Magnetic Resonance Imaging for the Etiology Diagnostics of Ventricular Arrhythmia

T. SIMOR, L. TOTH, K. PETRO, L. PAPP
Faculty of Medicine, Heart Institute, University of Pécs, Pécs, Hungary

I. REPA
Institute of Diagnostics, University of Kaposvár, Kaposvár, Hungary

Summary

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is among the major factors for mortality in young adults. Therefore, early diagnostics and institution of therapy, e.g. antiarrhythmics, radio frequency ablation, or implantable cardioverter/defibrillator, are unavoidable. Cardiac magnetic resonance imaging (MRI) is unique in the diagnosis of ARVD/C, since this non-invasive tool detects tissue-specific information with a simultaneous, direct measurement of the left- and right-ventricular function, regional wall motion abnormalities and morphology. A suitable T1 (spin-lattice relaxation time) sensitive MRI acquisition can differentiate pericardial, epicardial, and patchy or diffuse right ventricle lipid infiltration from the true myocardial tissue. We studied 31 patients with symptomatic ventricular arrhythmia with left bundle branch block morphology and a suspected diagnosis of ARVD/C. Only six out of 31 patients fulfilled the diagnostic criteria for ARVD/C. After a cardiac MRI, however, ARVD/C became evident in 16 and was excluded in 12 patients. Thus, a cardiac MRI is very effective in the assessment of ARVD/C. It is our opinion that cardiac MRI screening should be performed in all patients that have symptomatic ventricular arrhythmia with left bundle branch block morphology.

Key Words

Right ventricular dysplasia/cardiomyopathy, magnetic resonance imaging, arrhythmia

Introduction

The classification of cardiomyopathies was last revised in 1996. According to the new definitions and classifications, cardiomyopathies are divided into hypertrophic, dilated, and restrictive cardiomyopathies, as well as arrhythmogenic cardiomyopathies of the right ventricle (a new nosological entity), non-classified forms, and specific cardiomyopathies [1]. The wide clinical spectrum of arrhythmogenic right ventricular dysplasia/cardiomyopathies (ARVD/C), first described 23 years ago, appears to be the result of replacing most of the right ventricular myocardium with fatty/fibro-fatty tissue as well as genetic susceptibility to environmental agents (myocarditis) [2]. In the early stages of the disease, regional, and in late stages, diffuse fatty/fibro-fatty replacements, usually not involving the septum, are developed [3]. A familial history of ARVD/C is present in 30 % to 50 % of all cases, with the most common hereditary form being autosomal-dominant (chromosome 1, 3, 14), although an autosomal-recessive pattern has also been reported (chromosome 17 – palmoplantal keratosis – Naxos disease with 90 % familial history). A genetic test is currently not available.

Clinical diagnosis of ARVD/C is based on symptoms, right precordial ECG changes, right ventricular (RV) arrhythmias, and structural and functional RV abnormalities. Many cases are asymptomatic until first presentation of sudden death. A prospective investigation of sudden death involving the young in the region of

	Major	Minor
Family history	Familial disease confirmed at necropsy or surgery	Familial history of premature sudden death (age < 35 years) due to suspected RV dysplasia
ECG depolarization/conduction abnormalities	Epsilon waves or localized prolongation (110 ms) of the QRS complex in precordial leads V1, V2 or V3	Late potentials (signal averaged ECG)
ECG depolarization abnormalities		Inverted T waves in right precordial leads beyond V1 (age >12 years; RBBB absent)
Arrhythmias		NSVT or SVT; with LBBB from Holter ECG or stress testing; frequent VES (1000 in 24 h) with LBBB
Global and/or regional dysfunction and structural alterations detected by echocardiography, angiography, magnetic resonance imaging, or radionuclide scintigraphy	Severe dilatation and reduction of RV ejection fraction with no, or mild, LV impairment; localized RV aneurysms, i.e., akinetic/dyskinetic areas of diastolic bulging	Minor global RV dilatation; and/or ejection fraction reduction with normal LV; mild segmental RV dilatation; regional RV hypokinesia
Histology	Fatty/fibrofatty replacement of RV myocardium (endomyocardial biopsy)	

Table 1. McKenna's criteria [3] for the clinical diagnosis of right-ventricular dysplasia and cardiomyopathy. RV = right ventricle, EF = ejection fraction, NSVT = non-sustained ventricular tachycardia, SVT = sustained ventricular tachycardia, RBBB = right bundle branch block, LBBB = left bundle branch block. VES = ventricular extrasystole.

Venice, Italy showed that 20 % of fatal events in young people and athletes were due to previously undiagnosed ARVD/C. The other extreme are patients with congestive heart failure, with or without ventricular arrhythmias, who are often wrongly diagnosed as having dilated cardiomyopathy [4]. The most striking morphological feature of ARVD/C is the diffuse or segmental lack of myocardium in the RV free wall, which is replaced by fatty or fibro-fatty tissue. Usually subendocardial layers are preserved, in which some myocardium appears to be interspersed with fibrosis. Patchy acute myocarditis with myocyte death and focal round cell inflammatory infiltrates (mainly lymphocytes) is present in 66 % of cases. The purely adipose form of ARVD/C is characterized by partial/focal or diffuse replacement of the RV wall by fatty tissue, predominantly in the apex and infundibulum, in the absence of fibrosis and inflammatory infiltrates. The fibro-fatty form was the original type of description, characterized by fibrosis that either borders or is embedded with cardiomyocytes, RV-wall thinning with aneurysmal dilatation and inflammatory infiltrates. Aneurysms typically affecting inflow, apical, and outflow portions of the RV ("triangle of dysplasia") have been reported in 50 % of the cases in the autopsy series. In this variant, the left ventricle (LV) and, more rarely, the ventricular septum may be involved to a lesser extent [4].

Clinical diagnosis of ARVD/C is fulfilled in the presence of the major and minor criteria shown in Table 1 [3]. Thereby, two major, or one major and two minor, or four minor criteria indicate ARVD/C. The clinicopathological phases [4] are

- the concealed phase, characterized by slight RV structural changes, with or without minor ventricular arrhythmias, during which sudden death may occasionally be the first manifestation of the disease;
- the observable electrical disorder phase with symptomatic RV arrhythmias (may cause cardiac arrest) that are associated with RV functional and structural abnormalities;
- RV failure due to progression and extension of RV myocardial disease inducing global RV dysfunction with relatively preserved LV function;
- the final stage of biventricular pump failure due to significant LV involvement [5]. At this stage, ARVD/C mimics biventricular dilated cardiomyopathy.

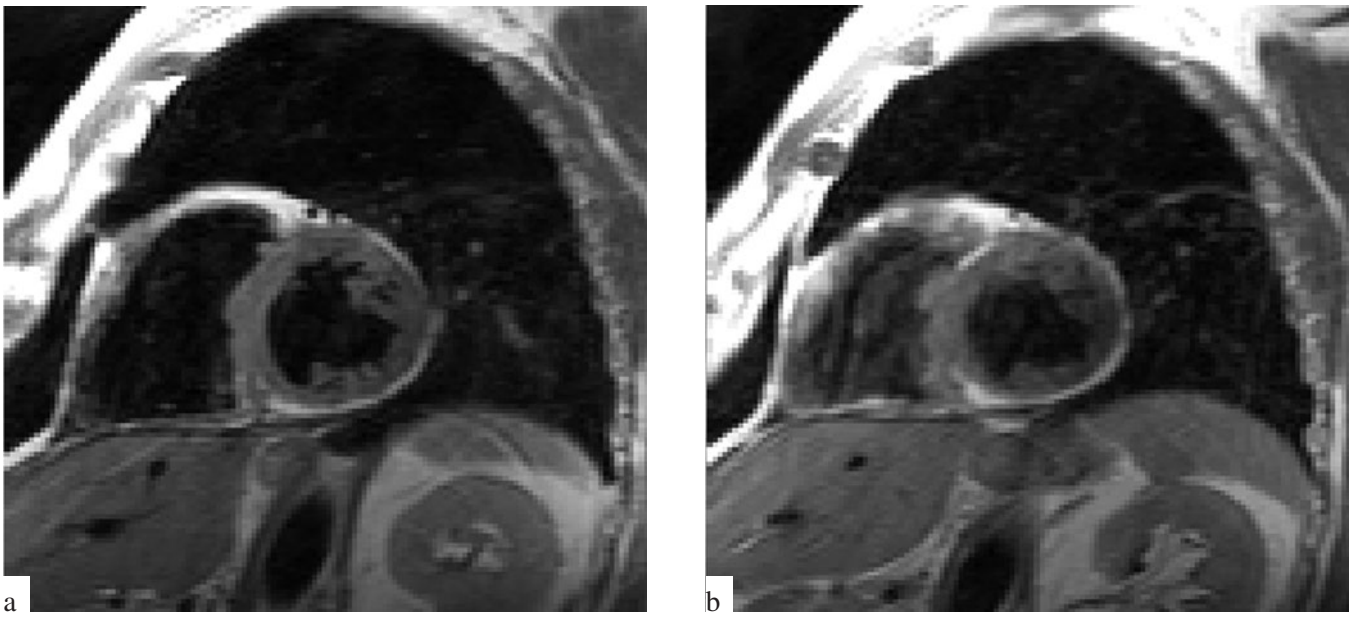

Figure 1. Magnetic resonance imaging: ECG-gated, 15 heartbeats long breath holding, double IR TSE short axis view images of a patient having a dilated right ventricle and normal left ventricular size. Note the epicardial and pericardial increase of the signal intensity and the patchy high regions of the signal intensity in the right ventricular free wall. Also note the antero-septal and postero-septal (left-ventricular epicardial, right-ventricular subendocardial) lipid infiltration signals in the more apical image (panel b) which is not visible 6 mm above (panel a). The patient is a 45-year old man having ventricular tachycardia with left bundle branch block morphology, epsilon wave in the precordial leads, positive echocardiography, and right ventricular angiography. IR = inversion-recovery, TSE = turbo spin echo.

Cardiac magnetic resonance imaging (MRI) is capable of providing high-resolution tissue specific information of ARVD/C, since the spin-lattice relaxation time (T1) values of lipid and heart muscle signals differ almost 10-fold. Thus, a suitable T1-sensitive MRI acquisition can differentiate pericardial, epicardial and patchy, or diffuse, RV lipid infiltration from the true myocardial tissue. Cardiac MRI is unique in the diagnosis of ARVD/C, since this non-invasive tool detects tissue-specific information with a direct measurement of cardiac function [6-10]. The following MRI criteria were employed for the ARVD/C diagnosis [11]:

- the presence of high signal intensity areas indicating the substitution of fat for myocardium,
- ectasy of the right ventricular outflow tract,
- dyskinetic bulges,
- dilatation of the right ventricle,
- enlargement of the right atrium (RA).

ARVD/C is indicated by MRI alone if at least three criteria are fulfilled [5].

Materials and Methods

The special MRI abbreviations used in this paragraph-stand for: TR = repetition time; time between two radiofrequency excitation pulses; FOV = field of view, size of the imaged slice; TE = echo time; IR = inversion-recovery; TSE = turbo spin echo; T1 = spin-lattice relaxation time, K-space = Fourier space, data matrix which contains the digitized information of all the signals.
A 1.5-Tesla magnetic resonance imager (Vision Plus, Siemens, Germany) equipped with a phase array body coil was used for cardiac imaging. Prospective ECG triggering, TR of 85 % of the RR interval, no signal average, slice thickness of 6 mm with no interslice gap, FOV of 45 cm and 256 x 256 image matrix were set during each acquisition. MRI cine technique was used with an ECG-gated, breath holding for 19 heartbeats, segmented K-space sequence with TR/TE/flip angle of 341 ms/4.8 ms/20 degrees and 40 ms time resolution within the heart cycle. The standard long axis planes – four-chamber view, two-chamber views showing aorta and anterior and posterior left ventricular wall – were set rotating around the long axis of the left ventricle.

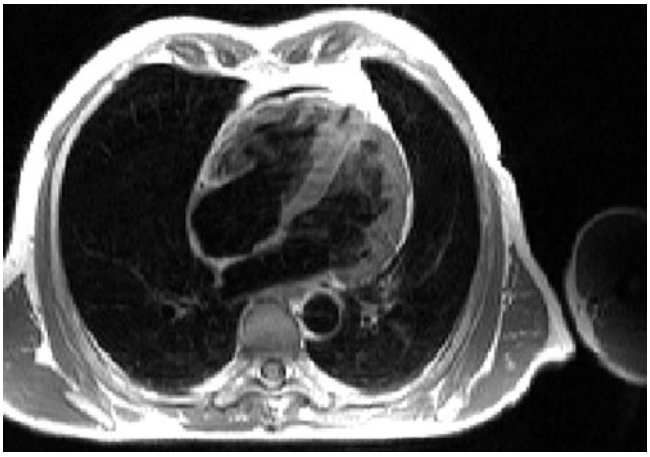

Figure 2. Magnetic resonance imaging: ECG-gated, 15 heartbeats long breath holding, double IR TSE four chamber view image of a patient having a dilated right atrium and right ventricle. Note the normal left atrial and left ventricular size. IR = inversion-recovery, TSE = turbo spin echo.

Separately, the long axis view was set for the entire right heart. Finally, consecutive, contiguous short axis slices (8 mm slice thickness) from the great vessels to the apex of the heart were acquired to visualize the whole heart. Each acquisition, i.e., each breath holding took approximately 20 s, and thus the acquisitions for the four long axis and 15 short axis slices were collected in 15 min. An ECG-gated, T1-weighted, breath holding for 15 heartbeats, double IR (flip of 160°) TSE, segmented K-space sequence with TR/TE of 700 – 1000 ms/32 ms was used for dark blood, morphology imaging, while using the same anatomical positions as during time resolved MRI. The latter acquisition took an additional 10 min.

From October 1999 to January 2001, 31 patients (19 men and 12 women; mean age 33.4 years; range 8 to 65 years) with a suspected diagnosis of ARVD/C were studied. Only six out of 31 patients fulfilled McKenna's criteria (Table 1), but all patients showed symptomatic ventricular arrhythmia with left bundle branch block morphology. Three groups of patients were created:

- MRI negative, where not even patchy MRI signal intensity increase was present in the right ventricular free wall in the T1-weighted image;
- MRI positive, where patchy (single or multiple) MRI signal intensity increase was present infiltrating across the right ventricular free wall;
- patients in whom the study could not be evaluated due to technical problems (primarily irregularities in the heart rhythm).

Results

None of our patients showed an increased size of the left atrium (LA) and LV. MRI was negative in 16 cases. However, RA and RV were dilated in four patients out of the latter 16 and therefore fulfilled McKenna's criteria. ARVD/C became evident in 12 other patients (McKenna's criteria fulfilled). These latter 12 patients showed positive MRI results (Figures 1 and 2):

- in seven patients, the apex of the RV,
- in two cases, the mid portion of the RV (two to three spots) and the inter-ventricular septum,
- in one patient, a single spot in the mid portion of the RV, and
- in two patients, the RV outflow tract showed patchy rises in MRI signal intensity.

MRI cine technique in this group showed
- dilated RA and RV in three patients,
- dyskinetic RV wall motion in two patients,
- and ectatic RV outflow tract in two patients.

From these findings, as compared to the classification of Corrado [4],

- five MRI-positive and 12 MRI-negative patients would correspond to the concealed phase
- four MRI-positive and four MRI-negative patients to the observable electrical disorder phase with symptomatic RV arrhythmias, functional and structural abnormalities, and
- three MRI-positive patients to the RV muscle disease phase inducing global RV dysfunction.
- The last three patients even fulfilled the MRI criteria of Midiridi [11], i.e. MRI alone provided the diagnostic criteria for ARVD/C.

Conclusion

Cardiac MRI is very important in the diagnosis of ARVD/C, since it detects tissue specific information

with a simultaneous, direct measurement of LV and RV function, regional wall motion abnormalities and morphology.

It is our plan to collect and compare more clinical data sets (MRI, ECG, Holter, stress testing, electrophysiology mapping, echocardiography, RV angio-graphy) to optimize our diagnostic and therapeutic (pharmacological treatment, ablation, ICD) strategies in ARVD/C. In our opinion, cardiac MRI screening should be performed in all patients having symptomatic ventricular arrhythmia with left bundle branch block morphology.

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Contact
Tamás Simor, MD, PhD
University of Pécs
Faculty of Medicine
Heart Institute
Ifjuság u. 13
H-7624 Pécs
Hungary
Telephone: +36 72 536001/5303
Fax: +36 72 536399
E-mail: tamas.simor@aok.pte.hu