

Arrhythmogenic Right Ventricular Dysplasia: cardiomyopathy current opinions on diagnostic and therapeutic aspects

Franco Naccarella, MD, FACC, FESC,* Gerald Naccarelli, MD, FACC,[†] Rosella Fattori, MD,[‡] Andrea Nava, MD, FESC,[§] Bortolo Martini, MD,* Domenico Corrado, MD, FESC,[§] Andrea Masotti, MD,* and Mauro Gatti, MD[¶]

Right Ventricular Dysplasia constitutes a genetic cardiomyopathy characterized by fibrous-adipose substitution of the right and rarely of the left ventricular myocardium. This disorder is associated with ventricular arrhythmias ranging from frequent ventricular ectopic beats, nonsustained and sustained ventricular tachycardia of left bundle branch morphology and sudden death. Therefore, the syndrome has been labelled Arrhythmogenic RVD Cardiomyopathy.

Diagnostic criteria, preliminary genetic data, and clinical manifestations are summarized and critical addressed, using data from the literature and from our own experience. The most important aspects of the ECG in this syndrome are reviewed and stressed with particular attention to initial versus advanced clinical subsets. The typical anatomical abnormalities and biopsy or pathology material are presented. *Curr Opin*

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*Cardiology Azienda USL Città di Bologna, Italy; [†]Penn State University, Cardiology Hershey PA, USA (Chief Prof. Gerald Naccarelli); [‡]Radiology Department University of Bologna, Italy (Chief Prof. Gianpaolo Gavelli); [§]Cardiology Ospedale di Thiene (Padova) Italy; [¶]Cardiology and Medical Genetic Departments University of Padova, Italy (Chief Prof. Sergio Dalla Volta), Cardiology Ospedale di Thiene (Padova) Italy

Correspondence to Prof. Franco Naccarella, Cardiology Department, Azienda USL Città di Bologna via Mascarella 77/5, Bologna 40/26.

Part of the data has been collected at the Cardiology Department Maggiore Hospital, USL Città di Bologna, Italy (Chief Prof. Daniele Bracchetti).

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Abbreviations

ARVDC	arrhythmogenic RVD Cardiomyopathy
ECHO	echocardiography
FEVB	frequent ectopic ventricular beats
NMR	nuclear magnetic resonance
NSVT	nonsustained ventricular tachycardia
PDC	primary dilated cardiomyopathy
PES	programed electrical stimulation
RVD	right ventricular dysplasia
SD	sudden death
VA	ventricular arrhythmias
VC	ventriculography
VT	sustained ventricular tachycardia

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Right ventricular dysplasia (RVD) is a genetic cardiomyopathy characterized by fibrous-adipose substitution of the right and (rarely) of the left ventricular myocardium. This disorder is associated with ventricular arrhythmias (VA) and sudden death (SD) [1•–94••]; therefore, the syndrome has been labelled Arrhythmogenic RVD Cardiomyopathy (ARVDC).

A family history is present in 30 to 70% of the cases [74]. An autosomal dominant pattern [1•–36••] is the most common form of transmission of the disease. (In rare cases, a recessive transmission of the disease has been noted in the Naxos form of ARVDC [35].)

Arrhythmogenic RVD Cardiomyopathy (ARVDC) is a heterogeneous syndrome from the genetical point of view. Six chromosomal loci have already been identified (Table 1) [4,5••,23•–36••]. The disease has been frequently recognized in the North of Italy (the Veneto [1•,3•,22•,23•–36••,59•,80•,82••,93••,94••] and the Emilia Romagna [11,58•,77••–79••] regions), France [8•,9••,10•,21••,88], Germany [57,84,86•,91••], Greece [35], Japan [14,56] and rarely in the North American Indian population [37].

It is now well accepted that the disease is not an abnormality of the development of the myocardium, as the name announces, but a progressive cardiomyopathy, because the ventricle may be normal at birth; however, a progressive fatty replacement may develop over time [1•,2••,4,5••,7••,20•–22•]. Numerous papers report the clinical characteristics of ARVDC and two recently published books summarize the most important clinical and prognostic aspects of the disease [1•–4]. The genetic evaluation of this disease has allowed researchers to define different chromosomal loci in various families, by linkage analysis, as reported in Table 1 [1•,5••,23•–36••].

Diagnostic criteria and clinical manifestations

The diagnosis of ARVDC is a sum of different anatomic features and electrical characteristics, including a positive family history for SD or ventricular

Table 1. Chromosomal loci in families with ARVDC by linkage analysis [5]

Locus, no.	Families, no.	Locus	References
1	6	14q24.3	[29,4,5]
2	4	1q42/3	[30]
3	3	14q12–q22	[31]
4	4	2q32.1–q32.3	[32]
5	1	3p23	[33]
6	1	10p12–14	[34]
7	9	17q21	[35]

Locus 1–6, Autosomal Dominant transmission; Locus 7, Autosomal recessive.

arrhythmias [1•–22•,39•–49•,79••]. Patients who have ARVDC usually present different ventricular arrhythmias such as frequent ectopic ventricular beats (FEVBs) with a left bundle branch morphology configuration, repetitive EVBs, nonsustained ventricular tachycardia (NSVT) and sometimes sustained monomorphic VT with the same left bundle branch morphology [1•–7••,8•–22•,39•].

Internationally recognized criteria for the diagnosis have been defined and published as early as 1994 [39•]. At least 2 major criteria, from different groups, one major and two minor criteria or four minor criteria, are necessary for an accurate diagnosis. Of major importance are the presence of global and/or regional dysfunction and structural abnormalities, as documented by echocardiography (ECHO), nuclear magnetic resonance (NMR), and a positive family history. Less important, but sometimes useful to deepen the clinical suspicion of ARVDC, is the presence of EVBs and repolarization abnormalities in subjects between 12 and 45 years old [1•–7••,19,23•,70–73]. There is a predominance of males [1•–7••]. Sometimes, SD could be the first manifestation of ARVD, frequently occurring during sportive activities (2–5% of SD in this context) [18,19].

Furthermore, four phases of the natural history of the disease have been defined by Nava *et al.* [1•,5••,7••,22•,74]: (1) The so called “silent or hidden phase”, with sporadic EVBs or minor or no abnormalities documented at the ECHO evaluation, or typical anatomic changes in RV myocardium, found at necropsy, in subjects died of SD; (2) “a self-evident phase” with clinical manifestation, including sustained ventricular tachycardia associated with diffuse structural abnormalities of the RV and sometimes of the LV; (3) “a phase characterized by right heart failure”, due to the progressive dilatation and reduction of the contractile force of the RV; (4) “a phase characterized by congestive heart failure” (“CHF) due to progressive involvement of both the RV and the LV.

Electrocardiographic aspects

Typical ECG aspects have been identified [39•–49•, 50•–59•]:

1. Epsilon waves have been documented in right precordial leads (V1 and V2). They represent, after the end of the QRS, delayed repolarization of some parts of the RV. They are usually present in patients with an advanced form of the disease characterized by a dilatation of the RV [9••].
2. A negative T-wave, beyond V3, and sometimes extending to V5 and V6 in a subject over 13 years of age, could be important for the diagnosis. African Americans should be carefully evaluated because these ECG aspects can be observed, even at older ages. Negative T-wave can be correlated also with the dilatation of the RV [51] and can become more evident in the follow-up of a given patient due to the evolutive pattern of the disease [52].
3. QRS duration in V1 more than 110 milliseconds and QRS duration, in right precordial leads more than the duration of QRS in left precordial leads, have been identified as other criteria for ARVDC. They represent conduction delay of the right ventricular free wall [55].
4. Late potentials have been documented by signal averaging in many of these patients. They are due to the delayed depolarization of some parts of the RV. They are more evident in patients who have reduced EF% of the RV [50•]. They have been associated with sustained ventricular tachycardia [50•,53].
5. Ventricular arrhythmias, of left bundle branch morphology, arise from the RV. If they have a left axis deviation they originate from the free wall of the RV; conversely if they show a QRS axis inferiorly directed, they originate from the infundibulum of the RV [1•–22•].
6. Left axis deviation and intraventricular conduction delay, namely right bundle branch block can be identified in standard ECG. Sometimes, a pattern of ST-T elevation in right precordial leads can be also documented, similarly to what can be observed in the Brugada Syndrome as it can be seen also in Table 2 [50•–59•].

Anatomical abnormalities

The changes observed in the RV, in patients who have ARVDC, are mainly a dilatation of the RV and of the outflow tract, but several other abnormalities have been described in different subjects, or in the same patient over time [1–7••, 60•–68].

Echocardiographic and NMR imaging have also demonstrated the presence of akinetic and dyskinetic areas, localized mainly in the outflow tract, in the apex of the RV, or below the tricuspid valve and in the inferior wall of the RV [40,60•–68].

Table 2. Arrhythmogenic right ventricular dysplasia cardiomyopathy (personal experience)

Patient's name	Age	ECG	A QRS (frontal plane)	Observed arrhythmias	Brugada pattern	Echo-NMR (areas of cardiac involvement)
1 RK ♂ (SP)	16	N	30°	NSVT couplets	no	↑ thickness of the moderator band (ARVDC in family's member)
2 AR ♂	19	LAD	-30°	NSVT EVBS	no	Infund Dil
3 GC ♂	29	neg T V1 V4	30°	FEVBS	no	Loc dil RV
4 ML ♂ (SP)	18	LAD	-45°	FEVBS couplets	no	RV Dil
5 ER ♂ (+) (SP)	18	RPP neg T V2-V4	-30°	VT VF	no	RV Hypo Diffuse RV Dil severe Diffuse RV Hypo
6 GB ♂	53	LAH neg T V1-V4	-45°	VT VF NSVT	yes	Aneurysms of the pulmonary infundibulum and RV
7 AP ♂	65	neg T V1 V5	20°	NSVT	no	Diffuse RV infiltration and LV involv
8 GC ♀ (+)	45	neg T V1 V5 LAH	-30° wide QRS	SVT-NSVT FEVBS	yes	Diffuse infil RV, aneurysms IVS involv LV involv
9 BR ♀ (SP)	29	LAH neg T V1 V6	±0°	VT-VF FEVBS	yes	RV diffuse infiltrat Biventricular infiltrat
10 BG ♂ (+)	35	LAH neg T V1 V6	-20°	NSVT-VF FEVBS	yes	RV diffuse infiltrat Infundibular involv Biventricular infiltrat

Clinical, ECG picture, and observed arrhythmias pattern in 10 consecutive, nonrelated patients (10 families). +, deceased. FEVBs, frequent ectopic ventricular beats; Infund Dil, localized infundibular dilatation; IVS involv, interventricular septum involvement; LAD, left axis deviation; LAH, left anterior emiblock; LV involv, left ventricle involvement; RPP, reduced potentials in peripheral lead; Diffuse RV dil, diffuse RV dilatation; Loc Dil, RV localized dilatation; RV Dil, RV dilatation; RV Hypo, RV hypokinesia; SP, sport activity; f, female; m, male. [11,77-79]

These areas are characterized by the thinning of the free wall due to disappearance of the normal myocardium and its substitution with fibrous or fibrous-fatty tissue [60•-68].

Diagnostic aspects

Bidimensional echocardiography

The most valuable method to assess patients who have suspected ARVDC is bidimensional echocardiography [39•-49•,60•-69•]. The most specific aspects for the diagnosis are reduced global or regional EF%, and different degree of dilatation of the RV and outflow tract.

The inferior wall, the area beyond the tricupid valve and the outflow tract should be carefully assessed by echocardiography, because these are the most frequently affected areas. It is important also to visualize, with an apical projection, the apex of the RV, which is frequently involved [60•]. This view is also useful for the evaluation of the intraventricular septum (infrequently involved) and for the exclusion of the extension of the disease to the LV (only found in some

specific subgroups of ARVDC, probably genetically determined) See also our personal experience reported in Table 2 [77••-79••].

Nuclear magnetic resonance

Nuclear magnetic resonance has been used as a more accurate diagnostic tool. In fact, it is characterized by a high sensitivity but a low specificity in the identification of the disease [62,63•,68]. In patients who have an advanced form of the disease, NMR can be only confirmatory; conversely its diagnostic efficiency can be of limited value, for patients who have frequent EVBs of left bundle branch morphology, associated with no structural abnormalities of the RV. However, it can be very useful in assessing the thickness of the free wall of both ventricles, global-regional contractile functions, and patterns of contractions [62,63•,68]. It should be used in association with other clinical and noninvasive or family history criteria, as pointed out by the Commission, which has defined the multiple criteria for diagnosing ARVDC [39•].

Table 3. Criteria for diagnosis of arrhythmogenic right ventricular dysplasia

Global and/or regional dysfunction and structural alterations*	Depolarization/conduction abnormalities
Major	Major
Severe dilatation and reduction of right ventricular ejection fraction with no (or only mild) LV impairment	Epsilon waves or localized prolongation (>110 ms) of the QRS complex in right precordial leads (V1–V3)
Localized right ventricular aneurysms (akinetic or dyskinetic areas with diastolic bulging)	Minor
Severe segmental dilatation of the right ventricle	Late potentials (signal-average ECG)
Minor	Arrhythmias
Mild global right ventricular dilatation and/or ejection fraction reduction with normal left ventricle	Minor
Mild segmental dilatation of the right ventricle	Left bundle branch block type ventricular tachycardia (sustained and nonsustained) on ECG, Holter monitoring, or exercise test
Regional right ventricular hypokinesia	Frequent ventricular extrasystoles (>1000/24 h) on Holter monitoring
Tissue characterization of wall	Family history
Major	Major
Fibrofatty replacement of myocardium on endomyocardial biopsy	Familial disease confirmed at necropsy or surgery
Repolarization abnormalities	Minor
Minor	Family history of premature sudden death (< 35 yrs) due to suspected right ventricular dysplasia
Inverted T-waves in right precordial leads (V2–V3) (people aged > 12 yrs, in absence of right bundle branch block).	Familial history (clinical diagnosis based on present criteria)

*Detected by echocardiography, angiography, magnetic resonance imaging, or radionuclide scintigraphy. ECG, electrocardiogram; LV, left ventricle. The diagnosis of ARVDC would be fulfilled by the presence of 2 major, 1 major plus 2 minor criteria, or 4 minor criteria from different groups. [39]

In our experience, NMR has been used to differentiate ARVDC from the Brugada Syndrome. In many cases of the Brugada Syndrome, a structurally normal heart has been found at NMR, confirming that the Brugada Syndrome is most of the time a functional disease due, as recently documented to a Na channels pathology (Primary Brugada Syndrome [25–28]. Conversely, in some cases, subtle structural changes of the RV (reduced thickness and mild dilatation of the RV and outflow tract without fatty-fibrous infiltration) have been recognized [11]. In other cases, a typical pattern of ARVDC has been identified in association with the specific ECG pattern of the Brugada Syndrome secondary to ARVDC [77••–79••] (Table 3 and 4).

Ventriculography

Ventriculography (VC) has been found to be the gold standard for the diagnosis of ARVDC, but according to recent reports and our own experience, it should be considered as only one of the methods to identify the anatomic abnormalities of the RV [60•,61]. These structural changes, together with the other criteria for ARVDC

diagnosis, could help defining what should be considered a “probabilistic” diagnosis as shown in Table 3 [39•].

When performing the ventriculography, a standard approach should be used, including a 60° LAO with a 25° to 30°caudal-cranial tilt, and a 30° RAO projection with a 15° to 20°caudal cranial tilt. Sometimes also AP and LL views are necessary. Particular attention should be paid to the apex, the outflow tract of the RV, and the anterior border of the RV, where a typical “pile of dishes” can be sometimes recognized [60•,61]. It should be emphasized again that clinical data, depolarization and conduction abnormalities, morphology of the observed arrhythmias, family distribution, and global or regional areas of dysfunction of the RV should be considered altogether to confirm the diagnosis [39•].

Personal experience

We selected from our own experience on ARVDC, ten consecutive subjects belonging to ten different families (Table 2) [11,77••—79••]. These subjects were characterized by VA with different degrees of complexity (from frequent EVBS to VF) on the one hand. At the same time, on the other hand, we related the observed VA to the extent of structural abnormalities, which ranged from an isolated thickness of the moderator band to a severe and diffuse extension of the disease to both the RV and the LV [79••]. Structural abnormalities, similar to the ones observed in the candidate member, were observed in other members of the same families.

From our own experience, we can summarize the following major aspects of ARVDC:

In patients who have major ventricular arrhythmias and diagnosis of ARVDC, a definite relation exists between the severity and the frequency of ventricular arrhyth-

Table 4. Differential diagnosis between ARVDC and Brugada Syndrome, and as proposed by Brugada

	ARVD	Brugada
Age	Any	Any
Sex	M > F	M > F
Inheritance	Autosomal Dominant	Autosomal
Dominant ECG	Inverted T, ST elev Fixed abnormality	Epsilon ± RBB, V1-3 Dynamic changes
H-V Interval	Normal	1/3 normal
Echo/angio	RV dilation or aneurysms	Normal (almost)
MRI	Fatty infiltration	Normal
Pathology	Fibrosis, fatty infiltration	Normal
VT Type	Monomorphic	Polymorphic (VF)
Exercise	No effect	Normal or worsening
Isoproterenol	No effect	Normalization
Class I Drugs (Flecainide) (77) (Ajmaline) (7)	No effect (some)	↑ ST elevation

From [7,25,39,58,78].

mias and the extent of the disease (degree of RV dilatation and/or LV involvement) (Table 2).

A continuous spectrum of anatomic involvement, from localized abnormalities of the moderator band, to pulmonary infundibulum involvement to localized or to diffuse RV involvement to biventricular involvement, can be documented. The reasons could both be a genetic heterogeneity of the disease in different families [79••] or a different evolution of the disease over time, with the increasing age of the subjects.

In younger patients, less serious ventricular arrhythmias can be demonstrated at rest, and a less diffuse disease can be anatomically evident. Nevertheless, life-threatening arrhythmias cannot be excluded during stress or competitive sport activity.

In older patients who did not practice sport, a more diffuse disease can be demonstrated and more serious arrhythmias were documented, in our experience, in everyday life. Furthermore, sudden death was observed in two subjects with VT, who did not practice sport.

Conversely, FV was the only documented arrhythmia in the Brugada Syndrome. In our own experience, which concerns 9 families, we had 7 out of 9 subjects with VF as the only documented arrhythmia, with the exception of one subject who had also frequent EVBS and NSVT of left bundle branch morphology [11].

Although genetic screening is always positive in patients who have ARVDC (9 out of 10 families, in our experience), in the Brugada Syndrome, genetic screening was negative for ARVDC in our experience [11], while it has been documented a Na channel pathology in only 1 out of 9 of our families. Even in the literature, a positive genetic screening was found only in 15 to 20% of the cases of the Brugada Syndrome [24–28,77••–79••].

Differential diagnosis

In the differential diagnosis, a primary dilated cardiomyopathy (PDC) should be easily excluded because, in this condition, the involvement of both ventricles and a global reduction of contractility, with a diffuse dilatation of both the RV and the LV, are present [8•,10•,23•–38, 39•–49•].

We already considered the differential aspects of ARVDC in comparison to the Brugada Syndrome. Cases of uncertain diagnosis should be ruled out by genetic screening, and confirming the presence of genes mutations, observed in association with ARVDC (Table 1) [1•–7••,11,25–29••,38]. Differential criteria between the two diseases have been reported Table 4.

Table 5. Differentiation of ARVD/C from RVOT tachycardia on surface ECG, and as proposed by Markus

	ARVC	RVO-VT	Control
T-wave inversion > V2	54.3%*	33.0%	1.4%
max QRS duration (V1-3)	114±19 ms*	104±13 ms	98±11 ms
max QRS > 100 ms (V1-3)	51.7%*	21.0%*	12.9%
QRS dispersion	40±13 ms*	34±10 ms	33±9 ms
QT dispersion	54±21 ms	47±16 ms	40±13 ms
Epsilon potential	22.5%*	2.8%	0
Late potentials (25 Hz)	41.4%*	11.7%	3.0%

*P = 0.001 for ARVD/C versus RVOT tachycardia and control [5,45].

The differential diagnosis with RVOT should include the morphology of the wide QRS tachycardia. RVOT, which is not associated with a structural heart disease, usually presents itself with an inferior QRS axis and a negative QRS in a VL. A small positive R-wave in AVL indicates an origin from the anterior part of the infundibulum tract (Table 5) [5••,45•].

It has been demonstrated by Marcus that a T-wave inversion is more common in ARVDC (54%) versus RVOT (33%); epsilon potential and late potential are more frequent in ARVDC (22.5% and 41.4% respectively) versus RVOT (2.8% and 11.7% respectively) (Table 5) [5••,45•]. (An underlying structural heart disease is recognizable more frequently in ARVDC.)

Other differential diagnosis should include abnormalities of the right atrium and ventricle, such as the atrial septal defect, anomalous pulmonary venous return, Ebstein malformation, and some types of myocarditis, sarcoidosis, diseases of the glycogen metabolism or of the adipose tissue, primarily affecting the RV.

Pathology and biopsy material

The most important structural abnormality recognized in ARVDC is fatty-fibrous substitution of the RV epicardium and midmyocardium. Intraventricular septum is rarely involved. A reduction in the thickness of the RV wall, mainly at the apex, the inferior wall, behind the tricuspid valve, and the outflow tract of the RV has been found. Accurate morphologic description of the pathology of the disease has been provided by Thiene *et al.* and others [1•–7••,9••,10•,20•–22•,46–49•].

From the histologic point of view, the disease is characterized by myocardial atrophy, with residual myocytes in the context of a fatty-fibrous infiltration. Evidence of myocyte death and of a primary or secondary lymphocytes infiltration is present in 30 to 50% of the cases. [46,47].

Thiene *et al.* tested different causes of these abnormalities, including an inflammatory etiology, a degenerative disorder, or apoptosis [1•–7••,9••,20•–22•,46,48•].

At the present time, the more widely accepted hypothesis for these structural changes is that they are due to a congenital disease, with polymorphic expressions of the different involved genes (localized versus diffuse involvement of the RV, with and without extension to the LV) [49•,59•] Table 2. A genotype/phenotype correlation has not been completely demonstrated, even if suspected [49•,59•,79••]. Furthermore, RVDC should be considered a progressive disease over time, with differences in any individual case [49•,52,59•,79••]. Biopsy can be performed to confirm the diagnosis in selected cases, only in the free wall of the RV, not forgetting the high risk of perforating the myocardium [64–67].

Risk stratification

In patients who have ARVDC, the risk of SD is higher than in the normal population [69•–83•]. The risk of SD has been associated with different markers, including patients who have loci localized to chromosome 1q42.3 [1•–7••,36••].

Risk stratification of affected subjects and of their family members can be performed using ECG, signal averaged ECG, 24 hours holter monitoring, stress test, bidimensional echocardiography (or other imaging techniques), and programmed electrical stimulation (PES). It has been shown that a normal echocardiographic examination, in a family member affected by ARVDC, has a very low probability (<3%) of developing ventricular arrhythmias during an 8 year-long follow-up and no probability at all of SD. Conversely, subjects who have an abnormal echo showed a higher incidence of developing arrhythmias (almost 90%); 54% showed a progression of the disease over time [69•].

We know that the diagnosis of ARVDC is incompatible with competitive sport activities, and the first clinical manifestation of the disease has been found frequently in young athletes, sometimes dying of SD [17–19,23•,39•,41,75] (Table 2 and 3). A previous history of syncopal attacks has been related to an increased risk of SD [5••].

Other clinical variables, electrocardiographic, and echocardiographic parameters have been investigated or are under clinical evaluation as possible prognostic factors and indicators of SD in this patient population. Some of those variables have been recently discussed by Marcus at the NASPE meeting [5••].

A higher incidence of SD is usually found in subjects who have previous CA or polymorphic VT or VT at high heart rate [72]. Patients with chromosome 1q42.43, as previously stated, show polymorphic VT during stress test, associated with an increased risk of dying suddenly, have been reported by the Padova group [36••].

In our own experience, major ventricular arrhythmias have been always observed in subjects with diffuse structural abnormalities, with the exception of one case of VF in a subject with a diffuse dilatation of the RV, but a normal LV. Cases of SD in athletes, associated to ARVDC of limited extension, have also been documented. These data, in association with the data of the Padova group, stress the fact that SD can occur during sport activity, even in subjects with a localized or a minor form of the disease [41,75].

In conclusion, risk factors for SD in ARVDC can be considered the following ones, as summarized by Marcus [5••]:

- (1) History of CA or syncope
- (2) Extension of ARVDC as expressed by T-wave inversion in V3 or beyond
- (3) Markedly abnormal late potentials
- (4) Marked RV dilatation or enlargement and multiple wall
- (5) Motion abnormalities, assessed by ECHO or angiography
- (6) Left ventricular involvement and dilatation
- (7) ARVDC, with a genetic locus on chromosome 1q42.43, associated with exercise-induced polymorphic VT and right ventricular apical aneurysms

Actual treatment

A large variety of antiarrhythmic drugs have been used in this disease to control ventricular arrhythmias [84–94••]. The most effective drugs have been proved to be amiodarone by French [9••–10•] and Italian authors and propafenone and sotalol by German authors [84,86•].

Breithardt [89–91••] recently reported at the NASPE meeting his own experience on the pharmacological (DT) and nonpharmacological treatment (NDT) of these patients. Sotalol appeared to be the most effective DT for ventricular arrhythmias in ARVDC patients, with and without PES evaluation. But it is not known, whether this drug is able to prevent SD, even in patients tested by PES.

On the other hand, empirically administered amiodarone in our own experience [79••] and in the largest French experience by Frank and Fontaine, appeared to be as effective as sotalol. None of these experiences have been prospective controlled clinical studies. It should be mentioned that a high recurrence-rate of life-threatening ventricular arrhythmias has been reported during pharmacological therapy [9••–10•,79••,88,89–91••].

The indication to ablation therapy is limited to patients with monomorphic ventricular tachycardia, but the frequency of recurrences is very high because ARVDC is a progressive disease, with progressive involvement of new

areas of the RV [86•,91••]. The implantable cardioverter defibrillator (ICD) is clearly recommended for patients with aborted SD, polymorphic VT during stress, and considered to be at high risk for the family history or for previous syncopal episodes [89–91••]. At the present time, we do not know if subjects with sustained monomorphic VT, without overt manifestations of the disease, are a clear indication for an ICD implantation. Clinical, but also emotional, factors are sometimes important in guiding this difficult clinical decision.

Current indications to ICD therapy can be defined as drug refractory VT, side effects on AA drugs, or noninducible VT/VF after a survived cardiac arrest. Breithard [91••] recently pointed out the predictors of arrhythmic events in patients with ARVDC and defined some guidelines for risk stratification and the most correct therapeutic approach to these patients [91••].

Predictors of arrhythmic events can be considered: extensive ARVDC (RV), LV involvement, inducible VT, drug refractoriness, noncompliance to treatment, survived cardiac arrest, history of syncope or familial SD and late potentials (SAECG).

A clinically useful risk stratification of patients with ARVDC can be performed on inducibility at PES [89–91••]. In patients with noninducible VT, an accurate evaluation of the history, of the presence and the types of VT, and of the occurrence of syncope or SD in the family can be excluded.

In case of resuscitated SD, the most correct approach is ICD implantation. In case of sporadic, hemodynamically well tolerated, sustained VT, an ablation procedure can be proposed. Conversely, in patients with sustained inducible VT/VF at PES, sotalol should be tested as the first drug. In case of VT suppression at PES, the patient should be followed on AA, with probably further PES testings over time. In case of non suppressible VT/VF, with 2 or more VT morphologies, or VT intolerance, or in the presence of extensive ARVDC, an ICD should be implanted, avoiding catheter ablation or a surgical approach with should be considered today as on historical therapy [1•,88,90•]. Catheter ablation should be considered as the treatment of choice only for patients with a limited extension of the disease, monomorphic VT or VT hemodynamically stable [85,86•,89,91••].

For the future, we support the idea of enrolling our patients in an International Data Base coordinated by the Padova Group. In this way, as our experience confirms, we could verify, in a larger patient population, the utility of the genetic screening, as a means of identifying patients at the highest risk [73,93••]. The prospective database will be also useful to assess new and old prognostic factors, and at

the same time, the prognostic value of pharmacological or nonpharmacological interventions.

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- Of special interest
- Of outstanding interest

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