Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia: An Update

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Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is a genetic cardiomyopathy characterized by ventricular arrhythmias and structural abnormalities of the right ventricle (RV). The diagnosis is based on the International Task Force criteria. Cardiologists may not be aware of these diagnostic criteria for ARVC/D and may place too much importance on the results of MRI imaging of the right ventricle. Patients with ARVC/D usually have an abnormal 12-lead electrocardiogram, abnormal echocardiogram, and ventricular arrhythmias with a left bundle branch block morphology. If noninvasive testing suggests ARVC/D, invasive testing with an RV angiogram, RV biopsy, and electrophysiologic study is recommended. Once a diagnosis of ARVC/D is established, the main treatment decision involves whether to implant an implantable cardioverter-defibrillator. We also recommend treatment with β blockers. Patients with ARVC/D are encouraged to avoid competitive athletics. Recent advances in the understanding of the genetic basis of ARVC/D have revealed that ARVC/D is a disease of desmosomal dysfunction.

Introduction

Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is an inherited cardiomyopathy characterized by ventricular arrhythmias and structural abnormalities of the right ventricle (RV). ARVC/D results from progressive replacement of right ventricular myocardium with fatty and fibrous tissue. The precise prevalence of ARVD in the United States has been estimated to be 1 in 5000 of the general population. This article provides a brief update on the cause, approach to diagnosis, and management of patients with ARVC/D.

Clinical Presentation and Natural History

Patients with ARVC/D typically present because of ventricular arrhythmias. The ventricular arrhythmias, which originate in the RV, may be asymptomatic and detected by routine electrocardiogram (ECG) or may cause palpitations, syncope, or sudden death. It has been estimated that ARVC/D accounts for 1% to 3% of sudden cardiac deaths (SCDs) in individuals under the age of 35 years, except in endemic areas such as in the Veneto region of Italy [1,2].

Dalal et al. [3••] recently reported the presentation, clinical features, survival, and natural history of ARVC/D in a US cohort of 100 patients. The median age at presentation was 26 years. The most common presenting symptoms were palpitations, syncope, and SCD in 27%, 26%, and 23% of patients, respectively. Among those who were diagnosed while living (n = 69), the median time between first presentation and diagnosis was 1 year (range, 0–37 years). During a median follow-up of 6 years, implantable cardioverter-defibrillators (ICDs) were implanted in 47 patients, 29 of whom received appropriate ICD discharges. At follow-up, 66 patients were alive, five developed signs of heart failure, two had a heart transplant, and 18 were on antiarrhythmic drug therapy. Thirty-four patients died at presentation (n = 23) or during follow-up (n = 11), of whom only three were diagnosed while living and one had an ICD implanted. On Kaplan-Meier analysis, the median survival in the entire population was 60 years. This study's results confirmed and extended the findings of prior studies. ARVC/D patients usually present between the second and fifth decades of life with symptoms of palpitations, syncope, or sudden death. Once they are diagnosed and treated with an ICD, mortality is low. This study also demonstrated a wide variation in presentation and course of ARVC/D patients, which may be explained in part by this disease's genetic heterogeneity.

Diagnosis of ARVC/D

The diagnosis of ARVC/D is established based on the criteria set by the Task Force of the Working Group of Myocardial and Pericardial Disease of the European Society of Cardiology and of the Scientific Council on Cardiomyopathies of the International Society and Federation

Table 1. Diagnostic criteria for ARVC/D*

Variable	Major criteria	Minor criteria
Structural or functional abnormalities	1. Severe dilation and reduction of RVEF with mild or no LV involvement	1. Mild global RV dilation and/or EF reduction with normal LV
	2. Localized RV aneurysm (akinetic or dyskinetic areas with diastolic bulging)	2. Mild segmental dilation of the RV
	3. Severe segmental dilatation of the RV	3. Regional RV hypokinesis
Tissue characterization	Infiltration of RV by fat with presence of surviving strands of cardiomyocytes	
ECG depolarization/ conduction abnormalities	1. Localized QRS complex duration > 110 ms in V1, V2, or V3	Late potentials in SAECG
	2. Epsilon wave in V1, V2, or V3	
ECG repolarization abnormalities		Inverted T waves in right precordial leads (V2-V3 above age 12 y in absence of RBBB)
Arrhythmias		1. LBBB VT (sustained or nonsustained) on ECG, Holter, or ETT
		2. Frequent PVCs (> 1000/24 h on Holter)
Family history	Family history of ARVC/D confirmed by biopsy or autopsy	1. Family history of premature sudden death (< 35 y) due to suspected ARVC/D
		2. Family history of clinical diagnosis based on present criteria

*The criteria state that an individual must have 2 major, or 1 major plus 2 minor, or 4 minor criteria from different categories to meet the diagnosis of ARVC/D.
ARVC/D—arrhythmogenic right ventricular cardiomyopathy/dysplasia; ECG—electrocardiogram; EF—ejection fraction; ETT—exercise treadmill test; LBBB—left bundle branch block; LV—left ventricle; PVCs—premature ventricular contractions; RBBB—right bundle branch block; RV—right ventricle; RVEF—right ventricular ejection fraction; SAECG—signal-averaged electrocardiogram; VT—ventricular tachycardia.

of Cardiology [4]. These criteria are shown in Table 1. Specific cardiac tests recommended for all patients suspected of having ARVC/D include an ECG, a signal-averaged ECG (SAECG), a Holter monitor, and an echocardiogram. Analysis of RV size and function can also be obtained by cardiac MRI and/or CT. If the noninvasive test results suggest the diagnosis of ARVC/D, invasive testing including right ventricular angiography, endomyocardial biopsy, and electrophysiology testing is recommended to establish the diagnosis and help provide further information to guide treatment recommendations.

Electrocardiographic Evaluation

ECG abnormalities are detected in more than 90% of ARVC/D patients [3••,5]. T-wave inversion (TWI) in leads V1-V3 is a well-established ECG feature of ARVC/D, and is considered as a minor diagnostic criterion in the absence of right bundle branch block. TWI's juvenile pattern in leads V1-V3 or beyond is a normal variant in children less than 12 years old and is present in 1% to 3% of a healthy population 19 to 45 years old. This finding is present in 50% to 87% of patients with ARVC/D. TWI beyond V1 in a patient in the above age group who has no apparent heart disease but has ventricular arrhythmias of left bundle branch block (LBBB) morphology should raise the suspicion of ARVC/D [6].

Another typical ECG feature of ARVC/D is the "epsilon wave," which is a "postexcitation" electrical potential of small amplitude that occurs in the ST segment after the end of the QRS complex. Epsilon waves—seen in 33% of ARVC/D patients—are considered a major diagnostic criterion for ARVC/D [5]. Slowed electrical conduction in the RV, as a result of ARVC/D, may also cause localized widening of QRS complex (≥ 110 ms) in the right precordial leads and is seen in 64% of the patients. Prolonged S-wave upstroke (defined as a prolongation from the S wave to the end of the QRS complex in V1-V3 ≥ 55 ms) is a common ECG feature of ARVC/D. Another term for this evidence of delayed activation is "terminal activation delay" (TAD). This term was coined recently by Cox et al. [7•], who defined TAD as the time from the nadir of the S wave to the end of all depolarization deflections, thereby including not only the S-wave upstroke but also late fractionated signals and epsilon waves, to the completion of the QRS complex. In this recent study, a prolonged TAD (≥ 55 msec) was observed in 71% of ARVC/D patients and 4% of control patients.

Late potentials on SAECG recordings are the counterpart of the epsilon waves and are considered a minor criterion for the diagnosis of ARVC/D. The Task Force on SAECG defines an SAECG as abnormal when two or more of the following are present: 1) the duration of the signal-averaged, high-frequency filtered QRS complex ≥ 114 ms;

2) the duration of the low-amplitude signal of less than 40 μV in the terminal portion of the filtered QRS complex ≥ 38 ms; and 3) the root mean square voltage of the terminal 40 ms of the filtered QRS complex less than 20 μV. The results of several recent studies have shown that the probability of an abnormal SAECG, as defined by these criteria, is related to the degree of structural disease [8,9].

Imaging of the RV and Myocardial Biopsy

Right ventricular size and function can be evaluated using several imaging modalities, including echocardiography, angiography, cardiac MRI, and CT. According to the Task Force criteria, a major criterion for ARVC/D is defined as the presence of severe dilatation and/or functional loss of the RV. A less severe abnormality of RV size and/or function is considered to be a minor criterion for ARVC/D. It can be appreciated that many of the Task Force criteria are nonspecific, since they are not quantitative. Although each of the available modalities for evaluating RV size and function can detect severe structural abnormalities of the RV, these tests' diagnostic accuracy is less certain when evaluating patients with mild disease. Right ventricular angiography has historically been regarded as the best imaging test for diagnosing ARVC/D and has been shown to be highly specific (90%).

Indik et al. [10] recently reported promising results with a new automated system for detecting RV wall motion abnormalities in patients with ARVC/D. Compared with right ventricular angiography, echocardiography is noninvasive and represents the first-line imaging approach in evaluating patients with suspected ARVC/D or in screening family members [11•]. Tissue Doppler echocardiography and strain echocardiography can reliably differentiate ARVC/D from controls without RV disease with approximately 70% sensitivity and 90% specificity [12]. MRI is an attractive imaging method because it is noninvasive and can differentiate fat from muscle [13–17,18•]. Gadolinium-enhanced MRI can localize fibrosis in the RV myocardium [16,17]. MRI also allows for a highly accurate and quantitative evaluation of right ventricular size and function. Regional wall motion abnormalities limited to the RV have been shown to have 75% sensitivity and 97% specificity for ARVC/D [18•,19].

Although MRI is well suited for evaluating patients with suspected ARVC/D, it is also important not to overinterpret minor abnormalities detected on MRI. It is our experience that cardiac MRI is a common cause of ARVC/D overdiagnosis [20]. Physicians should be hesitant to diagnose ARVC/D when the only anatomic abnormalities are those seen on cardiac MRI. In our experience, an abnormality detected with MRI will virtually never be the sole abnormality detected in a patient with ARVC/D. It is also important to recognize that the presence of "fat" in the right ventricular myocardium may be normal and that subtle wall motion abnormalities and thinning of the RV wall are common in normal populations and that these findings should not be considered diagnostic of ARVC/D [21,22]. Although CT imaging can also be used to image the RV, limited experience exists with this imaging modality compared with MRI [23].

An endomyocardial biopsy should be performed in selected patients suspected of having ARVC/D. This technique is most sensitive when performed on the free wall at a site adjacent to regional RV dysfunction. ARVC/D can be a patchy disease; definitive pathologic evidence for the diagnosis by myocardial biopsy will be obtained in approximately one third of affected individuals. However, when the biopsy shows myocyte loss (< 45% residual myocytes) with fibrosis and fatty infiltration along with surviving strands of myocytes, the diagnosis of ARVC/D is clearly established. An endomyocardial biopsy is also useful in identifying other conditions such as sarcoidosis, which can be confused with ARVC/D [24]. Myocardial perforation has been reported as a complication of endomyocardial biopsies. Precautions to prevent myocardial perforation include gently withdrawing the biopsy sample. If resistance occurs, it may indicate a thin fibrotic area, and another site should be selected. If the biopsy is guided by CARTO mapping (Biosense Webster, Diamond Bar, CA), the border of the low voltage should be targeted.

Electroanatomic Mapping

The presence of low voltage areas in the RV has been proposed to aid in diagnosing patients with ARVC/D. This is based on several studies that have shown that the results of electroanatomic mapping correlate well with pathologic findings on endomyocardial biopsy in addition to the other imaging modalities [25–29]. More recently, Corrado et al. [28] showed that low-amplitude areas found at voltage mapping were associated with myocyte loss and fibrofatty replacement at endomyocardial biopsy. These investigators evaluated 31 patients who fulfilled Task Force criteria for ARVC/D after noninvasive evaluation and performed RV electroanatomic voltage mapping and endomyocardial biopsy to validate the diagnosis. Twenty of 31 patients had an abnormal RV electroanatomic voltage mapping showing more than one area with bipolar electrograms with voltage values less than 0.5 mV. Low-voltage areas were sharply demarcated and typically surrounded by a border zone with reduced signal amplitudes (0.5–1.5 mV), which merged into normal myocardium (> 1.5 mV). These low-voltage areas were also significantly correlated with echocardiographic or angiographic RV wall motion abnormalities and pathologic findings at biopsy. However, 11 of 31 patients showed preserved electrogram voltage, histopathologic evidence of inflammatory cardiomyopathy, and a more benign clinical course [28]. In 2008, these same investigators extended their findings and performed voltage mapping and endomyocardial biopsy

in 27 patients with presumed right ventricular outflow tract (RVOT) tachycardia and no echocardiographic/angiographic evidence of right ventricular dysfunction. Electroanatomic voltage mapping was normal in 20 of 27 patients. However, the other seven patients showed electroanatomic scar areas that correlated with fibrofatty myocardial replacement at biopsy. They concluded that electroanatomic mapping can identify a subgroup of patients with RVOT tachycardia and concealed ARVC/D by detecting RVOT electroanatomic scars on voltage mapping that correlates well with fibrofatty myocardial replacement at biopsy [29].

Although voltage mapping is not a specific Task Force criterion for ARVC/D diagnosis, in cases of clinical uncertainty, voltage mapping may confirm the diagnosis. Multiple areas of low voltage specifically surrounding the tricuspid valve are considered to be highly suggestive of the disease and correlate with biopsy findings. Performance and interpretation of voltage mapping requires considerable experience. Low voltage does not necessarily imply diseased myocardium but may result from poor tissue contact. This is particularly true in regions of the RV near the tricuspid valve. We have seen several patients overdiagnosed or misdiagnosed with ARVC/D because of low voltage observed at the time of electroanatomic mapping. Based on this experience, we urge electrophysiologists to use great caution when considering an ARVC/D diagnosis when the only evidence for this disease is low voltage on an electroanatomic map. Further research is needed to determine if electroanatomic mapping provides information that will facilitate the early diagnosis of ARVC/D. Most studies to date have been performed in patients with overt ARVC/D in which the diagnosis is not in question. Therefore, although the initial studies appear promising, we do not recommend widespread use of voltage mapping as a diagnostic strategy at this time, particularly at centers without considerable experience in performing and interpretating electroanatomic mapping studies.

Left Ventricular Involvement in ARVC/D

ARVC/D was first described as a cardiomyopathy predominantly affecting the RV. Consequently, the Task Force criteria for ARVC/D diagnosis that were proposed in 1994 were designed to exclude left ventricular disease [4]. The ensuing clinical description of ARVC/D in several large cohorts relied on inclusion of patients who fulfilled the Task Force criteria, and therefore resulted in the exclusion of "left-sided arrhythmogenic cardiomyopathy."

More recently, ARVC/D has been shown to be a disease of the cardiac desmosome. Because the desmosomal structure is similar on both sides of the heart, the existence of left-sided arrhythmogenic cardiomyopathy has been hypothesized. Three studies investigating the RV and left ventricle (LV) characteristics in relation to the presence of desmosomal mutations are particularly noteworthy. Bauce et al. [30] reported their echocardiographic findings in 26 desmoplakin mutation carriers among 38 individuals from four families. Of the 14 individuals with an abnormal echocardiogram, 13 had RV involvement and seven had LV involvement. Right ventricular ejection fraction and right ventricular end-diastolic volume were similar (or slightly worse) in patients with LV involvement; only one individual had an abnormal LV with no abnormalities detected in the RV. In a subgroup of 22 mutation carriers among 28 genotyped individuals who underwent cardiac MRI with delayed enhancement, Sen-Chowdhry et al. [31••] reported LV delayed enhancement in 100% of the mutation carriers. In the same study, 54% of the mutation carriers were reported to have LV systolic dysfunction. Subsequently, the same group reported LV involvement in 85% and predominantly left-sided disease in 15% of the 39 desmosomal mutation carriers [32]. These studies' results suggest that although left ventricular involvement can occur, the overall structure and function are well preserved in the early disease stages. Independent LV involvement is rare and is consistent with the traditional notion that right-sided disease precedes left-sided disease in most cases.

Differential Diagnosis

Although it is not difficult to diagnose an overt case of ARVC/D, differentiating ARVC/D at its early stages from idiopathic ventricular tachycardia (IVT) (a usually benign and not familial arrhythmic condition that also presents with VT with an LBBB morphology) remains a clinical challenge [24,33,34]. The major differences in the two conditions include the following: 1) IVT is not familial, whereas ARVC/D is; 2) IVT is not associated with an increased sudden death risk, whereas ARVC/D is; 3) patients with IVT have normal ECGs and SAECGs, whereas patients with ARVC/D do not; 4) IVT results from triggered activity and usually presents with a single LBBB morphology. In contrast, patients with ARVC/D have reentrant VT, often with multiple LBBB; and 5) IVT responds to treatment with catheter ablation, whereas catheter ablation plays only a palliative role in managing patients with ARVC/D. It is extremely important to determine if the patient has IVT or ARVC/D for two reasons. First, IVT is a benign condition that is not associated with a risk of sudden death and therefore is not an indication for ICD placement. In contrast, when ARVC/D diagnosis is established, there needs to be serious consideration for ICD implantation because of SCD risk. Second, ARVC/D is frequently hereditary, whereas IVT is not. As a result, when an ARVC/D diagnosis is made, screening of all first-degree family members is recommended.

Histology

ARVC/D pathology is characterized by myocyte loss and later replacement with fatty and/or fibrotic tissue mainly in the RV. These changes are most prominent in the so-called triangle of dysplasia: the inflow, outflow, and apical

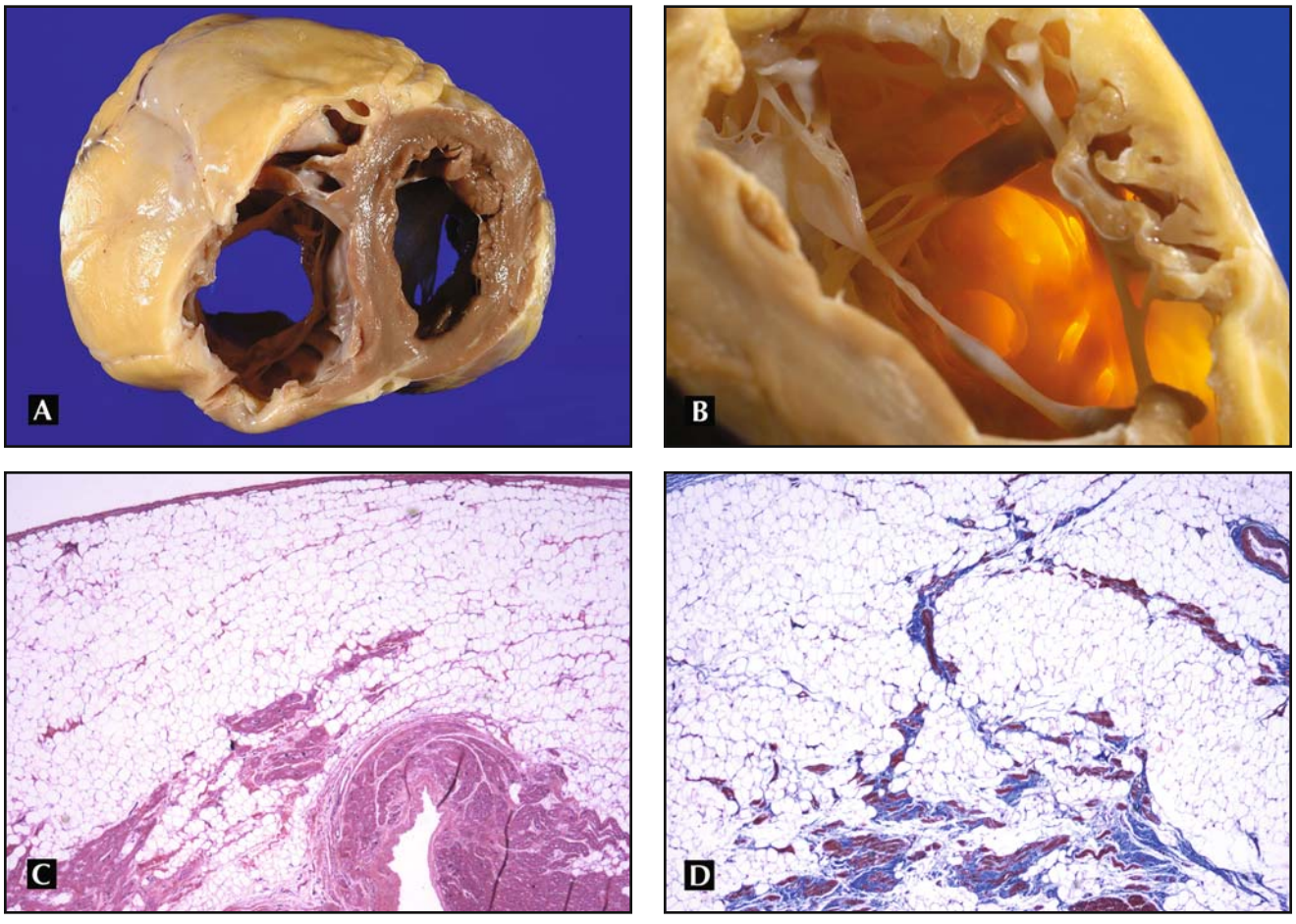

Figure 1. Pathologic examination of an arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) heart. **A and B,** Gross pathology. The right ventricle is so dilated as to be translucent in some areas, typical of late ARVC/D. **C,** Hematoxylin and eosin stain demonstrating replacement of right ventricular myocytes by fatty and fibrotic tissue. **D,** Trichrome stain demonstrating replacement of right ventricular myocytes by fatty and fibrotic tissue.

areas. Patchy acute myocarditis with myocyte death and inflammatory infiltrates is also present in nearly two thirds of the cases. As the disease progresses, myocytes are replaced by fatty and/or fibrous tissue, and changes extend to the posterolateral wall of the LV and sometimes the interventricular septum.

Tandri et al. [35] recently reported the case of a 28-year-old man with ARVC/D who eventually underwent orthotopic heart transplant for incessant VT and heart failure. Genetic testing revealed a mutation in plakophilin-2 (2146-1G>C splice product mutation). The pathology of his explanted heart is typical of the changes seen in ARVC/D. As shown in Figure 1, he had a markedly dilated RV and areas of translucency consistent with the loss of myocytes. A trichrome stain demonstrated the presence of fibrosis and fatty infiltration. Immunostaining revealed a marked decrease in the presence of plakophilin-2, plakoglobin, desmoplakin, and the gap junction protein connexin 43 at the intercalated discs. This suggests that the patient had significantly fewer desmosomes and gap junctions compared with controls [35]. These changes are particularly instructive in relation to ARVC/D genetics.

Genetics

ARVC/D is a heritable condition, typically with an autosomal-dominant pattern of inheritance and variable penetrance [35–38]. A familial pattern of disease exists in approximately one third of probands. To date, 12 genetic abnormalities of ARVC//D have been identified (Table 2).

Several variants involve a polymorphism in a gene encoding a desmosomal protein, which are part of the intercalated disc and are responsible for providing electrical and mechanical coupling and transmission of contractile force between cardiac myocytes. The desmosome consists of three parts: the transmembrane adhesion molecules, which provide the bridge between the two myocytes; the intracellular linker proteins, which link to the cytoskeleton; and the cytoskeletal proteins. *Desmoglein* and *desmocollin,* the genes responsible for ARVC/D11 and ARVC/D12, respectively, are the transmembrane adhesion molecules. *Plakoglobin* (responsible for ARVC/D9), *plakophilin* (responsible for ARVC/D10), and *desmoplakin* (linked to ARVC/D8) are the intracellular linker proteins. *Desmin*, responsible for ARVC/D7, is an intermediate filament that is part of the cytoskeleton.

Table 2. Genetic abnormalities associated with ARVC/D

Classification	Gene	Chromosome	Prevalence, %	Comments
ARVC/D1	*$TGFB_3$*	14q24.3	Rare	Characterized by progressive degeneration of RV myocardium. Causes cytokine-stimulating fibrosis and modulates cell adhesion
ARVC/D2	Cardiac ryanodine receptor	1q42-q43	Rare	Associated with catecholaminergic polymorphic VT
ARVC/D3	—	14q11-q12	—	Reported in 3 small families [50]
ARVC/D4	—	2q32.1-q32.3	—	Associated with localized LV involvement
ARVC/D5	*TMEM43*	3p23	—	Reported in ARVC/D cases in Newfoundland [38]
ARVC/D6	—	10p12-14	—	Early onset, high penetrance. Initially thought to be due to a missense mutation in *PTPLA*
ARVC/D7	*ZASP, desmin*	10q22, 2q35	—	Associated with myofibrillar myopathy
ARVC/D8	*Desmoplakin*	6p24	10	Associated with palmoplantar keratoderma and woolly hair (Carvajal syndrome)
ARVC/D9	*Plakoglobin*	17q21	Rare	Associated with palmoplantar keratoderma and woolly hair (Naxos disease)
ARVC/D10	*Plakophilin-2*	12p11	25	—
ARVC/D11	*Desmoglein-2*	18q12.1-q12.2	10	—
ARVC/D12	*Desmocollin*	18q12.1	3	Reported in 1 patient [51]

ARVC/D—arrhythmogenic right ventricular cardiomyopathy/dysplasia; LV—left ventricle; RV—right ventricle.

That so many of the causative mutations for ARVC/D are in genes that encode parts of the desmosome highlight that ARVD is principally a disease caused by abnormal desmosomes. It is thought that the dysfunctional desmosome can be mechanically torn apart when exposed to shear stress, leading to cell membrane damage and direct cell death, accompanied by inflammation and repair by fibrofatty replacement. Cell adhesion defects most likely reach a critical point at places where the ventricular wall is thinnest, in part explaining why ARVC/D preferentially affects the RV. It also helps to explain why familial ARVC/D is more likely to be seen in individuals who have led physically active lives because they have placed more mechanical stress on their hearts [35].

Implantable Defibrillators, Catheter Ablation, and Other Treatment Options

Once the ARVC/D diagnosis has been established, the main management decision concerns whether to implant an ICD to prevent sudden death [39•,40–42]. ARVC/D patients who are at the highest risk for arrhythmic death include those patients with a history of having been resuscitated from SCD, patients with syncope, and those who have marked right ventricular involvement. The presence of left ventricular involvement is also a risk factor. Risk stratification based on the above characteristics is of value. However, these risk factors have not been prospectively verified and therefore cannot determine which patients with ARVC/D have a sufficiently low risk that ICD placement is not warranted.

A recent study reported on the outcome of ICDs in 67 patients with definite or probable ARVC/D [39•]. Over a mean follow-up of 4.4 ± 2.9 years, 40 (73%) of 55 patients who met Task Force criteria for ARVC/D and four (33%) of 12 patients with probable ARVC/D had appropriate ICD therapies for ventricular tachycardia/ventricular fibrillation (VT/VF; $P = 0.027$). The mean time to ICD therapy was 1.1 ± 1.4 years. Eleven of 28 patients (39%) who received an ICD in the absence of a prior episode of sustained VT or VF and 33 of 35 (94%) patients who received an ICD for secondary prevention experienced appropriate ICD therapies ($P = 0.001$). Electrophysiologic testing did not predict appropriate ICD interventions in patients who received an ICD for primary prevention. Fourteen patients (21%) received ICD therapy for life-threatening arrhythmias (VT/VF > 240 bpm). No difference was noted in the incidence of life-threatening arrhythmias in the primary and secondary prevention groups. Based on these findings, the authors concluded that patients who meet Task Force criteria for ARVC/D are at increased risk for SCD and should undergo ICD placement for primary and secondary prevention, regardless of electrophysiologic testing results. Further research

is needed to confirm that a low-risk subset of patients can be identified who may not require ICD placement. We currently recommend ICD implantation in patients who meet the strict diagnostic criteria for ARVC/D. This approach applies particularly to probands. Uncertainty remains as to whether patients with probable ARVC/D and/or asymptomatic family members of probands with ARVC/D who meet criteria for ARVC/D should also undergo ICD implantation [43].

In addition to ICD placement, we recommend that patients with ARVC/D avoid competitive athletics. Also, we advise patients with definite or probable ARVC/D to avoid strenuous activities, such as long-distance biking or running and long-distance swimming and/or weight training. Activity should be limited to low-intensity activities, such as walking or golf.

Little data exist concerning the use of pharmacologic agents in treating patients with ARVC/D to prevent SCD. Symptomatic ventricular arrhythmias are treated initially with β-blocker therapy and/or sotalol [44••]. If β blockers cannot control a patient's symptoms or prevent recurrent VT, membrane active antiarrhythmic agents, such as sotalol and, if necessary, amiodarone, are considered. Further research is needed to determine if other commonly used treatments for heart failure, such as angiotensin-converting enzyme inhibitors, are of value for treating patients with ARVC/D.

The progressive, widespread ARVC/D pathology suggests that catheter ablation would not be a long-term curative procedure [45,46••,47–49]. Dalal et al. [46••] recently published their experience with catheter ablation of VT in 24 patients with ARVC/D. These patients underwent 48 ablation procedures at institutions throughout the United States. The cumulative VT-free survival was 75% at 1.5 months, 50% at 5 months, and 25% at 14 months. The immediate success of the procedure had no bearing on recurrence, nor did the use of an assistive mapping technique or repetition of the procedure [46••]. Somewhat more promising results were reported by Satomi et al. [47]. In this report, catheter ablation was acutely successful in ablating 23 of 26 VTs in 17 patients. During a mean follow-up of 26 ± 15 months, 13 of 17 patients were free of recurrent VT. Yao et al. [49] also reported favorable results of catheter ablation in 32 patients, with an 84% acute efficacy of catheter ablation and an 82% long-term efficacy with 28 ± 16 months of follow-up.

Catheter ablation's proper role in ARVC/D remains poorly defined. At the present time, it is best used as a palliative measure for patients with refractory VT. Further research is needed to better define the role of VT catheter ablation in ARVC/D.

Cardiac transplantation is considered in patients with progressive heart failure and intractable recurrent ventricular arrhythmias [37]. In our experience, few patients with ARVC/D require cardiac transplantation [3••].

Conclusions

ARVC/D is an inherited cardiomyopathy associated with ventricular arrhythmias and fibrofatty replacement of the right ventricular myocardium. Recent advances in the understanding of the genetic basis of this disease indicate that ARVC/D should be considered a disease of desmosome dysfunction. The diagnosis of ARVC/D is based on the Task Force criteria and should be approached with great caution. Once a diagnosis is established, placement of ICD is recommended in most patients. Further research is needed to better determine which patients and/or family members may be at low enough risk of sudden death to avoid ICD therapy.

Disclosures

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