at CS diagnosis, low LVEF values, abnormal findings on ^{67}Ga scintigraphy or ^{18}F-FDG PET of the heart, and concomitant NSVT with abnormal findings on ^{67}Ga scintigraphy or ^{18}F-FDG PET of the heart were independent predictors of lethal ventricular arrhythmias in CS patients with mildly impaired cardiac function.[6] These findings suggest that the need for ICD insertion should be assessed in these patients.

Late gadolinium enhancement (LGE) in CMR was not significantly different as a predictor of lethal ventricular arrhythmias in the present study. However, a meta-analysis including 10 studies reported that the presence of LGE on CMR is associated with increased odds of both all-cause mortality and arrhythmogenic events in patients with CS.[7] Furthermore, in another meta-analysis including 9 studies with suspected or diagnosed sarcoidosis, a positive LGE finding on CMR was associated with an 8.6-fold increased risk of ventricular arrhythmia.[8] As the investigators mentioned, this difference may be caused by selection bias.

^{18}F-FDG PET is widely used to evaluate patients with suspected CS. With respect to prognostic outcomes, Blankstein et al[9] demonstrated that abnormal FDG uptake in the heart was associated with arrhythmic events and remained significant after adjusting for LVEF, which is consistent with the present study. A recent meta-analysis revealed that FDG uptake was also associated with major adverse cardiac events including death, ventricular arrhythmia, and heart failure hospitalization.[10]

Although it is a nonspecific marker of inflammation, an abnormal finding on ^{67}Ga scintigraphy of the heart has been used for the diagnosis of CS.[11] A

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previous study showed that accumulation of ^{67}Ga in the heart at the time of CS diagnosis was detected more frequently in the VT patients than in the non-VT patients.[12]

AVB is the most common initial manifestation of CS. Nordenswan et al[13] revealed that the rate of sudden cardiac death in 5 years is 14% in patients with AVB and an ejection fraction of 35% to 50%. AVB in CS is not a benign condition, and all patients who require permanent pacing should be considered for insertion of an ICD.

NSVT is reported to be associated with sustained ventricular arrhythmias in nonischemic dilated cardiomyopathy.[14] However, the prognostic significance of NSVT in CS remains unclear.

In the present study,[6] concomitant NSVT with AVB at CS diagnosis and NSVT with abnormal ^{67}Ga scintigraphy or ^{18}F-FDG PET of the heart were independent predictors of lethal ventricular arrhythmias. These results suggests that AVB, NSVT, ^{67}Ga scintigraphy, and ^{18}F-FDG PET may be helpful in predicting sudden cardiac death in patients with CS.

In conclusion, this work[6] provides important information for the use of ICDs in patients with mildly impaired cardiac function. The presence of NSVT, AVB at CS diagnosis, and ^{67}Ga scintigraphy or ^{18}F-FDG PET of the heart should be assessed in CS patients with mildly reduced LV function. Further studies are needed to validate the results of the present study.

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