

## CARDIOVASCULAR MEDICINE

# Electrophysiological characteristics and outcome in patients with idiopathic right ventricular arrhythmia compared with arrhythmogenic right ventricular dysplasia

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**Background:** Idiopathic right ventricular arrhythmias (IRVA) are responsive to medical and ablative treatment and have a benign prognosis. Arrhythmias caused by right ventricular dysplasia (ARVD) are refractory to treatment and may cause sudden death. It is difficult to distinguish between these two types of arrhythmia.

**Objective:** To differentiate patients with IRVA and ARVD by a conventional electrophysiological study. **Methods:** 56 patients with a right ventricular arrhythmia were studied. They had no history or signs of any cardiac disease other than right ventricular dysplasia. They were classified as having IRVA (n = 41) or ARVD (n = 15) on the basis of family history, ECG characteristics, and various imaging techniques. They were further investigated by standard diagnostic electrophysiology.

**Results:** The two groups were clearly distinguished by the electrophysiological study in the following ways: inducibility of ventricular tachycardia by programmed electrical stimulation with ventricular extrastimuli (IRVA 3% v ARVD 93%,  $p < 0.0001$ ); presence of more than one ECG morphology during tachycardia (IRVA 0% v ARVD 73%,  $p < 0.0001$ ); and fragmented diastolic potentials during ventricular arrhythmia (IRVA 0% v ARVD 93%,  $p < 0.0001$ ). Data from the clinical follow up in these patients supported the diagnosis derived from the electrophysiological study.

**Conclusions:** Patients with IRVA or ARVD can be distinguished by specific electrophysiological criteria. A diagnosis of ARVD can be made reliably on the basis of clinical presentation, imaging techniques, and an electrophysiological study.

Ventricular arrhythmias with left bundle branch block morphology are often observed in apparently healthy people and usually arise from the right ventricle. In this situation it is important to differentiate between idiopathic right ventricular arrhythmias (IRVA), which are responsive to medical and ablative treatment and have a benign prognosis,<sup>1,2</sup> and arrhythmias originating from right ventricular dysplasia (ARVD), which are refractory to treatment and carry a significant risk of sudden death.<sup>3–6</sup> The pathogenesis of myocardial fatty-fibrous degeneration in ARVD is unknown, and the disease presents in different forms and with variable outcome.<sup>3,7–11</sup>

Thus the diagnosis of ARVD is a clinical challenge, and the gold standard for making the diagnosis has not yet been defined. Endomyocardial biopsy is of limited value because the affected area may be missed, and biopsy of the right ventricular free wall—the region most often affected—is considered hazardous. Echocardiography and right ventricular angiography may fail to identify subtle forms of dysplasia.<sup>12–14</sup> With the more sensitive technique of nuclear magnetic resonance imaging (MRI), no standards have yet been established for the diagnosis of ARVD, and abnormal findings of uncertain significance are often reported.<sup>15–17</sup> Furthermore, from MRI and histological findings it has been suggested that at least some cases of right ventricular arrhythmia that have been classified as “idiopathic” in fact represent an early stage, or forme fruste, of ARVD.<sup>18–21</sup>

In this study we sought to differentiate patients with IRVA and ARVD by a conventional electrophysiological study. We show that a diagnosis of ARVD can be made reliably on the

basis of the clinical presentation, appropriate imaging, and electrophysiology.

## METHODS

### Study population

We studied 56 consecutive patients who were referred to our centre between January 1993 and February 2000 with right ventricular arrhythmia and no history or signs of cardiac disease other than suspected right ventricular dysplasia. Clinical history, physical examination, a 12 lead ECG with documentation of the arrhythmia, a 24 hour Holter ECG, and routine laboratory analysis were available for all patients. Four patients had coronary and left ventricular angiography, which excluded coronary artery disease and left ventricular dysfunction.

### Rating of symptoms and arrhythmias

A score of 0–5 was used for rating the symptoms as follows: 0, no symptoms; 1, 2, 3, mild, moderate, and severe palpitations, respectively; 4, dizziness, near syncope; 5, syncope. A score of 0–3 was used for rating the arrhythmias: 0,

**Abbreviations:** ARVD, arrhythmogenic right ventricular dysplasia; IRVA, idiopathic right ventricular arrhythmia; LBBB, left bundle branch block; MRI, magnetic resonance imaging; RBBB, right bundle branch block; RFCA, radiofrequency catheter ablation; VT ventricular tachycardia

no arrhythmia; 1, premature ventricular beats; 2, non-sustained ventricular tachycardia (runs of three beats or more, duration less than 30 seconds); 3, sustained ventricular tachycardia.

### Diagnostic criteria

The diagnosis of right ventricular dysplasia was made according to the recommendations of the task force of the working group on myocardial and pericardial disease of the European Society of Cardiology and the Scientific Council on Cardiomyopathies of the International Society and Federation of Cardiology.<sup>12</sup> In each patient, the family history and the characteristics of the 12 lead ECG were assessed in relation to a possible diagnosis of ARVD. Echocardiography was carried out in 54 patients. Right ventricular dysplasia was defined as severe dilatation and reduction of right ventricular function (with no or only subtle involvement of the left ventricle), or localised right ventricular aneurysms. If there was mild global or segmental dilatation, or mild reduction of right ventricular function, the findings were considered suspicious or uncertain. The same criteria were used for the findings obtained at right ventricular angiography ( $n = 15$ ).

An MRI was done in 22 cases, exclusively at other institutions, and the interpretation was left to the discretion of the physician who carried out the procedure. In none of the patients classified as having ARVD was the diagnosis based solely on MRI results.

All patients with ARVD had, as major diagnostic criteria, either severe dilatation and reduction of right ventricular ejection fraction, localised right ventricular aneurysms, or severe segmental dilatation of the right ventricle, without major impairment of the left ventricle. Furthermore, all the ARVD patients had at least one of the major or minor ECG criteria of this condition when they were in sinus rhythm, and when tachycardias occurred there was always a left bundle branch morphology. Hence, all patients in our ARVD group had at least one major and two minor criteria of the condition, thereby fulfilling the proposed diagnostic criteria.<sup>12</sup> The initial diagnosis of IRVA was made by excluding the cases of ARVD.

### Electrophysiological study

The procedure was performed after the patient had given written consent. Studies were carried out with the patient in the fasting state and with no sedation whenever possible. If sedation was necessary, a combination of midazolam and morphine was used. Except for amiodarone (two patients with IRVA, seven with ARVD), antiarrhythmic drugs were discontinued for at least five half lives before the study.

Under local anaesthesia, standard quadripolar catheters were advanced through the right femoral vein to the right atrium, His bundle, and right ventricle. Right ventricular mapping, including pace mapping, was performed using a 4 mm tip quadripolar steerable catheter (Medtronic Mariner) which was subsequently used to perform temperature guided radiofrequency endocardial ablation (RFCA) when indicated.

Standard 12 lead surface ECG and bipolar endocardial electrograms were recorded on a multichannel recorder and stored on optical disk for later analysis.

After completion of the recordings during sinus rhythm, programmed right ventricular stimulation was undertaken at three basic drive rates (600, 500, and 430 ms), with up to three extrastimuli, and rapid burst pacing was carried out with varying cycle lengths. If no arrhythmia could be induced, the same stimulation protocol was used at a different right ventricular site and during the infusion of isoprenaline (isoproterenol) (1 to 5  $\mu\text{g}/\text{min}$ ). The induction of polymorphic ventricular tachycardia or ventricular fibrillation was considered a non-specific feature. In 10 patients (all from the IRVA group) with frequent premature ventricular beats or runs of non-sustained or sustained ventricular tachycardias, no

programmed electrical stimulation was carried out before ablation. All patients underwent a programmed electrical stimulation study after ablation.

Endocardial activation mapping was performed during sinus rhythm and during any type of haemodynamically tolerated arrhythmia, to allow analysis of the electrogram morphology (fragmented *v* normal) and of the prematurity of the local electrogram at the ablation site, and to enable the variables to be compared between the two groups. The site of ablation was chosen as the site of earliest endocardial activation during ventricular arrhythmia or from a pace mapping that best reproduced the arrhythmia on the 12 lead surface ECG. In some cases where a re-entry mechanism was suspected, the tachycardia was entrained at cycle lengths of 20–40 ms below the cycle length of the tachycardia to guide the site of ablation, though entrainment studies were not carried out systematically. Immediate ablation success was defined as termination of sustained ventricular tachycardia or the cessation of the spontaneous arrhythmia followed by a failure to reinduce a previously inducible arrhythmia.

### Follow up

Follow up was achieved in all patients. Information was obtained during outpatient visits ( $n = 21$ ) or by telephone inquiry ( $n = 35$ ). Patients were asked about symptoms in general, and specifically about palpitations, dizziness, syncope or near syncope, and current drug treatment. Fifty three of the 56 patients had undergone a 24 hour Holter ECG.

### Statistics

A one tailed paired Student *t* test was used for statistical analysis of score changes during follow up. An unpaired two tailed *t* test was used to compare the two patient groups.

## RESULTS

### Symptoms and ECG

Baseline characteristics of the patients are shown in table 1. Patients were of similar age in the two groups. There was a predominance of male patients in the ARVD group. Patients classified as having IRVA had milder symptoms, with only two patients (5%) presenting a history of syncope compared with a 33% incidence of syncope in the ARVD group. Two patients in the ARVD group (14%) had suffered from a cardiac arrest, but none in the IRVA group. In the IRVA group 34% of the patients had a documented sustained ventricular tachycardia, compared with 80% in the ARVD group. Although the patients classified as having ARVD presented with more severe symptoms than those with IRVA, ventricular ectopy was a more common finding in the IRVA patients on the 12 lead surface ECG taken at admission or during the hospital stay (80% *v* 43%). Thus overall, patients with mild symptoms but with frequent isolated ectopy or non-sustained ventricular tachycardia were more likely to suffer from an idiopathic form of arrhythmia.

Additional information obtained from the baseline ECG included the presence of an epsilon wave, right bundle branch block (incomplete or complete), and negative T waves in the precordial leads (other than V1) which were observed in 0%, 2.5%, and 23% of patients with IRVA, and in 14%, 33%, and 87% of patients with ARVD, respectively (table 2).

A left bundle branch block morphology with an inferior axis during arrhythmia—which is the typical presentation in IRVA—was present in 37 of the 41 patients with IRVA (90%) and in seven of the 15 with ARVD (47%). Hence this typical morphology did not exclude right ventricular disease, nor could a different morphology be taken as proof of ARVD. In the other patients with IRVA, an intermediate axis was present in two and a left or superior axis in a further two. In patients with ARVD with other than an inferior axis during arrhythmia, an

**Table 1** Characteristics of the study population

Characteristic	IRVA (n=41)	ARVD (n=15)	p Value
Age (years)	40.1 (13.4)	37.4 (16.4)	NS
Age range	14 to 69	16 to 64	NS
Family history	0/41	2/15	NS
<i>Symptoms (score)</i>			
<i>Palpitations</i>			
None/mild (0;1)	13 (32%)	1 (7%)	
Moderate (2)	15 (36%)	4 (27%)	
Severe (3)	13 (32%)	10 (66%)	
Presyncope (4)	11 (27%)	4 (27%)	
Syncope (5)	2 (5%)	5 (33%)	
Cardiac arrest (5)	0	2 (14%)	
Mean score	2.3 (1.5)	3.7 (1.3)	0.0058
<i>Presenting arrhythmia (score)</i>			
Detection on baseline ECG (Halter)	33 (80%)	7 (43%)	0.0126
PVB (1)	10 (24%)	1 (7%)	
Non-sustained VT (2)	17 (42%)	2 (14%)	
Sustained VT (3)	14 (34%)	12 (80%)	
Mean score	2.1 (0.8)	2.7 (0.6)	0.0054
<i>ARVD: positive/uncertain/negative</i>			
Echocardiography	0/3/36	12/2/1	
RV angiography	0/1/8	5/1/0	
MRI	0/4/11	4/2/1	
Antiarrhythmic drugs at presentation	32 (78%)	13 (87%)	NS

Values are n (%) or mean (SD).

ARVD, arrhythmogenic right ventricular dysplasia; IRVA, idiopathic right ventricular arrhythmia; MRI, magnetic resonance imaging; PVB, premature ventricular beats; RV, right ventricular; VT, ventricular tachycardia.

**Table 2** ECG characteristics during sinus rhythm and during ventricular ectopy

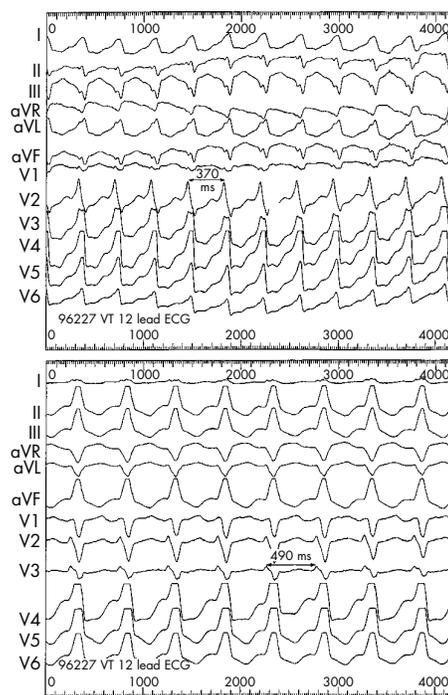
Characteristic	IRVA (n=41)	ARVD (n=15)	p Value
<i>During sinus rhythm</i>			
Epsilon wave	0	2 (14%)	NS
RBBB	1 (2.5%)	5 (33%)	0.0006
Negative precordial T wave (other than lead I)	9 (23%)	13 (87%)	<0.0001
<i>During VT (all LBBB)</i>			
Inferior axis	37 (90%)	7 (48%)	0.0016
Intermediate axis	2 (5%)	4 (27%)	0.0016
Left/superior axis	2 (5%)	3 (20%)	

ARVD, arrhythmogenic right ventricular dysplasia; IRVA, idiopathic right ventricular arrhythmia; LBBB, left bundle branch block; RBBB, right bundle branch block; VT, ventricular tachycardia.

intermediate axis was present in four and a left or superior axis in three (table 2).

### Diagnostic criteria

For the purpose of this study, a diagnosis of IRVA was made in those cases where a diagnosis of ARVD could not be established on the basis of the currently accepted criteria.<sup>12</sup> Two patients in the ARVD group had a positive family history (a parent with premature sudden death (minor criterion) caused by suspected ARVD); on the other hand, no patient in the IRVA group had a familial history of ARVD or any suspicious premature sudden deaths. Two patients classified as having ARVD had an epsilon wave on the surface ECG (major criterion). None of the patients with a diagnosis of IRVA had clear evidence of dysplasia of the right ventricle on echocardiography (n = 39), right ventricular angiography (n = 9), or MRI (n = 15), though suspicious or uncertain



**Figure 1** Example of multiple morphologies of ventricular tachycardia in right ventricular dysplasia (96227). In this patient, a left bundle branch block VT with left axis deviation, cycle length 370 ms (upper panel), and a second VT, with inferior axis, cycle length 490 ms (lower panel), could be induced. Recording made at 50 mm/s.

results were found in three, one, and four cases, respectively. In contrast, patients classified as having ARVD had at least one positive imaging study. However, in this group, five of 29 examinations (two echocardiograms, one angiogram, and two MRI studies) gave uncertain results, and two were actually negative (one echocardiogram, one MRI study; table 1).

### Electrophysiological study

Programmed ventricular stimulation using up to three extrastimuli before ablation was carried out in 31 of the 41 patients with IRVA (76%), inducing ventricular tachycardia in only one. In nine patients rapid burst stimulation or isoprenaline induced a ventricular tachycardia. In the remaining 10 patients with IRVA—who all presented with frequent premature ventricular beats or non-sustained/sustained ventricular tachycardias—programmed electrical stimulation with ventricular extrastimuli was done only after successful catheter ablation (100% immediate success, defined as the cessation of the spontaneous arrhythmia), and no form of ventricular tachycardia was inducible. In contrast, in 14 of the 15 patients with ARVD, induction of 34 forms of sustained ventricular tachycardia with ventricular extrastimuli was documented by programmed electrical stimulation, and multiple ventricular tachycardia morphologies were induced in 11 of the 15 patients (73%) (fig 1; table 3).

Fragmented diastolic potentials during ventricular tachycardia were not seen in any of the patients with IRVA but were observed in 13 of the 14 patients with ARVD (93%) (one patient was not mapped in this group). However, narrow, spiky shaped potentials—preceding by (mean (SD)) 28 (10.8) ms the onset of the QRS—were observed in 26 of the 41 patients with IRVA (64%) (fig 2). In comparison, prematurity of the diastolic fragmented potentials seen in patients with ARVD preceded the onset of the QRS complex by an average of 80.7 (51.3) ms (mean difference 52.5 ms, 95% confidence interval (CI) 31.2 to 73.7 ms, p < 0.0001; table 3; fig 3).

**Table 3** Electrophysiological characteristics

Characteristic	IRVA (n=41)	ARVD (n=15)	p Value
<i>Mode of VT induction</i>			
PVS	1/31 (3%)	14/15 (93%)	<0.0001
Burst/isoprenaline	9/31 (30%)	0	
<i>Mapping</i>			
Fragmented diastolic potentials	0	13/14 (94%)	<0.0001
Earliest diastolic activity (ms)	-28 (10.8)	-80.7 (51.3)	<0.0001
<i>RF ablation</i>			
Primary success	28/30 (93%)	6/13 (46%)	0.0016
Not attempted	11/41 (7%)	2/15 (14%)	
Acute failure	2/30 (7%)	7/13 (54%)	0.0003

Values are n (%) or mean (SD).

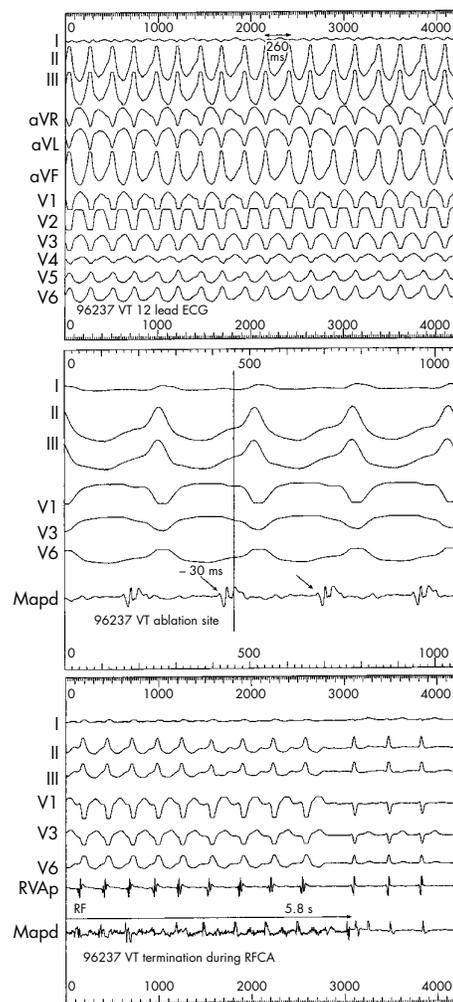
ARVD, arrhythmogenic right ventricular dysplasia; Burst/isoprenaline, rapid ventricular stimulation at varying cycle lengths and/or isoprenaline; Earliest diastolic activity, prematurity of local endocardial electrical activity preceding the onset of the QRS complex in the surface ECG; IRVA, idiopathic right ventricular arrhythmia; PVS, programmed ventricular stimulation using ventricular extra beats; RF, radiofrequency; VT: ventricular tachycardia.

Although catheter ablation of the ventricular arrhythmia was considered in all patients, it was not attempted in 11 of the 41 patients with IRVA or in two of the 15 patients with ARVD, either because of the absence of any significant arrhythmia, or because the patient refused it. The immediate success rate of radiofrequency catheter ablation was 93% in the IRVA group, compared with 46% in the ARVD group ( $p = 0.0016$ ) (table 3).

### Decisions about the diagnosis

The decision as to whether or not ARVD was present was based on findings suggesting right ventricular dysplasia in at least one of the three imaging techniques employed. In addition, all patients classified in this group had some abnormality on their resting ECG, and all presented with a ventricular tachycardia of left bundle branch morphology. Hence the published diagnostic criteria for ARVD<sup>12</sup> were fulfilled in all these patients. Of relevance to the aim of the study is the fact that the findings of the electrophysiological study confirmed the diagnosis—thus none of the patients classified as having IRVA showed features of ARVD in the electrophysiological study. The one patient who had an inducible ventricular tachycardia on programmed electrical stimulation with ventricular extrastimuli had a single morphology of tachycardia and no diastolic fragmented potentials. This patient underwent a successful ablation procedure and during a follow up of three and a half years she remained free from symptoms and arrhythmias. In one other IRVA patient, both the echocardiography and the MRI were suspicious (but not positive) for ARVD, but biopsies taken from the right ventricle were negative. This patient suffered from severe symptoms with near syncope, and had non-sustained ventricular tachycardias on the Holter ECG. Electrophysiological study showed no signs of right ventricular disease, and the patient underwent a successful ablation procedure. Antiarrhythmic drugs were withdrawn and during a follow up of 32 months the patient complained only of mild palpitations, no further ventricular tachycardia episodes being documented.

All patients classified as having ARVD had at least one positive diagnostic imaging test. A clear pattern of ARVD was demonstrable on electrophysiology in 14 of the 15 patients. The most striking example in this group was a patient whose diagnosis was based on a positive echocardiogram and a positive right ventricular angiogram. This patient presented with recurrent syncope and a non-sustained ventricular tachycardia with left bundle branch block and a superior axis, and was

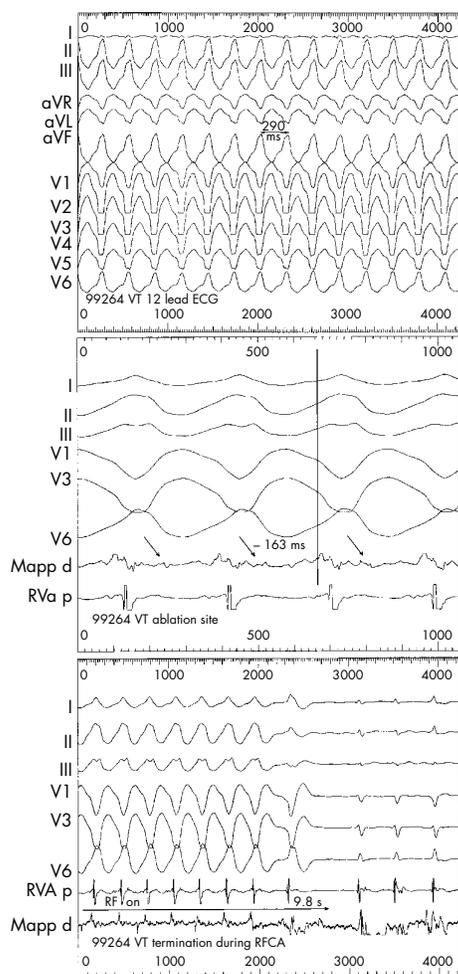


**Figure 2** Surface ECG 12 lead morphology (upper panel) and related intracavitary recording (middle and lower panels) during ventricular tachycardia caused by idiopathic right ventricular arrhythmia (IRVA). Compare with fig 3: the surface ECG pattern is indistinguishable from ARVD, but there is no diastolic activity on the intracavitary recording in this patient. Earliest activation has a lesser degree of prematurity (-30 ms) at the ablation site (96237) than in ARVD. Radiofrequency current was delivered at this site resulting in termination of ventricular tachycardia. ARVD, arrhythmia caused by right ventricular dysplasia; Mapd: mapping catheter recording, distal tip; RFCA: radiofrequency catheter ablation; RVAp, right ventricular apex electrogram, proximal tip; VT, ventricular tachycardia. ECG and intracavitary recording at 50 and 200 mm/s, respectively.

the only patient in the group who did not show the typical electrophysiological patterns of ARVD—that is, no tachycardia was inducible and no fragmented diastolic potentials were documented during spontaneous non-sustained ventricular tachycardia in the electrophysiological study. This patient did not undergo ablation and did not receive an implantable cardioverter-defibrillator. Treatment with a  $\beta$  blocker was initiated during hospital stay. During a follow up of 29 months the patient has been free of any symptoms, though non-sustained ventricular tachycardias have been documented on Holter ECG. The clinical course over the follow up period suggested that the information derived from the electrophysiological study in this patient was more relevant than that obtained from the morphological examination.

### Follow up

Follow up data were obtained in all patients in the study. Over a period of around two years in both groups, no deaths



**Figure 3** Surface ECG 12 lead morphology (upper panel) and related intracavitary recording (middle and lower panels) during ventricular tachycardia arising from right ventricular dysplasia (ARVD). The surface ECG pattern is indistinguishable from IRVA (fig 2), but a diastolic fragmented potential ( $-163$  ms with respect to QRS onset) was recorded at the ablation site (99264). Radiofrequency current was delivered at this site, resulting in termination of ventricular tachycardia. Mapp d, mapping catheter recording; RF, radiofrequency; RFCA, radiofrequency catheter ablation; RVa p, right ventricular apex electrogram, proximal tip; VT, ventricular tachycardia. ECG and intracavitary recording at 50 and 200 mm/s, respectively.

occurred. Patients were asked to report their symptoms and current drug treatment. An ECG was available in all patients, and a 24 hour Holter recording in 53 of the 56 patients.

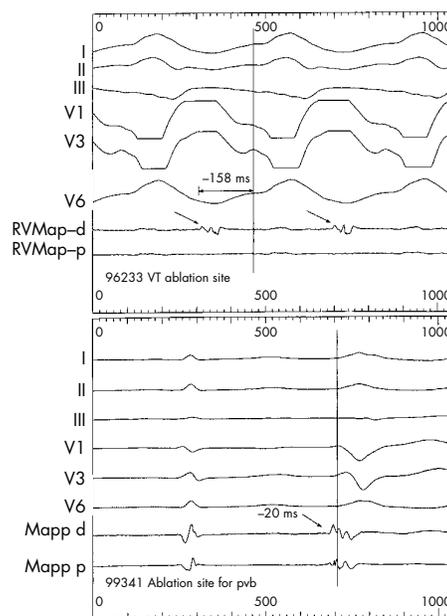
Among the patients with IRVA, 33 of 49 (80%) reported improved symptoms by at least one score unit, and in 32 of 39 (80%) the Holter ECG showed a decreased tachycardia score (table 4). The mean (SD) symptom score was 2.4 (1.5) on initial evaluation and decreased to 0.5 (0.6) at the time of the most recent follow up (mean score difference 1.88, 95% CI 1.43 to 2.32;  $p < 0.0001$ ). The Holter score decreased from 2.1 (0.78) to 0.68 (0.52) (mean score difference 1.46, 95% CI 1.16 to 1.77;  $p < 0.0001$ ; fig 4). In 18 of 32 patients with IRVA (56%), antiarrhythmic drug treatment was discontinued; a new drug regimen was started in five (12%).

An implantable cardioverter-defibrillator was implanted in eight patients with ARVD and recurrent sustained ventricular tachycardia. Syncope had occurred in four and cardiac arrest in two; six of these patients had adequate device treatment during follow up. Eleven of 15 patients with ARVD (73%) reported improved symptoms by at least one score unit, but in

**Table 4** Follow up

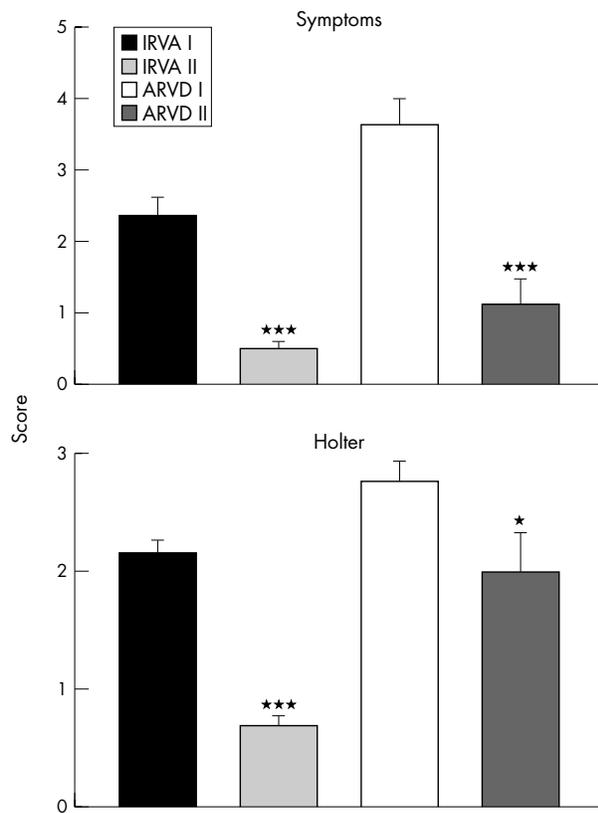
Outcome	IRVA (n=41)	ARVD (n=15)	p Value
Number of patients	41 (100%)	15 (100%)	
Duration (months) (mean, range)	24 (1 to 84)	23 (3 to 50)	NS
Death	0	0	
ICD implant	0	8	$<0.0001$
Improved symptom score	33 (80%)	11 (73%)	NS
p Value for improvement	$<0.0001$	$<0.0001$	
Improved Holter score	32 (78%)	5 (33%)	0.0013
p Value for improvement	$<0.0001$	$<0.035$	
AAD discontinued	18/32 (56%)	2/13 (15%)	0.0035
AAD added	5 (12%)	2 (14%)	NS

AAD, antiarrhythmic drug treatment; ARVD, arrhythmogenic right ventricular dysplasia; ICD, implantable cardioverter-defibrillator; IRVA, idiopathic right ventricular arrhythmia.



**Figure 4** Activation mapping at the ablation site during sustained ventricular tachycardia in right ventricular dysplasia (96233, upper panel) and during idiopathic ventricular ectopies (99341, lower panel), in both cases with left axis deviation morphology. In right ventricular dysplasia, the intracavitary recording shows an isolated and fragmented diastolic potential ( $-158$  ms with respect to QRS onset), while the earliest presystolic activity for idiopathic premature beat is recorded at the ablation site 20 ms before the QRS. RVMa-p, right ventricular mapping catheter, distal and proximal tip; VT, ventricular tachycardia. Recording made at 200 mm/s.

only five of 14 (33%) did the Holter ECG show a decreased score (table 4). The mean (SD) symptom score was 3.75 (1.34) on initial evaluation and decreased to 1.19 (1.38) at the time of last follow up (mean score difference 2.5, 95% CI 1.53 to 3.53;  $p < 0.0001$ ). The Holter score decreased from 2.7 (0.56) to 1.9 (1.25) (mean score difference 0.77, 95% CI 0.65 to 1.47;  $p = 0.035$ ; fig 5). In 2/13 (15%) of the patients with ARVD, antiarrhythmic drug treatment was discontinued, and new treatment was started in two (14%). In patients who had undergone RFCA, the procedure was considered successful over the long term if no episodes of the ventricular arrhythmia treated with ablation or any form of sustained ventricular tachycardia were documented during follow up. Long term success of RFCA was 73% (22/30) in patients with IRVA and 15% (2/13) in patients with ARVD.



**Figure 5** Improvement in symptoms and ventricular arrhythmias recorded on a 24 hour Holter ECG after treatment in patients with idiopathic right ventricular arrhythmia (IRVA) and arrhythmogenic right ventricular dysplasia (ARVD). I and II, scores before admission and during follow up, respectively. \* $p=0.035$ ; \*\*\* $p<0.0001$ .

## DISCUSSION

Our aim in this study was to investigate whether data obtained during a conventional electrophysiological study can be used to guide the management of patients with a right ventricular arrhythmia. To do this, we analysed data retrospectively from 56 patients with this type of arrhythmia referred to our hospital over a seven year period; these patients had no clinical evidence of structural heart disease other than suspected right ventricular dysplasia. This type of patient selection is a limitation of the present study, as most of the patients were referred to us after primary assessment in other institutions, so a referral bias must be assumed. Furthermore, the physicians who performed the electrophysiological study were not blinded to the clinical history and imaging data. However, the electrophysiological testing was carried out according to a standardised protocol.

For the purpose of this study, patients were classified as having ARVD by previously suggested criteria.<sup>12</sup> Clinical decision making in these patients was based on imaging, clinical presentation, and the results of the electrophysiological study. The validity of this approach was assessed during long term follow up.

Not unexpectedly, data from a standard 12 lead ECG (signal averaged ECGs were not taken in these patients) and the clinical presentation alone do not allow a diagnosis to be made in the majority of the patients. Although patients with a completely normal ECG during sinus rhythm are unlikely to suffer from ARVD, 66% of the ARVD patients in the present study had only repolarisation abnormalities in the precordial leads, a feature that was also observed in 23% of the patients with IRVA. These results are in line with previous observations.<sup>22</sup>

The documented arrhythmias consisted of premature ventricular beats or non-sustained ventricular tachycardias in

about 20% of patients with ARVD, with a left bundle branch block/inferior axis morphology in half the cases. This is also regarded as the presenting arrhythmia in patients with IRVA.<sup>23</sup> These data are in accordance with previous findings.<sup>3,7</sup> On the other hand, 34% of our patients with IRVA had documented sustained ventricular tachycardia, and 10% did not show the “classic” inferior axis during arrhythmia. Catheter mapping in these patients showed that the origin of the tachycardia was not in the right ventricular outflow tract. This contrasts with the commonly held view that idiopathic arrhythmias from the right ventricle originate only from the outflow tract area—which has given rise to the term “idiopathic right ventricular outflow tract tachycardia”—and confirms the difficulty in classifying these patients correctly.

These factors give weight to the finding that a diagnosis of ARVD can be made from data obtained in a conventional electrophysiological study. We found a high concordance between the diagnostic electrophysiological criteria (induction of ventricular tachycardia by programmed electrical stimulation with ventricular extrastimuli, presence of diastolic fragmented potentials, multiple ECG morphologies of the tachycardia) and the results of imaging tests. A clear discordance—that is, positive results on both echocardiography and right ventricular angiography, and a negative result on electrophysiological study—was noted in only one patient. Interestingly, treatment success (with a  $\beta$  blocker alone) and a benign course during follow up suggest that data from the electrophysiological study were highly predictive of the correct management in that patient. As it seems unlikely that the results of both types of imaging were false positives, it appears that the criteria used during electrophysiological examination may help detect some patients with right ventricular dysplasia who will not experience severe tachycardias. The same good response to treatment and benign course were observed in a patient who was classified as belonging to the IRVA group in the light of suspicious (but not positive) results on echocardiography and MRI and who had a negative electrophysiological study. Had these patients been classified only on the basis of the electrophysiology, their diagnosis would have been correct in the light of the other data collected in this study, including the long term follow up.

In agreement with our present findings, previous studies on patients with right ventricular tachycardias and without other cardiac disease have shown that the tachycardias can often be induced by rapid pacing and isoprenaline, and very rarely by programmed electrical stimulation with ventricular extrastimuli.<sup>23–25</sup> In one report, “polyphasic widened electrograms” were observed in three of nine patients mapped during tachycardia.<sup>25</sup> However, these electrograms were not described further and may represent early activation in the area of focal ectopy, as seen in patients with IRVA—which is a pattern clearly different from the (mid)diastolic fragmented potentials that are observed in patients with ARVD (figs 1–3).

The effectiveness of the diagnostic electrophysiological variables in differentiating IRVA from ARVD is not surprising if one takes into account the underlying anatomical and pathophysiological properties. Previous studies have suggested that IRVA is a result of cAMP dependent triggered activity,<sup>26</sup> which is a focal form of tachycardia clearly distinguishable from re-entry tachycardia on the basis of its electrophysiological properties. Ventricular tachycardias in diseased myocardium—as in ischaemic heart disease and right ventricular dysplasia—are characterised by areas of slow conduction within the diseased tissue that allow continuous electrical activity (shown as fragmented diastolic potentials) in an expanded area, creating a circuit pathway.<sup>27</sup> If the diseased area supports more than one circuit pathway, or if the disease affects different areas of the ventricle, more than one type of tachycardia can occur. This explains why most patients with ARVD have more than one ECG morphology of ventricular tachycardia.<sup>3</sup> Finally, re-entry tachycardias are generally

inducible by programmed electrical stimulation with ventricular extrastimuli, as were the ventricular tachycardias of patients with ARVD in the present and previous studies.<sup>3 6 10</sup> In contrast, focal ventricular tachycardias cannot be induced by programmed electrical stimulation with ventricular extrastimuli but may be induced by burst stimulation, and in the setting of IRVA are particularly sensitive to  $\beta$  adrenergic agonists. Thus in the present study, ventricular tachycardia was induced in nine patients in the IRVA group by burst stimulation or isoprenaline.

Previous studies have shown that radiofrequency catheter ablation has a high rate of success in patients with IRVA and a much lower primary success rate in patients with ARVD.<sup>28 29</sup> Our findings are consistent with these previous reports. However, they do suggest that ablation may be a valuable therapeutic option in selected patients. It is not yet clear how this group should be defined, but it may include patients with no history of cardiac arrest, only mild right ventricular dysfunction, moderately fast or slow ventricular tachycardias, no involvement of the left ventricle, and a reliable primary success.<sup>7</sup> Ablation may be also considered as an adjunct to an implantable cardioverter-defibrillator where the need for other treatments is excessively burdensome.

It has been speculated that IRVA may represent an early stage of ARVD,<sup>18-21</sup> and as ARVD is regarded as a progressive disorder,<sup>5 30</sup> some of the patients who are diagnosed as having IRVA may develop overt ARVD. However, the similar age of patients in the two groups and the follow up data from the present study suggest that evolution of IRVA to ARVD is not a common pattern.

## Conclusions

The major finding of this study is that a diagnosis of ARVD can be made reliably on the basis of clinical presentation, imaging techniques, and an electrophysiological study. In addition, we have confirmed in a substantial series that patients with IRVA respond well to ablation and medical treatment. On the other hand patients with ARVD respond less well to ablation and medical treatment and often require an implantable cardioverter-defibrillator to prevent fatal arrhythmias.

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