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Original article

Arrhythmogenic Cardiomyopathy. Patterns of Ventricular Involvement Using Cardiac Magnetic Resonance

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ABSTRACT

Introduction and objectives: Biventricular arrhythmogenic cardiomyopathy and left dominant arrhythmogenic cardiomyopathy forms had recently been included in the spectrum of arrhythmogenic cardiomyopathy. The aim of the study was to describe, using cardiovascular magnetic resonance, the patterns of ventricular involvement as well as late gadolinium enhancement in these conditions.
Methods: Medical databases and records from the cardiology units of 3 hospitals were reviewed to obtain data from patients with arrhythmogenic cardiomyopathy.
Results: Twenty-six consecutive patients were included (40 [16] years, 16 males). Right ventricle involvement was present in 19 patients (73%). Among them, 13 patients (50%) had volumes over the upper limit of normality, 11 (42%) patients had late gadolinium enhancement in right ventricle and 6 patients (23%) had just mild involvement with wall motion abnormalities or microaneurysms. Left ventricle involvement was present in 24 patients (92%), all of them with late gadolinium enhancement. In 15 patients (57%) left ventricular systolic dysfunction was observed, and dilatation in 3 patients (11%). Late gadolinium enhancement was more frequent in the inferior, lateral, and inferolateral walls (65%, 57%, and 61% of patients, respectively) while septum was seldom affected (26% of cases). The pattern of late gadolinium enhancement was mainly subepicardial (46% of patients) or transmural (19%), and was intramyocardial in only 12% of the cases.
Conclusions: In this sample, left ventricle involvement is very common. The most frequent finding was late gadolinium enhancement, while the least frequent was dilatation. The pattern of late gadolinium enhancement was more frequently subepicardial and located in the inferior and inferolateral walls.

Resonancia magnética cardiaca en miocardiopatía arritmogénica. Tipos de afección y patrones de realce tardío de gadolinio

Palabras clave:
Miocardiopatía arritmogénica
Cardiorresonancia magnética
Realce tardío de gadolinio

RESUMEN

Introducción y objetivos: La miocardiopatía arritmogénica biventricular y la miocardiopatía arritmogénica izquierda han sido incluidas recientemente en el espectro de la miocardiopatía arritmogénica. El objetivo del estudio es describir con cardiorresonancia magnética el tipo de afección observada y describir los patrones de realce tardío de gadolinio.
Métodos: Se revisaron las bases de datos y la historia clínica informatizada de tres hospitales, para obtener datos de enfermos consecutivos con miocardiopatía arritmogénica.
Resultados: Se incluyó a 26 pacientes consecutivos, con una media de edad de 40 ± 16 años, de los que 16 eran varones (67%). Se observó afección de ventrículo derecho en 19 pacientes (73%), con volúmenes aumentados en 13 pacientes (50%), 11 pacientes (42%) con realce tardío de gadolinio en ventrículo derecho y 6 (23%) presentaban únicamente alteraciones de la contractilidad segmentaria. Se observó afección de ventrículo izquierdo en 24 pacientes (92%), todos con realce tardío de gadolinio; 15 pacientes (57%) presentaron disfunción sistólica ventricular izquierda. En 3 pacientes (11%) se observó dilatación de ventrículo izquierdo y ninguno de ellos fue diagnosticado de miocardiopatía arritmogénica izquierda. La localización del realce tardío de gadolinio fue predominantemente inferior (65%), inferolateral (61%) y lateral (57%), mientras que la localización septal fue menos frecuente (26%). El patrón de realce tardío de gadolinio fue fundamentalmente epicárdico (46%) y transmural (19%), raramente intramiocárdico (12%).
Conclusiones: En esta muestra, la afección del ventrículo izquierdo es muy frecuente; el hallazgo observado en el mayor número de pacientes fue el realce tardío de gadolinio y el menos frecuente, la

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dilatación. El patrón de realce tardío de gadolinio es subepicárdico y afecta a territorios inferior, inferolateral y lateral.

Abbreviations

AC: arrhythmogenic cardiomyopathy
BVAC: biventricular arrhythmogenic cardiomyopathy
LDAC: left-dominant arrhythmogenic cardiomyopathy
LGE: late gadolinium enhancement
RDAC: right-dominant arrhythmogenic cardiomyopathy

INTRODUCTION

In arrhythmogenic cardiomyopathy (AC), myocardial tissue is replaced with fatty and fibrous tissue, initially in the epicardium. This process usually affects the regions posterior and inferior to the right ventricle (RV) entry tract, adjacent to the tricuspid valve. The infiltrate is an electrically unstable substrate that produces phenomena ranging from isolated ventricular extrasystoles to sustained ventricular tachycardia or ventricular fibrillation.[1]

Within the spectrum of AC, biventricular arrhythmogenic cardiomyopathy (BVAC) and left-dominant arrhythmogenic cardiomyopathy (LDAC) phenotypes have been reported.[2]

The introduction of cardiac magnetic resonance imaging (cMRI) in clinical practice has significantly improved assessment of the RV. This imaging technique is the most accurate and reproducible for quantifying volumes and biventricular function. Likewise, detection of late gadolinium enhancement (LGE) after administration of gadolinium-DPTA (gadopentate dimeglumine) acid represents progress in the characterization of myocardial tissue in a number of diseases.[3]

Recent data indicate the importance of LGE for identifying fibroadipose lesions. Tandri et al.[4] first reported the clinical usefulness of these sequences in AC. These investigators found LGE in the myocardium of the RV in 67% of patients with this condition, and this was associated with inducible monomorphic ventricular tachycardia in electrophsyiologic studies.

Subsequently, Sen-Chowdhry et al.[5] demonstrated that finding LGE in the left ventricle (LV) allows a more sensitive and specific diagnosis than LGE in the RV. Recently, an update of the Task Force diagnostic criteria has been published[6] and these now include genetic diagnosis. With the new criteria, more patients with LDAC will be diagnosed. Little has been published with regard to the clinical usefulness of LGE in the LV for diagnosis of AC and particularly in left phenotypes, and therefore it was not included in the 2010 diagnostic criteria.

The objectives of the present study were therefore to describe the type of disease observed with cMRI in patients with AC, describe the prevalence and patterns of LGE, and establish a scoring system to enable a structured diagnosis of the different phenotypes.

METHODS

This was a retrospective study of the databases of the cMRI units (Filemaker Pro, version 8.1, United States) of 3 hospitals (*Hospital Clínico Universitario, Hospital Universitario La Fe, Hospital General Universitario de Valencia*) between 2006 and 2010, and subsequently the computerized medical records of the patients selected from these databases.

Entries compatible with AC were selected from the databases of the cMRI units. The computerized medical records were then examined to extract clinical data (form of presentation, presence of arrhythmias, electrocardiographic [ECG] findings, and Holter-ECG monitoring).

Of the 5685 entries reviewed, 32 had suspected AC. In 6 of these, there was no conclusive clinical diagnosis and they were excluded (3 with severe dilatation and RV dysfunction, 2 with segmental contraction abnormalities and mild RV dysfunction, and 1 with RV segmental contraction abnormalities only).

Scoring System Biventricular Involvement

A scoring system for biventricular involvement was drawn up to define the distribution of morphological characteristics and to establish a structured diagnosis of the different phenotypes. To calculate the score, it was first necessary to diagnose single-ventricular involvement (LDAC or right-dominant arrhythmogenic cardiomyopathy [RDAC]) or biventricular involvement from examination of cMRI images. Subsequently, the following was assessed for both ventricles: segmental contraction abnormalities, ventricular dilatation, systolic dysfunction, and LGE.

If these characteristics were observed in the LV, they counted as -1 whereas if they pertained to the RV they counted as –1. The score was obtained by summing all individual components (Table 1). Thus, the presence of balanced characteristics in both ventricles yielded an overall score of 0, that is, purely biventricular involvement, whereas negative values or positive values corresponded to prominently left or right involvement, respectively. For example, LDAC diagnosed only by LGE in the LV would have a score of –1, as would BVAC with segmental contraction abnormality in the RV, LGE in the LV, and systolic dysfunction in the LV. To differentiate between them, they would be denominated BVAC with a score of –1 or an LDAC with a score of –1. The score comprised the diagnosis of single-ventricular or biventricular involvement based on inspection of the cMRI images (LDAC, RDAC, or BVAC) along with the score obtained. This score is not an indicator of severity but rather a morphological indicator of ventricular predominance that enables a structural definition of purely biventricular involvement (score 0), biventricular involvement with left or right predominance (any score other than 0), and single-ventricular forms with limited involvement (score 1, 2, –1, or –2) or multiple characteristics of involvement (score –3, –4, 3, or 4).

Table 1
Morphologic Score of Ventricular Predominance (Sum of Morphological Characteristics)

	LV	RV
Segmental contraction abnormalities	–1	1
Ventricular dysfunction	–1	1
Dilatation	–1	1
Late gadolinium enhancement	–1	1

LV, left ventricle; RV, right ventricle.

Diagnosis

Patients with cMRI compatible with AC and clinical diagnosis of AC were included in the study.

In patients with LDAC or left-dominant BVAC, clinical diagnosis was made by the presence in the cMRI of an epicardial pattern of LGE in the LV with a familial history of the condition in first-degree relatives. The index cases (3 patients in total) that were assessed after sudden death resuscitation or sustained ventricular tachycardia (2 patients) or exercise-induced syncope (1 patient) had LGE and the same involvement in a first-degree relative, but genetic confirmation was considered necessary for clinical diagnosis. We currently have genetic confirmation in all cases of LDAC and 4 cases of BVAC.

Cardiac Magnetic Resonance Imaging

The cMRI studies were performed by 5 cardiologists dedicated to MRI and who had extensive experience in the field.

After inclusion, the studies were reassessed by 2 observers who agreed on the diagnosis with respect to the qualitative variables.

Intraclass correlation coefficients (ICCs) were calculated. Interobserver agreement was investigated by randomly selecting 11 patients from the sample to be reassessed by 1 of the participating cardiologists. The following values were recorded: left ventricular ejection fraction (LVEF) (ICC=0.92; confidence interval [CI], 0.8-0.9), right ventricular ejection fraction (RVEF) (ICC=0.7; CI, 0.3-0.9), left ventricular end-diastolic volume (LVEDV) (ICC=0.83; CI, 0.5-0.9), and right ventricular end-diastolic volume (RVEDV) (ICC=0.72; CI, 0.4-0.9). Segmental contraction abnormalities and the presence of LGE in the LV had an interobserver κ of 0.83 and 0.74, respectively ($P<.01$); the presence or absence of LGE in the RV had a κ of 0.5 ($P=.05$) and RV segmental contraction abnormalities a κ of 0.8 ($P<.01$).

The studies were conducted with a 1.5 T system (Magnetom Avanto or Magnetom Sonata), Syngo MR 2004 V version (Siemens Medical Solutions, Erlangen, Germany).

The protocol followed included 3 sequences:

1. Cinematic sequences: True FISP (true fast imaging with steady-state precession sequence), repetition time 2.8 ms, echo time 1.2 ms, flip angle 58°, matrix 225×192, field of view 370 mm to 270 mm, segmented while holding breath, with retrospective ECG synchronization, obtained in 2-chamber view, LV outlet tract, 6 to 8 slices of the RV outlet tract (slice thickness, 8 mm with no space between slices), and 6 to 8 slices along the short axis taken sequentially from base to apex (slice thickness, 8 mm, with 2 mm between slices), and 6 to 8 slices of 4-chamber views (slice thickness, 8 mm with no space between slices).
2. Morphologic sequences: TSE T1–repetition time, 70 ms; echo time, 26 ms; field of view 340×81, matrix 256×192, and the same sequence at the same site with fat saturation pulse; TSE T2–repetition time, 800 ms; echo time, 81 ms; matrix 256×192, in the same site as the functional sequences (slice thickness, 8 mm with 2 mm between slices).
3. Viability sequences: segmented Turbo FLASH (turbo fast low angle shot); repetition time, 700 ms; echo time, 1.55 ms; flip angle, 45°; matrix 256×192; field of view, 340 mm to 78 mm; slice thickness, 8 mm with 2 mm between slices, 2 R-R. In the same views as the functional cinematic sequences, acquired 5 min to 8 min after bolus administration of 0.1 mol/kg of gadolinium-DTPA via a peripheral vein.

The volume and ejection fraction data for both ventricles were analyzed using MASS software (QMass MR 6.1.5 for Windows) from Medis.

Genetic Study

Patients from 1 of the participating centers (*Hospital Universitario La Fe*, n=11) were included in a genetics study, with prior approval of the ethics committee of the hospital and approval for each of the participants. Thus, the proband (the most symptomatic patient or the one with most severe disease within a family) was screened for mutations using conventional sequencing (ABI Prism 3100 sequencer, Applied Biosystems) of exon and intron regions adjacent to the 4 main desmosome genes: plakoglobin, plakophilin-2, desmoglein-2, desmocollin-2, and desmoplakin in DNA from peripheral blood.

Causal mutations were considered as those genetic variants previously identified as such and new ones that caused relevant changes in the protein structure and showed cosegregation with the familial phenotype.

Once 1 or more mutations had been identified in a proband, other first-degree relatives were screened for the same mutations. The presence of mutations identified previously in the proband was considered a positive confirmatory result.

Statistical Analysis

The following variables were analyzed:

1. The indexed end-diastolic volumes of both ventricles were considered abnormal as follows[6,7]: an RVEDV index >100 mL/m^2 and an LVEDV index> 98 mL/m^2.
2. A LVEF< 55%[7] and RVEF <40%, which is the quantitative figure obtained from cMRI that is considered a major diagnostic criterion for AC, in presence of segmental contraction, according to the 2010 Task Force criteria.[6]
3. The presence or absence of segmental contraction abnormalities in both ventricles. The following were considered abnormalities in the RV: aneurysms (extensive areas of narrowing of the wall with increased systolic volume or dyskinesia) and microaneurysms (small areas that protrude from the RV wall during diastole with asynchronous movement during systole).
4. Presence of LGE in either ventricle.
5. Presence of fatty infiltrates in either of the 2 ventricles.
6. LGE pattern (epicardial, transmural, intramyocardial, or mixed).
7. LGE site (inferior, septal, anterior, lateral, or inferolateral).

Table 2
Clinical Data of the Study Population

	RDAC	LDAC	BVAC
Reason for study, no. (%)	2	5	19
Family study		5 (100)	4 (21)
Clinical	2 (100)		15 (78)
Syncope	1 (50)		5 (26)
Palpitations	1 (50)		1 (5)
Dyspnea			1 (5)
Sudden death resuscitation or SVT			8 (42)
Males, no. (%)	2 (100)	1 (20)	14 (74)
Age, years	(32-43)	44 (13-68)	38 (11-60)
Meet TFC	2 (100)	3 (60)	13 (68)
1994 criteria	2 (100)		7 (37)
2002 criteria, relatives		1 (20)	4 (21)
2010 criteria		2 (40)	2 (10)

BVAC, biventricular arrhythmogenic cardiomyopathy; LDAC, left-dominant arrhythmogenic cardiomyopathy; RDAC, right-dominant arrhythmogenic cardiomyopathy; SVT, sustained ventricular tachycardia; TFC, Task Force Criteria.

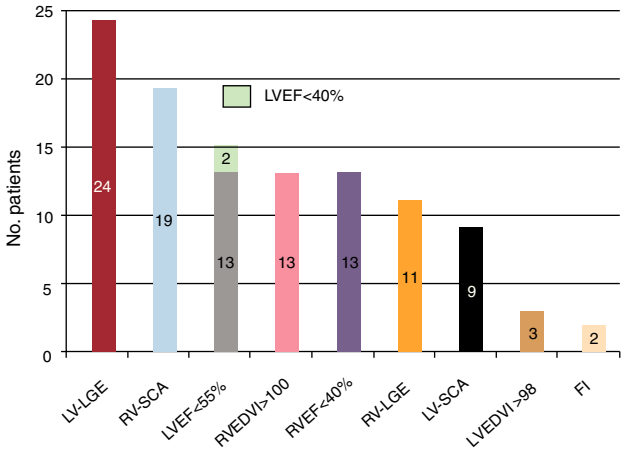

Figure 1. Frequency of morphological characteristics in the sample. FI, fatty infiltration of right ventricle; LVEDVI, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LV-LGE, left ventricular late gadolinium enhancement; LV-SCA, left ventricular segmental contraction abnormalities; RVEDVI, right ventricular end-diastolic volume index; RVEF, right ventricular ejection fraction; RV-LGE, right ventricular late gadolinium enhancement; RV-SCA, right ventricular segmental contraction abnormalities.

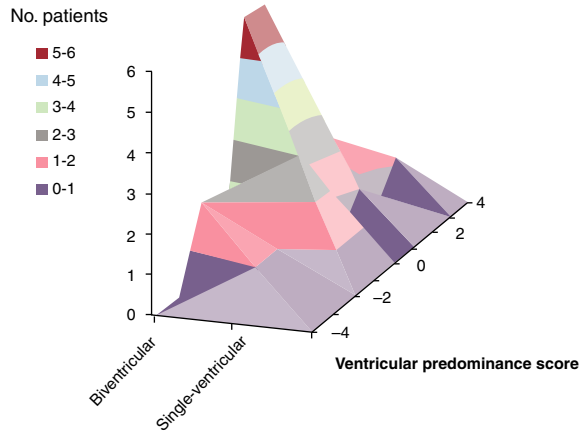

Figure 2. Distribution of patients according to score for biventricular involvement.

The statistics package SPSS 15.0 was used for the analysis. Qualitative variables were expressed as means (SD) and qualitative ones as percentages. The Kolmogorov-Smirnov test was used to test the normal distribution of the score.

RESULTS

Twenty-six consecutive patients with diagnosis of AC were included; 67% were male and the mean age was 40 (16) years.

Table 2 shows the data on clinical presentation of the patients according to the different AC phenotypes and the percentage of patients who met the Task Force Criteria (1994,[8] 2002,[9] and 2010[6]) according to the information in the medical records.

Eight patients were admitted after sudden death resuscitation or sustained ventricular tachycardias and admission to hospital occurred in BVAC, without RV dilatation or dysfunction in 3 cases (38%).

Analysis of the Morphological Characteristics of the Sample

RV involvement was observed in 19 patients (73%). Of these, 13 patients (50%) had RV dilatation and dysfunction and 6 (23%) had only mild involvement, with aneurysms or microaneurysms. We observed LGE in the RV in 11 patients (42%). Fatty infiltration in the RV was only observed in 2 patients (7%). No such infiltration was observed in the LV.

LV involvement was observed in 24 patients (92%), all with LGE in the LV. Of these, 15 patients (57%) had systolic dysfunction and in 2 cases the LVEF was less than 40%. We also observed LV segmental contraction abnormalities in 9 patients (34%). In 3 patients (11%), left ventricular dilatation was observed, and

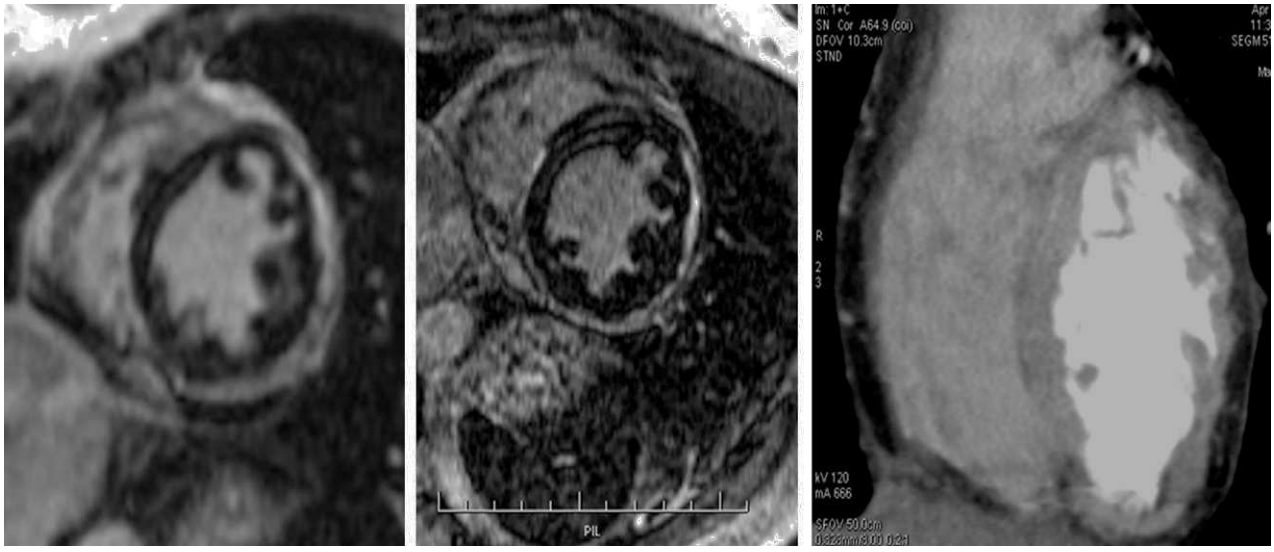

Figure 3. Left ventricular arrhythmogenic cardiomyopathy. Turbo FLASH viability images obtained in cuts along the short axis at the basal level with fatty saturation (central image) and without fatty saturation (left image) and multiplanar reconstruction of multislice computed tomography images to obtain a slice of the basal short axis, in which an undulating epicardial border is observed indicative of fibroadipose epicardial infiltration.

none of these had been diagnosed with LDAC. The number of patients with each of the anatomical characteristics is shown in Figure 1.

There was an inferior LGE in the LV site in 17 patients (65%), inferolateral in 16 (61%), and lateral in 15 (57%). The least common site of infiltration was septal, occurring in 7 patients (26%).

The LGE was epicardial in 12 patients (46%), transmural in 5 (19%), and intramyocardial in 3 (11%); 4 patients (15%) showed mixed enhancement, epicardial and transmural.

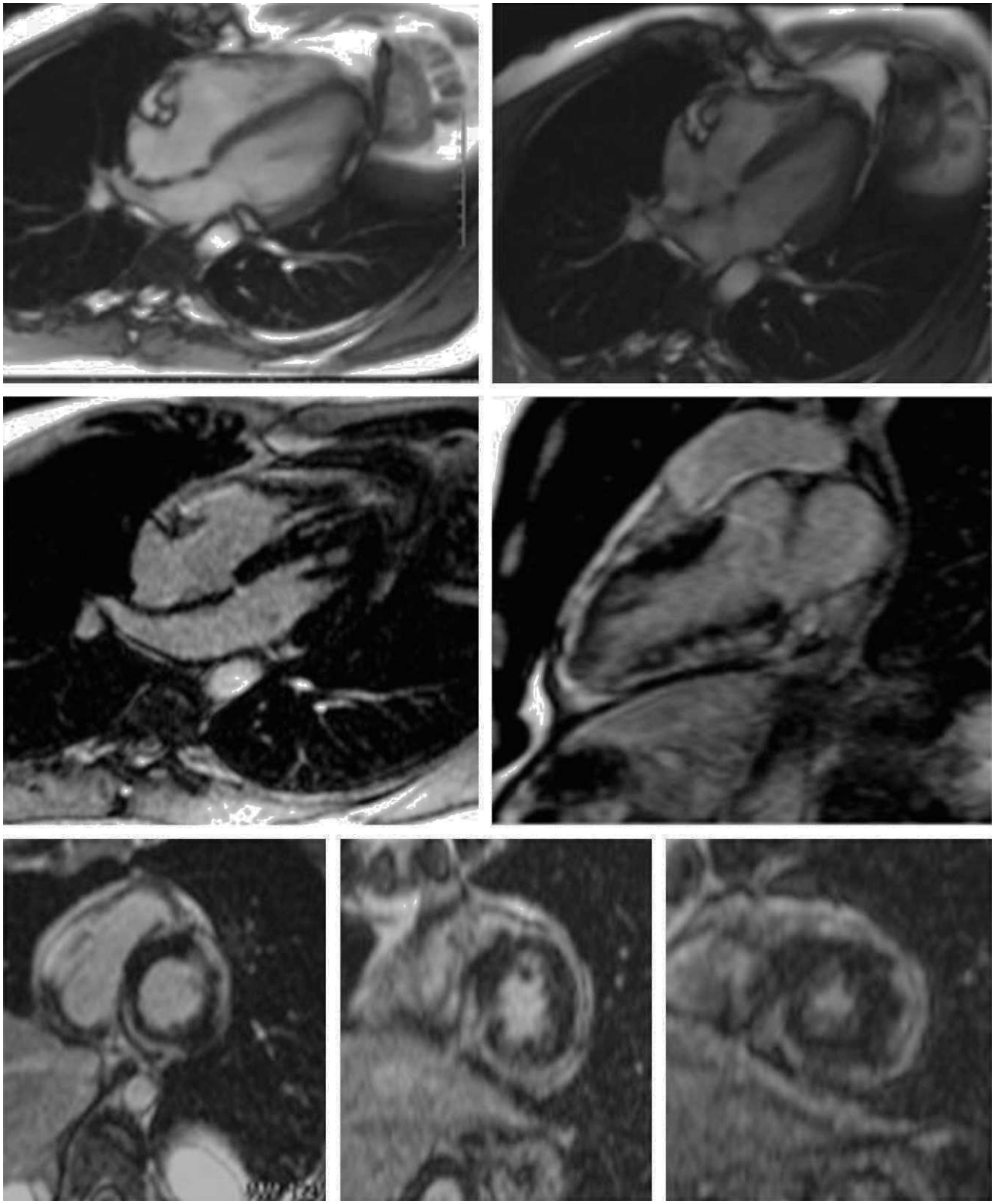

Figure 4. Left ventricular arrhythmogenic cardiomyopathy. True FISP cinematic images in the 4-chamber view during systole and diastole (upper row) and viability images (center and lower row) in 2- and 4-chamber views and along the short axis, showing both ventricles with normal volumes. Subtricuspid aneurysm in the right ventricle with late gadolinium enhancement. Pattern of severe late epicardial gadolinium enhancement on the inferior, inferolateral, and lateral walls of the left ventricle.

Phenotype Analysis by Score

The mean (SD) score obtained was 0.46 (1.6). Diagnosis of anatomic subtypes was established according to single or biventricular involvement and score. The distribution of the scores is shown in Figure 2. We observed 7 patients (26%) with single-ventricular involvement, 5 patients with LDAC, 4 with few characteristics of involvement (score −1, −2), and just 1 patient with multiple characteristics of involvement (LV segmental contraction abnormalities, mild dysfunction, and LGE [score −3]) (video 1). Of the 2 patients with RDAC, 1 had few characteristics of involvement (score 2) and the other had multiple characteristics (score 4).

There were 19 patients (73%) with biventricular involvement (BVAC): 6 (23%) with pure BVAC (score 0) (video 2), 2 patients with left predominance (score −2), and 11 patients with right predominance, which was mild in 6 cases (score 1).

The most frequently observed phenotype was BVAC with right predominance (video 3), observed in 11 patients (42%), followed by pure BVAC in 6 (23%) and LDAC in 5 (19%). The least common phenotypes were RDAC and BVAC with left predominance, accounting for 2 patients each.

Analysis of Characteristics According to Phenotypes

Within the LDAC phenotype (5 patients) (Fig. 3), the most frequently observed characteristic was presence of epicardial LGE in the LV, observed in all cases, followed by mild LV dysfunction in 2 patients and LV segmental contraction abnormalities in 2 patients.

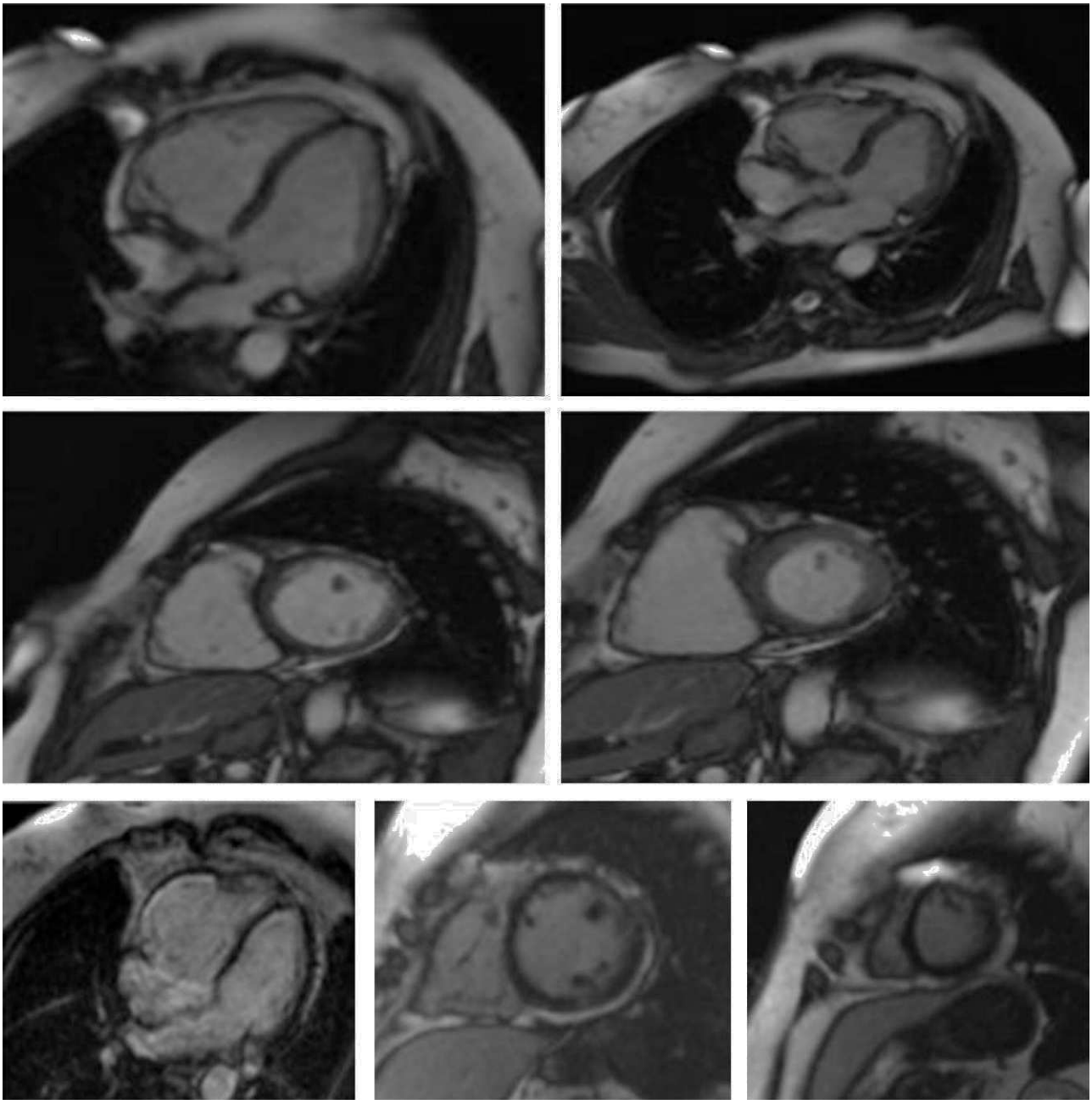

Figure 5. Right ventricular arrhythmogenic cardiomyopathy. True FISP cinematic images (upper and center rows) in the 4-chamber and basal short-axis view during systole and diastole and Turbo FLASH viability images (lower row), showing a dilated right ventricle with subtricuspid aneurysm.

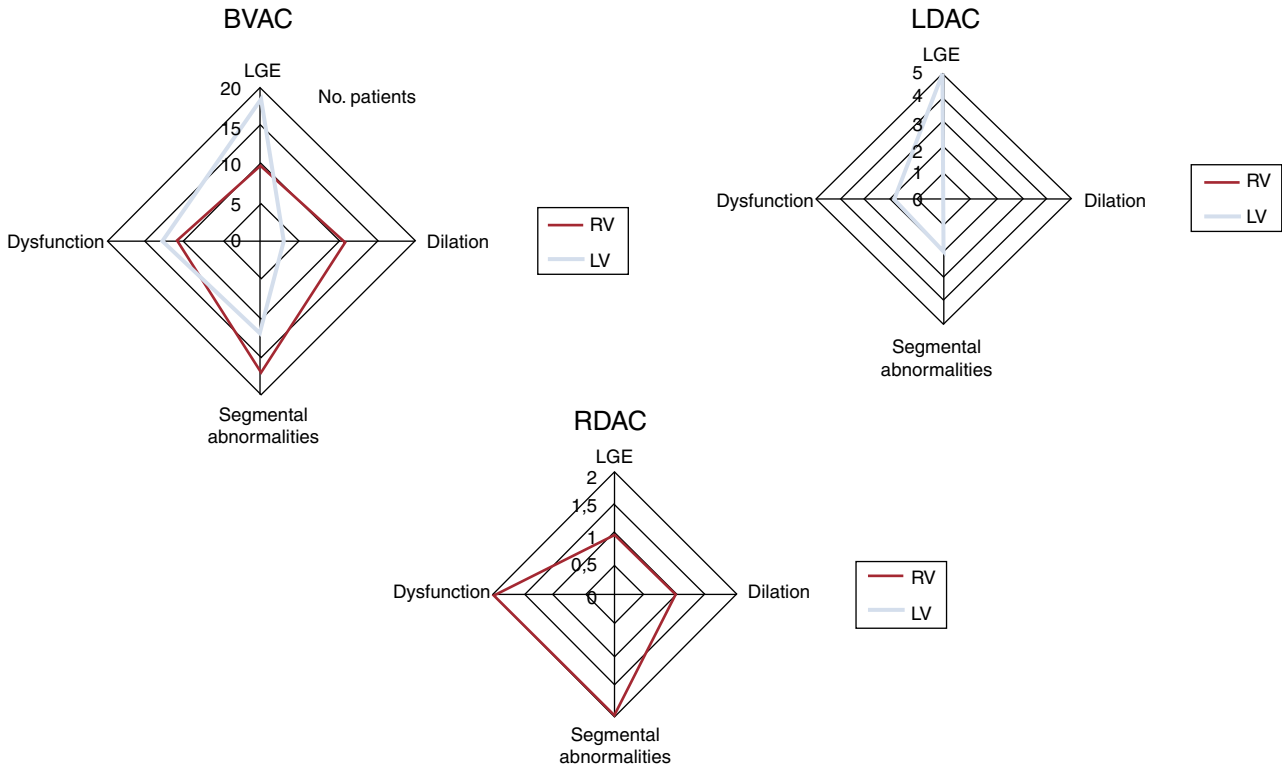

Figure 6. Distribution of characteristics according to phenotypes. The different values show the patients affected in each group. BVAC, biventricular arrhythmogenic cardiomyopathy; LDAC, left-dominant arrhythmogenic cardiomyopathy; LV, left ventricle; LGE, late gadolinium enhancement; RDAC, right-dominant arrhythmogenic cardiomyopathy; RV, right ventricle.

In the BVAC phenotype (19 patients) (Fig. 4), the characteristic most frequently observed was presence of LGE in the LV in all cases, followed by RV segmental contraction abnormalities in 17 patients, LV dysfunction in 13, RV dysfunction in 11, increased RV volume in 12, LGE in the RV in 10, and LV dilatation in 3.

In the RDAC phenotype (2 patients) (Fig. 5), we observed segmental contraction abnormalities and RV dysfunction in 2 patients and RV dilatation and LGE in 1 patient. Figure 6 shows the distribution of characteristics according to phenotype.

Genetic Study

Genetic study was performed for 11 patients (42%), of whom 5 had been diagnosed with LDAC and 6 with BVAC. Mutations in desmoplakin were observed in 6 patients; 2 patients had double mutations (desmoplakin and desmocollin variant), and 1 patient had a mutation of a desmoplakin variant and a plakophilin-2 mutation. Finally, in 2 patients diagnosed with BVAC, no confirmatory mutation was found.

DISCUSSION

The most common finding in our sample was the presence of epicardial LGE in the inferior, inferolateral, and lateral walls of the LV (92%). In a significant number of patients (62%), LV systolic dysfunction was observed, but this involvement was mild, and only in 2 patients was the ejection fraction below 40%. In our series, LV dilatation was reported less frequently, and was observed only in those patients with severe biventricular involvement. The LV involvement was not associated with severe dilatation or dysfunction, but rather with abnormalities that were difficult to detect with conventional echocardiographic techniques, although clearly clinically relevant, as studies have identified these as among the most powerful predictors of sudden death and/or recurrence of ventricular arrhythmias.[10–12]

Houlot et al.[13] prospectively studied a cohort of 130 patients and identified right heart failure and presence of LV dysfunction as independent risk factors for cardiac death.

Of the patients who experienced resuscitated sudden death or sustained ventricular tachycardia in our sample, 38% occurred in biventricular phenotypes, with no increases in RV volumes or dysfunction.

This series is one of the first with a substantial percentage of pure LDAC with clinical, imaging, and genetic diagnosis. It is important to highlight that in these patients diagnosis was performed initially with cMRI and genetic confirmation was then obtained in all cases. This suggests that the diagnosis in left phenotypes by cMRI with contrast techniques is a valid and recommendable tool in the context of clinical suspicion, although the studies that support this are few. Currently, therefore, diagnostic suspicion after cMRI should be confirmed with familial study and genetic techniques.

This fundamental finding of the study is, at the same time, an important limitation, as the left forms and biventricular forms with predominantly left-sided involvement are not fully represented in the current Task Force Criteria. Thus, among patients who present with arrhythmia, even with genetic confirmation and cMRI evidence of anatomic involvement, there are some who do not meet the Task Force Criteria because left ventricular involvement still had not been included in the imaging criteria.

Our study notably extends the anatomic spectrum of this cardiomyopathy and illustrates that the left and right phenotypes

form a continuum, given that we often observed RV segmental contraction abnormalities in left phenotypes and LGE in the LV in right phenotypes.

This was a retrospective study in which patients were selected according to imaging criteria, and therefore selection bias cannot be ruled out. Since LV involvement is very common, even in predominantly right phenotypes, this might reflect a selection bias as these patients have substantial structural involvement. On the other hand, our results show few cases of mild RDAC, perhaps because it is unlikely that an imaging unit would diagnose AC in presence of mild segmental contraction abnormalities or mild degrees of RV dysfunction, given that the observer is aware of the possibility of false positives.[14]

Dalal et al.[15] have recently published a prospective study of a series of patients with AC studied with cMRI using protocols that included LGE sequences and even genetic study. These authors did not find the same prevalence of LV involvement or LGE, given that, of the 25 patients genotyped for AC, only 4 had LV involvement, and this took the form of the presence of intramyocardial fat in the LV. The explanation of this difference in results might be that these were different populations, that the cMRI technique might have been different, and that the method for selecting patients was different. The genotype of the patients studied in our series shows essentially desmoplakin mutations, whereas plakophilin mutations were the most prevalent in the series reported by Dalal et al.

With regard to the cMRI technique used, it is noteworthy that Dalal et al. found fatty infiltration in the LV in all patients with LV involvement, when fatty infiltration of the LV is a relatively rare finding in the literature. Fatty infiltration was not a clinically useful finding in our series, as it was only detected in 2 patients. The underlying problem is the narrowness of the RV wall, which forms a continuum with the epicardial fat; this leads to errors in partial volume, and so is associated with low reproducibility. On the other hand, the series reported by Dalal et al. included family members with a positive genotype, whereas in our series the patients were selected according to initial diagnosis by imaging techniques.

Other series have, however, reported similar findings to our own,[4,16] with substantial LV involvement and LGE in the LV, and as in our study found a substantial proportion of desmoplakin mutations. The authors of these series also highlighted the value of LGE in the LV and observed greater sensitivity and specificity in the diagnosis of AC for this characteristic compared to other anatomic characteristics.

In the context of this disease, it is difficult to find series that allow extrapolation of the data obtained, and the findings have to be analyzed in view of the population included and the selection criteria used.

It is also necessary to bear in mind that there is a small number of patients with pure LDAC phenotypes and biventricular phenotypes with LV predominance who cannot be diagnosed with the current Task Force Criteria, even in the case of genetic confirmation, ECG disorders, and cMRI evidence of LV involvement.

We hope that the introduction of MRI into clinical practice will enable more frequent detection of these phenotypes, thereby increasing the evidence base and generating specific diagnostic tools for these phenotypes.

CONCLUSIONS

LV involvement was very common in this series; the presence of epicardial LGE in the inferior, inferolateral, and lateral walls of the LV was observed in most patients, while dilatation was the least observed characteristic. This condition is therefore not associated with severe dilatation and dysfunction, but with abnormalities that are hard to detect with the usual imaging techniques.

With regard to the score of ventricular predominance, the most frequently observed phenotype in the participating cMRI units was BVAC with RV predominance.

We also note that cMRI with LGE techniques, in the context of compatible clinical signs and symptoms, will lead to high suspicion of LDAC that should be confirmed with familial and genetic study.

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CONFLICTS OF INTEREST

None declared.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found in the online version available at doi:10.1016/j.rec.2011.07.013.

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