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Cardiac Magnetic Resonance Predicts Outcome in Patients With Premature Ventricular Complexes of Left Bundle Branch Block Morphology

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Objectives We investigated whether the presence of right ventricular (RV) abnormalities detected by cardiovascular magnetic resonance (CMR) predict adverse outcome in patients presenting with frequent premature ventricular complexes (PVCs) of left bundle branch block (LBBB) morphology.

Background CMR is a component of the diagnostic workup for the differential diagnosis between arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) and idiopathic RV tachycardia. RV abnormalities evaluated by CMR could have prognostic importance.

Methods Four hundred forty consecutive patients with >1,000 PVCs of LBBB morphology (minor diagnostic criterion of ARVC/D) and no other pre-existing criteria were prospectively enrolled. RV wall motion (WM), signal abnormalities, dilation, and reduced ejection fraction evaluated by CMR were considered imaging criteria of ARVC/D. Follow-up was performed evaluating an index composite end point of 3 cardiac events: cardiac death, resuscitated cardiac arrest, and appropriate implantable cardiac-defibrillator shock.

Results Subjects with multiple RV abnormalities (RVA-2 group) had worse outcome than the no-RVA group (hazard ratio [HR]: 48.6; 95% confidence interval [CI]: 6.1 to 384.8; $p < 0.001$). Of the 61 patients in the RVA-2 group, only 6 had a definite diagnosis of ARVC/D applying the Task Force Criteria. Also, subjects with a single imaging criterion (RVA-1 group) had worse outcome than the no-RVA group (HR: 18.2; 95% CI: 2.0 to 162.6; $p = 0.01$). Patients with only WM abnormalities had higher prevalence of cardiac events than no-RVA (HR: 27.2; 95% CI: 3.0 to 244.0; $p = 0.03$).

Conclusions In subjects with frequent PVC of LBBB morphology, CMR allows risk stratification. RV abnormalities were associated with worse outcome. (J Am Coll Cardiol 2010;56:1235–43) © 2010 by the American College of Cardiology Foundation

Premature ventricular complexes (PVCs) of left bundle branch block (LBBB) morphology and inferior axis arise from the right ventricular (RV) outflow tract or, less frequently, from the higher portion of the interventricular septum. PVCs of such morphology constitute a manifestation of idiopathic right ventricular tachycardia (IRVT) or an initial arrhythmic manifestation of arrhythmogenic RV cardiomyopathy/dysplasia (ARVC/D) (1–3). These 2 diseases initially have similar manifestations but are completely opposite in terms of the prognosis (4–6). IVRT is a disease with excellent prognosis, whereas ARVC/D is characterized by a great risk of sudden cardiac death, especially in young people involved in competitive sports (7). In Italy, where this study was conducted, ARVC/D has high incidence and is one the major causes of sudden death in the young (8). The diagnosis of ARVC/D is based on the presence of concomitant major and minor signs: functional and morphological abnormalities of the RV, electrocardiographic abnormalities, arrhythmias, and family history (9,10). Cardiac magnetic resonance (CMR) has been proposed as a valuable component of the diagnostic workup for ARVC/D (11). CMR frequently shows only minimal morphological and functional alterations that are not sufficient to diagnose ARVC/D. In the present study, we enrolled a selected group of subjects who

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Abbreviations and Acronyms

ARVC/D = arrhythmogenic right ventricular cardiomyopathy/dysplasia
CI = confidence interval
CMR = cardiovascular magnetic resonance
ECG = electrocardiogram
HR = hazard ratio
ICD = implantable cardiac-defibrillator
IRVT = idiopathic right ventricular tachycardia
LBBB = left bundle branch block
LV = left ventricle/ventricular
NYHA = New York Heart Association
PVC = premature ventricular complex
RV = right ventricle/ventricular
RVA = right ventricular abnormalities
VT = ventricular tachycardia
WM = wall motion

only had a history of PVCs, without other clinical, electrocardiographic, and echocardiographic criteria associated with ARVC/D. The aims of the study was to evaluate the relationship between RV abnormalities detected by CMR and the clinical end points of cardiac death, resuscitated cardiac arrest, and appropriate implantable cardiac-defibrillator (ICD) shock using a long-term follow-up.

Methods

Study population. Four hundred forty consecutive subjects with frequent PVCs of LBBB morphology and inferior axis on referring clinical exam of CMR from January 2002 to March 2005 were prospectively enrolled. In order to select patients with minimal confounding factors, the following inclusion criteria were applied: 1) 1,000 or more PVCs of LBBB morphology and inferior axis on 24-h Holter electrocardiogram (ECG) monitoring; 2) normal resting echocardiogram; 3) maximal exercise test negative for ischemia; 4) normal 12-lead rest electrocardiogram; 5) no familial history of sudden death; 6) no history of coronary artery disease, cardiomyopathy, systemic hypertension, or diabetes mellitus; and 7) absence of contraindications to CMR.

Patients with frequent PVCs or ventricular bigeminism during examination were treated with an oral antiarrhythmic agent (propafenone, flecainide, or amiodarone) for 1 week before CMR examination in order to optimize ECG trigger and to obtain optimal image acquisition.

Of the initial study population, 44 subjects were excluded for claustrophobia (n = 18), body dimension above the scanner diameter (n = 5), and very frequent PVCs despite antiarrhythmic drugs during CMR (n = 21). Thus, the final population included 396 patients (mean age 33 years, 257 males).

CMR. CMR examination was performed using a 1.5-T Signa CVi scanner (GE, Milwaukee, Wisconsin) with a cardiac phased-array 8-channel coil. For the assessment of regional wall motion (WM) and left ventricular (LV) and RV volumes and mass, cine images were used with a steady-state free precession (Fast Imaging Employing Steady-State Acquisition [FIESTA]) pulse sequence in short-axis views (from atrioventricular valve plane to the apex, 8-mm slice thickness, no gap) and in para-axial views (from diaphragm to the entire outflow tract, 5-mm slice thickness, no gap). The following acquisition parameters were applied: 30 phases, 10 to 25 views per segment depending on heart rate, NEX 1, FOV 40 cm, a matrix of 224 × 224, a 45° flip angle, TR/TE equal to 3.5/1.5, and a bandwidth of 125 kHz.

For the evaluation of fat infiltration, a fast spin echo image was acquired in the same short-axis view (8-mm slice thickness, no gap) and para-axial view (5-mm slice thickness, no gap) with the following parameters: NEX 1, FOV 40 cm, matrix of 256 × 256, a 90° flip angle, TR/TE of 1,791/41.5, and a bandwidth of 62.5 kHz. Fast spin echo images were also reacquired using a fat saturation pulse to selectively null signals from fat.

Post-processing. Using dedicated software (Mass Analysis, MEDIS, Leiden, the Netherlands), the following functional parameters were obtained from the short-axis images: RV and LV end-diastolic volume index, RV and LV end-systolic volume indexes, LV mass index, and RV and LV ejection fraction. The RV and LV volume indexes were compared with the respective reference values clustered for class age and sex (12,13). RV WM was evaluated by 2 independent expert investigators (G.D.A. and E.S.) from the short-axis and para-axial cine views and were classified as normal WM, minor WM abnormalities (hypokinetic segment), or major WM abnormalities (akinetic or bulging segment) (Fig. 1).

Similarly, fast spin echo images with and without fat saturation were evaluated by 2 independent expert investigators, and the signal from the RV wall was classified as follows: 1) normal signal if there was no evidence of hyperintense myocardium with infiltrative characteristics; or 2) signal alteration (myocardial area hyperintense in fast spin echo images and hypointense in fat saturation fast spin echo images) diffuse (more than 1 segment) if focal, but infiltrating or associated with wall thinning (Fig. 2).

Any discrepancies between the investigators were then independently adjudicated by a blinded third investigator (M.L).

Group definition. According to the Task Force diagnostic criteria for ARVC/D, CMR findings accepted as major diagnostic criteria are severe WM abnormalities (akinesia, bulging) and severe RV dilation with dysfunction (defined as mean end-diastolic volume index >4 SD above the mean reference value, and RV ejection fraction lower than 40%) (10). Minor CMR diagnostic criteria of ARVC/D are: mild WM abnormalities (hypokinesia), mild RV dilation defined as mean end-diastolic volume index >2 and <4 SD about the mean of the reference, or RV ejection fraction between 40% and 50%). Considering that all patients were positive for only a minor criterion (>1,000 PVCs in 24 h with LBBB morphology and inferior axis), the diagnosis of ARVC/D was based on the evidences of major or minor CMR criteria for ARVC/D. Therefore, on the basis of the presence or absence of these criteria, subjects were clustered in 2 groups: no-RVA group (patients without RV abnor-