Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is a heart muscle disorder characterized pathologically by fatty or fibrofatty replacement and electrical instability of the right ventricular myocardium. Clinical manifestations include structural and functional malformations (fatty infiltration, dilatation, aneurysms) of the right ventricle, ECG abnormalities, and presentation with ventricular tachycardias with left bundle branch block pattern or sudden death. The disease often is familial with an autosomal inheritance. The typical hallmarks of ARVD/C are distributed in the so-called “triangle of dysplasia.” The functional and morphologic characteristics are relevant to clinical imaging approaches such as contrast angiography, echocardiography, radionuclide angiography, ultrafast computed tomography, and cardiovascular magnetic resonance imaging. Evident forms of the disease are straightforward to diagnose based on a series of diagnostic criteria proposed by the International Task Force for Cardiomyopathy. However, the diagnosis of early and mild forms of the disease often is difficult. Treatment is directed toward preventing life-threatening ventricular arrhythmias in which radiofrequency ablation and implantable defibrillators play an increasing role. Despite new diagnostic and therapeutic approaches in ARVD/C, uncertainties about the etiology of the disease, the genetic basis, the appropriate diagnosis and therapy, and the clinical course of patients with ARVD/C have resulted in several registries to increase our knowledge of this intriguing disease.

KEYWORDS Arrhythmogenic right ventricular dysplasia (ARVD/C); Screening; Diagnosis; Treatment (Heart Rhythm 2006;3:225–234) © 2006 Heart Rhythm Society. All rights reserved.

The name arrhythmogenic right ventricular dysplasia (ARVD) was coined for the first time in 1978 by Frank and Fontaine. At that time, the disease was defined as “total or partial replacement of right ventricular muscle by adipose and fibrous tissue associated with arrhythmias of left bundle branch block configuration.” In 1996, the World Health Organization (WHO) and the International Society and Federation of Cardiology (ISFC) decided that ARVD had to be considered as a manifestation of a cardiomyopathy (ARVD/C).

In recent years, ARVD/C has drawn considerable attention because of better understanding of the underlying mechanisms, genetic background, improved diagnostic capabilities for early detection of ARVD/C, and use of more advanced therapies.

Incidence/prevalence

ARVD/C occurs in young adults with a male-to-female ratio of 2.7/1.0, but the true incidence is unknown. The prevalence of the disease in the general population is estimated at 0.02% to 0.1% (average 1:5,000) but is dependent on geographic circumstances. In certain regions of Italy (Padua, Venice) and Greece (Island of Naxos), an increased prevalence of 0.4% to 0.8% for ARVD/C has been reported. Eighty percent of the disease is diagnosed in patients younger than 40 years. ARVD/C should be suspected in all young patients presenting with syncope, ventricular tachycardia, or cardiac arrest. Similar to the incidence, the true prevalence of the disease is unknown because the diagnosis may be missed in a substantial number of patients.
Genetic factors

A familial predilection of ARVD/C has been recognized. The clinical findings related to ARVD/C suggested a familial occurrence of 30% to 50% with autosomal dominant inheritance, various degrees of penetrance, and polymorphic phenotypic expression. The diagnosis of ARVD/C may have important consequences for direct relatives because they have an increased chance of having the disease. Genetic screening for early detection of healthy carriers may play a fundamental role in primary prevention, considering that sudden death often occurs as a first manifestation of the disease. The genes involved and the molecular defects are not fully known, although several ARVD/C loci have been identified. Genetic disorders have been identified on chromosomes 14q23-q24 (ARVD1), 1q42-q43 (ARVD2), 14q12-q22 (ARVD3), 2q32 (ARVD4), 3p23 (ARVD5), 10p12-14 (ARVD6), 10q22, 6p24 (ARVD8), and 12p11 (ARVD9). An autosomal recessive variant of ARVD/C that is associated with palmoplantar keratosis and woolly hair (Naxos disease) has been mapped on chromosome 17q21, whereby plakoglobin and desmoplakin have been identified as the responsible genes. Plakoglobin participates in cell-to-cell junctions, and it is postulated that inadequate cell adherence injures the cardiac cell membranes, leading to cell death and fibrofatty replacement. Mutations in the desmosomal protein plakophilin-2 reportedly are common in ARVD/C patients. In addition, the cardiac ryanodine receptor gene may be involved in the disease. The ryanodine receptor probably plays an important role in inducing catecholamine-related ventricular tachycardia. It has been suggested that the advent of genetic testing will provide the gold standard for diagnosis. However, the findings of polymorphisms in ARVD/C and the fact that 50% of ARVD/C families do not show any linkage with the identified chromosomal loci stress the need to exploit an ARVD/C registry and to install tissue DNA banks.

Anatomy/histology

The most striking morphologic feature of the disease is the diffuse or segmental loss of right ventricular myocytes with replacement by fibrofatty tissue and thinning of the right ventricular wall (Figure 1). Fatty infiltration of the right ventricle per se probably is a different process that may not be considered synonymous with ARVD/C. Therefore, the diagnosis of ARVD/C should only be made in the presence of fibrosis, which probably is more arrhythmogenic than just fatty infiltration. Fibrofatty replacement usually begins in the subepicardium or mediomural layers and progresses to the subendocardium. Only the endocardium and the myocardium of the trabeculae may be spared. Anatomic malformations of the right ventricle consist of mild-to-severe global right ventricular dilation, right ventricular aneurysms, and segmental right ventricular hypokinesia. The sites of involvement are found in the so-called “triangle of dysplasia,” namely, the right ventricular outflow tract, apex, and infundibulum. However, the fibrofatty pattern of ARVD/C is limited not only to the right ventricle; the disease also might migrate to the interventricular septum and the left ventricular free wall, with a predilection for the posteroseptal and posterolateral areas. Left ventricular involvement may even be the first manifestation of the disease. The affected areas may form an “electricophysiologic hole” potentially constituting a substrate for reentrant arrhythmias.

Etiology

The exact etiology of ARVD/C is not fully understood. Four theories on the etiology of ARVD/C have been introduced: dysontogenic, degenerative, inflammatory, and apoptotic. D’Amati et al5 proposed a transdifferentiation theory, which is based on the hypothesis that cells can change from muscle to adipose tissue. A viral component also has been suggested in the pathogenesis of ARVD/C. Basso et al6 described a novel, genetically transmitted animal model in boxer dogs, which may aid in understanding the pathogenic mechanism in ARVD/C.

ECG findings

The anatomic damage present in ARVD/C may modify electrical activation and repolarization. Generally, ECG ab-
normalities can be observed in almost 90% of patients with ARVD/C. The ECG in patients with ARVD/C usually shows sinus rhythm, QRS duration >110 ms in lead V1, a terminal deflection within or at the end of the QRS complex (called epsilon wave) in leads V1–V3 (30% of patients), and inversion of T waves in the right precordial leads (50%–70% of patients) (Figure 2). Complete right bundle branch block is found in approximately 15% of patients and incomplete right bundle branch block in 18% of patients with ARVD/C. In the presence of right bundle branch block pattern, selective prolongation of the QRS duration in leads V1–V3 compared with lead V6 (>25 ms, parietal block) is an important hallmark of ARVD/C. Additional ECG markers have been reported, such as the ratio of QRS duration in leads V1+V2+V3 vs V4+V5+V6 ≥1.2 and a prolonged S wave upstroke in V1–V3 ≥55 ms in the absence of right bundle branch block. Several studies have shown a relation between ARVD/C and the Brugada syndrome. This syndrome is associated with an ECG pattern of right bundle branch block and right ventricular precordial ST-segment elevation, which may be responsible for the sudden death of young adults at rest or during sleep.

**Exercise and ventricular arrhythmias**

ARVD/C usually is characterized by the occurrence of symptomatic right ventricular arrhythmias during exercise. Islands of fibrofatty tissue may form the arrhythmogenic substrate underlying these arrhythmias that typically are induced by adrenergic stimulation. During exercise testing, 50% to 60% of patients with ARVD/C show ventricular arrhythmias, which are characteristically monomorphic and have a predominant left bundle branch block pattern in 96% (Figure 3). An inferior QRS axis during ventricular tachycardia reflects the right ventricular outflow tract as site of origin, whereas a superior axis reflects the right ventricular inferior wall as site of origin. The occurrence of arrhythmic cardiac arrest due to ARVD/C is significantly increased in athletes. Particularly in certain regions in Italy, ARVD/C has been shown to be the most frequent disease (22%) leading to exercise-induced cardiac death in athletes. As a result, a diagnosis of ARVD/C is considered incompatible with competitive sports and/or moderate-to-high intensity level recreational activities.

**Clinical presentation**

The clinical presentation varies widely because ARVD/C includes a spectrum of different conditions rather than a single identity. Different pathologic processes may manifest a diversity of symptoms, such as fatigue, atypical chest pain, syncope, or acute coronary syndrome. ARVD/C is a disease that may have a temporal progression, and the disease may present differently according to the time of presentation. There may be (1) a symptomatic form with transient or sustained ventricular tachycardia of left bundle branch block configuration, although right bundle branch block configuration also can be observed; (2) an asymptomatic form consisting of ventricular ectopic beats (>1,000/24 hours); (3) right ventricular failure with or without arrhyth-
mias; and (4) a masked form in which sudden death, usually during exercise, is the first clinical presentation. Overall, judging the accurate position of the patient on the time scale of the spectrum is difficult, and some patients may remain stable for several decades.

Natural history

The natural history of ARVD/C is determined by both cardiac electrical instability and progressive right ventricular dysfunction. In the major reported studies, mortality rates ranged from 4% to 20% for similar follow-up periods. In ARVD/C, both sexes have similar mortality risk, with a peak of risk during the fourth decade. ARVD/C may account for up to 5% of sudden deaths in young adults in the United States and 25% of exercise-related deaths in the Veneto region of Italy. Unless sudden cardiac death occurs, progressive impairment of cardiac function may result in right or biventricular heart failure late in the evolution of ARVD/C, usually in a time course of 4 to 8 years after typical development of complete right bundle branch block. Fontaine et al11 evaluated the natural history of 130 ARVD/C patients who were followed from 1977 to 2000. The authors reported 21 cardiac deaths, of which 14 were due to progressive heart failure and 7 to sudden cardiac death, resulting in an annual mortality of 2.3%. In most patients, the mechanism of sudden death in ARVD/C is acceleration of ventricular tachycardia with ultimate degeneration into ventricular fibrillation. Generally, right ventricular failure and left ventricular dysfunction were independently associated with cardiovascular mortality.

Diagnosis

A definite diagnosis of ARVD/C is based on histologic demonstration of transmural fibrofatty replacement of right ventricular myocardium at either autopsy or surgery. Myocardial biopsy lacks sufficient sensitivity because, for safety reasons, the biopsy is performed mostly in the interventricular septum, whereas the typical pathologic changes of ARVD/C are more pronounced in the right ventricular free wall. In 1994, McKenna et al7 established the criteria for diagnosing ARVD/C in a Task Force report on ARVD/C. The diagnosis of ARVD/C is based on several major and minor criteria involving structural, histologic, ECG, arrhythmic, and genetic factors (Table 1). In 2002, Hamid et al12 proposed a modification of the Task Force criteria for diagnosing ARVD/C in first-degree relatives of patients with proven ARVD/C. When standard criteria were applied, 28% of patients had ARVD/C, but when all cardiovascular parameters were taken into account, 48% of relatives had evidence of the disease. At variance with the Task Force criteria, minor abnormalities of the current ECG, Holter, or echocardiographic criteria may indicate familial involvement. As the Task Force criteria were reached by expert consensus opinion, based primarily on tertiary center experience, the criteria are highly specific but lack sensitivity. An additional drawback of the criteria is that the Task Force did not specify the preferred order of imaging techniques to
examine and score right ventricular morphology and function. A standardized imaging protocol for the different imaging techniques and a quantification of the criteria were not provided. Consequently, evident forms of the disease are straightforward to diagnose, but diagnosis of early and mild forms of the disease often is difficult. Based on our experience, serial reevaluation of Task Force-negative patients suspected of having ARVD/C with minor ECG abnormalities is indicated because frequently functional/structural abnormalities only become apparent over time.13

Differential diagnosis

The most important differential diagnosis consists of Uhl disease, which is characterized by a paper-thin right ventricle due to almost complete absence of myocardial muscle fibers probably as a result of apoptotic destruction. Uhl disease can be differentiated from ARVD/C by the absence of a major gender difference (male-to-female ratio 1.3), absence of a family history, and presentation in early childhood, usually with congestive heart failure as the first symptom. Also, the differentiation of ARVD/C from myocarditis and biventricular cardiomyopathy may be difficult, particularly when the left ventricular ejection fraction is slightly below 50%.

Many patients with ARVD/C present with right ventricular outflow tract tachycardias as a first sign of the disease. However, right ventricular outflow tract tachycardias with a left bundle branch block pattern and inferior QRS axis represent a broad clinical spectrum. These tachycardias are not only observed in ARVD/C patients; they may be of idiopathic origin and can be seen in patients with coronary artery disease, right or biventricular cardiomyopathy, sarcoidosis, and congenital heart disease. Based on electrophysiologic characteristics such as inducibility of ventricular tachycardia, the mechanism underlying the ventricular tachycardia (reentry vs triggered automaticity), presence of more than one ECG morphology, and fragmented potentials, usually one can distinguish between idiopathic right ventricular outflow tract arrhythmias and arrhythmias due to ARVD/C.14

Myocardial imaging

In addition to the Task Force criteria, imaging modalities such as contrast angiography, echocardiography, radioiso-

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Table 1  Task Force diagnostic criteria for arrhythmogenic right ventricular dysplasia/cardiomyopathy

<table>
<thead>
<tr>
<th>Major criteria</th>
<th>Minor criteria</th>
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<tbody>
<tr>
<td><strong>I Global and/or regional dysfunction and structural alterations</strong></td>
<td>Severe dilation and reduction of right ventricular ejection fraction with no (or only mild) left ventricular impairment</td>
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<tr>
<td></td>
<td>Localized right ventricular aneurysms (akineti or dyskinetic areas with diastolic bulging)</td>
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<tr>
<td></td>
<td>Severe segmental dilation of the right ventricle</td>
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<tr>
<td><strong>II Tissue characterization of walls</strong></td>
<td>Fibrofatty replacement of myocardium on endomyocardial biopsy</td>
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<tr>
<td><strong>III Repolarization abnormalities</strong></td>
<td>Epsilon waves or localized prolongation (&gt;110 ms) of the QRS complex in right precordial leads (V1–V3)</td>
</tr>
<tr>
<td><strong>IV Depolarization/conduction abnormalities</strong></td>
<td>Left bundle branch block-type ventricular tachycardia (sustained and nonsustained) (ECG, Holter, exercise testing)</td>
</tr>
<tr>
<td><strong>V Arrhythmias</strong></td>
<td>Familial disease confirmed at necropsy or surgery</td>
</tr>
<tr>
<td><strong>VI Family history</strong></td>
<td>Familial disease confirmed at necropsy or surgery</td>
</tr>
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</table>

To fulfill the appropriate criteria for arrhythmogenic right ventricular dysplasia/cardiomyopathy, patients must meet either two major criteria, one major plus two minor criteria, or four minor criteria

Adapted from McKenna et al.7

ECG = electrocardiogram; LV = left ventricle; RV = right ventricle
tope techniques, computed tomography, and cardiovascular magnetic resonance imaging may play a specific and unique role in establishing and affirming the diagnosis of ARVD/C. However, one should realize that imaging techniques are always dependent upon technical aspects of the study, focusing on the right side of the heart, the expertise of the technician, the type of equipment used, and the expertise of the interpreter. Whenever possible, an abnormality observed with one imaging technique should be verified using another imaging modality.

Right ventricular contrast angiography

Right ventricular contrast angiography usually is regarded as the reference standard for the diagnosis of ARVD/C. Angiographic evidence of ARVD/C consists of akinesis/dyskinetic bulgings localized in the anatomic triangle of dysplasia and the presence of hypertrophic trabeculae (Figure 4). However, one should realize that imaging techniques are always dependent upon technical aspects of the study, focusing on the right side of the heart, the expertise of the technician, the type of equipment used, and the expertise of the interpreter. Whenever possible, an abnormality observed with one imaging technique should be verified using another imaging modality.

Echocardiography

Echocardiography is the most widely used noninvasive technique for assessing cardiac performance in patients with ARVD/C. The most conspicuous findings by echocardiography are right ventricular dilation, enlargement of the right atrium, isolated dilatation of the right ventricular outflow tract, increased reflectivity of the moderator band, localized aneurysms, and decreased fractional area change. There also is akinesis/dyskinesis of the inferior wall and the right ventricular apex. Due to its restricted acoustic window in obese patients and in patients with pulmonary emphysema, transthoracic echocardiography is not always the optimal imaging technique for visualizing the right ventricle; in these patients, transesophageal echocardiography is the preferred approach. Peters et al compared intracardiac ultrasound with contrast angiography in 25 patients with ARVD/C and showed additional details in 12 patients with the ultrasound technique. In the near future, contrast echocardiography may help in diagnosing ARVD/C because of improved endocardial border delineation and enhanced right ventricular opacification (Figure 5). In clinical practice, echocardiography will remain the initial diagnostic approach in patients suspected of having ARVD/C.

Radioisotope techniques

Radionuclide angiography, by showing abnormal right ventricular function with left ventricular involvement, is useful for predicting subsequent cardiac death in ARVD/C. Myocardial perfusion scintigraphy allows noninvasive assessment of right ventricular damage in patients with arrhythmias due to ARVD/C. This technique may distinguish patients with ARVD/C from those with idiopathic right ventricular outflow tract tachycardias.

Use of radioisotopes with specific affinity for the beta-adrenoceptor allows investigation of the neuronal mechanisms of the heart. In patients with ARVD/C, cardiac sympathetic innervation is diminished, which may have implications for early recognition and treatment of arrhythmias. Current limitations of radioisotope imaging, such as suboptimal spatial resolution and inherent radiation burden, prohibit the use of radionuclide imaging as a first-line approach in patients with ARVD/C.
Computed tomography

Computed tomography is capable of diagnosing patients with ARVD/C. Electron-beam computed tomography provides superior resolution, enabling improved visualization of the right and left ventricles because of its ability to acquire cardiac images in cross-section. Dery et al. were the first to demonstrate a dilated hypokinetic right ventricle in a patient with ARVD/C. Specific findings of ARVD/C on electron-beam computed tomography are the presence of epicardial fat, intramyocardial fat deposits, conspicuous trabeculations with low attenuation, dilated hypokinetic right ventricle, and scalloped appearance of the right ventricular wall. At present, there are no reports on the use of multislice computed tomography in ARVD/C patients. In the near future, this advanced modality may improve the capability to detect the disease by virtue of its enhanced temporal and spatial resolution. In addition, computed tomography may be of value in serially evaluating ARVD/C patients with an implantable cardioverter-defibrillator. Because the radiation burden is high, multislice computed tomography currently is not the optional imaging modality for initial screening of patients suspected of having ARVD/C.

Cardiovascular magnetic resonance imaging

Theoretically, cardiovascular magnetic resonance imaging offers the optimal noninvasive imaging approach in patients with right and left ventricular dysfunction, in view of its high spatial resolution and unlimited field of view. This modality allows visualization of the right ventricle, not only anatomically and morphologically but also in functional and flow dynamic terms. Anatomic and morphologic abnormalities in patients with ARVD/C include intramyocardial fat deposits, focal wall thinning, wall hypertrophy, trabecular disarray, and right ventricular outflow tract enlargement. The ability of this technique to characterize adipose infiltration by showing myocardial areas with high signal intensity is unique in diagnosing ARVD/C. Functional abnormalities consist of right ventricular aneurysms, regional thinning, right ventricular dilation, failure of systolic thickening, and impaired global and diastolic right ventricular function. In addition, cardiovascular magnetic resonance imaging allows velocity mapping of tricuspid flow, which may be an early but nonspecific sign of the disease. Cardiovascular magnetic resonance imaging is more accurate in analyzing right ventricular function than most other imaging modalities because it allows a truly three-dimensional calculation of ventricular volumes.

Midiri et al. used the following five anatomic, morphologic, and functional cardiovascular magnetic resonance criteria for diagnosis of ARVD/C: (1) presence of high-signal intensity areas indicating the substitution of myocardium by fat, (2) ectasia of right ventricular outflow tract, (3) dyskinetic bulges, (4) right ventricular dilation, and (5) right atrial enlargement (Figure 6). However, much experience in interpretation of cardiovascular magnetic resonance imaging is required because of the normal variants of the right ventricle, which in general are greater than for the left ventricle. Of interest, studies revealed that focal wall-motion abnormalities are much more reliable indicators than intramyocardial fat infiltration, which appears to have a poor interreader agreement. Bomma et al. demonstrated that the diagnosis of ARVD/C cannot rely solely upon qualitative features noted by cardiovascular magnetic resonance imaging as 77% of patients with initial abnormal cardiovascular magnetic resonance imaging findings of intramyocardial fat/wall thinning could not be confirmed at reevaluation.

Consequently, there was a high rate of misdiagnosis of ARVD/C based on the supposed finding of adipose infiltration by cardiovascular magnetic resonance. Because fibrosis may be more specific than intramyocardial fat, Tandri et al. used an improved imaging approach to visualize the intramyocardial fibrotic process. The authors showed for the first time that contrast-enhanced cardiovascular magnetic resonance imaging allowed identification of myocardial fibrosis by increased signal enhancement in the majority of patients with ARVD/C.

Several studies have addressed the value of cardiovascular magnetic resonance imaging in patients showing right ventricular outflow tract tachycardias as a first manifestation of ARVD/C. Patients with idiopathic right ventricular outflow tract tachycardias were shown to be morphologically indistinguishable from healthy individuals. Kayser et al.
showed a high diagnostic accuracy for detecting ARVD/C in patients with ventricular tachycardia with a left bundle branch block pattern.

In summary, cardiovascular magnetic resonance imaging provides important anatomic, morphologic, functional, and flow-dynamic criteria for diagnosing ARVD/C. Although fatty infiltration has been shown to have less diagnostic accuracy than wall-motion abnormalities, cardiovascular magnetic resonance imaging is an important technique for detecting structural abnormalities suggestive of ARVD/C, but the imaging findings should be confirmed by other imaging modalities such as echocardiography and/or angiography.19 Accordingly, the diagnosis of ARVD/C must be made based on Task Force criteria and not on structural abnormalities alone. As a result, echocardiography will be the initial diagnostic approach in most centers.

**Treatment**

There are five therapeutic options in patients with ARVD/C: (1) antiarrhythmic agents, (2) radiofrequency ablation, (3) implantable cardioverter-defibrillator therapy, (4) heart failure treatment, and (5) surgical treatment.

1. The effects of antiarrhythmic drug therapy are difficult to assess because of small series of patients and limited time to follow-up. Wichter et al26 found sotalol was more effective than beta-blocking agents or amiodarone both in patients with inducible ventricular tachycardia and those with noninducible ventricular tachycardia. However, it is not known whether sotalol is able to prevent sudden death, even in patients tested by programmed electrical stimulation.

2. Catheter ablation can be considered in case of drug intolerance or ineffectiveness.27 To guide radiofrequency ablation, electroanatomic mapping constitutes a suitable way to visualize the myocardium in patients with ARVD/C. Boulos et al28 were the first to describe three-dimensional electroanatomic mapping using the CARTO technique. By studying spatial association of endocardial electrograms, significant loss of myocytes was shown to result in the recording of low-amplitude, fractionated endocardial ECGs with a prolonged duration (Figure 7). There was an excellent concordance with echocardiography and cardiovascular magnetic resonance imaging in detecting the pathologic substrate.

   Success of the ablation procedure may be affected by the progressive and diffuse nature of the disease, resulting in multiple arrhythmogenic foci, which are difficult to abolish. Fontaine et al29 studied 50 patients who were followed for a mean of 5.4 years, and the authors reported success rates of 32%, 45%, and 66% after one, two, and three ablations, respectively. Most of these patients had not responded to pharmacologic therapy.29 In our institution, radiofrequency ablation proved to be successful in 32 patients with ARVD/C and drug-refractory ventricular tachycardia, with an initial success rate of 88%. However, we observed procedure-related complications, such as myocardial perforation, in two patients. In addition, one patient required pericardiocentesis for pericardial effusion. In line with previous studies, we observed recurrences in 7 (29%) patients during follow-up (Figure 8).30

3. Implantable cardioverter-defibrillator therapy is indicated in case of serious risk of sudden death.31 Patients at highest risk are those who have been resuscitated, those who are unresponsive or intolerant of antiarrhythmic therapy (secondary prevention), and those with the disease who have a family history of cardiac arrest in first-degree relatives (primary prevention). There is no evidence that patients who have a positive family history but no evidence of the disease are at exceptional high risk. Although an implantable cardioverter-defibrillator has been shown to be the most effective safeguard against sudden arrhythmic death in large patient populations with ARVD/C, its precise role still needs to be defined.32,33 Programming the implantable cardioverter-defibrillator is difficult in ARVD/C patients because they may develop supraventricular and ventricular tachyarrhythmias with similar rates. In addition, the fibrofatty nature of the right ventricle may preclude proper sensing of the implantable cardioverter-defibrillator. Wichter et al32 showed a high incidence of lead-related adverse events in 60 patients with ARVD/C who received implantable cardioverter-defibrillator therapy because of resuscitated cardiac arrest or sustained ventricular tachycardia. In a series of 132 patients, Corrado et al33 showed that five patients required placement of an additional septal lead due to loss of ventricular sensing and/or pacing, and that four patients had an increase in defibrillation threshold. Overall, the major clinical question remains whether it would be possible to identify those
patients with ARVD/C who could benefit most from implantable cardioverter-defibrillator placement based on anticipated knowledge such as genetic screening. In our institution, placement of an implantable cardioverter-defibrillator is indicated in patients with ventricular arrhythmias and a positive family history, ventricular tachycardia/fibrillation prone to collapse, hemodynamically unstable ventricular tachycardias, or frequently occurring stable ventricular tachycardias that are difficult to abolish by radiofrequency catheter ablation. In all other patient categories, we prefer to start with sotalol as the primary drug of choice.

4. When the disease has progressed to right ventricular or biventricular failure, treatment consists of the current therapy for heart failure, including diuretics, beta-blocking agents, angiotensin-converting enzyme inhibitors, and anticoagulants. In case of intractable right ventricular failure, cardiac transplantation may be the only remaining alternative.

5. More than 20 years ago, surgical treatment was introduced, initially consisting of right ventriculotomy. Total disconnection of the right free wall then was tried. This approach was abandoned because of the risk of developing right ventricular failure, the increased availability of cardiac transplantation, and the improvement in the technology of implantable cardioverter-defibrillators. Occasionally, disconnection surgery or right ventricular cardiomyoplasty is a useful therapeutic option.

Conclusion

ARVD/C is a heart muscle disorder of unknown course that is characterized pathologically by fibrofatty replacement of the right ventricular myocardium and electrical instability. Clinical manifestations include structural and functional malformations of the right ventricle, ECG abnormalities, and presentation with ventricular tachycardia with left bundle branch block pattern or sudden death. Although in most centers echocardiography will remain the initial screening approach for patients suspected of having ARVD/C, cardiovascular magnetic resonance imaging provides important anatomic, morphologic, functional, and flow-dynamic criteria to aid in the diagnosis of ARVD/C. Nevertheless, the diagnosis of ARVD/C consists of a combination of ECG and morphologic abnormalities as well as evidence of familial disease. Genetic evaluation is becoming increasingly important in confirming the diagnosis in probands and family members. Pharmacologic treatment remains useful, but radiofrequency ablation and implantable cardioverter-defibrillator therapy are increasingly important therapeutic approaches in patients with ARVD/C. However, remaining uncertainties about the etiology of the disease, the genetic basis, the appropriate diagnosis and therapy, and the clinical course of patients with ARVD/C have resulted in initiation of several registries to increase our knowledge of this intriguing disease. Currently, large clinical trials of ARVD/C patients are in progress, such as the European ARVD Registry and the Multidisciplinary Study of Right Ventricular Dysplasia (US ARVD Study). Hopefully these registries will improve our knowledge of ARVD/C.

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