



Risk management in early stage arrhythmogenic cardiomyopathy associated with Provocable Brugada ECG

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DOI: <https://doi.org/10.33545/26649020.2019.v1.i1a.2>

Abstract

Risk factors of malignant tachyarrhythmias should be assessed in cases with early stage arrhythmogenic cardiomyopathy and provokable Brugada ECG. Spontaneous right precordial coved-type ST segment elevation, tall R wave in lead aVR, QRS fragmentation, 1° AV block, inducibility during electrophysiological examination, low amplitude coved-type ST elevation and localised right precordial QRS prolongation should be tested in 20 out of 128 patients.

Only QRS fragmentation and localised right precordial QRS prolongation were positive in these patients. QRS fragmentation was positive in two patients, one with aborted sudden cardiac and one patient without any further arrhythmic events. Localised right precordial QRS prolongation was positive in five patients with serious arrhythmic events – four cases with previous ventricular fibrillation and one case with subsequent slow ventricular tachycardia. All other risk factors could be ruled out.

In summary, localised right precordial QRS prolongation seems to be the strongest risk marker in cases of developing arrhythmogenic cardiomyopathy and provokable Brugada ECG.

Keywords: arrhythmogenic cardiomyopathy; Brugada ECG; localised right precordial QRS prolongation; QRS fragmentation; r-wave sign

Introduction

The risk of aborted sudden cardiac death is very high in cases with developing arrhythmogenic cardiomyopathy and provokable Brugada ECG [1]. In about 10 - 15% of cases there seems to be an association between arrhythmogenic cardiomyopathy and Brugada syndrome by the so-called connexome – a linkage of desmosomal proteins, sodium channel complexes and gap junctions including desmosomal genes like plakophilin-2 [2], desmoglein-2 [3], desmoplakin [4], and plakoglobin (in animal models).

Risk assessment in these cases is of utmost importance by spontaneous coved-type ST elevation in right precordial leads as the only independent risk marker [5], QRS fragmentation [6], positive R wave in lead aVR [7], 1° AV block [8], inducibility during electrophysiological examination [9], low amplitude coved-type right precordial ST elevation, and as a new finding localized right precordial QRS prolongation demonstrated in the last ESC meeting in Barcelona 2017 [10] with a sensitivity of 78% and a specificity of 87%.

Above mentioned risk factors were analysed in cases with possible or typical developing arrhythmogenic cardiomyopathy and provokable Brugada ECG.

Method

In a cohort of 128 patients the diagnosis of typical (n=7, two major diagnostic criteria) and possible (n=13, one major and one minor diagnostic criteria) arrhythmogenic cardiomyopathy (72 males, mean age 46.1 +/- 13.6 years) was made. Diagnostic criteria were evaluated according to the paper published by Frank Marcus in 2010 [11]. Cardiac MRI (n=2) and right ventricular angiography (n=18) applied as imaging technique. In all cases right ventricular outflow

tract were involved. Right ventricular dilatation and aneurysms could be excluded. Ajmaline challenge was used to provoke Brugada ECG that was positive in 20 cases (15%). In provoked Brugada ECG cases localised right precordial QRS prolongation, spontaneous Brugada ECG, tall R wave in lead aVR, 1° AV block, inducibility during electrophysiological examination, and low amplitude coved-type ST elevation was analysed. Three young female cases had symptoms of vasovagal syncope with positive tilt table and one female patient had a syncope possibly due to epilepsy. In these four patients an ICD was not implanted.

Results

Localized right precordial QRS prolongation Localised right precordial QRS prolongation could be detected in 6 cases – four cases with aborted ventricular fibrillation before ICD implantation with the diagnosis of an early stage of arrhythmogenic cardiomyopathy and Brugada syndrome and one case of slow ventricular tachycardia 2 years after ICD implantation with the same diagnosis. The sixth case had no arrhythmic event in a six years follow-up.

QRS fragmentation QRS fragmentation was positive in two cases – one case with QRS fragmentation in two right precordial leads in aborted sudden cardiac death, and in a second case with QRS fragmentation in one right precordial lead with no arrhythmic event in a six years follow-up.

Spontaneous coved-type ST elevation in right precordial leads, tall R wave in lead aVR, 1° AV block, and inducibility during electrophysiological examination could be excluded.

Low amplitude right precordial ST elevation Low amplitude right precordial ST elevation after ajmaline challenge was positive in all but one patients.

Discussion

Since 2014 it is known that arrhythmogenic cardiomyopathy and Brugada syndrome have a common relationship in 10 – 15% of patients. The so-called connexome - an association between gap junctions, desmosomal proteins and sodium channel complexes – is the cause of this phenomenon and was first described in 2014 [1].

In isolated Brugada syndrome without structural abnormalities some risk factors for the development of arrhythmic events have been described: a positive R wave in lead aVR [7], spontaneous coved-type ST elevation [5], QRS fragmentation [6], inducibility of tachyarrhythmias during electrophysiological examination [9], and I° AV-block [8]. The best results could be achieved by a combination of Tpeak-Tend intervals in precordial leads, spontaneous Brugada type 1 patterns in a peripheral lead, and early repolarization in inferolateral leads [12]. Similar results can be obtained with the number of positive risk factors [13]. A phenotype of Brugada syndrome with positive tilt table testing was associated with ventricular tachycardia or ventricular fibrillation [14]. A differentiation between vasovagal and arrhythmic syncope is difficult to make.

In early stages of arrhythmogenic cardiomyopathy with provokable Brugada ECG the situation is different. Generally, the risk of ventricular fibrillation is extremely high, supporting the theory that Brugada syndrome is the main disease with developing arrhythmogenic cardiomyopathy [15].

In the majority of patients (n=13) there was the diagnosis of possible arrhythmogenic cardiomyopathy without dilatation and aneurysms of the right ventricle. In our group of patients there are no spontaneous cove-type ST-elevation in right precordial leads, no I° AV block and during electrophysiological examination there were no inducibility of ventricular tachyarrhythmias in the cohort of 20 patients. In this group of patients a positive R wave of 3mm or more could be excluded; typical electrocardiographic appearance in lead AVR with significant Q wave, small R wave (2 mm or less), and negative T wave (2 mm or less) characterizes arrhythmogenic cardiomyopathy [16, 17].

QRS fragmentation after ajmaline administration was positive in a two cases, one female case with QRS fragmentation in two leads in aborted sudden cardiac death, one male case with QRS fragmentation only in one lead, without arrhythmic events in a 72 months' follow-up.

During a last ESC meeting in Barcelona 2017 another risk factor gained further importance: localized right precordial QRS prolongation [10]. This risk factor was tested in more than 200 patients with a sensitivity of 78% and a specificity of 87%.

In four patients (3 females) with aborted ventricular fibrillation before the diagnosis of arrhythmogenic cardiomyopathy was made and in one female patient with slow ventricular tachycardia after the diagnosis of arrhythmogenic cardiomyopathy with provokable Brugada ECG localized right precordial QRS prolongation was positive.

In this small study sensitivity was 83.3% and specificity 92, 9%, suggesting that localised right precordial QRS prolongation is a strongest predictor of previous and future arrhythmic events.

Localized right precordial QRS prolongation is a strong diagnostic marker of arrhythmogenic cardiomyopathy [18]

and - as it appears – the strongest risk factor in cases with developing arrhythmogenic cardiomyopathy and provokable Brugada ECG.

The value of drug-induced type 1 Brugada ECG and cardiac arrest is controversially discussed: newest register data reveal an increasing risk for cardiac arrest of about 50% [19].

These results should be tested a larger collective of patients to gain statistically significant results. This aim is difficult to reach: arrhythmogenic cardiomyopathy is a rare diagnosis and ajmaline testing in these patients is positive in only 15%.

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