ORIGINAL ARTICLE

Low Voltage in Limb leads in Arrhythmogenic Cardiomyopathy

Stefan Peters

Department of Cardiology, Ubbo Emmius Hospital Norden, Lower Saxony, Germany

ABSTRACT

Aims: Low voltage in limb leads characterizes left ventricular involvement in arrhythmogenic cardiomyopathy. A large collective of patients with arrhythmogenic cardiomyopathy including 439 patients (268 males, meanage 46.8±11.6 years) were analyzed. **Methods:** Low voltage in limb leads was analyzed in typical patients with arrhythmogenic cardiomyopathy. Several other electrocardiogram (ECG) features including low voltage in precordial leads, typical appearance in lead a VR, and developing complete right bundle branch block (RBBB) were additionally analyzed. **Results:** Low voltage in limb leads was found in 61 patients (15%). Three patients represented with low voltage in limb leads and T wave inversions in inferolateral leads characterizing arrhythmogenic left ventricular cardiomyopathy or phospholamban (PLN) cardiomyopathy. In 38 patients low voltage in limb leads and typical ECG findings of arrhythmogenic cardiomyopathy were found. These patients had arrhythmogenic biventricular cardiomyopathy. Low voltage in limb and precordial leads was found in 14 patients with two cardiac deaths due to heart failure. In six cases low voltage in limb and precordial leads and developing complete RBBB were found. Four patients were tranplanted, two cases died due to heart failure. **Conclusions:** Standard ECG can differentiate between arrhythmogenic left ventricular, arrhythmogenic biventricular, and arrhythmogenic advanced end-stage or PLN-induced cardiomyopathy.

Key words: Advanced form, arrhythmogenic cardiomyopathy, arrhythmogenic left ventricular cardiomyopathy, low voltage

INTRODUCTION

Low voltage in limb leads characterizes significant left ventricular involvement.[1] Additional inferolateral T wave inversions or flattened T waves represent arrhythmogenic left ventricular cardiomyopathy (ARLC).[2]

Low voltage in limb leads and other electrocardiogram (ECG) parameters should be analyzed in a large collective of patients with arrhythmogenic cardiomyopathy to differentiate between arrhythmogenic biventricular or left ventricular cardiomyopathy. The question is whether low voltage in limb leads characterizes left ventricular involvement in the whole phenotype, and additional inferolateral abnormalities of the T wave (inversion or flattening) characterizes arrhythmogenic left dominant cardiomyopathy or phospholamban (PLN) cardiomyopathy.

METHOD

The ECG's of 439 patients (264 males, meanage 46.4+/-11.6 years) were analyzed with regard to low voltage in limb leads (</=5 mm) or precordial leads (</=7.5 mm) or both, and abnormalities of the T waves in right precordial (inversion) or inferolateral leads (inversion or flattening). The question is to differentiate between arrhythmogenic biventricular cardiomyopathy (ARBC), arrhythmogenic left dominant cardiomyopathy, and end-stage or PLN cardiomyopathy as a rare mutation.

In all patients gathered between 1985 and 2020 the diagnosis was made by ECG, echocardiography, right and left ventricular angiography. In seldom cases magnetic resonance imaging (MRI) was used. Coronary artery disease was excluded by coronary angiography in all cases. Most cases

Address for correspondence:
Dr. Stefan Peters, Department of Cardiology, Ubbo Emmius Hospital, Osterstr. 110, 26506 Norden, Lower Saxony, Germany

were included between 1985 and 1995; MRI scanning and genetic testing were not done in period of time.

As imaging technique left and right ventricular angiography were performed to make a statement of left and right ventricular dilatation, left and right ventricular ejection fraction and segmental wall disturbances. These features to diagnose arrhythmogenic cardiomyopathy are published elsewhere.[3]

Several ECG scenarios are possible:

- Low voltage in limb leads and T wave inversion or flattening in inferolateral leads a direct sign of arrhythmogenic left dominant cardiomyopathy or PLN mutation (Group 1).
- Low voltage in limb leads and epsilon waves and T wave inversions in right precordial leads as a sign of arrhythmogenic biventricular disease (Group 2).
- Low voltage in limb and precordial leads with epsilon waves and T wave inversion in right precordial leads as a sign of rare (Group 3) or
- Low voltage in limb and precordial leads, developing complete right bundle branch block (RBBB) with localized right precordial QRS prolongation, epsilon wave, and T wave inversions in right precordial leads (Group 4) as sign of advanced end-stage ARBC or PLN-induced disease [Table 1].

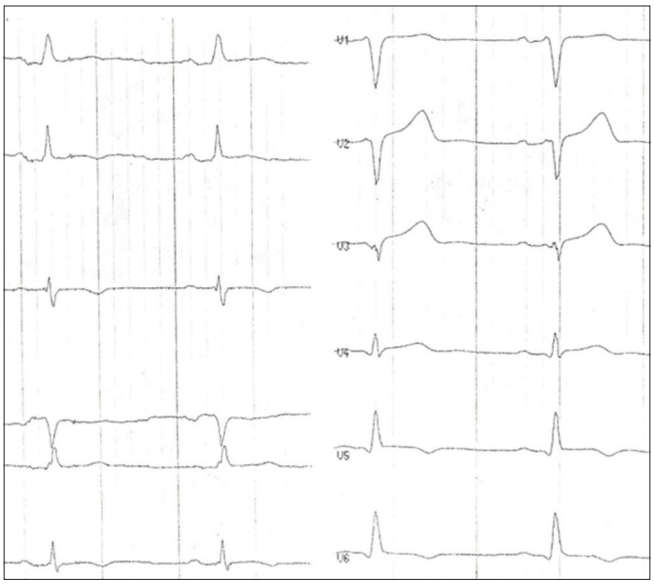

Figure 1: Typical example of arrhythmogenic left ventricular cardiomyopathy with low voltage in limb leads, T-wave inversions in inferolateral leads

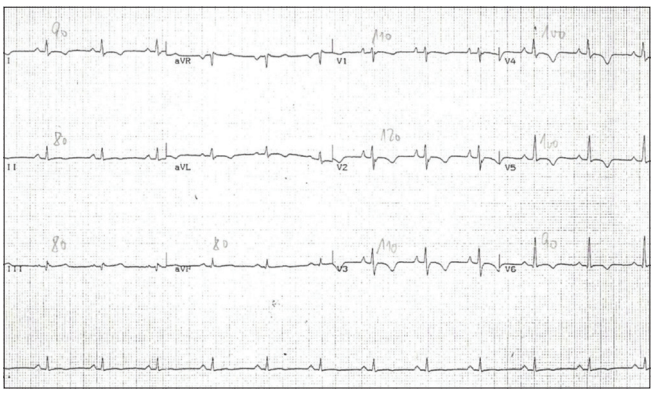

Figure 2: Example of arrhythmogenic biventricular cardiomyopathy with low voltage in limb leads, epsilon waves, T-inversions in right and left precordial leads

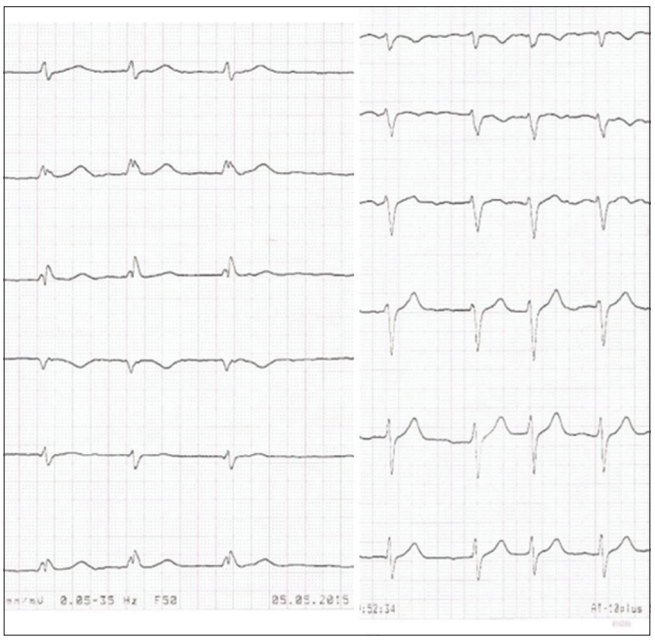

Figure 3: Example of advanced form of arrhythmogenic cardiomyopathy with low voltage in limb and precordial leads, epsilon waves, and right precordial T inversions

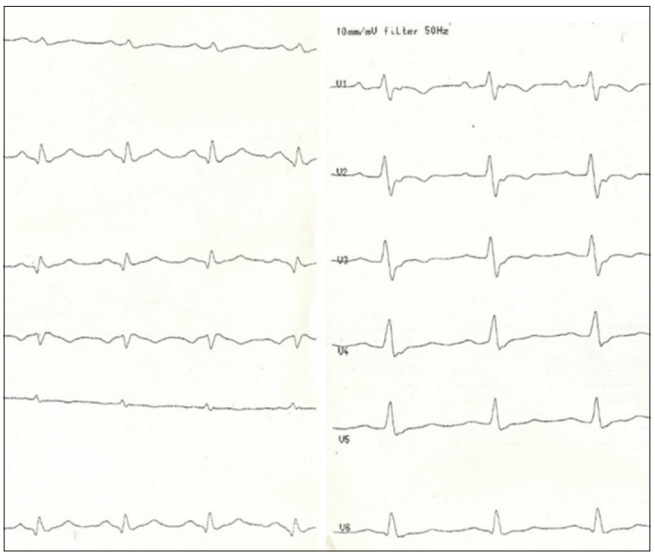

Figure 4: Example of developing right bundle branch block with low voltage in limb leads, complete right bundle branch block, epsilon waves, and right precordial T inversions

Table 1: Possible scenario of ECG abnormalities and actual number of patients

	Eps.	Ri. prec. neg.T	Inf.lat.neg. T/flatt	Low voltage limb leads	Devel. RBBB	Terminal activation delay	No.
ARLC	-	-	+	+	-	-	2
ARBC	+	+	-	+	+	+	38
Adv. Dis.	+	+	-	+	-	+	14
PLN?	+	+ (6)	+ (1)	+	+ (6)	+	7

Eps: Epsilon wave; ri.prec.neg. T: Right precordial T-inversion; in.lat.neg. T/flatt.: Inferolateral T inversion/flattening; devel. RBBB: Developing right bundle branch block; No.: Number of patients; ARLC: Arrhythmogenic left ventricular cardiomyopathy; ARBC: Arrhythmogenic biventricular cardiomyopathy; adv.dis.: Advanced disease; PLN: Possible phospholamban mutation

RESULTS

Electrocardiographic sign of advanced left ventricular dysfunction is low voltage in limb leads in n = 61 patients (15%). In many cases with segmental left ventricular involvement without reduction of left ventricular function no low voltage criteria could be found.

In two male patients low voltage in limb leads and T wave inversion in inferolateral leads could be found. In the first patient left ventricular ventricle was dilated with a large aneurysm at apical site. The ejection fraction was moderately low with 45% with sustained ventricular tachycardia. Both patients presented with RBBB like sustained ventricular tachycardia. In addition, in one female patient genetic screening found familial PLN mutation.

In 38 cases low voltage in limb leads with typical electrocardiographic appearance of arrhythmogenic right ventricular cardiomyopathy (epsilon waves, right precordial T wave inversion, typical appearance in lead a VR large Q waves, small R waves, and negative T-waves with an amplitude of less than 2 mm), localized right precordial QRS prolongation, and inverted T waves in lead V1 with an amplitude of 2 mm and more. Left ventricular ejection fraction was in these cases between 40 and 50%. All cases had mild signs of heart failure and an increase of ventricular premature beats, non-sustained or in a small number of patients sustained ventricular tachycardia.

Low voltage in limb and precordial leads were present in 14 cases with modest (n = 8) or severe (n = 6) signs of heart failure, left ventricular rejection fraction ranging between 35 and 45%. Two patients died due to therapy-resistant heart failure, in one case with a LV end diastolic diameter of more than 8 cm.

In 6 cases the ECG of patients developed right complete RBBB, low voltage in limb and precordial leads with T wave inversions in all precordial leads. These patients suffered from therapy-resistant heart failure and sustained ventricular tachycardia several months before heart failure appeared. Four patients were transplanted, two patients died from therapy-resistant heart failure.

CONCLUSIONS

Low voltage in limb leads in arrhythmogenic cardiomyopathy can be identified in segmental hypokinesia, non-dilated left ventricle with reduction of ejection fraction with positive posterolateral plate enhancement on MRI.[2] In these patients low voltage in limb leads and T wave inversion or flattening in inferolateral leads could be identified. These features represent ARLC (left dominant) cardiomyopathy. Without late enhancement these features characterize a unique form of dilated cardiomyopathy.[4] In this large cohort of patients with arrhythmogenic cardiomyopathy studied only two patients represent the specific type of electrocardiographic abnormalities. ARLC is caused by desmoplakin or desmoglein-2 [Figure 1]. PLN mutations are characterized by low voltage in limb leads and inferolateral T-wave inversions, whereas T inversions in lateral leads originate from V3[4] to V6. Late gadolinium enhancement is strictly inferoseptal.

But there are other forms of ECG findings associated with low voltage in limb leads. In arrhythmogenic right ventricular cardiomyopathy with significant left ventricular dysfunction and reduction of left ventricular rejection fraction these form of disease represents classical ARBC including signs of ventricular arrhythmia and heart failure. In about 60% of cases arrhythmogenic right ventricular cardiomyopathy has slight left ventricular involvement with increased risk of sudden cardiac death.[5,6] Significant ARBC has been first described by Pinamonti [Figure 2].[7]

Low voltage in limb and also precordial leads[1] with and without complete RBBB characterize patients with very high risk of sudden cardiac death and heart failure. These patients have either advanced end-stage disease with certain similarities to dilated cardiomyopathy [Figure 3].[8] Developing RBBB possibly represent advanced form of ARBC or PLN-induced disease,[9] particularly if the initial ECG show low voltage in limb leads and T-wave inversions inferolateral. There are three other cases of developing complete RBBB, but without low voltage ECG. These patients suffered from aborted sudden cardiac death, but without signs of heart failure and without left ventricular involvement [Figure 4].[10] QRS fragmentation in several leads was found in all patients as a

sign of increased arrhythmic death. Low voltage ECG is in this respect a valuable marker of significant left ventricular disease shown by cardiac MRI.[1]

But not all aspects of different diagnostic methods are conclusive: In a 71-year old female patient ECG revealed incomplete RBBB with localized right precordial QRS prolongation and low voltage in limb and precordial leads. By cardiac MRI arrhythmogenic cardiomyopathy was diagnosed by myocardial edema at the apex of the right ventricle masque rending arrhythmogenic right ventricular cardiomyopathy and positive late enhancement of the inferior site of a non-dilated left ventricle with normal function.[11]

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