

Brugada syndrome: 2017 update (RCD code: V-1A.1)

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Introduction

Brugada Syndrome (BrS) is traditionally considered a primary channelopathy, most commonly due to reduced inward sodium current with an increased risk of syncope and sudden cardiac death (SCD). According to the recent guidelines, BrS is diagnosed in patients with ST-segment elevation with type 1 morphology among the right precordial leads V_1 and V_2 , occurring either spontaneously or after provocative drug test with intravenous administration of Class I antiarrhythmic drugs. Moreover, BrS is diagnosed in patients with type 2 or type 3 ST-segment elevation in ≥ 1 lead among the right precordial leads when a provocative drug test with intravenous administration of Class I antiarrhythmic drugs induces a type I ECG morphology. Risk stratification of SCD is the most important aspect of the concise management of those patients. Importantly, once considered pure arrhythmic syndrome, nowadays, there is growing understanding that some structural abnormalities may be present in BrS. Therefore, imaging is actively investigated in this field. Brugada syndrome can be considered as a rare disease, with the prevalence of 1 in 1000 to 1 in 10 000, being more frequent in south-east Asia than in the western countries. Thus, this topic has been already explored in the Journal of Rare Cardiovascular Disease (see references below). The purpose of this Review is to update the Readers with the main developments in this entity.

Risk stratification

Risk stratification and management of patients with BrS is a major challenge. The well-known individual risk predictors are as follows: gender, arrhythmic syncope, familial sudden death, spontaneous type 1 pattern ECG (in V_1 , V_2 and aVR), fragmented

QRS, early repolarization pattern in the lateral or inferior leads, inducibility of ventricular arrhythmias during electrophysiological study (EPS) and presence of a SCN5A mutation. Recently, the Shanghai Score System that include: clinical history, detailed assessment of 12-lead ECG, ambulatory ECG monitoring, family history, and genetic tests was proposed as diagnostic algorithm. In the recent study, The Shanghai score was not superior to conventional risk stratification in BrS. Furthermore, in another study it was observed that the Shanghai scoring system excluded a significant number of relatives from families with a history of SCD, who are likely to carry BrS. In line with this, it was reported that the presence of a spontaneous type 1 ECG pattern was not a predictor of higher risk in BrS pediatric cohort. Spontaneous type 1 ECG pattern is considered a risk factor for major arrhythmic events. However, its prevalence is probably underestimated because of its variability. It was shown that 12-lead 24-hour Holter monitoring allowed the identification of substantial number of subjects with a spontaneous type 1 pattern who would not be appropriately identified with conventional measures. Male sex clearly predispose to BrS and majority of studied populations mainly consisted of men. Thus, the clinical characteristics of BrS in women is unknown. In one of the largest BrS registry, women represented a significantly lower risk group than men. Clinical presentation in women affected by BrS was less severe than men with less spontaneous type 1 ECG and less symptomatic patients. Syncope is considered a major risk factor for arrhythmic events in patients with BrS. However, it is often difficult to differentiate arrhythmogenic from neurally mediated syncope. During long-term follow-up it was shown that inducible ventricular arrhythmias during EPS is a strong factor influencing the outcome. This, it was concluded that patients with arrhythmogenic syncope had a higher risk of events and EPS is a useful tool for risk stratification in patients with syncope. Additionally, it was suggested

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that QRS fragmentation may be associated with the increased risk of ventricular arrhythmias. Of note, abnormal fragmentation of the QRS complex (fQRS) is defined as the presence of multiple spikes within the QRS (≥ 4 spikes in 1 or ≥ 8 spikes in all of the leads V_1 , V_2 , and V_3). In the cohort of 1358 patients, fQRS was found in only 16 patients (1%); however, it was highly related to ventricular arrhythmias. Fever is considered as one of the SCD precipitating factors. However, studies that clearly support this association are lacking. In one study it was found that among 628 BrS patients only 26 (4.1%) presented with fever at time of the arrhythmic event. Thus, fever-induced SCD is rather rare in BrS patients. Interestingly, this group of patients tends to include more females and Caucasians, which is contrast to common SCD presentation in BrS. Although clinical presentation in older patients with BrS closely resemble presentation in younger patients, the authors from France found that patients >65 years or more seem to represent a lower risk group than younger people.

Imaging

Increasing number of evidence suggests that BrS, that was traditionally considered as an electrical disorder, may in fact encompass numerous morphological abnormalities including features of right ventricular outflow tract (RVOT) pathology. In one study patients were characterized using a “multimodality assessment matrix” encompassing three domains: electrical [fragmented QRS, inferolateral ST change, burden of Brugada changes on Holter monitor, and late ECG potentials], morphologic [abnormal RVOT volume or wall motion], and genotype. Comprehensive multimodality assessment confirms that BrS is a heterogeneous disorder with cardiac arrhythmias and some features of cardiomyopathy, particularly in the RVOT area.

Genetics

It is widely appreciated that Copy Number Variants (CNVs) are responsible for cardiac diseases associated with SCD. In this large study, a total of 1765 European patients were analyzed with a homemade algorithm for the assessment of CNVs, using High Throughput Sequencing, in whom 36 (2%) pathogenic CNVs were identified. Detection rates were particularly high for dilated cardiomyopathy (4.4%), arrhythmogenic cardiomyopathy (5.1%) and long QT syndrome (4.7%). Probably, the identification of CNVs (along with Single Nucleotide Variants and small insertions and deletions) will soon change the clinical work-up of patients being suspected of arrhythmic backgrounds.

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