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Arrhythmogenic Right Ventricular Cardiomyopathy in Chinese Patients

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Introduction

Arrhythmogenic right ventricular cardio-myopathy (ARVC) is a familial form of cardiomyoapthy with autosomal dominant inheritance in most cases.[1] The most tragic characteristic of this condition is that it causes sudden arrhythmic death in relatively healthy young persons without any preceding symptom. The manifestation of the disease varies between different ethnic groups. In Naxos disease affecting Greece, ARVC is strongly associated with the dermatological condition, palmoplantar keratosis.[2] In Veneto region of Italy, however, sudden cardiac death (SCD) in young athletes is the major manifestation of ARVC with one-fifth of SCD related to the disease.[3] There is very limited information about ARVC in Chinese population. This article aims to provide information about the clinical characteristics of ARVC in local population and a brief review of management of this disease.

Pathology and Genetics

ARVC is characterized pathologically by fibrofatty replacement of right ventricular myocardium. The arrhythmogenic substrate may be explained by the slow conduction between surviving fibres interlaced in fibrous tissue and fat.[4] Increased automaticity by enhanced adrenergic tone may be the triggering factor and possibly account for induction of ventricular tachycardia during exercise.[5] By linkage analysis, 6 chromosomal loci responsible for ARVC were identified.[6] Recently, the gene accounting for Naxos disease, ARVC with palmoplantar keratosis, was also delineated. In this autosomal recessive disease, deletion of plakoglobin accounted for the disorder.[7]

Diagnostic Criteria

The most commonly adopted diagnostic criteria for ARVC were proposed by the working group on myocardial and pericardial disease of the European Society of Cardiology and of the scientific council on cardiomyopathies of the International Society and Federation of Cardiology.[8] It comprised of 6 categories for diagnosis of ARVC (Table 1). Each category was subdivided into major and minor criteria. The diagnosis of ARVC was established if two major or one major plus two minor or four minor criteria from different categories were fulfilled.

Table 1. Diagnostic criteria for arrhythmogenic right ventricular cardiomyopathy.[8]

	Major	Minor
Global and/or regional dysfunction and structural	• Severe dilatation and reduction of RV EF with no	• Mild global RV dilatation and/or EF reduction with

alterations	LV impairment • Localized RV aneurysms • Severe segmental RV dilatation	normal LV • Mild segmental RV dilatation • Regional RV hypokinesia
Tissue characterization of wall	Fibrofatty replacement of myocardium on endomyocardial biopsy	
Repolarization abnormalities		Inverted T-waves in right precordial leads (V2-V3) in the absence of RBBB
Depolarization/conduction abnormalities	Epsilon waves or localized prolongation (>110ms) of the QRS complex in right precordial leads (V1-V3)	Late potentials (signal-average ECG)
Arrhythmias		• LBBB type VT (sustained and nonsustained) on ECG, Holter monitoring or exercise test • Frequent ventricular extrasystoles (>1000/24hr) on Holter monitoring
Family history	Familial disease confirmed at necropsy or surgery	• Family history of premature sudden death (<35 years) due to suspected RV dysplasia • Family history (clinical diagnosis based on present criteria)
RV=right ventricle; LV=left ventricle; EF=ejection fraction; RBBB=right bundle branch block; LBBB=left bundle branch block; ECG=electrocardiograph		

Clinical Characteristic in Chinese Patients

In addition to our previous report,[9] there are now a total of 12 patients with ARVC being followed up in our arrhythmia clinic at April 2001 based on the above diagnostic criteria. The latest diagnosed patient was detected during family screening. Her clinical work-up was still incomplete though one major and two minor criteria were already fulfilled. For the remaining 11 patients who have completed the clinical work-up, the commonest presenting symptoms were palpitation and dizziness. Their mean age of clinical presentation was 42.6±14.8 years. Ventricular tachycardia (VT) with left bundle branch block (LBBB) morphology as the initial presentation was present in 6 patients. One patient presented with resuscitated sudden cardiac death. Two patients had positive family history of premature sudden death. The latest diagnosed patient detected by family screening was the sister of the patient with a positive family history. With regards to the electrocardiograph (ECG), 6 patients showed evidence of repolarization abnormality with T wave inversion in V2-3 in the absence of right bundle branch block. In addition to the 6 patients who had spontaneous VT as initial presentation, one patient had VT with LBBB morphology during treadmill test. For the 9 patients who agreed for electrophysiology study (EPS), 4 patients had inducible monomorphic VT of same morphology as clinical VT. All patients had normal left ventricular function by echocardiography. Right ventricular dilatation was detected in 5 patients. Eight patients had undergone cardiac catheterization and 3 patients had dilated right ventricle (RV) with global hypokinesia. Ten patients had magnetic resonance imaging (MRI) examination. All patients had RV abnormality, either with RV dilatation with wall thinning or fibrofatty replacement. The most commonly affected area in RV was free wall. The mean

follow-up period for the 11 patients was 42.3±58.3 months. Five patients had implantable cardioverter defibrillator (ICD) implanted. These patients had either history of cardiac arrest or haemodynamically unstable VT or unexplained syncope with inducible VT. Six patients were prescribed with antiarrhythmic agents. The most commonly used antiarrhythmic agents were amiodarone and beta-blockers. Two patients had successful radiofrequency ablation (RFA) done for either VT or symptomatic ventricular ectopics because of either failure or intolerable side effects of antiarrhythmic therapy. No patients died during the follow up period.

Investigation

The primary aim of investigation for patients suspected to have ARVC is two-fold. First to confirm the diagnosis and secondly is for risk stratification. One of the major diagnostic criteria for ARVC is global or regional RV dysfunction.[8] Available imaging techniques to assess RV anatomy and function include echo-cardiography, RV angiography and MRI. RV angiography was the gold standard of investigation modality for ARVC in early 1990's.[10] However, it was an invasive procedure and was soon replaced by MRI and echocardiography. Echocardiography is a non-invasive technique and useful for family screening. However, the detection rate in our cohort by echo-cardiography was less than 50%. MRI seems to be the most promising investigation modality. MRI has the unique property to differentiate fatty tissue from myocardium. Cine MRI is even better to show RV regional dysfunction. However, experience played an important role in the correct interpretation of MRI for diagnosis of ARVC.

Risk stratification for future arrhythmic events in patients with ARVC is vital. Unfortunately, there is no reliable method to predict these tragic events. Young age of onset, strenuous exercise, strong family history of sudden death, extensive right ventricular disease, left ventricular involvement, syncope or VT are associated with worse outcome.[11-13] The role of EPS in stratifying the risk of ARVC patients is controversial.

Treatment and Prognosis

There is no universally accepted guideline for the management of patients with ARVC. Available treatment modalities for symptomatic patients are antiarrhythmic therapy, RFA, ICD and surgery. It is unclear whether these modalities of therapy are useful in asymptomatic subjects identified by family screening. ICD is indicated in patients who have survived an episode of ventricular fibrillation cardiac arrest or haemodynamically unstable VT. For patients with haemodynamically stable VT, EPS guided antiarrhythmic therapy may be adopted though the effectiveness of such approach has not been tested in any randomized prospective study.[14] RFA may be useful for drug-resistant arrhythmia but its role for prevention of SCD is unclear. Surgical RV disconnection is now less commonly performed. In a recent report involving 37 families with ARVC,[15] the risk of death was only 0.08 patient/year during a 8.5 year follow up. The overall prognosis in patients with ARVC is not bad. The most important clinical issue is how to risk stratify these patients and implement appropriate therapy.

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