

A new electrocardiographic marker of sudden death in brugada syndrome: the S-wave in Lead I

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Brugada syndrome (BrS) is a genetic disease, characterized by a coved-type ST-segment elevation in right precordial leads at ECG and increased risk of sudden cardiac death (SCD) [1]. An implantable cardioverter defibrillator (ICD) is recommended for patients with documented VT or VF [2]; however, it is unclear how to manage asymptomatic BrS subjects.

Recently, interstitial fibrosis [3] and dispersion of repolarization [4] as well as delayed activation on endocardial and epicardial mapping [3], have been demonstrated in the right ventricular outflow tract (RVOT) of BrS patients, particularly in those with increased arrhythmic risk.

Various electrocardiographic parameters have been investigated for risk stratification in asymptomatic BrS patients, with inconsistent results regarding their clinical impact [5-7].

The depolarization of the RVOT is reflected by an S-wave in lead I [8]. Interestingly, a prominent S wave in lead I is associated with right ventricular (RV) enlargement and fibrosis, such as in congenital valvular heart diseases, and cor pulmonale [8]. Thus, we hypothesized that a deep and/ or large S-wave in lead I in BrS, revealing a conduction delay over the RVOT, could be used to identify high-risk patients.

In our study [9], we prospectively enrolled 347 (78.4% male; mean age 45 ± 13.1 years) consecutive BrS patients with spontaneous

type 1 ECG and without a previous history of VF or aborted SCD, from four Italian cardiology centres. Eighteen patients (5.2%) had a history of persistent or paroxysmal atrial fibrillation (AF) and 14 (4.03%) experienced syncope at presentation. Electrophysiological study (EPS) and ICD implantation were performed in 186 (53.6%) and 98 (28.2%) patients respectively.

During follow-up (48 ± 39 months), 276 (79.5%) patients remained asymptomatic, 39 (11.2%) developed syncope, and 32 (9.2%) had VF/SCD. Among subjects who developed VF/SCD during follow-up, 3 died suddenly, 14 had aborted SCD, and 15 had appropriate ICD shocks.

In the multivariate analysis, a history of AF (HR: 3.7) and an S wave in lead I with amplitude ≥ 0.1 mV (HR: 13.30), duration ≥ 40 ms (HR 39.1), and S-wave area ≥ 1 mm (HR: 17.1) were 0073 significantly associated with VF/SCD events during follow-up. Otherwise, parameters such as SCN5A mutation, syncope, family history of SCD, and inducible VF at EPS, failed to predict VF/SCD during follow-up.

Finally, we performed a detailed RV endocardial electroanatomic mapping in 12 patients, randomly selected. The endocardial activation time was significantly longer in BrS patients with an S wave in lead I compared with the others, mostly due to a significant delay in the anterolateral RVOT. Thus we

could conclude that an S wave in lead I reflects late conduction in the RVOT.

In summary, in our prospective study, focusing on a large population of asymptomatic BrS patients, we demonstrated for the first time, that an electrocardiographic parameters, a wide S wave in lead I, reflecting late conduction in the RVOT, can predict VF/SCD. An S wave in lead I may indeed suggest fibrosis and dispersion of repolarization in the RVOT, that in turn, may favour re-entrant VT and SCD in BrS individuals.

However, this electrocardiographic marker should probably be implemented within multiparametrical models for risk stratification in BrS. Moreover, since

several promising prognostic parameters in BrS finally failed to prove useful in larger studies, an independent confirmation cohort should confirm our results.

Future studies should also confirm the presence of increased fibrosis in the RVOT in BrS patients with a prominent S wave in lead DI, by systematic assessment of the right ventricle with magnetic resonance imaging and high density epicardial and endocardial electroanatomic mapping. Moreover, eventual distribution of a prominent S wave in lead DI among BrS members of the same family should be explored, in order to investigate on possible specific genetic mutation involved in fibrosis of the RVOT.

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