ORIGINAL ARTICLE

Role of Electrocardiography in Filamin C-positive Arrhythmogenic Cardiomyopathies

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ABSTRACT

Arrhythmogenic cardiomyopathies (ADCM) include arrhythmogenic dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy (ARVC), and arrhythmogenic left ventricular cardiomyopathy (ALVC). This mixture of arrhythmogenic syndromes can be caused by filamin C mutations. **Materials and Methods:** The question is whether standard electrocardiography (ECG) can differentiate between these three forms of cardiomyopathies. Typical features of ADCM are epsilon waves, T-wave inversions in the right precordial leads, but also low voltage in limb leads, typical features in lead aVR, and an amplitude of negative T-waves in lead V1 of 2 mm or more. ECGs of arrhythmogenic dilated cardiomyopathy ($n = 7$), ALVC ($n = 2$), and ARVC ($n = 2$) were analyzed. **Results:** Arrhythmogenic dilated cardiomyopathy presented by ECG with the left bundle branch block in four cases and left ventricular hypertrophy in three cases. Arrhythmogenic left dominant cardiomyopathy was characterized by low voltage in limb leads and T-wave inversions or flattening in inferolateral leads. ARVC was presented by either complete right bundle branch block with a T-wave inversion in lead V1 of 2 mm or more. The other ECG presented with T inversions in the right precordial leads (amplitude in lead V1 of 2 mm or more), epsilon waves, and typical features in lead aVR. **Conclusions:** Standard ECG is an excellent parameter for the differentiation of ADCM (ADCM, ALVC, and ARVC).

Key words: Arrhythmogenic dilated cardiomyopathy, arrhythmogenic left ventricular cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, filamin C

INTRODUCTION

Filamin C mutations can cause either arrhythmogenic dilated, arrhythmogenic left ventricular (ALVC), or arrhythmogenic right ventricular cardiomyopathy (ARVC).[1-3]

Beyond imaging techniques, the question is whether simple standard electrocardiography (ECG) is able to differentiate all forms of arrhythmogenic cardiomyopathies (ADCM) mentioned above.

ECG criteria of ADCM are well described: Epsilon waves,[4] right precordial T-wave inversions,[5] incomplete or complete right bundle branch block,[6] localized right precordial QRS prolongation,[7] QRS fragmentation,[8] and low voltage of limb or precordial leads or both[9] belong to diagnostic armamentaria.

ECGs of arrhythmogenic dilated cardiomyopathy include left bundle branch block and signs of the left ventricular hypertrophy. ALVC is electrocardiographically characterized by low voltage in limb leads and T-wave abnormalities inferolateral (inversions or flattening). ARVC can be identified by a large number of ECG criteria mentioned above. This case report of 11 patients would be conducted to clarify the question whether standard ECG is of help to differentiate the sort of ADCM diagnosed by imaging techniques.

MATERIALS AND METHODS

In the studies of Luisa Mestroni and Matthew Taylor, only a few ECGs in rare filamin C mutations exist including extensive imaging techniques. These authors send the ECGs of seven patients with arrhythmogenic dilated cardiomyopathy, two

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patients with arrhythmogenic left dominant cardiomyopathy, and two patients with ARVC to me for analyzing new criteria in lead aVR and the amplitude of T inversions in lead V1. The role of lead aVR in ARVC is described as the lead is directed to the right ventricle. The same is true for lead V1.[10]

A correlation to imaging techniques was expressed by sensitivity and specificity with $P < 0.05$.

RESULTS

Patients with arrhythmogenic dilated cardiomyopathy revealed four ECGs with complete left bundle branch block without typical configuration in lead aVR and three ECGs with signs of the left ventricular hypertrophy by positive Sokolow Lyon index. Two ECGs with signs of the left ventricular hypertrophy presented with typical appearance in lead aVR suggestive for ADCM, and positive T waves in lead V1, not typical for ADCM [Figure 1].

Patients with ALVC presented with low voltage in limb leads and T-wave inversions inferolateral in one patient and T-wave flattening in the other patient [Figure 2].

ARVC in two patients presented in one case with complete right bundle branch block with right precordial QRS prolongation and with an amplitude or inverted T-wave in lead V1 of more than 2 mm [Figure 3]. The ECG of the other patient revealed typical epsilon wave, T-wave inversions in the right precordial leads and right precordial QRS

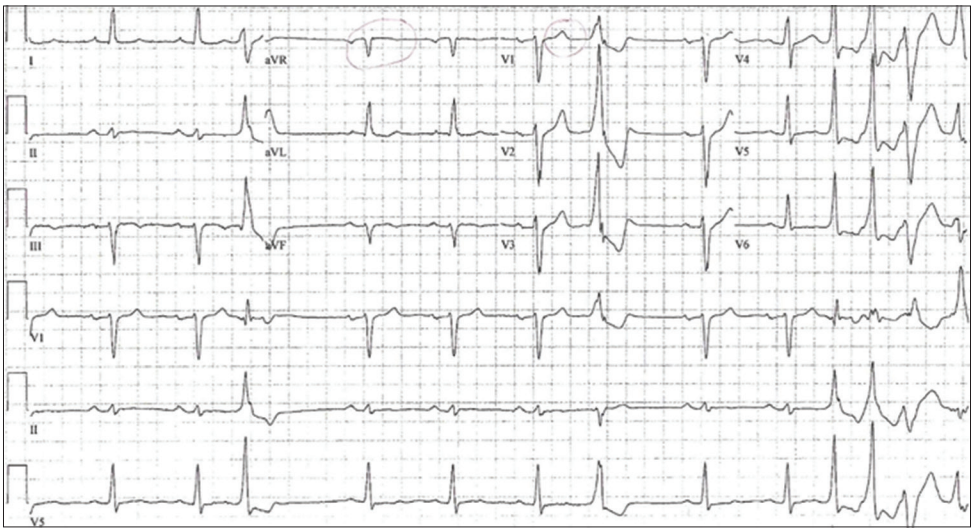

Figure 1: Electrocardiography in arrhythmogenic dilated cardiomyopathy: Left ventricular hypertrophy, typical pattern in lead aVR, but positive T-wave in lead V1

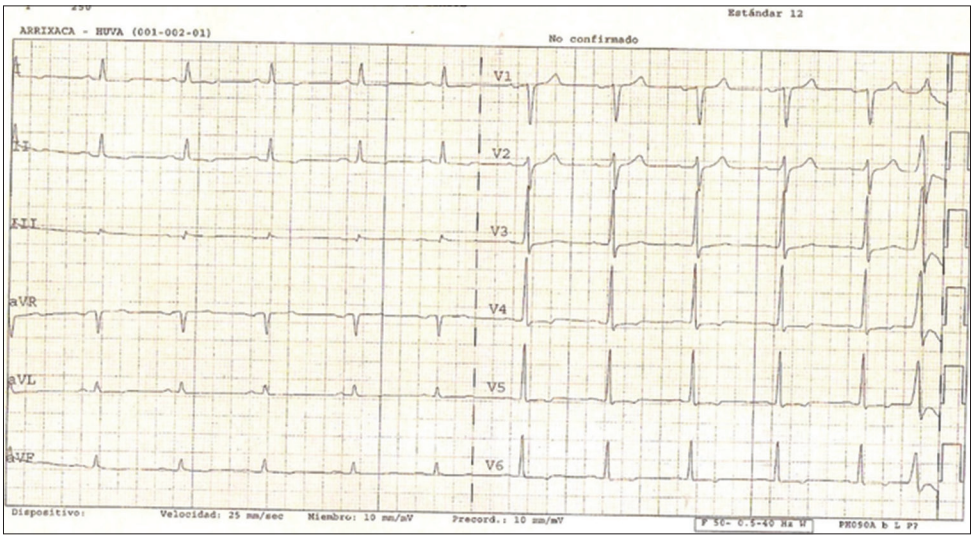

Figure 2: Electrocardiography in arrhythmogenic left ventricular cardiomyopathy: Low voltage in limb leads, inferolateral T inversions

prolongation [Figure 4]. The appearance in lead aVR was typical for ARVC. In this case, the amplitude of inverted T-wave in lead V1 of more than 2 mm was again highly typical for ARVC. Table 1 presents typical signs at standard ECG.

DISCUSSION

Little is known of electrocardiographic features in rare filamin C-positive ADCM. A differential diagnosis can be reached by imaging techniques, especially including cardiac magnetic resonance [Table 2]. Filamin C mutations in cardiomyopathies have a very high risk of sudden cardiac death. Primary ICD implantation at early stages of the cardiomyopathies should be done. Similar recommendations are known for lamin A/C and RBM20.[11]

Electrocardiographic study is very small and includes only 11 ECGs. Despite this fact, the electrocardiographic prediction of the phenotype is high by extensive imaging techniques done the authors. By simple ECG presentation, a differentiation of the type of ADCM is absolutely safe. The correlation to imaging techniques revealed a sensitivity and specificity of 100%, respectively. Merely, ECG signs of complete left bundle branch block or left ventricular hypertrophy characterize all forms of dilated cardiomyopathy whether arrhythmogenic or non-arrhythmogenic. Lead aVR is of doubtful help.

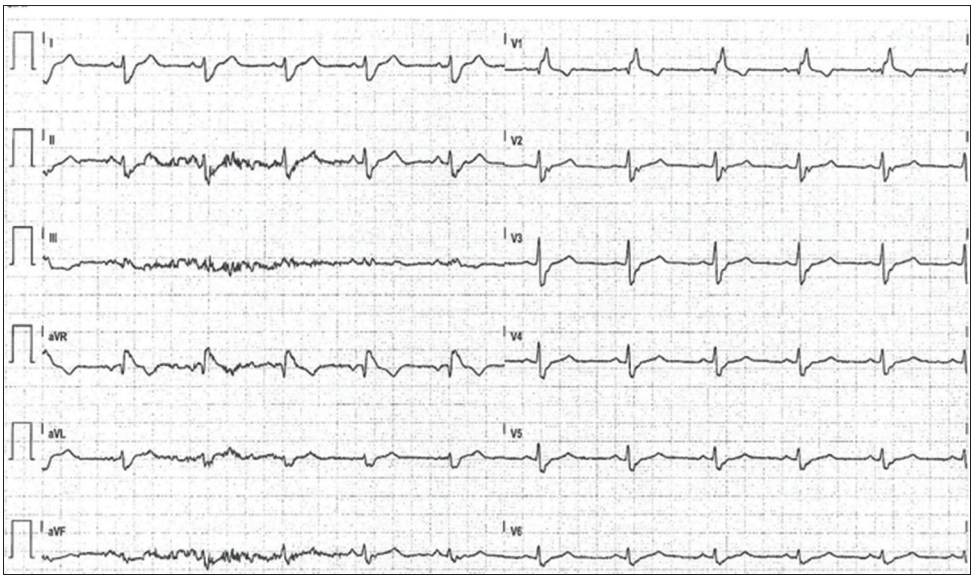

Figure 3: Electrocardiography in arrhythmogenic right ventricular cardiomyopathy: Complete RBBB, terminal activation delay, T inversion in lead V1, QRS fragmentation in several leads

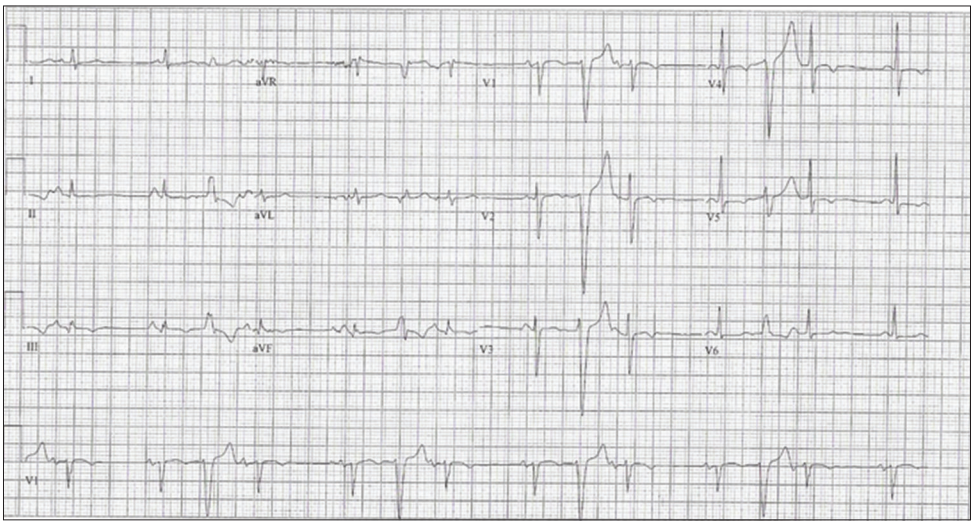

Figure 4: Electrocardiography in arrhythmogenic right ventricular cardiomyopathy: Right precordial epsilon waves and T-wave inversions, typical pattern in lead aVR, and terminal activation delay

Table 1: Electrocardiography signs of arrhythmogenic cardiomyopathy

Pat. right	LBBB	LVH inferolat	RBBB	Epsilon voltage	T-inv.	T.inv. typical	Low	aVR
No.1	+							
No.2	+							
No.3	+							
No.4	+							
No.5		+						+
No.6		+						+
No.7		+						
No.8						+	+	
No.9						(+)	+	
No.10			+	+	+			+
No.11				+	+			+

LBBB: Left bundle branch block, LVH: Left ventricular hypertrophy, RBBB: Right bundle branch block

Table 2: Reports of filamin C and arrhythmogenic cardiomyopathy

Author	Title	Journal	Year
Spezzacatene *et al.*	Arrhythmogenic phenotype in dilated cardiomyopathy: Natural history and predictors of life-threatening arrhythmias	J Am Heart Ass	1995
Augusto *et al.*	Dilated cardiomyopathy and arrhythmogenic left ventricular cardiovasc cardiomyopathy: A comprehensive imaging cardiovascular genotype-imaging phenotype study	Eur Heart	2020
Brun *et al.*	FLNC truncations cause arrhythmogenic right ventricular cardiomyopathy	J Med Genet	2020

ALVC is characterized by low voltage in limb leads and inverted or flattened T waves in inferolateral leads.[2]

ARVC is characterized by typical electrocardiographic features such as epsilon waves, right precordial T-wave inversions, localized right precordial QRS prolongation, QRS fragmentation, typical appearance in lead aVR, incomplete or complete right bundle branch block, and an amplitude of inverted T-wave in lead V1 of 2 mm or more.

The same is true for imaging techniques like cardiac magnetic resonance imaging with late enhancement to differentiate between ALVC or ARVC. A differentiation between arrhythmogenic or non-arrhythmogenic dilated cardiomyopathy by imaging techniques is not possible, although the left ventricular ejection fraction (LVEF) is insignificantly higher in arrhythmogenic dilated cardiomyopathy (LVEF 34% vs. 32%).[1]

A clear distinction exists for arrhythmogenic right ventricular or left ventricular cardiomyopathy by standard ECG and imaging techniques. In arrhythmogenic biventricular cardiomyopathy, the ECG signs overlap a lot.

In dilated cardiomyopathy, the prediction of severe arrhythmias is difficult and the need for ICD implantation is not easy to obtain. There is lack of clear recommendation by at last two ICD studies.[12,13] Typical appearance in lead aVR or amplitude of inverted T waves in lead V1 of 2 mm or more does not characterize patients with an arrhythmogenic phenotype of dilated cardiomyopathy. However, due to very small ECG sample size, the prediction is uncertain.

CONCLUSIONS

Although ECG features in different forms of cardiomyopathies seem to be unspecific,[14] in this study, ECG can differentiate between arrhythmogenic dilated, ALVC, and ARVC ARVC.

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