Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia: Mechanisms and Management

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Abstract: Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is a primary cardiac myocytes disorder that predominantly affects the right ventricle. It is mainly inherited as autosomal dominant with variable expressivity; it also has been recognized as one of the major genetic causes of sudden cardiac death in the young and in athletes. The desmosomal protein is the most commonly affected structure and around 60% of diagnosed cases have an identified genetic mutation. ARVC is characterized histologically by the replacement of cardiomyocytes with fibro-fatty tissue that is progressive over time. The most commonly involved sites in the heart are right ventricle inflow tract, right ventricular outflow tract and posterolateral wall of the left ventricle. New diagnostic criteria have increased the sensitivity and specificity for ARVC/D. These include imaging evidence of RV regional wall motion abnormalities and RV dilatation using echocardiography, cardiac magnetic resonance imaging and angiography. Other diagnostic criteria include fibrous replacement of the RV-free wall on biopsy, repolarization and conduction abnormalities on the electrocardiogram as well as ventricular tachyarrhythmias and significant family history. Management involves assessing for implantable-cardioverter implantation, pharmacological therapy for prevention of ventricular arrhythmias and treatment of any ventricular dysfunction. Patients with ARVC/D who are engaged in strenuous/endurance/competitive physical activity have 2–5-fold increased risk of sudden cardiac death and restriction from competitive/endurance sports is important. Family screening is important to identify asymptomatic patients.

Keywords: arrhythmogenic right ventricular dysplasia, sudden cardiac death, ventricular tachycardia, arrhythmogenic cardiomyopathy

Introduction

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) also known as arrhythmogenic right ventricular dysplasia (ARV) was first well-described in 1982 in a case series of 24 patients by Marcus et al.¹ ARVC/D is an inherited, autosomal dominant disease with variable expressivity and penetrance,² that is characterized histologically by the replacement of cardiomyocytes with fibro-fatty tissue and is progressive over time. The new infiltrates act as a substrate for ventricular arrhythmias and eventually lead to right ventricular failure and sudden cardiac death (SCD).³ While the disease predominantly affects the right ventricle, recent studies and improved imaging has allowed the discernment of left ventricular involvement in a substantial proportion of patients.⁴

Due to variable expression, it is difficult to diagnose, and thus, to estimate the incidence and prevalence of ARVC/D. The disease spectrum varies between silent

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clinical features such as electrocardiographic changes, to florid right ventricular failure, malignant arrhythmias and SCD.^{5,6} Around 40% of cases are diagnosed through testing of first-degree relatives.⁷ The estimated prevalence of ARVC/D is 1:1000 to 1:5000.^{8,9} This disease might be responsible for about 20% of cases of SCDs in the young across Europe and up to 27% of sports-related SCD.^{6,10} A recently published nationwide study on SCD in patients aged 13–25 years from USA national registry between 1980 and 2011 suggested that ARVC is responsible for about 5% of SCD.¹¹ The disease is more prevalent in men with a ratio of 3:1, and a family history is present in 30–50% of cases.^{12–15}

Efforts have been made to improve our understanding of this disease, resulting in new strategies that focus on early diagnosis based on evaluating the functional and structural cardiac alterations characteristic of this entity, as well as genetic testing for patients considered at high risk. This culminated in the development of the updated International Task Force Criteria for the clinical diagnosis of ARVC/D in 2010.¹⁶ The main objective of treatment is to reduce the risk of sudden cardiac death and improve the quality of life for patients suffering from this disease. This is achieved mainly by appropriate pharmacological and device therapy, as well as restriction of strenuous physical activity. The latter has a direct relationship with disease progression and severity of

arrhythmias.¹⁷ ARVC is a common cause of sudden cardiac death (SCD) in athletes.¹⁸ This review focuses on mechanisms underlying ARVC and how they relate to the clinical presentation and diagnostic criteria. In addition, all aspects of the clinical management of ARVC will be addressed.

Mechanisms of ARVC/D

Genetics

It is now well established that the primary-diseased structure is a desmosomal protein in most cases.^{19–21} It was later discovered that other non-desmosomal proteins play a role in the pathogenesis of this disease. This is evident by the number of isolated disease-causing genes (Table 1). Of all patients diagnosed with ARVC, causative mutations can be identified in 60% of patients, with the majority involving genes that encode mechanical junction proteins in the intercalated disk.²²

Pathogenesis

Desmosomal proteins are specialized proteins that span the cell membrane, facilitate communication and provide structural support between myocytes. Desmosomal proteins perform an important role in 1) gene transcription and regulation of differentiation 2) electrical current conduction through regulation of gap junction and 3) calcium homeostasis.^{21,23} Multiple theories have been proposed to

Table 1 Some of the Principal Disease-Associated Genes in Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia

Gene	Protein	Function	Mode of Inheritance	Phenotype
Desmosomal proteins				
JUP ²⁴	Plakoglobin	Desmosomal protein	AD/AR	Cardiocutaneous syndrome (Naxos disease)
DSP ⁸⁴	Desmoplakin	Desmosomal protein	AD/AR	Cardiocutaneous syndrome (Carvajal syndrome)
PKP2 ⁸⁵	Plakophilin-2*	Desmosomal protein	AD/AR	ARVC/D
DSG2 ⁸⁶	Desmoglein-2	Desmosomal protein	AD/AR	ARVC/D
DSC2 ⁸⁷	Desmocollin-2	Desmosomal protein	AD/AR	ARVC/D
Non-desmosomal proteins				
TGFB3 ⁸⁸	Transforming growth factor-Beta-3	Cytokine	AD	ARVC/D
TMEM43 ⁸⁹	Transmembrane protein 43	Nuclear membrane protein	AD	ARVC/D
DES ⁹⁰	Desmin	Intermediate filament	AD	Overlap syndrome (between HCM and DCM phenotype) with early conduction disease
TTN	Titin	Cytoskeleton protein	AD	Overlap syndrome with early conduction disease
CTNAA3	Alpha-T-Catenin	Cytoskeleton protein	AD	ARVC/D

Note: *Most common (Frequency in ARVC/D 20–45%). The table is modified from Basso et al²⁶ and Mazurek et al.²³

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; ARVC/D, arrhythmogenic right ventricular cardiomyopathy/dysplasia; HCM, hypertrophic cardiomyopathy; DCM, dilated cardiomyopathy.

explain the mechanism by which desmosomal abnormalities are related to the pathogenesis of ARVC/D and creation of fibrofatty infiltrates instead of the normal myocardium (Figure 1A).

An example of this pathogenesis is better understood in Naxos disease, a cardiocutaneous syndrome characterized by a triad of non-epidermolytic palmoplantar keratoderma, woolly hair and ARVC/D.²⁴ The single causative protein in common between the triad is a mutant plakoglobin protein which is a part of cell-to-cell adhesion complex. Abnormalities in adhesion would promote myocytes detachment, apoptosis²⁵ and subsequently, replacement by fibrofatty tissue.²⁶ It is important to note that exercise increases the rate of myocytes detachment; athletic mutation-carriers become symptomatic earlier than non-athletics, and have a worse phenotype.²⁷

Desmosomes are important proteins in transcription regulation. In normal myocardial cells, Canonical Wnt signaling is active and it prevents the degradation of cytoplasmic β -catenin protein. β -catenin is a protein that travels to the

nucleus to facilitate and aid in the recognition and transcription of target genes by binding to TCF/LEF complexes.²⁸ Plakoglobin (AKA γ -catenin) is one of the desmosomal proteins similar in properties to β -catenin, but with antagonizing effects.^{21,23,26} In patients with defective Desmoplakin (another desmosomal protein), free Plakoglobin is enabled to travel and localizes the nucleus where it replaces β -catenin, and switches transcription from myogenesis to adipogenesis²⁹ (Figure 1B).

Arrhythmia is a common feature of dilated cardiomyopathy, and patients are at increased risk of developing sudden cardiac death with worsening structural abnormalities.³⁰ However, arrhythmias in ARVC/D are one of the early manifestations of the disease, which can develop even before any obvious cardiac pathology.^{31,32} This is likely secondary to gap-junction remodeling associated with the ARVC/D. For example, there is a clear evidence of downregulation of Connexin 43, one of the major gap-junction proteins,^{33,34} this phenomena is not specific to ARVC/D, but also found in other cardiomyopathies.³⁵ Another observation is the decreased I_{Na} secondary to decreased formation of sodium

Figure 1 Schematic representation of molecular basis and pathogenesis of Arrhythmogenic right ventricular cardiomyopathy/dysplasia. (A) Tight gap junctions and close intercellular connection between cardiomyocyte is essential in normal function and signal transduction between cardiac cells. (B) When there is a defective plakophilin 2, plakoglobin is freed to localize the nucleus and replaces beta-catenin in the TCF/LEF to form a complex that inhibits canonical Wnt signaling pathway thus increasing beta-catenin destruction and switching the cell to lipogenesis. This event will result in increased intercellular space, impaired cell-to-cell adhesion and malfunctioning of gap junctions. The steps of pathogenesis are numbered 1–3.

Abbreviations: TCF, t-cell factor; LEF, lymphoid enhancer factor.

pores evident by paucity of Nav1.5 (a pore-forming protein) at the intercalated disks in patients with ARVC/D.^{36,37}

Pathology

ARVC/D is a misleading name, as the disease may also affect the left ventricle (LV) instigating a shift to the use of the term arrhythmogenic ventricular cardiomyopathy.⁵ Right ventricular (RV) involvement can be generalized or localized as well. Grossly there will be dilation and thinning of the affected myocardium. The most commonly involved sites in the heart are right ventricle inflow tract, RV outflow tract and posterolateral wall of the LV. These three sites have been termed “the new triangle of dysplasia”.³⁸ The RV apex, which was part of the “original triangle of dysplasia”,³² is also frequently affected but commonly only seen in severe and end-stage disease. Its worth mentioning that in some cases LV involvement may precede RV dysfunction.³⁹ ARVC/D is a progressive disease, and typically starts in the RV and, with age, continues to invade the LV.^{5,40} LV involvement is commonly seen in patients with PKP2 mutation, which is the most frequently seen genotype in ARVC/D.² On a microscopic level, the main characteristic of the disease is the replacement of normal myocardium by fibrofatty or fatty infiltrates, which are inherently a substrate for macro-reentrant circuits.^{41,42} Frequently noted, and specially in autopsies of patients who had sudden cardiac death, the presence of inflammatory infiltrates in areas of dying myocardium.^{5,41}

Clinical Features and Diagnostic Criteria

One of the challenging features of ARVC/D is that it may remain silent for decades. In addition, it has variable presentations ranging from totally asymptomatic patients, palpitations and sudden cardiac death. Many cases of ARVC/D come to medical attention following screening because of ARVC/D diagnosis in a relative.⁴³ The mean age at diagnosis is 30 years with a range of 10 years to 50 years of age. Presentation appears to be earlier in athletes, and more malignant in males. There are specific features of some mutations and these are listed in Table 2.

Palpitations, presyncope and syncope are the most common complaints occurring in >90% of patients. Other symptoms include atypical chest pain, dyspnea and right ventricular failure.⁴⁴ Palpitations and presyncope/syncope are most commonly associated with ventricular arrhythmia, which can be premature ventricular beats, or even ventricular tachycardia, most commonly originating from

Table 2 Mutations and Associated Features

Mutation	Features
Plakoglobin (AR)	<ul style="list-style-type: none"> • “Naxos Disease” <ul style="list-style-type: none"> ◦ Woolly hair ◦ Palmoplantar keratosis ◦ 100% penetrance of ARVC
Desmoplakin (AR)	<ul style="list-style-type: none"> • “Carvajal Syndrome” <ul style="list-style-type: none"> ◦ Woolly hair ◦ Epidermolytic palmoplantar keratoderma ◦ Biventricular ARVC
Desmoplakin (AD)	<ul style="list-style-type: none"> • Early LV involvement, may exceed the severity of RV disease
Plakophilin 2 (AD)	<ul style="list-style-type: none"> • Classic ARVC
Desmoglein (AD)	<ul style="list-style-type: none"> • Arrhythmia
Desmocollin (AD)	<ul style="list-style-type: none"> • SCD
TMEM43 (AD)	<ul style="list-style-type: none"> • Worse outcomes in males • Full penetrance • More aggressive disease

Note: Data from these studies.^{24,84,89,91–93}

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; ARVC, arrhythmogenic right ventricular cardiomyopathy; LV, left ventricle; RV, right ventricular; SCD, sudden cardiac death.

the RV (LBBB morphology).⁷ In addition, ARVC/D patients are at increased risk of SCD and this can be the initial presentation.^{7,13} Given the non-specific signs and symptoms of ARVC/D, the original Task Force criteria in 1994 was updated in 2010.¹⁶ The new criteria increased the sensitivity and specificity of ARVC/D diagnosis. These include imaging evidence of RV regional wall motion abnormalities and RV dilatation using echocardiography, cardiac magnetic resonance imaging and angiography. Other diagnostic criteria include fibrous replacement of the RV-free wall on biopsy, repolarization and conduction abnormalities on the electrocardiogram as well as ventricular tachyarrhythmias and significant family history.¹⁶

Management

In patients with ARVC/D, the main goal of clinical management is to prevent sudden cardiac death and slow the progression of disease. Other aims include anticipation and management of complications as they arise in order to improve quality of life as well as the early detection of asymptomatic ARVC/D patients once a proband is identified to trigger cascade screening in first-degree relatives. In patients with symptomatic ventricular arrhythmias or those experiencing ICD therapies, interventions to reduce the burden of ventricular arrhythmias are needed. The

avoidance of strenuous physical activity is essential to prevent progression of the disease. One should consider a multidisciplinary approach to manage ARVC/D patients, as this disease affects patient's activity, habits, and mental status.

Once diagnosis is confirmed, a stepwise evaluation of the patient's risks and clinical situation should be commenced. This would serve in determining prognosis, anticipate adverse outcomes and appropriateness of ICD therapy. Patients who have had a prior SCD or a hemodynamically significant sustained ventricular tachycardia have a clear indication for an ICD; in this population, the annual risk of requiring appropriate ICD therapy is around 7% to 10%.⁴⁵ If a patient has not had a prior SCD or VT, then a risk stratification approach is needed to identify those who would benefit from an ICD; in high-risk patients, appropriate ICD therapy can occur in around 5% of patients per year, a substantial risk. Interestingly, in a recent study by Zorzi and colleagues, found that phenotypic expression of ARVC/D as defined by the presence of syncope, non-sustained ventricular arrhythmias or ventricular dysfunction as compared to gene-positive non-phenotypic patients portends a substantially greater risk of sustained VT and SCD.⁴⁶ The incidence of VT or SCD was 2.3%/year among patients with definite ARVC with phenotypic expression and 0.2%/year in phenotype negative or borderline patients ($P = 0.002$).⁴⁶

Risk Stratification

Most of the information on ARVC/D is from retrospective studies, which makes it difficult to create a precise risk stratification model. A recently developed risk model published by an international collaboration in six countries (18 centers) from Europe and North America reported that variables associated with higher risk for VT/VF are: male sex, young age, extent of T-wave inversion across precordial and inferior leads on ECG, imaging features reflecting more extensive RV disease and severity of ventricular arrhythmia.⁴⁷

Multiple studies examined independent risk factors associated with poor outcomes (defined as malignant arrhythmia, appropriate ICD interventions, death or heart transplant) in ARVC/D by the means of multivariable analysis. Most commonly reported significant (or at borderline statistical significance) factors are aborted SCD, either VT or VF related;^{48–50} Unexplained syncope;^{48,50,51} non-sustained ventricular tachycardia;^{51,52} premature ventricular contraction frequency >1000/24 hrs;⁵³ atrial fibrillation;⁵⁴ inducible VT in

electrophysiology studies;^{52,53,55,56} proband status;⁵⁷ young age at first presentation;^{48,49,53} male sex;^{54,57–59} multiple genetic mutations;⁵⁸ amount of myocardial scarring;^{60–62} extent of T-wave inversion on ECG;^{49,57,63} LV dysfunction^{44,48,55,64,65} and RV dysfunction or dilatation.^{55,66}

Electrophysiologic study (EPS) is a powerful diagnostic tool in situations where there is a doubt about the diagnosis, specially between ARVC/D and idiopathic right ventricular outflow tract tachycardia.⁶⁷ EPS can also serve as a prognostic tool, as mentioned above. Even with the presence of conflicting data regarding usefulness of VT-inducibility as a risk factor to predict long-term outcomes in ARVC/D, EPS can be helpful in optimization of the detection/discrimination algorithms and anti-tachycardia pacing protocols in ICD recipients.⁶⁸ It is recommended that EPS should be considered in the diagnosis and/or evaluation of patients with suspected ARVC/D, it is also reasonable for risk stratification in asymptomatic patients.⁶⁸

ICDs to Prevent SCD

Initial attempts at prevention of SCD through surgical fulguration were unsuccessful. ICDs made it possible to prevent SCD in patients with ARVC/D; however, it is important to target patients at risk of developing lethal arrhythmias (VT/VF) to avoid unneeded short or long-term complications of ICD therapy.⁶⁹ Deciding on ICD placement is usually the best next logical step after patient's presentation and risk stratification. It can be placed for primary or secondary prevention. ICD placement should be a shared decision made between patients and treating physicians. No randomized trials have yet been performed to compare ICDs with medical therapy in patients with ARVC/D. Patients with ARVC/D have a high burden of VT requiring ICD therapy or leading to SCD in those without an ICD. This is compounded by a prolonged period of exposure given the young age at diagnosis. On the other hand, the young age of ICD implantation also exposes patients to ICD complications, inappropriate ICD shocks and the requirement for multiple generator replacements. Appropriateness of ICD therapy in high-risk patients has been demonstrated in multiple studies. In a cohort of 131 patients with ARVC/D who did not have an ICD, 29% experienced significant ventricular tachycardia including SCD with an annualized rate of 5.6%.⁷⁰ In a meta-analysis reported by Schinkel⁷¹ it was found that in high-risk ARVC/D patients, the rate of appropriate ICD intervention was 9.5%/year.

Recently, the Heart Rhythm Society published their expert consensus⁷² on ICD placement in arrhythmogenic cardiomyopathy; ARVC/D-specific recommendations were as follows: class I recommendation for patients with ARVC/D who had experienced SCD or hemodynamically not tolerated VT; class IIa recommendation for patients with ARVC/D that had stable sustained VT, or patients with multiple risk factors (Figure 2) (three major, two major and two minor, or one major and four minor); class IIb recommendation for patients with multiple risk factors (two major, one major and two minor, or four minor).⁷²

Another set of recommendations for ICD therapy in ARVC/D patients were published in 2015 by Corrado et al⁶⁸ with similar recommendations. Class I indications for ICD placements were in patients who have: 1) ≥ 1 episode of unstable sustained VT/VF (secondary prevention) or 2) Severe systolic dysfunction of the RV, LV, or both regardless of the presence of arrhythmia (primary prevention). Class IIa indications for ICD placement were in patients who have 1) ≥ 1 episode of stable sustained VT or 2) Major risk factors (NSVT, moderate ventricular dysfunction, unexplained syncope). Class IIb indication is reserved for asymptomatic

patients with minor risk factors. In patients with low risk for SCD (asymptomatic, no risk factors and healthy gene carriers), ICD implantation is not indicated and thus given a class III recommendation as risks of ICD placement outweighs the benefits. Device selection should be based on individualized clinical scenario; for example, cardiac resynchronization therapy (CRT) is reasonable in cases where there is EF of $<35\%$ and LBBB morphology on 12-lead ECG. Figure 3 depicts our current approach to the management of ARVC/D.

Activity Restriction and Lifestyle Modification

One of the modifiable risk factors is engagement in competitive/endurance sports. The link between high-intensity exercise and early onset of ARVC/D symptoms has been demonstrated in prospective, retrospective and animal studies. Patients with ARVC/D who are engaged in strenuous/endurance/competitive physical activity have 2-5-fold increased risk of sudden cardiac death.^{73,74} In addition, in the population of ARVC/D, athletes showed reduced LV and RV function compared

Figure 2 Risk factors for sudden cardiac death in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia who have not experienced sudden cardiac death or sustained ventricular tachycardia. Criteria from 2019 Heart Rhythm Society expert consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy.⁷² *Major criteria; **Minor criteria.

Abbreviation: PVC, premature ventricular contraction.

Figure 3 Suggested algorithm for the management of arrhythmogenic right ventricular cardiomyopathy/dysplasia. *Treatment with angiotensin converting enzyme inhibitor/angiotensin receptor blocker, beta blocker and mineralocorticoid receptor antagonists. **See Figure 2.

Abbreviations: AAD, anti-arrhythmic drugs; ECG, electrocardiogram; ICD, implantable-cardioverter defibrillators; LVEF, left ventricular ejection fraction; RV, right ventricle; SCD, sudden cardiac death; VA, ventricular arrhythmias; VT, ventricular tachycardia.

with non-athletes in a mutation-positive family.¹⁷ Exercise restriction is associated with a 70–80% reduction in the risk of VT and ICD therapy including patients who never had ventricular arrhythmias beforehand.⁷⁵ Given the clear association, it is recommended that all patients diagnosed with ARVC/D not participate in competitive or endurance exercises (Class

I recommendation).⁷² It is also recommended for those patients to abstain from non-competitive high-intensity sports (such as hockey, football, basketball, and activities that require sprinting). Patients who are engaged in low-intensity recreational activities did not show a higher risk for early onset phenotype or SCD compared with patients who are inactive.⁷⁴

Pharmacological Therapy

There is limited data for the use of anti-arrhythmic drugs (AAD) in patients with ARVC/D; however, most recommendations are based on clinical experience, registries and retrospective studies. AAD should not be prescribed prophylactically for asymptomatic patients. They are only indicated in patients who experience symptoms such as frequent PVCs and/or non-sustained VT, or patients who have an existing ICD and experience frequent appropriate device discharges.⁶⁸

The choice of AAD is variable across literature, most commonly used medications are amiodarone or sotalol.⁷⁶ Wichter et al assessed AAD efficacy in low and intermediate-risk patients with ARVC/D and found that sotalol was more effective in preventing ventricular arrhythmia than amiodarone.⁷⁷ Amiodarone was more effective (although only in smaller number of patients) in another study published by Marcus et al.⁷⁸ These conflicting results could be explained by the differences in the target dose used in both studies, specially sotalol dose.

Amiodarone and sotalol are both class III AAD, and both have a degree of beta blockade. In addition, both block potassium channels which slows repolarization of cardiac cells and increases the effective refractory period in ventricular cardiomyocytes thus increasing the action potential period. These effects are key features in the mechanism by which class III AADs can suppress arrhythmias. Interestingly, the distribution of the fibrosis with lower fibrotic density compared to ischemic scar and the cellular electrical uncoupling linked to molecular disjunction indicate that arrhythmic mechanisms such as abnormal automaticity and trigger activity are ore likely causative compared to re-entry in the genesis of ventricular arrhythmias.³²

The current guidelines recommended the use of amiodarone when indicated and acknowledged the conflicting evidence for AAD.⁷⁶ However, they recommend using a beta-blocker as a first-line agent in ARVC/D patients with either atrial or ventricular arrhythmia, and AADs should be an adjunct therapy, it is also recommended to avoid prophylactic use of beta blockers or AADs in asymptomatic patients.⁶⁸ For patients with concomitant heart failure, pharmacological therapy should be based on guide-directed medical therapy.⁷²

Catheter Ablation

VT ablation (both endocardial and epicardial) is not a curative solution for VT in patients with ARVC/D due to

the progressive nature of the disease and patchy distribution. Multiple studies demonstrated high recurrence rate of VT in both short and long term follow up.^{79–82} It is recommended however, in cases refractory to maximal pharmacological therapy or if there is a contraindication to medical therapy.

Heart Transplant

If indicated heart transplant is a final therapeutic option in ARVC/D patients who are eligible for the procedure. Most common indications are severe heart failure or intractable ventricular arrhythmias.⁸³

Family Screening

Current guidelines recommend that all ARVC/D patients should be seen by a genetic counselor or by an experienced clinician to obtain a comprehensive family history spanning three generations. In addition, first-degree relatives should submit to clinical evaluation every 1–3 beginning at the early age of 12 years. The cardiovascular evaluation should include a 12-lead ECG, 24–48 hr Holter monitoring to assess for ventricular arrhythmias, and cardiac imaging such as echocardiography or cardiac magnetic resonance imaging to assess for RV regional wall motion abnormalities or dilatation. As an adjunct to cardiovascular evaluation, exercise stress testing to provoke arrhythmias may be considered.

Conclusions

ARVC is as one of the major genetic causes of sudden cardiac death in the young and in athletes. The desmosomal protein is the most commonly affected structure and around 60% of diagnosed cases have an identified genetic mutation. New diagnostic criteria have improved the sensitivity of testing for ARVC. Management revolves around ICD implantation for primary or secondary prevention of ventricular arrhythmias. Future research should focus on curative approaches as well as interventions to improve quality of life.

Disclosure

The authors report no conflicts of interest in this work.

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