

# Arrhythmogenic right ventricular cardiomyopathy/dysplasia in Iraq

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## Abstract

**Background:** *Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is a disorder that involves replacement of the right ventricular myocardium with fibro-fatty tissue. Ventricular tachycardia is a main presenting feature. There are no known reports of this disease from the Arab countries in the Middle East. This is the first report of 34 patients from Iraq.*

**Methods:** *Thirty four patients with ARVC/D diagnosed from January 2003 to May 2007 according to the International Task Force criteria were included in this study.*

**Results:** *All patients presented with ventricular tachycardia of left bundle branch block morphology. The following findings were seen on the 12-lead electrocardiography during sinus rhythm: T wave inversion V1–V3 or beyond in 80%, epsilon wave in 28%, and parietal block in 48%. Right ventricular enlargement by echocardiography was seen in 69%. Twenty two per cent had a family history of sudden cardiac death. All patients were treated with implanted cardioverter-defibrillators.*

**Conclusions:** *ARVC/D is a disease seen in Iraq. It requires a high diagnostic suspicion with verification using the international task force criteria. (Cardiol J 2010; 17, 2: 172–178)*

**Key words:** *arrhythmogenic right ventricular cardiomyopathy/dysplasia, Iraq*

## Introduction

Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is a disorder that involves replacement of right ventricular myocardium with fibro-fatty tissue [1, 2]. It generally presents in adolescents and young adults, with the first symptoms appearing at  $33 \pm 14$  years, mostly in males [3, 4]. Pediatric cases have been also reported [4–6]. The prevalence is uncertain but there is more pre-

valence of different types of the disease like Naxus disease in certain localities. The most accepted prevalence rate is 6/10,000 [1, 3, 4, 7].

The common presenting symptoms are due to ventricular arrhythmias, including sustained ventricular tachycardias (sVT) of right ventricular origin with a left bundle branch block pattern causing palpitations or syncope. Sudden cardiac death (SCD) due to ventricular fibrillation (VF) can occur [1, 8–12]. These symptoms may be observed during

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competitive sports and strenuous exercise, but also occur at rest or during sleep [13, 19]. Other presentations are: palpitations due to ventricular premature beats or non-sustained ventricular tachycardias documented during routine electrocardiography or by Holter monitoring, family screening for SCD at a young age and unexplained right ventricular (RV) enlargement by echocardiography or cardiomegaly by chest X-ray, especially due to RV enlargement [1, 2, 7, 19]. Recently it has been observed that ARVC/D may primarily affect the left ventricle or both ventricles [14].

Right sided heart failure is a rare presenting symptom, but right or left congestive cardiac failure may occur as a late manifestation of the disease [1, 2]. Supraventricular tachycardia including atrial fibrillation, flutter and atrial extrasystoles is an unusual feature of ARVC/D, but may be an initial marker of the disease [15, 16].

Electrocardiographic abnormalities in ARVC/D are:

- T-wave inversion in right precordial leads V1–V3, sometimes extending to the left precordial leads;
- QRS duration > 110 ms;
- QRS duration in V1 longer than V6 by  $\geq 20$  ms (parietal block);
- epsilon wave in V1 or V2 [1, 4, 5].

Angiographic RV features include: RV dyskinesia or aneurysms and reduced right ventricular ejection fraction (RVEF) with relatively normal left ventricular ejection fraction (LVEF) [7, 17]. Magnetic resonance imaging is a diagnostic tool which can characterize the fatty and fibrous infiltrate in the RV wall but its specificity and sensitivity of interpretation is still unknown [1, 2, 17].

Myocardial biopsy from the interventricular septum is not reliable since the interventricular septum is the usual site of myocardial biopsy and this area is not usually involved. Therefore RV biopsies must be done from the RV free wall and a free RV wall [2, 7, 18].

This study presents a cohort of Iraqi patients who presented with sVT of left bundle branch block (LBBB) pattern and were diagnosed as having ARVC/D. To our knowledge, this is the first report of this disease from Iraq or the Arab countries.

## Methods

All the patients presented with sVT to the emergency room of the University Hospital, Kadhimiya, Baghdad, and the Nasrya Heart Centre, Nasrya, Iraq, from January 2003 to May 2007.

Following termination of the sVT, either by DC-shock in the majority of patients or by IV medications in a few, investigation of the underlying cause of the ventricular tachycardia showed that it was due to ARVC/D.

The diagnosis was initially suspected when the electrocardiography (ECG) during sinus rhythm showed T wave inversion in the anterior precordial leads and/or complete or incomplete right bundle branch block (RBBB/IRBBB). Chest X-ray and echocardiography were done in all patients. Coronary angiography was done in patients who were 40 years old or above. Magnetic resonance imaging was not available. Myocardial biopsies were not done in any patient. In addition to the presenting sVT, criteria for the diagnosis of ARVC/D included.

- T wave inversion in the anterior precordial leads V1–V3 (**RBBB is not a criterion for ARVC/D**).
- An epsilon wave seen in V1 or V2 by recording with a double standard speed (50 ms), double standard amplitude (20 mm/mV) and using a 40 Hz filter.
- Echocardiography that revealed an enlarged RV of variable severity with diminished RVEF; localized RV aneurysmal dilatation, with normal or nearly normal left ventricle size and function. These diagnostic criteria are consistent with the international task force diagnostic criteria [3]. Thirty patients fully met the diagnostic Task Force criteria; four patients were borderline but almost fulfilled the criteria by meeting three minor criteria plus an additional fourth borderline minor criterion.

Twenty patients had an electrophysiological study to induce ventricular tachycardia by programmed ventricular stimulation (PVS) using triple extrastimuli.

A cardioverter-defibrillator (ICD) was implanted in all patients, either because of recurrent symptomatic ventricular tachycardia, resuscitated VF, and induced VT/VF by PVS or a family history of premature sudden death. Thirty ICDs were single chamber (Profile), four were dual chamber (Photon DR), and all were made by St. Jude Medical.

The patients were followed for 18 months. All events and ICD therapies were recorded and the ICD detection criteria, pacing therapies, and other functions were programmed according to the patient's arrhythmia characteristics.

The study was approved by the local bioethical committee and all patients gave their informed consent.

### Results

As shown in Table 1 and 2, there were 34 patients, 20 females and 14 males. Thirty patients were Arabs from the middle, south and north of Iraq and four patients were Kurds from Kurdistan in the north of Iraq. Their ages ranged from 22 to 42 years, mean age 31 years. All presented with sVT of LBBB configuration (Fig. 1). The cycle length (CL) of the VT ranged from 400–200 ms (rate 150–300 bpm). In five patients CL was 200 ms (rate 300 bpm), in 20 patients CL 240–280 ms (rate 240–250 bpm), and in eight patients CL of the VT was 360–320 ms (167–188 bpm). In one patient the VT CL was 400 ms (rate 150 bpm). Eighty per cent of patients had T wave inversion in the anterior precordial leads V1–V3. Seven patients had T wave inversion (TWI) in V1 and V2; 20 patients had TWI in V1–V3 and seven patients showed TWI extending from V1 to V6 (Fig. 2). The axis of the VT was inferior in 15 patients and superior in 19 patients. Epsilon waves were observed in 28% of patients (Fig. 2B). Sixty eight per cent of patients had RV enlargement of more than 3.5 cm diameters by echocardiography. The normal values of RV diameter at the mid RV in the two-dimensional echocardiography long axis view and the guided M-mode is 2.7–3.4 cm (Fig. 3). Thirty nine per cent of patients had decreased RVEF < 40%. Two patients had an enlarged cardiac shadow by standard chest X-ray due to RV enlargement.

Twenty per cent of patients had a family history of premature SCD. One woman had two brothers who died suddenly at the ages of 22 and 19. One

**Table 1.** Clinical findings in the patients diagnosed with arrhythmogenic right ventricular cardiomyopathy.

Total no.	34 patients
Date of initial observation	January 2003 – May 2007
Age (years)	22-42 (mean 31)
Female/male	20/14
Sustained VT of LBBB pattern	34 (100%)
Electrocardiography findings:	
Epsilon wave	9 (27%)
T wave inversion	34 (100%)
V1 and V2	7 (20%)
V1–V3	20 (60%)
V1–V6	7 (20%)
Parietal block (QRS V1 > V6 by ≥ 20 ms)	16 (48%)
Echocardiography findings:	
Enlarged RV > 3.5 cm	23 (68%)
RVEF < 40%	13 (39%)
RV aneurysmal dilatation	2 (6%)
Diffuse hypokinesia	25 (75%)
Family history	7 (22%)

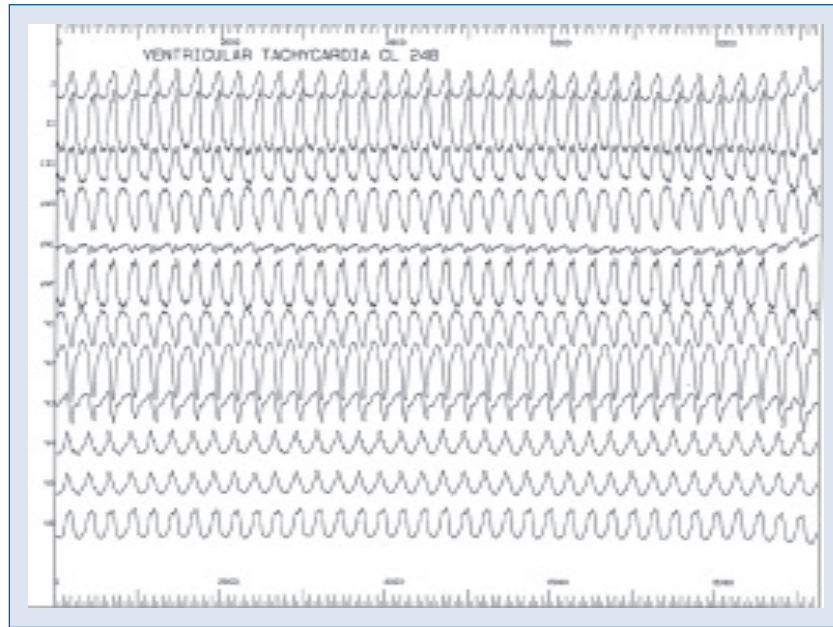
VT — ventricular tachycardia; RV — right ventricle; RVEF — right ventricular ejection fraction; LBBB — left bundle branch block

living brother, aged 25, had recurrent palpitation and VT was recorded during one of the attacks that was converted by DC-shock. He refused further evaluation or ICD implantation. Another 38 year-old male patient had a son who died suddenly at the age of 12. An autopsy was not done.

**Table 2.** Patients fulfilling the International Task Force criteria: 30 patients fully fulfilled the Task Force criteria, four patients fulfilled three minor criteria and one borderline minor criterion.

Task Force criterion	Number of patients (%)
1. Family history	
Major: Familial disease confirmed at autopsy or surgery	0 (0%)
Minor: Familial history of premature sudden cardiac death	7 (22%)
2. Electrocardiography depolarization/conduction abnormalities	
Major: Epsilon wave or localized prolongation (> 110 ms) of QRS in the right precordial leads (V1–V3)	9 (27%)
3. Electrocardiography repolarization abnormalities	
Minor: Inverted T wave in right precordial V1–V3	27 (80%)
4. Arrhythmias	
Minor: Sustained ventricular tachycardia of LBBB	34 (100%)
5. Global or regional dysfunction and motion abnormalities	
Minor: Mild global or segmental right ventricular dilatation and regional hypokinesia	25 (75%)
Major: Severe dilatation and reduction of RVEF > 40%	13 (39%)

LBBB — left bundle branch block; RVEF — right ventricular ejection fraction



**Figure 1.** Left bundle branch block pattern of ventricular tachycardia with superior axis. Cycle length of 248 ms (rate of 242 bpm).

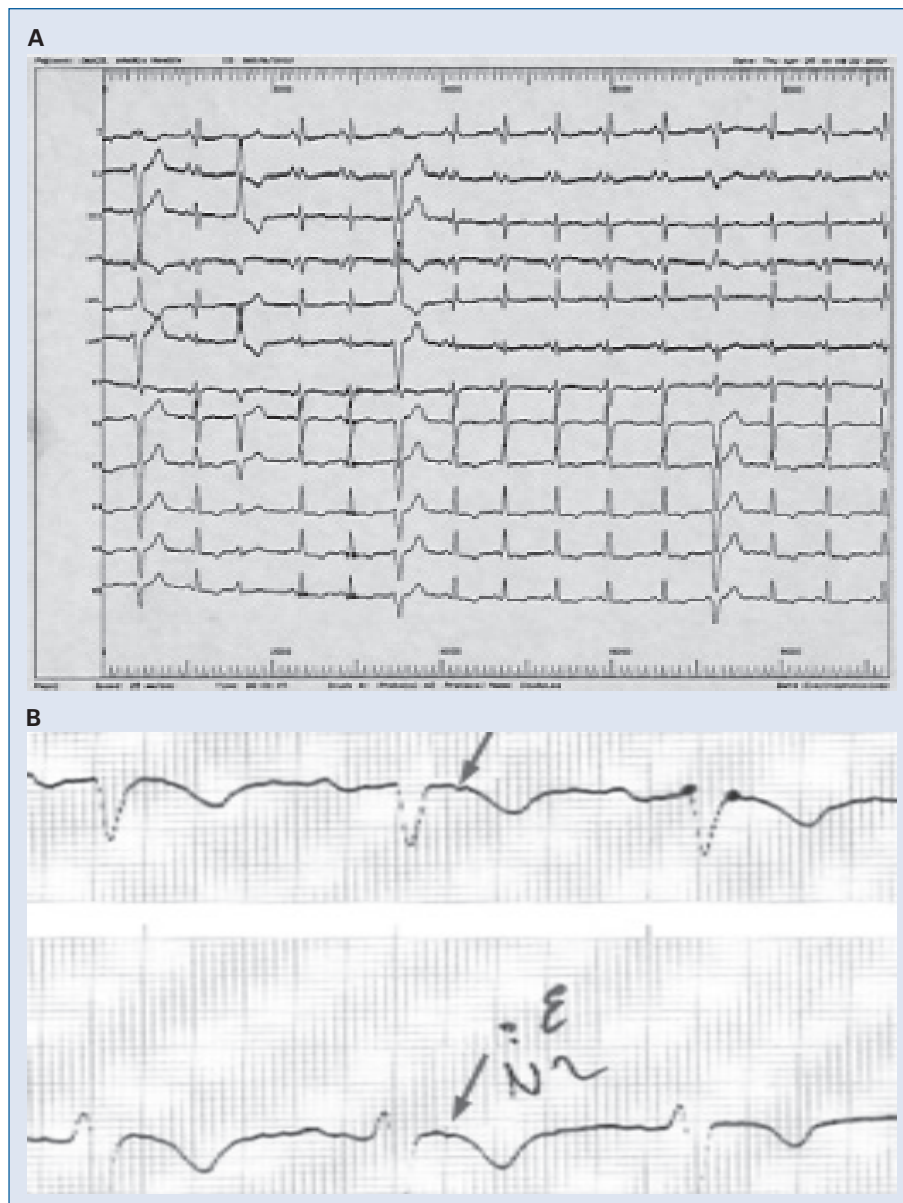
Twenty patients had electrophysiological study for VT induction by PVS. Thirteen patients had induced VT of similar morphology to the clinical presenting VT. Two patients had induced VF. In the remaining five patients, VT was not induced by PVS.

The post-implantation ICD therapies within the 18 months follow-up revealed 45 episodes of VT in 22 patients successfully treated, by antitachycardia pacing (ATP) in 34 episodes (75%) and by DC-cardioversion after failed ATP or fast VT in 11 episodes (25%). Five patients developed VF that was successfully reverted to NSR by shocks. Fifteen patients received amiodarone due to recurrent VT in a frequency of more than two episodes per month after the implantation of the ICD. Before treatment with amiodarone, these patients had one shock or three ATP per month; after amiodarone the episodes of tachycardia decreased to one shock or one ATP every five months. Three patients continued to have recurrent VT in spite of amiodarone therapy. They are being referred to another center for VT ablation. Two patients developed device pocket infection. One was treated with antibiotic irrigation for two weeks with complete healing. The other did not improve after intensive systemic and local antibiotic irrigation and the device was removed and replaced on the other side.

## Discussion

Patients with ARVC/D commonly present with VT [1, 7, 8]. Patients may rarely have supraventricular arrhythmias, including atrial flutter [15, 16]. Right and left heart failure are uncommon, but occur due to deterioration of right, and sometimes left, ventricular function [1, 14]. Late potentials may be visible in the ECG as an epsilon wave seen in V1 or V2 which can be enhanced by the recording at a speed of 50 mm/s, an amplitude of 20 mV and with a 40 Hz filter [18]. ARVC/D may be seen as sporadic cases, but reports of family members with the disease illustrate the influence of genetic factors [1, 7, 20–22]. Familial history of ARVC/D is present in at least 30–50% of cases [1, 2, 22]. The commonest pattern of inheritance is autosomal, dominant with variable penetrance, although an autosomal, recessive pattern has also been reported [20–22].

ARVC/D has been found to be mainly a disease of the cardiomyocyte junction and plakophilin-2 is the most frequently targeted gene [20, 21]. Extradysmosomal genes implicated in ARVC/D include desmoplakin, junctional plakoglobin, the cardiac ryanodine receptor plakophilin-2, and the transforming growth factor (beta3 and the TMEM43 genes) [20, 21]. ARVC/D may show slow continu-



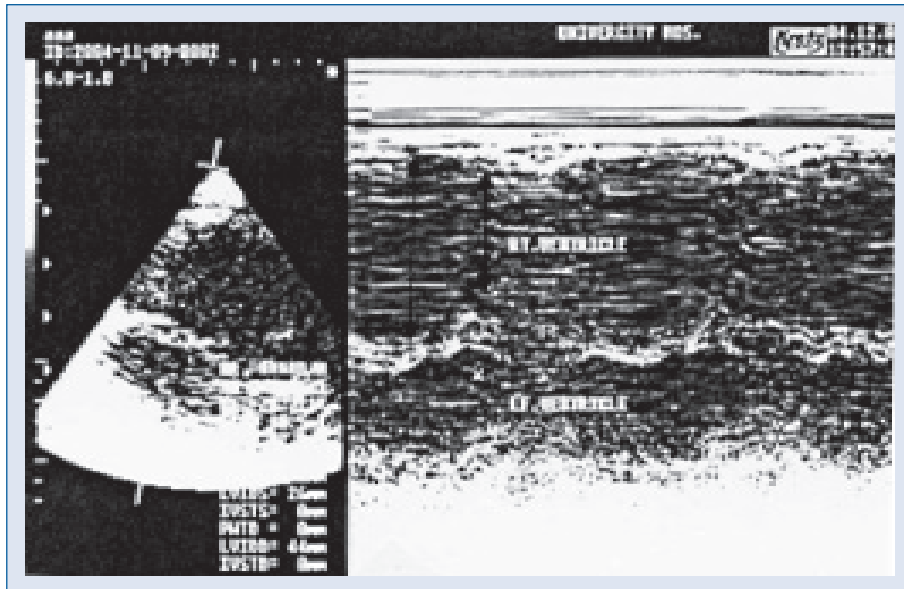
**Figure 2.** A. Twelve-lead electrocardiography showing T wave inversion in all the precordial leads; B. Magnified V2, V3 showing epsilon wave (arrow).

ous progression or may have periodic 'bursts' of arrhythmias and/or deterioration of RV function in an otherwise stable disease [10, 11, 20, 21].

From autopsy data of SCD, the incidence of ARVC/D has been reported to differ in different parts of the world. In Lyon, France it was found in 5% of postmortem examinations of SCD [10, 11]. In Veneto, Italy it was seen in 20% of 12 SCD autopsies, seven males and five females ranging in age from 13 to 30 years, all undiagnosed before death but frequently with a history of palpitation [11]. ARVC/D was thought to be a cause of SCD during

sports in 26% [10, 11, 13]. In a survey of athletes who were found to have VT/VF, ARVC/D was present in 18% [19].

We are not aware of any reports of ARVC/D in the Arab countries of the Middle East and North Africa. In this series of 34 patients reported from Iraq, all patients presented with sVT causing significant hemodynamic effects. The diagnosis of ARVC/D was based on findings of two major criteria, two minor and one major or four minor criteria according to the international Task Force standardized diagnostic criteria and the European Society



**Figure 3.** Echocardiograph; long axis view in two dimensions and M-mode showing right ventricular enlargement; right ventricular diastolic diameter (RVDD) = 35 mm, right ventricular systolic diameter (RVSD) = 28 mm, black arrows.

of Cardiology working group on cardiomyopathies and dysplasia [3]. No patient in the present series showed RV failure or LV failure. Coronary angiography was normal in patients aged over 40. The predominance of females in this series is unusual [5]. The ECG abnormalities are similar to those in previous reports. We noticed features of diffuse conduction disease in two patients, consisting of alternating RBBB and LBBB with atrioventricular conduction delay and variable prolongation of the PR interval.

ARVC/D is a worldwide disease, although it has been noted as being more common in specific localities such as Padua in northern Italy [2]. The patients with ARVC/D in this report are the first such cases in Iraq. If we consider the previously estimated prevalence of this disease (6/10,000 of the general population) we can expect the about 13,200 patients in Iraq, a country with a 22 million population.

### Conclusions

ARVC/D is disease which is seen in Iraq, High levels of diagnostic suspicion are required, the International Task Force criteria should be followed to reach a diagnosis, and ARVC/D should be considered as a possible diagnosis in any patient presented with LBBB pattern ventricular tachycardia.

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