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Characterization of the Electroanatomic Substrate in Cardiac Sarcoidosis

Correlation With Imaging Findings of Scar and Inflammation

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ABSTRACT

OBJECTIVES This study sought to characterize the electroanatomic (EAM) substrate in patients with cardiac sarcoidosis (CS) and ventricular tachycardia and its relationship to imaging findings of inflammation and fibrosis.

BACKGROUND CS is characterized by coexistence of active inflammation and replacement fibrosis.

METHODS A total of 42 patients with CS based on established criteria and ventricular tachycardia underwent high-density EAM mapping. Abnormal electrograms (EGM) were collected and independently classified as multicomponent fractionated, isolated, late, and split according to standard criteria and regardless of the peak-to-peak bipolar/unipolar voltage. A total of 29 patients (69%) underwent pre-procedural cardiac magnetic resonance (CMR) and positron emission tomography (PET)/computed tomography (CT). The distribution of EAM substrate was correlated with regions of late gadolinium enhancement (LGE) on CMR and increased 18F-fluorodeoxyglucose uptake on PET/CT.

RESULTS Of 21,451 bipolar and unipolar EGM, 4,073 (19%) were classified as abnormal with a predominant distribution in the basal perivalvular segments and interventricular septum. Using the standard bipolar (<1.5 mV) and unipolar (<8.3 mV for left ventricle <5.5 mV for the right) voltage cutoff values, 40% and 22% of the abnormal EGM were located outside the EAM low-voltage areas, respectively. LGE was present in 26 of 29 patients (90%), whereas abnormal 18F-fluorodeoxyglucose uptake in 14 of 29 patients (48%) with imaging. Segments with abnormal EGM had more LGE-evident scar transmurality [median: 24% (interquartile range [IQR]: 4% to 40%) vs. median: 5% (IQR: 0% to 15%); $p < 0.001$] and lower metabolic activity (median: 20 g glucose [IQR: 14 g to 30 g] vs. median: 29 g glucose [IQR: 18g to 39 g]; $p < 0.001$). Overall, the agreement between the presence of abnormal EGM was higher with the presence of LGE ($\kappa = 0.51$; $p < 0.001$) than with the presence of active inflammation ($\kappa = -0.12$; $p = 0.003$).

CONCLUSIONS In patients with CS and ventricular tachycardia, pre-procedural imaging with CMR and PET/CT can be useful in detecting EAM abnormalities that are potential targets for substrate ablation. Abnormal EGM were more likely located in segments with more scar transmurality (LGE) at CMR and a lower degree of inflammation on PET. (J Am Coll Cardiol EP 2017;■:■–■) © 2017 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

CMA = cardiac metabolic activity

CMR = cardiac magnetic resonance

CMV = cardiac metabolic volume

CS = cardiac sarcoidosis

CT = computed tomography

EAM = electroanatomic

EGM = electrogram(s)

EPI = epicardial

FDG = 18F-fluorodeoxyglucose

FP = fractionated potential(s)

IQR = interquartile range

LGE = late gadolinium enhancement

LP = late potential(s)

LV = left ventricular

LVA = low voltage area(s)

PET = positron-emission tomography

RV = right ventricular

SP = Sharp fractionated Potential(s)

VT = ventricular tachycardia

Cardiac sarcoidosis (CS) is a unique type of nonischemic cardiomyopathy characterized by lymphocyte CD4+-mediated formation of non-necrotizing granulomas. The resulting myocardial damage is driven by active inflammation with myocyte loss and reparative fibrosis that may progress to biventricular dilation and dysfunction as well as refractory ventricular tachycardia (VT) (1-3). The pathologic substrate of inflammation and replacement fibrosis can be studied non-invasively with imaging techniques such as positron emission tomography (PET)/computed tomography (CT) or cardiac magnetic resonance (CMR) and constitute an ideal milieu for re-entrant VT (4-6). In patients with CS and VT, intramural, subepicardial, and septal re-entrant circuits are common (7-9), with heterogeneous substrates capable of sustaining multiple re-entrant circuits (10,11). An accurate characterization of the EAM substrate responsible for re-entrant VT in patients with CS is crucial to identify targets for substrate-based ablation approaches (12,13). High-density EAM mapping has been used to characterize the electrical correlates of arrhythmogenic substrate in different clinical settings. No previous study has specifically evaluated the EAM substrate characteristics of patients with CS and VT, and the relationship between EAM abnormalities and imaging findings of active inflammation or scar are unknown. In this study we sought to characterize the EAM substrate responsible for VT in patients with CS and the relationship with imaging findings of inflammation and scar.

METHODS

STUDY POPULATION. Forty-two consecutive patients with diagnosis of CS based on Heart Rhythm Society criteria and refractory VT referred for Catheter Ablation to our institution were included in the study (14). Before the procedure all patients underwent a diagnostic work-up, comprehensive of clinical evaluation, 12-lead electrocardiography, implantable cardioverter-defibrillator interrogation and transthoracic echocardiography. A total of 29 patients (69%) underwent a comprehensive CMR with late gadolinium enhancement (LGE) imaging for detection of necrosis/fibrosis and cardiac PET/CT for detection of abnormal 18F-fluorodeoxyglucose (FDG) as a surrogate of myocardial inflammation. Details on the CMR and PET/CT methods for imaging acquisition and analysis are reported in the Online Appendix. Patients gave written informed consent prior the procedures according to the institutional guidelines of the University of Pennsylvania Health System.

EAM MAPPING AND ANALYSIS OF EAM SUBSTRATE. Patients presented to the cardiac electrophysiology laboratory in the fasting state. Conscious sedation was used whenever possible. Catheters were positioned in the heart using fluoroscopic guidance. A 6-F quadripolar catheter with 5-mm interelectrode distance (Bard Inc., Delran, New Jersey) was placed at the right ventricular (RV) apex. A deflectable 8-F mapping/ablation catheter that had a 3.5-mm irrigated tip and a 2-mm ring electrode separated by 1 mm (Thermocool, Biosense Webster, Diamond Bar, California) was advanced to the RV (transvenous approach), left ventricle (LV) (retrograde aortic or transseptal approach), or epicardial (EPI) space according to the presumed site of origin of the VT or the underlying substrate. In particular, the decision for an EPI approach was made when: 1) the 12-lead electrocardiography of the VT suggested an EPI origin; 2) there was evidence of EPI substrate on imaging studies (e.g., magnetic resonance, intracardiac echocardiography); and 3) there was a failure of endocardial ablation procedure. Access to the pericardial space and epicardium was obtained using the percutaneous subxiphoid approach described by Sosa et al. (15). A 64-element phased-array intracardiac echocardiography catheter (AcuNav, Acuson, Mountain View, California) was used to assist catheter manipulation, radiofrequency energy delivery, and tissue-catheter contact and to monitor for complications. A high-density (color and surface fill threshold <15 mm) 3-dimensional EAM (CARTO, Biosense Webster Inc., Diamond Bar, California) was created during sinus or paced rhythm to identify abnormal electrograms (EGM) consistent with scar, as previously reported (10,11,16). Intracavitary points were manually eliminated. Bipolar and unipolar EGM were filtered at 10 to 400 Hz and 0.5 to 400 Hz, respectively, displayed at 400 mm/s on the CARTO system and analyzed for stability, peak-to-peak amplitude, duration, and morphology.

Low-voltage areas (LVA) were defined according to established criteria, namely: a bipolar signal amplitude ≤1.5 mV in the endocardium and ≤1.0 in the epicardium and an endocardial unipolar signal amplitude ≤8.3 mV in the LV and RV septum and ≤5.5 mV in the RV free wall (10,17). Careful attention was paid to define the valvular planes and to