Diagnosis of Arrhythmogenic Right Ventricular Dysplasia-Cardiomyopathy: Value of Standard ECG Revisited

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Background: The diagnostic dilemma in arrhythmogenic right ventricular dysplasia-cardiomyopathy (ARVD/C) is that a single diagnostic test does not exist and that there is a need for broadening diagnostic criteria. As standard ECG contributes significantly to clinical diagnosis and represents a tool for screening in family studies ECG data should be revisited.

Methods and Results: In a cohort of 265 patients (159 males, mean age 46.8 years) with ISFC/ESC criteria of ARVD/C ECG features were reevaluated.

QRS duration in $(V1 + V2 + V3)/(V4 + V5 + V6) \geq 1.2$ —called localized right precordial QRS prolongation—was present in 261/265 patients (98%) and represents the essential finding. Right precordial epsilon potentials were found in 23% in standard and in 75% in highly amplified and modified recording technique. Right precordial T wave inversions were present in 143 cases (54%) and ST-segment elevation of different types in 66 patients (25%). Localized prolongation of inferior QRS complexes could be found in 58 cases (22%), complete right bundle branch block with T inversions beyond V2 in most cases in 17 patients (6%), incomplete right bundle branch block in 38 cases (14%), pseudo-incomplete right bundle branch block in 8 patients (3%), and right precordial R wave reduction in 14 cases (5%).

Conclusion: With regard to sensitivity and already known specificity an ECG score for the diagnosis of ARVD/C was developed with high probability of ARVD/C in cases with ≥ 4 points, possibly without the need for an additional imaging technique.

Standard ECG with additional highly amplified and modified recording technique represents a single diagnostic test with high value in the clinical diagnosis of ARVD/C and should be used as a first line tool in noninvasive family screening.

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arrhythmogenic right ventricular dysplasia-cardiomyopathy; localized right precordial QRS prolongation; T wave inversions; epsilon potential; ECG score

Clinical diagnosis of arrhythmogenic right ventricular dysplasia-cardiomyopathy (ARVD/C) remains difficult despite certain progress in imaging techniques of the right ventricle,¹ molecular genetics,² and understanding of underlying mechanisms such as calcium overload of the sarcoplasmatic reticulum and disturbances of gap junctions.^{3,4} From family studies it is now well understood that there is a need for broadening the diagnostic criteria of ARVD/C.⁵ Difficulties in clinical diagnosis are mainly based on the fact that a single diagnostic test is not present, thus missing the diagnosis in cases with only subtle morphological changes.⁶ These considerations were the background for the reeval-

uation of electrocardiographic changes in ARVD/C as a simple diagnostic test.

METHOD

Since 1988 standard ECGs of 265 patients (159 males, mean age 46.8 years) with ISFC/ESC diagnostic criteria of ARVD/C have been analyzed. In 128 cases analysis also included highly amplified and modified ECG leads as proposed by Marcus and Fontaine in 1994.⁷

Patients included in this study had morphological and functional changes of the right ventricle demonstrated by echocardiography, angiography,

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and MRI (100%), left bundle branch block—like ventricular premature beats (64%) or nonsustained or sustained ventricular tachycardia (50%), positive findings of fibrolipomatosis in endomyocardial biopsy (20%), and positive family history with unexplained sudden cardiac death under the age of 40 years, and definite diagnosis by autopsy or clinical diagnosis by systematic family screening (36%).

Analysis of standard or highly amplified and modified ECG included QRS duration in right precordial and inferior leads, the correlation of QRS interval between right and left precordial leads, and inferior and other limb leads, the frequency of so-called epsilon potentials, the localization and extent of precordial T wave inversions, morphology (coved, saddle-back, or junctional), and the amplitude of ST segment elevation in right precordial leads, incomplete and complete right bundle branch block, and R amplitude in right precordial leads.

Finally, an attempt was made to develop an electrocardiographic score for the diagnosis of ARVD/C with regard to the sensitivity of the different ECG findings in the underlying cohort of patients and the already known specificity.

RESULTS

In the majority of the patients the underlying rhythm was sinus rhythm, only six patients were in atrial fibrillation. The electrical axis was balanced in 105 patients, superior in 75 patients, and inferior in 85 cases. The following special findings could be observed.

Localized Right Precordial QRS Prolongation

This specific phenomenon (Fig. 1) could be found in 261 cases (98%) if the definition of QRS interval in $(V1 + V2 + V3)/(V4 + V5 + V6) \geq 1.2$ and a necessary QRS duration in at least two right precordial leads of ≥ 100 ms was used. In 232/236 patients (98%), the localized right precordial QRS prolongation was positive in cases with right precordial QRS duration of ≥ 100 ms and a R/S ratio in $V2 < 1$, in 29 cases with a R/S ratio in $V2$ of ≥ 1 QRS duration in at least two right precordial leads was ≥ 110 ms. QRS interval in $V1 - V3 \geq 110$ ms as proposed by Fontaine as a diagnostic finding could be observed in 186 cases (70%).

Figure 1. Localized right precordial QRS prolongation with QRS duration ≥ 100 ms in $V1$ and $V2$.

Epsilon Potential

Constant or inconstant small afterdepolarizations in the transition of right precordial QRS complex and ST segment (=epsilon potentials) could be found in different frequencies in correlation to ECG recording technique (Fig. 2).

In the standard recording technique in 128 patients epsilon potentials in right precordial leads were seen only in 29 cases (23%). The frequency could be increased by a highly amplified recording technique of precordial leads (20 mV) in 63 cases (49%), and by a modified recording technique (bipolar leads in position $V2$, $V3$ and $V5$) in 78 cases (61%). When highly amplified and modified recording techniques were used in addition to standard leads the prevalence of epsilon potentials was 75% (98 cases). Another beneficial effect of high amplification was a higher resolution of the J-point in

Figure 2. Large epsilon potentials in V1–V3.

right precordial leads and measurements of QRS duration were easier to perform.

Right Precordial T Wave Inversions

Negative precordial T waves in cases with ARVD/C could be found in 143/265 cases (54%). These T inversions were limited to V1–V3 in 82 cases (57%) and were beyond V3 in 61 patients (43%).

Right Precordial ST Segment Elevation

ST segment elevation of different types (coved, saddle-back, junctional) was present in 66 patients (25%) with a maximum amplitude of 1.5 mm (Fig. 3). ST elevation was accompanied by incomplete right bundle branch block in 10 cases (17%) and by complete right bundle branch block in only one patient (2%).

In lead V1 a coved type of ST elevation was found in 25/37 cases (67%), saddle-back type in 4 cases (11%), and junctional type in 8 patients (22%).

In lead V2 17/50 cases presented with a coved type (34%), 15 patients with a saddle-back type (30%), and 18 cases with a junctional type (36%).

In lead V3 a coved type was present in 8/31 cases (26%), saddle-back type in 1 patient (3%), and junctional type in 22 cases (71%).

Localized Inferior QRS Prolongation

A QRS duration in inferior leads II, III, and aVF of ≥ 100 ms, longer than in other limb leads (Fig. 4), could be demonstrated in a total of 58 cases (22%). The prolongation of the QRS interval was due to afterdepolarizations resembling epsilon potentials in 27 cases (47%). An inferior electrical axis as a possible explanation for prolongation of QRS interval in inferior leads was present only in 19 cases (33%). Forty-eight patients (83%) with localized inferior QRS prolongation presented with

Figure 3. ST segment elevation of saddle-back type in V1 and V2 and of junctional type in V3.

Figure 4. Localized QRS prolongation in inferior leads with afterdepolarizations at the end of the QRS complex in lead II and aVF.

inferior and/or posterobasal abnormalities of the left ventricle demonstrated by echocardiography and left ventricular angiography.

Right Bundle Branch Block

Complete right bundle branch block was found in 17 cases (6%). In all cases RBBB was accompanied by localized right precordial QRS prolongation (for definition see the above explanation). T wave inversion beyond V2 was seen in 13/17 cases (76%).

Incomplete Right Bundle Branch Block

Incomplete RBBB was present in 38/265 cases (14%) with the phenomenon of localized right pre-

cordial QRS prolongation in all cases. T wave inversions beyond V2 were present in 16 cases (42%).

Pseudo-Incomplete Right Bundle Branch Block

The phenomenon of rSR'-configuration in V1 and/or V2 without persisting S waves in V5 and V6 (Fig. 5) as so-called pseudo-incomplete RBBB could be observed in eight cases (3%) with T wave inversions beyond V2 in only two patients (25%).

R Reduction in Right Precordial Leads

R wave reduction in septal or right precordial leads resembling chronic anterior myocardial

Figure 5. Pseudo-ICRBBB with rSR' in V2 without S wave in V5 and V6.

Figure 6. R wave reduction in V1–V3 with slight junctional ST segment elevation.

infarction (Fig. 6) first described in a large Canadian family with ARVD/C by Norman could be found in this cohort in 14/265 cases (5%). Abnormal apical left ventricular function without the presence of coronary artery disease was present in nine cases (64%). R reduction in right precordial leads was accompanied in 12 cases (86%) by right precordial ST segment elevation.

According to the sensitivity of ECG findings (5–5%, 0.5 points, >15–25%, 1 point, >25–75%, 2 points and >75%, 3 points) a score for the electrocardiographic diagnosis of ARVD was defined (Table 1). The score of the right precordial T wave inversions was limited to one point and R reduction in the right precordial leads was excluded because of low specificity in both cases. The probability of ARVD/C was high in cases with ≥ 4 points, moderate in cases with 3 points, and low in cases with ≤ 2 points. All cases included in this analysis presented with ≥ 4 points (range from 4 to 7 points).

DISCUSSION

ARVD/C represents a pathologically well-defined cardiac entity; what remains highly controversial is

its clinical diagnosis. In 1994 McKenna et al. published diagnostic criteria with major and minor criteria taken from right ventricular morphology and function, depolarization, and repolarization abnormalities at standard ECG, tissue characterization by endomyocardial biopsy or autopsy, arrhythmias, and family history.⁸ What was not specified was the question of which imaging technique should be preferred in order to examine right ventricular morphology and function. Furthermore, MRI technique and electron beam tomography were mentioned in this article without defining the role of MRI in the diagnosis of ARVD/C. Although there is definitely certain progress in the MRI technique,¹ some crucial points remain: sensitivity of MRI in ARVD/C is limited in cases with larger amount of fibrosis, and specificity is only moderate due to the fact that there is another anomaly of the right ventricle, pure lipomatosis, which is completely different from ARVD/C.⁹ Echocardiography and angiography have certain limitations in tissue characterization. Only the consequences of fibrolipomatosis—sacculations, aneurysms, localized dilatation of different parts of the right ventricle—are visible. Endomyocardial biopsy is rarely used in ARVD/C due to sampling error and potential complications.

What remains in the clinical diagnosis is ECG in different techniques in order to demonstrate conduction delay in the right ventricular free wall due to fibrolipomatosis and to document typical ventricular arrhythmias by Holter monitoring. Other electrocardiographic techniques are also relevant for the diagnosis of ARVD/C: exercise testing for the documentation of stress-induced monomorphic or polymorphic ventricular tachycardia,¹⁰ highly amplified and modified ECG leads in order to demonstrate epsilon potentials,⁷ signal-averaging ECG technique using modified FRANK leads for the presentation of late potentials, which play a role in the diagnosis of ARVD/C,¹¹ risk stratification¹² and vectorcardiography, and signal-averaging technique per standard leads in order to reveal right ventricular free-wall conduction delay.¹³

The most important result of the analysis of standard ECG is that the phenomenon of localized right precordial QRS prolongation, defined as $QRS \text{ duration in } (V1 + V2 + V3)/(V4 + V5 + V6) \geq 1.2$, has a sensitivity of 98% and a specificity of 100%, which could be demonstrated in already published work comparing ARVD/C with other forms of cardiomyopathies and a normal population.¹⁴ As discussed before the underlying

Table 1. Proposed ECG Score Including Findings of Standard ECG (and Highly Amplified and Modified Leads) and Typical Forms of Arrhythmias

ECG Changes	Score
Localized right precordial QRS prolongation: QRS interval in (V1 + V2 + V3) with ≥ 100 ms in ≥ 2 leads/(V4 + V5 + V6) ≥ 1.2 or	
Localized right precordial QRS prolongation: QRS interval in (V1 + V2 + V3) with ≥ 110 ms in ≥ 2 leads in cases of R/S in V2 ≥ 1 /(V4 + V5 + V6) ≥ 1.2 or	3
QRS interval ≥ 110 ms in V1–V3 after exclusion of incomplete or complete RBBB and	2
Epsilon potential (constant or inconstant) in V1–V3 at normal or highly amplified and modified recording technique and	2
Right precordial T wave inversions $\geq V2$ and	1
Right precordial ST elevation (coved, saddle-back, or junctional) and	1
Localized QRS prolongation in inferior leads II, III, and aVF after exclusion of inferior electrical axis and	1
Complete right bundle branch block with T inversion beyond V2 and	0.5
Incomplete right bundle branch block with T inversion $\geq V2$	0.5
<i>ECG changes in cases of arrhythmias</i>	
Sustained or nonsustained VT or multiple VPBs with LBBB configuration and superior electrical axis or	2
Sustained or nonsustained VT or multiple VPBs with LBBB configuration and inferior electrical axis	1

≥ 4 points = high probability of ARVC without additional imaging techniques.

3 points = moderate probability of ARVC, additional imaging technique for confirmation of diagnosis required.

≤ 2 points = low probability of ARVC.

mechanism of right ventricular free-wall conduction delay could be confirmed by vectorcardiography and a signal-averaging technique as per standard leads.¹³ Furthermore, the frequency of localized right precordial QRS prolongation is identical in patients with the diagnosis of ARVD/C made by clinical aspects or definite tissue characterization¹⁵ and in cases of so-called nonarrhythmogenic right ventricular dysplasia-cardiomyopathy.¹⁶ In this respect ARVD/C has an essential ECG finding similar to the right precordial RBBB and ST elevation in Brugada syndrome and QT prolongation in long QT syndrome.¹⁷

Epsilon potential was the ECG finding described in the first four published cases of the working group of Guy Fontaine.¹⁸ In these four patients who had surgical intervention for therapy-resistant ventricular arrhythmias, epsilon potentials and afterdepolarizations at different areas of the right ventricle

during electrophysiological study could be demonstrated. The prevalence of epsilon potentials is low in standard ECG but much higher when alternative recording techniques such as high amplification of precordial leads and modification of bipolar limb leads are used. Specificity of right precordial epsilon potentials is high although similar potentials in other leads could be demonstrated in single cases of severe coronary heart disease.¹⁹

Right precordial T wave inversions were one of the first findings described in cases with ARVD/C. They are useful in risk stratification of patients with ARVD/C as T inversions beyond V3 represent cases with left ventricular involvement²⁰ characterizing a higher risk of sudden cardiac death.²¹ Nevertheless, the specificity of T wave inversions is low.

ST segment elevation with different morphology in right precordial leads in ARVD/C has been described for many years and plays an important

role in risk stratification of sudden cardiac death. Only in a minority of patients with ARVD/C and right precordial ST segment elevation incomplete or complete right bundle branch block were additional findings.²² This can be confirmed by the present analysis of ECG findings. According to a personal communication by Domenico Corrado at the CARDIOSTIM meeting in Nice in 2002 and systematic ajmaline testing the typical Brugada phenomenon can be provoked by class I antiarrhythmics in 8–10% of patients with ARVD/C.²³

The phenomenon of localized QRS prolongation in inferior leads II, III, and aVF is another interesting finding in ARVD/C, which appears predominantly in cases with additional left ventricular involvement in inferior and posterobasal segments. Inferior electrical axis is only evident in one third of the cases so that in the majority of cases this phenomenon cannot be explained by electrical axis as demonstrated in a normal population.²⁴

Complete and incomplete right bundle branch block are rare findings but in all cases accompanied by the phenomenon of localized right precordial QRS prolongation. The prognosis of cases with ARVD/C and complete right bundle branch block is poor as in a lot of cases the development of complete right bundle branch block precedes evolving right heart failure.²⁵

According to the findings of Mark Norman in Canadian families with ARVD/C and dilated cardiomyopathy R wave reduction in right precordial leads without coronary artery disease seems to be a frequent and specific ECG finding for mutations on the short arm of chromosome 3.²⁶ From the present analysis it seems that R reduction in right precordial leads represents a rare finding in other populations.

With the essential finding of localized right precordial QRS prolongation and other ECG abnormalities summarized in the proposed ECG score standard ECG (with highly amplified precordial leads and modified limb leads in addition) provides a powerful diagnostic tool as a single test for diagnosing ARVD/C.⁶ In cases with four or more points from the ECG score it has to be discussed whether the diagnosis of ARVD/C can be made without additional imaging techniques. Standard ECG should be used as the first diagnostic step in noninvasive family screening for ARVD/C, which is in good accordance with recommendations in hypertrophic cardiomyopathy.

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