Electrocardiographic Features of Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy According to Disease Severity

A Need to Broaden Diagnostic Criteria

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Background—The purpose of this study was to systematically study diagnostic and prognostic electrocardiographic (ECG) characteristics of arrhythmogenic right ventricle dysplasia/cardiomyopathy (ARVD/C).

Methods and Results—The patient population included 50 patients with ARVD/C (27 males, 23 females; mean age 38±15 years). We also analyzed the ECG of 50 age- and gender-matched normal control subject and 28 consecutive patients who presented with right ventricular outflow tract (RVOT) tachycardia. Right bundle-branch block (RBBB) was present in 11 patients (22%). T-wave inversions in V_1 through V_3 were observed in 85% of ARVD/C patients in the absence of RBBB compared with none in RVOT and normal controls, respectively ($P<0.0001$); epsilon waves were seen in 33%, and a QRS duration ≥110 ms in V_1 through V_3 was present in 64% of patients. Among those without RBBB, our newly proposed criterion of "prolonged S-wave upstroke in V_1 through V_3" ≥55 ms was the most prevalent ECG feature (95%) and correlated with disease severity and induction of VT on electrophysiological study. This feature also best distinguished ARVD/C (diffuse and localized) from RVOT.

Conclusions—A prolonged S-wave upstroke in V_1 through V_3 is the most frequent ECG finding in ARVD/C and should be considered as a diagnostic ECG marker. **(*Circulation*. 2004;110:1527-1534.)**

Key Words: cardiomyopathy ■ diagnosis ■ electrocardiography

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is a myocardial disease that primarily affects the right ventricle (RV) and is characterized histologically by the replacement of myocytes by adipose and fibrous tissue.[1] The anatomic damage present in ARVD/C modifies electrical activation and repolarization, particularly of the RV.[2] Marcus et al[1] described the ECG features of ARVD/C in their original description of this disease more than 20 years ago. Subsequently, the Task Force on Right Ventricular Myopathies of the European Society of Cardiology and of the Scientific Council on Cardiomyopathies of the International Society and Federation of Cardiology included several ECG features of the disease in the criteria for diagnosis of ARVD/C.[3] These criteria included (1) T-wave inversions in V_1 through V_3, (2) QRS duration (QRSd) ≥110 ms in V_1 through V_3, and (3) the presence of an epsilon wave (electric potentials after the end of the QRS complex). Additional ECG markers of ARVD/C that have been reported include (1) QRS and QT dispersion,[4] (2) parietal block, defined as a QRSd in leads V_1 through V_3 that exceeds the QRSd in lead V_6 by >25 ms,[5] and (3) a ratio of the QRSd in leads $V_1+V_2+V_3/V_4+V_5+V_6 \geq 1.2$.[6]

The purpose of the present study was to reexamine the ECG features of ARVD/C. Particular attention is focused on determining the relation of ECG parameters to disease severity; describing a novel ECG marker of ARVD/C; and identifying those ECG features that best distinguish ARVD/C from RV outflow tract tachycardia (RVOT), which is the most common differential diagnosis in the clinical setting, and assessing the association of ECG markers with clinical presentation and outcome of the electrophysiology study (EPS) in patients with ARVD/C.

Methods

Study Population

The patient population included 50 patients with ARVD/C (27 males, 23 females; mean age 38±15 years). We also analyzed the ECG of 50 age- and gender-matched individuals with no history of arrhythmia or syncope and a normal ECG pattern and 28 consecutive patients who presented with ventricular arrhythmias of left bundle-branch block morphology and who were classified as having RVOT

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TABLE 1. Clinical Characteristics of Patients With ARVD/C According to Task Force Criteria

	ARVD/C (n=50)
Family history	
Family history of ARVD/C confirmed by biopsy or autopsy	2 (4)
Family history of premature sudden death (age <35 years) due to suspected ARVD/C	1 (2)
Family history (clinical diagnosis based on present criteria)	8 (16)
ECG depolarization/conduction abnormalities	
Epsilon waves	16 (32)
Localized QRSd >110 ms in V_1, V_2, or V_3 (in absence of RBBB)	25/39 (64)
Late potentials on signal-averaged ECG	19 (56)
Repolarization abnormalities	
Inverted T waves in right precordial leads (V_2–V_3) above age 12 y in absence of RBBB	34/39 (87)
Tissue characterization of walls	
Fibrofatty replacement of myocardium in endomyocardial biopsy	6/14
Structural or functional abnormalities	
Severe dilatation and reduction of RV ejection fraction with mild or no LV involvement	28 (56)
Localized RV aneurysm (akinetic or dyskinetic areas with diastolic bulging)/severe segmental dilatation of the RV (diffuse RV disease)	
Mild global RV dilatation and/or ejection fraction reduction with normal LV/mild segmental dilation of the RV/regional RV hypokinesis (localized RV disease)	22 (44)
Arrhythmias	
Left bundle-branch block VT on ECG, Holter, or exercise tolerance test	
Sustained VT	21 (42)
Nonsustained VT	14 (28)
Frequent premature ventricular contractions (>1000/24 h on Holter)	11 (22)

LV indicates left ventricular. All values are n (%).

*Major ARVD/C diagnostic criteria are shown in bold. The criteria state that an individual must have 2 major, or 1 major plus 2 minor, or 4 minor criteria from different categories to meet the diagnosis of ARVD/C.[3]

after exclusion of structural heart disease. The majority (78%) of ARVD/C patients presented with palpitations. Syncope was reported by 17 patients (34%). The Task Force criteria were used for the diagnosis of ARVD/C[3] and the prevalence of minor and major criteria in these patients are shown in Table 1. For purposes of our analysis, ARVD/C was defined to be diffuse (n=28) when imaging techniques revealed widespread RV involvement that resulted in global RV dilatation and a reduction in the RV ejection fraction (Table 1). Localized RV disease (n=22) was diagnosed by the presence of regional RV lesions, such as segmental RV wall-motion abnormalities (hypokinetic or dyskinetic areas), with mild or no decrease in RV ejection fraction.[3] No patients or controls were receiving antiarrhythmic drugs or other drugs known to affect the QRS complex or the QT interval at the time of acquisition of the ECG tracings in the present study. All patients were in sinus rhythm.

ECG Analysis

The 12-lead ECGs were obtained in the traditional lead positions and recorded at 25 mm/s. To increase the accuracy of measurements, ECGs were enlarged 2 times. Digital calipers capable of measuring to within 1 ms (horizontal axis) and 0.01 mV (vertical axis) were used to determine the intervals (Sigma Scan). The intervals were measured in 3 consecutive beats in each lead; the mean value of the 3 beats was used. The ECG parameters, techniques for measurement, and definitions used are described in Table 2.

In addition to analysis of conventional ECG markers, we propose a novel marker for delayed right precordial activation. This feature is a prolonged S-wave upstroke in leads V_1 through V_3. Figure 1 demonstrates an illustration of the measurement of S-wave upstroke and examples of this feature in patients with ARVD/C in leads V_1 through V_3.

ECG leads in which the end of the QRS complex or T wave could not be identified were excluded from analysis from the study group. The percentage of missing leads for determination of QT and QRS dispersion was 9% and 6%, respectively. Two independent observers, blinded as to the clinical data, tested the repeatability of all ECG measurements in a random sample of 20 ECGs, and the percentage differences in measurements ranged from 1% to 6% for within-observer variability and from 1% to 7% for between-observer variability. A standardized EPS was performed in all of the ARVD/C patients.

Statistical Analysis

Data are presented as mean±SD and percentages. Continuous variables were compared with the use of Student's *t* test; categorical variables were compared with a χ^2 test. Dichotomous variables were created for each ECG marker to determine the optimal values to differentiate localized ARVD/C from RVOT and normal controls, respectively, as determined by the highest χ^2 value. ECG markers with the highest association with clinical features such as VT and a positive EPS were determined. Finally, stepwise logistic regression was performed to identify the independent ECG predictors of VT induction. A probability value of ≤ 0.05 was considered significant.

Results

Figure 2 shows 3 representative ECGs from ARVD/C patients in the present series. The ECG in Figure 2A was recorded from a 37-year-old male who presented with sustained VT. EPS revealed multiple morphologies of VT, and echocardiography showed a severely dilated RV. The

TABLE 2. Definition of ECG Variables and Measurements

Variables	Definition
PR interval	Beginning of P wave to first deflection of QRS complex[7]
PR segment	Calculated by subtracting P-wave interval from PR interval[7]
QRS complex	Beginning of QRS complex to its end[7]*
S-wave upstroke	Nadir of S wave to isoelectric line
QT interval	Onset of QRS complex to end of T wave[4]†
JT interval	QT interval minus QRSd[7]
QT/QRS/JT dispersions	Difference between maximum and minimum QT, QRS, and JT values occurring in any of the 12 ECG leads, respectively[4]
Epsilon waves	Distinct waves of small amplitude that occupy the ST segment in the right precordial leads[1]
Parietal block‡	QRSd in V_1-V_3 that exceeds the QRSd in lead V_6 by >25 ms (see reference 5)
T-wave inversions	T-wave negativity in V_1 and beyond[3]
ST-segment elevation	Maximal displacement of ST segment with upward convexity ≥0.5 mm from the isoelectric line[4]
Complete RBBB	QRSd ≥0.12 s, secondary R wave in right precordial leads, and wide S wave in leads I and V_6[7]
Incomplete RBBB	QRSd ≥0.10 and <0.12 s, secondary R wave in right precordial leads, and wide S wave in leads I and V_6[7]

*When the offset of the QRS complex was difficult to define because of a gradual slope toward a plateau, it was measured at the intersection of the S wave with the isoelectric baseline.

†When U waves were present, the QT interval was measured to the nadir of the curve between the T and U waves.

‡Parietal block may represent the presence of an epsilon wave that merges with the QRS complex and appears as a soft R wave.

12 lead-ECG demonstrates the typical ECG features of ARVD/C, including diffuse precordial T-wave inversions (V_1 through V_5), an epsilon wave in V_1, and a parietal block. In addition, a prolonged S-wave upstroke can be seen in V_2. The ECG in Figure 2B was obtained from an individual with a family history of ARVD/C who presented with palpitations and was diagnosed as having ARVD/C. The ECG shows T-wave inversion in V_1 through V_3 with an S-wave upstroke of 60 ms in V_2. The ECG in Figure 2C was obtained from a 45-year-old female who presented with syncope. An MRI revealed diffuse RV dilatation. The ECG showed a right bundle-branch block (RBBB) pattern with T-wave inversion in the right precordial leads. This ECG also demonstrated that the QRSd in V_1 was >25 ms higher than in V_6.

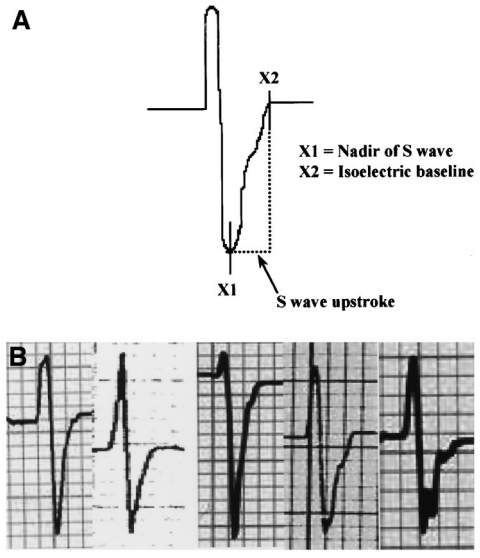

Figure 1. A, Illustration of determining S-wave stroke from QRS complex. B, Examples of QRS complex in V_1 through V_3 from several ARVD/C cases demonstrating prolonged S-wave upstroke.

ECG Characteristics of ARVD/C in the Absence of RBBB

Table 3 presents the prevalence of ECG characteristics in ARVD/C patients (39/50) in the absence of RBBB. The classic ECG feature of T-wave inversion in V_1 through V_3 was observed in 85% of ARVD/C patients compared with none of the RVOT or control patients ($P<0.0001$). Overall, among the 39 ARVD/C patients, T-wave inversion was observed in V_1 and V_2 in 4 patients (10%), V_1 through V_3 in 23 (59%), V_1 through V_4 in 7 (18%), V_1 through V_5 in 2 (5%), and V_1 through V_6 in 2 patients (5%). Epsilon waves and parietal block were seen in 33% and 52% of cases, respectively. A QRSd ≥110 ms in V_1 through V_3 was present in 64% of patients. A ratio of the QRSd in $V_1+V_2+V_3/V_4+V_5+V_6 \geq 1.2$ was detected in 30 ARVD/C patients (77%) compared with 7% of RVOT patients and 8% of normal controls ($P<0.0001$; Table 3). Our newly proposed criterion of prolonged S-wave upstroke in V_1 through V_3 ≥55 ms was the most prevalent ECG feature in ARVD/C, being seen in 95% of patients compared with its presence in 7% of patients with RVOT and 2% of controls. ST-segment elevation was seen only in 1 patient.

Table 4 shows the relative value of various ECG features of ARVD/C in differentiating patients with diffuse ARVD/C, localized ARVD/C, and RVOT and normal controls. There are several important results of this analysis. First, all previously described ECG criteria were more prevalent in ARVD/C patients with diffuse versus localized RV involvement. For example, T-wave inversion in V_1 through V_3 was present in ARVD/C cases with diffuse disease but only in 70% of ARVD/C patients with localized disease ($P=0.0009$). An epsilon wave was present in 53% of patients with diffuse RV involvement but

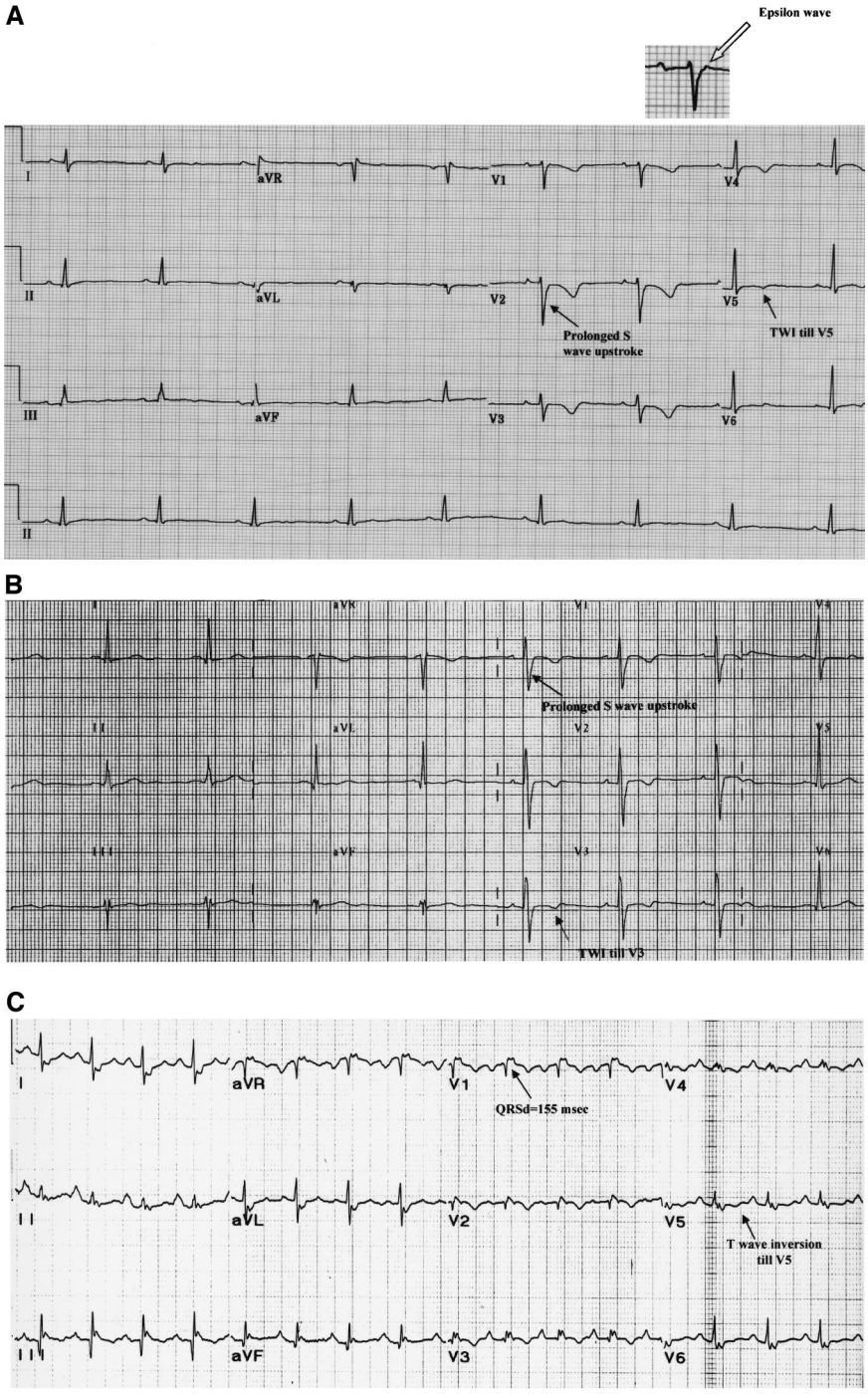

Figure 2. Sample ECGs of ARVD/C patients. A, Diffuse ARVD/C; B, localized ARVD/C; and C, ARVD/C with RBBB pattern. TWI indicates T-wave inversion.

only 15% of ARVD/C patients with localized disease ($P=0.01$). Similarly, the Task Force–recommended QRSd cutoff value of 110 ms was seen in 78% of ARVD/C cases with diffuse involvement but only 50% of ARVD/C patients with localized disease ($P=0.06$). The results of the present study indicate that by using a cutoff value of ≥105 ms for the QRSd in V_1 to V_3, we were able to identify an additional 20% of patients with the localized form of ARVD/C compared with the standard cutoff value of ≥110 ms with the same specificity. This table also shows the diagnostic value of the prolonged S-wave upstroke criteria in V_1 through V_3. The optimal cutoff value for this parameter was ≥55 ms (χ^2 value 36.7). Every patient with diffuse ARVD/C was identified with this criterion, as were 90% of patients with localized ARVD/C. Among patients with the localized form of ARVD/C, prolonged S-wave upstroke ≥55 ms was seen in 8 (80%) of 10 patients who did not have a QRSd ≥110 ms in V_1 through V_3. Four ARVD/C patients with diffuse RV involvement also demonstrated a QRSd <110 ms in the right precordial leads; interestingly, a prolonged S-wave upstroke ≥55 ms was present in all of these cases. In contrast, only 1 patient with RVOT and 1 control patient demonstrated this ECG feature.

TABLE 3. Relative Prevalence of ECG Features of ARVD/C in Patients With ARVD/C Without RBBB or RVOT and in Normal Controls

	ARVD/C (n=39)	RVOT (n=28)	Normal Controls (n=50)	P*	P†
T-wave inversion V_1–V_3	33 (85)	0 (—)	0 (—)	<0.0001	<0.0001
Epsilon wave	13 (33)	0 (—)	0 (—)	<0.0001	<0.0001
Parietal block	20 (52)	4 (14)	4 (8)	0.004	<0.0001
QRSd ≥110 ms in V_1–V_3	25 (64)	0 (—)	0 (—)	<0.0001	<0.0001
QRS $V_1+V_2+V_3$/QRSd $V_4+V_5+V_6$ ≥1.2	30 (77)	2 (7)	4 (8)	<0.0001	<0.0001
QRS dispersion ≥40 ms	17 (44)	1 (4)	0 (—)	<0.0001	<0.0001
QT dispersion ≥65 ms	27 (69)	3 (10)	1 (2)	<0.0001	<0.0001
S-wave upstroke ≥55 ms V_1–V_3	37 (95)	1 (7)	1 (2)	<0.0001	<0.0001

Values are n (%).
*ARVD/C vs RVOT.
†ARVD/C vs normal controls.

Association of ECG Variables With Clinical Presentation and Inducibility at EPS in the Absence of RBBB

Among patients without RBBB, no significant differences were observed in ECG characteristics according to presence or absence of family history, palpitations, or syncope. Fourteen patients (36%) presented with a history of sustained VT and 21 (54%) with nonsustained VT/premature ventricular contractions ≥1000/d, and 4 (10%) had no arrhythmic history. A positive EPS was seen in 26 (67%) of 39 of these patients. Figure 3 shows the most predictive univariate ECG markers associated with the presence of spontaneous and inducible VT on EPS. A stepwise logistic regression analysis of all the ECG-derived variables identified prolonged S-wave upstroke in V_1 through V_3 ≥70 ms (odds ratio 7.2; 95% CI 1.2 to 43.8; $P=0.03$) and QRS dispersion ≥40 ms (odds ratio 6.1; 95% CI 1.0 to 37.6; $P=0.05$) as the only significant predictors of inducibility of VT at EPS, respectively.

ECG Characteristics of ARVD/C With RBBB

Four (8%) and 7 (14%) patients presented with complete RBBB and incomplete RBBB, respectively. Diffuse RV involvement was seen in all patients with complete RBBB and in 5 of 7 patients with an incomplete RBBB (81%). All of these patients (100%) were inducible at EPS; 7 (64%) presented with a history of sustained VT, and 3 (27%) had a history of nonsustained VT/premature ventricular contractions ≥1000/d. The prevalence of an epsilon wave was not different among patients with an RBBB pattern than among the ARVD/C patients without RBBB (27% versus 33%, respectively). Another marker of delayed activation was the presence of parietal block (defined as a QRSd in leads V_1 to V_3 that exceeded the QRSd in lead V_6 by >25 ms). A parietal block was more commonly observed among patients with the RBBB pattern than among those without this RBBB pattern (82% versus 52%, respectively; $P=0.07$). No differences in dispersion measures were demonstrated according to the presence or absence of RBBB.

Discussion

In this study, we performed a systematic analysis of the 12-lead ECG in ARVD/C. In addition, we described a novel ECG finding in ARVD/C, which we termed "delayed S-wave upstroke," in the right precordial leads. We have also identified which ECG markers best discriminate the mild (localized) form of ARVD/C compared with RVOT and controls. In addition, we described ECG markers of VT inducibility on EPS in ARVD/C. Finally, we have characterized the ECG features of ARVD/C in the subset of patients with complete or incomplete RBBB.

Since the first description of ARVD/C, there has been considerable interest in describing the ECG features of this disease. The hallmark feature of ARVD/C, the epsilon wave, is a marker of delayed activation of the RV and is considered a major diagnostic criteria for ARVD/C according to the Task Force.[3] This is a highly specific but insensitive criterion for ARVD/C and is observed in 25% to 33% of ARVD/C patients when evaluated by the standard ECG.[4,6] In addition to the epsilon wave, several other markers of delayed activation of the RV have been described, such as QRSd ≥110 ms in V_1 through V_3,[3,6] the ratio of the sum of the QRSd in leads $V_1+V_2+V_3/V_4+V_5+V_6$ ≥1.2, and parietal block.[5,6] T-wave inversion in leads V_1 through V_3 in the absence of RBBB is considered a minor diagnostic criterion for ARVD/C,[5] and its prevalence in ARVD/C has been reported as 55% to 94% in different series.[2,6,9] The extent of right precordial T-wave inversion relates to the degree of RV involvement, as reported by Nava et al.[8] Despite the frequent association of T-wave inversion with ARVD/C, it is not specific for ARVD/C, particularly because it may be a normal finding in children less than 12 years of age and can also be seen in normal individuals.

The prevalence of previously described ECG features of ARVD/C reported here is consistent with prior reports The results of the present study further extend the existing literature in several ways. We have demonstrated that significant differences exist in most ECG features among ARVD/C patients, such as epsilon wave, T-wave inversion, QRSd ≥110 ms in V_1 through V_3, and parietal block, according to the degree of RV involvement, and that they are more prevalent in diffuse ARVD/C than in the localized form of the disease (Table 4). In the present study, we have described a new marker of delayed RV activation, the prolonged S-wave

TABLE 4. Relative Value of ECG Parameters in Differentiating Diffuse ARVD/C and Localized ARVD/C From RVOT and Normal Controls in Absence of RBBB

Variables	ARVD/C Diffuse (n=19)	ARVD/C Localized (n=20)	RVOT (n=28)	Normal Controls (n=50)	*P**	*P*†	*P*‡	χ^2 Value§
Epsilon wave‖	10 (53)	3 (15)	0 (—)	0 (—)	0.01	0.03	0.005	4.5
Parietal block	13 (73)	7 (35)	4 (14)	4 (8)	0.006	0.03	0.005	7.9
T-wave inversions								
V_1–V_2 and beyond	19 (100)	18 (90)	4 (14)	3 (6)	0.2	<0.0001	<0.0001	26.9
V_1–V_3 and beyond‖	19 (100)	14 (70)	0 (—)	0 (—)	0.009	<0.0001	<0.0001	27.6
V_1–V_4 and beyond	6 (32)	1 (5)	0 (—)	0 (—)	0.03	0.2	0.2	1.4
V_1–V_5/V_1–V_6	4 (21)	0 (—)	0 (—)	0 (—)	0.03	...	...	...
QRSd V_1–V_3								
≥100 ms	19 (100)	18 (90)	5 (18)	2 (6)	0.8	<0.0001	<0.0001	23.9
≥105 ms	16 (84)	14 (70)	1 (4)	0 (—)	0.3	<0.0001	<0.0001	24.3
≥110 ms‖	15 (78)	10 (50)	0 (—)	0 (—)	0.06	<0.0001	<0.0001	17.7
≥120 ms	12 (63)	4 (20)	0 (—)	0 (—)	0.03	<0.0001	<0.0001	6.8
QRSd $V_1+V_2+V_3/V_4+V_5+V_6$								
≥1.1	19 (100)	18 (90)	14 (50)	21 (42)	0.1	0.004	<0.0001	2.5
≥1.2	18 (95)	12 (60)	2 (7)	4 (8)	0.01	<0.0001	<0.0001	15.7
≥1.3	13 (73)	5 (25)	0 (—)	0 (—)	0.001	0.005	<0.0001	7.8
S-wave upstroke V_1–V_3								
≥50 ms	19 (100)	19 (95)	3 (11)	4 (8)	0.3	<0.0001	<0.0001	33.3
≥55 ms	19 (100)	18 (90)	1 (7)	1 (2)	0.2	<0.0001	<0.0001	36.7
≥60 ms	17 (84)	15 (75)	0 (—)	0 (—)	0.2	<0.0001	<0.0001	30.5
≥70 ms	13 (68)	5 (25)	0 (—)	0 (—)	0.007	0.005	0.005	7.8
QRS dispersion								
≥30 ms	17 (89)	15 (75)	3 (10)	5 (10)	0.2	<0.0001	<0.0001	20.5
≥35 ms	13(68)	10 (50)	3 (10)	2 (4)	0.2	0.003	<0.0001	9.1
≥40 ms	10 (53)	7 (35)	1 (4)	0 (—)	0.2	0.004	<0.0001	8.3
QT dispersion								
≥50 ms	18 (95)	14 (70)	5 (17)	7 (14)	0.04	<0.0001	<0.0001	13.3
≥65 ms	15 (78)	12 (60)	3 (10)	1 (2)	0.2	<0.0001	<0.0001	13.2
≥80 ms	12 (63)	6 (30)	0 (—)	0 (—)	0.03	<0.0001	<0.0001	9.6
JT dispersion								
≥35 ms	14 (73)	12 (60)	4 (14)	6 (12)	0.4	0.001	<0.0001	10.9
≥40 ms	11(58)	8 (40)	3 (10)	4 (8)	0.3	0.01	0.002	5.7
≥45 ms	5 (26)	3 (15)	1 (4)	1 (2)	0.4	0.1	0.01	1.9

Values are n (%).
*Diffuse vs localized disease.
†Localized vs RVOT.
‡Localized vs control.
§χ^2 Differences between localized ARVD/C and RVOT.
‖Task Force ECG criteria of ST elevation in V_1 were observed in one case of diffuse ARVD/C.

upstroke, which was present in all cases with diffuse ARVD/C and which was also highly prevalent (90%) in the localized form of the disease. In the absence of an RBBB pattern, a prolonged S-wave upstroke was observed in 12 (86%) of 14 ARVD/C patients who did not have QRSd ≥110 ms in the right precordial leads, which is a major criterion for diagnosis of ARVD/C.[3] Notably, in 4 (20%) of 20 patients with localized disease in the absence of RBBB, a prolonged S-wave upstroke ≥55 ms was the only ECG abnormality detected. The slight delay in the S wave may be present early in the course of disease without evidence of marked prolongation in QRSd, as observed in the present study, and may be a better diagnostic marker than the current ECG criteria.[3] If these results are confirmed by other studies, we think that the current ECG diagnostic criteria should be modified in recognition of a broader spectrum of disease severity to identify an earlier form of disease.

In this study, we also addressed how to best distinguish localized ARVD/C from patients with RVOT with the information obtained from a 12-lead ECG. This analysis was performed because recognition of severe global ARVD/C is rarely a diagnostic dilemma. In contrast, it can be challenging

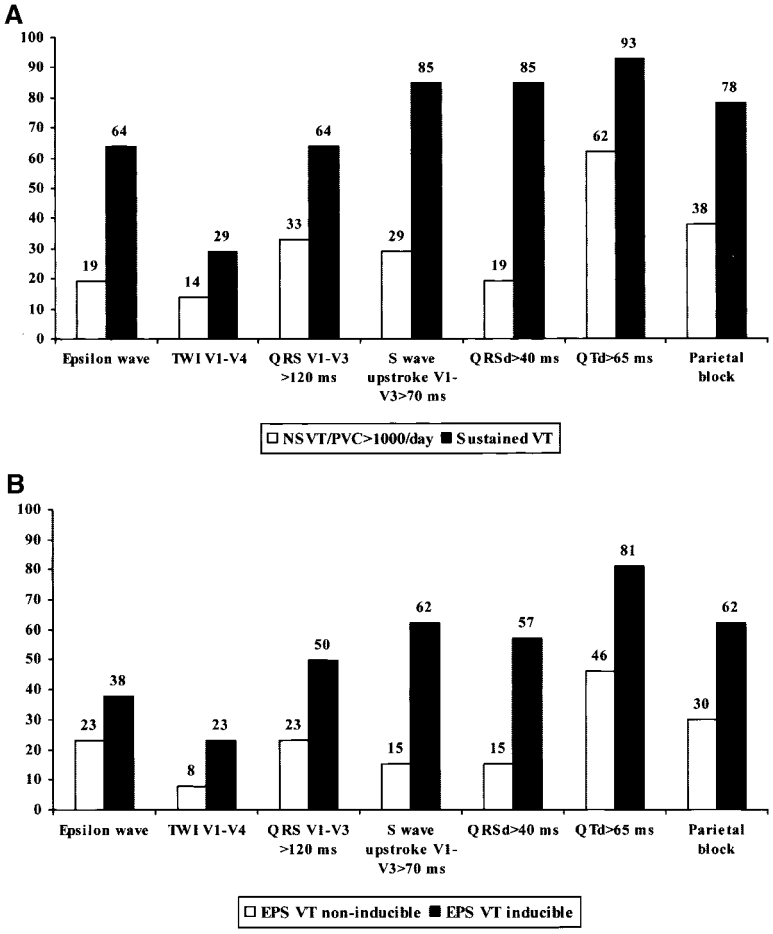

Figure 3. Prevalence (%) of ECG markers in (A) nonsustained VT/premature ventricular contractions (NSVT/PVC) ≥1000/d (n=21) vs sustained VT (n=14) and (B) EPS-noninducible VT (n=13) vs EPS-inducible VT (n=26) in absence of RBBB. TWI indicates T-wave inversion; QTd, duration of QT interval.

to attempt to distinguish patients or family members of probands from those with RVOT and normal controls. Previous studies have shown that the current ECG criteria are not sufficiently sensitive and specific to diagnose ARVD/C in patients presenting with VT of RV origin, and thus, additional imaging and invasive testing, such as EPS, are required for differentiation.[10] The present findings demonstrate that a prolonged S-wave upstroke ≥55 ms in V_1 through V_3 is sensitive and specific for distinguishing the 2 conditions. Another potentially important distinguishing ECG feature is T-wave inversion in the right precordial leads. None of the RVOT patients had T-wave inversion extending to V_3, whereas this feature was observed in 70% of patients with localized ARVD/C and 100% of those with diffuse ARVD/C (Table 4). We observed no differences in the ECG parameters studied between RVOT and normal controls, in agreement with previous findings.[11,12] However, some studies have demonstrated the presence of T-wave inversion in V_1 through V_3 in 6% to 20% of patients with RVOT.[10,13] Further studies are needed to ascertain the diagnostic value of T-wave inversion in right precordial leads in distinguishing ARVD/C from RVOT.

In a landmark study, Turrini et al[4] identified QRS dispersion ≥40 ms on the 12-lead ECG as an independent predictor of sudden cardiac death in patients with ARVD/C. We confirm that QRS dispersion is an independent predictor of arrhythmic risk (as assessed by VT induction at EPS). In addition, the present results also indicate that an S-wave upstroke ≥70 ms is an independent marker for VT induction in patients diagnosed with ARVD/C. Prolonged S-wave duration has recently been demonstrated to be a sensitive marker of VT inducibility in Brugada syndrome.[14] Broadening of the QRS complex, especially the S-wave upstroke, in the right precordial leads may be due to an important conduction delay in ARVD/C and may be an indicator of increased risk. Conduction delay has been suggested to have an important role in the pathogenesis of VT in ARVD/C.[3]

We also describe the ECG features of a subset of ARVD/C patients with a complete or incomplete RBBB. Fontaine et al[5] reported that 14% to 18% of ARVD/C patients have RBBB; the present study confirms this finding. In the present series, RBBB was associated with diffuse RV involvement. The presence of RBBB has also been described as a feature associated with heart failure in ARVD/C.[15] The study results suggest the diagnostic utility of parietal block, which was more frequent in ARVD/C patients with RBBB than in those with ARVD/C who did not have RBBB. Because it is not unusual to encounter ARVD/C patients presenting with RBBB, the presence of parietal block may be used as an ECG diagnostic criteria in these patients.

There are several limitations of this study. First, although the ECG analyses were performed carefully, interindividual variation in lead placement and day-to-day variation in voltages can result in variations in ECG pattern. Second, the

patients with ARVD/C in this study were selected on the basis of the Task Force diagnostic criteria. To the extent that these criteria lack sensitivity,[16] it is difficult to be certain whether the ECG features of ARVD/C reported in the present study adequately represent those with early forms of the disease, such as asymptomatic family members. Also, there is a possibility of an overrepresentation of ECG markers currently used as diagnostic criteria, because the same ECG abnormalities were used as criteria for entry into the classification of ARVD/C; however; the prevalence of these features in the present study was similar to that reported in the literature.[2,3,6,9] Third, it is recognized that a prolonged S-wave upstroke directly relates to QRS width in the right precordial leads; nonetheless, it was superior to localized QRS prolongation in distinguishing the mild form of ARVD/C from RVOT and was also an independent ECG marker for predicting VT induction. Finally, the prolonged S-wave upstroke parameter, which we describe for the first time in the present study, has not been validated prospectively. The cutoff criteria that we have proposed were selected on the basis of the present data set. Before this measure is relied on for diagnosis of ARVD/C, it will need to be evaluated prospectively in a separate patient population.

In summary, we have established the utility of ECG markers, including a new parameter, ie, prolongation of S-wave upstroke in V_1 through V_3. This measurement has the highest diagnostic utility for differentiating the localized form of ARVD/C from RVOT, correlates with the degree of RV involvement, and is an independent predictor of VT induction. Therefore, it should be considered as a diagnostic ECG marker for ARVD/C. Further prospective studies are needed to confirm these findings.

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