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EDITORIAL

Type 2 Brugada pattern: more doubts than certainties

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Early description of association between sudden cardiac death (SCD) and an electrocardiographic pattern characterized by right intraventricular conduction delay, ST segment elevation and negative T waves in leads V_1-V_3 dates back to 1989 by Martini *et al.*[1]

Subsequently, in 1992, the Brugada brothers described a similar association,[2] arousing a great scientific interest about this condition that was defined Brugada Syndrome (BrS). However, after almost 30 years, despite the incredible development of scientific knowledge on this topic, some doubts still exist. For instance, the latest European Guidelines on the prevention of SCD may generate a semantic misunderstanding defining the presence of only spontaneous or pharmacologically induced ECG type 1 Brugada pattern as sufficient for the diagnosis of BrS.[3] Although in medicine a syndrome is defined as a set of symptoms and/or signs that precisely characterize a given pathological condition, this concept does not seem to be applied to BrS.

However, ECG is essential for the diagnosis of BrS and among the various Brugada patterns, only type 1 (or "coved" type) is diagnostic for BrS, while type 2 (or "saddle back" type) may only be considered diagnostic if it converts to type 1 by IC-antiarrhythmic drug challenge.[3] Sometimes, a type 1 pattern can be found in right precordial leads at 2nd or 3rd intercostal space. For this reason, when a spontaneous type 2 ECG pattern is present in V_1-V_2 at the 4th intercostal space it is reasonable to investigate also the 2nd and 3rd intercostal space. Moreover, it is well known that ECG Brugada patterns are not always stable and the same patient may show different patterns in different conditions (Figure 1).[4] This feature provides evidence for the clinical use of simple diagnostic methods to unravel a concealed type 1 ECG pattern, such as ambulatory 12-lead ECG, exercise ECG testing or 12-lead ambulatory ECG monitoring.

Considerable efforts have been made to identify electrocardiographic criteria that could define precisely those ECG patterns.[5] However, ECG interpretation still represents a challenge for car-

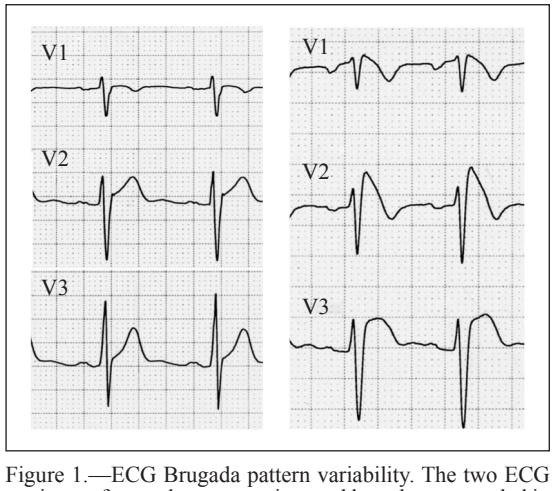

Figure 1.—ECG Brugada pattern variability. The two ECG tracings refers to the same patient and have been recorded in two different times. In the first panel no significant repolarization alterations are present in right precordial leads. In the panel on the right a typical type 1 diagnostic Brugada pattern is clearly evident in the same leads.

diologists and the difficulties seem even greater for type 2. Therefore, Crea *et al.* should be commended for their efforts in focusing their attention on this topic.[6] In particular, they highlighted the problem of the low inter-observer agreement and low accuracy in diagnosis of type 2 Brugada pattern between different categories of cardiologists.[6] In their paper, Fleiss K value was <0.20 in a pool of 42 cardiologists recruited to analyze in two stages, and in different order, 14 ECGs with a positive terminal deflection of the QRS in leads V_1-V_2, with electrodes positioned in the 4th intercostal space.[6]

The authors[6] conclude: "These finding could have serious consequences in term of prevention of arrhythmic events and risk stratification analysis." This introduces another major research issue on BrS: risk stratification for SCD. First of all, which is the risk of a patient with a drug-induced type 1 Brugada pattern? Moreover, is it always indicated to perform a IC drug challenge in type 2 patients to reveal a type 1?

The topic is currently under lively debate. From a general analysis of the literature, in clinical practice it seems clear that the arrhythmic risk of patients with spontaneous type 2 pattern is not high, therefore a wide use of IC-antiarrhythmic drug challenge in asymptomatic patients or subjects without risk factors is hardly sustainable.

In particular, a large study analyzed 1568 patients from 7 different papers (87% asymptomatic, 48% with drug-induced type 1 ECG pattern, all without ICD): in patients with drug-induced type 1 ECG pattern the incidence of sudden death was 0.08% per year,[7] and therefore even lower than that observed in the general population. By contrast, authors found a 0.9% per year incidence of sudden death in spontaneous type 1.[7] More precisely, the few (24 out of 1568) subjects who died suddenly had on average multiple risk factors, including spontaneous type 1 pattern, non-neurally-mediated syncope, familiarity for early sudden cardiac death (<45 years of age and not related to ischemic heart disease), ventricular inducibility at the electrophysiological study, while survivors had on average only one risk factor.[7] These data provide further evidence for the importance of a multiparametric assessment in risk stratification.

In 2011, Delise *et al.*[8] in a large prospective study analyzed the value of multiparametric evaluation to stratify the risk of sudden death in BrS. Specifically, they evaluated familiarity for sudden cardiac death, non-neurally-mediated syncope and positive electrophysiological study, as risk factors both in patients with spontaneous type 1 pattern and in subjects with a drug-induced pattern. During follow-up, they found no events in patients with 0 or 1 risk factor, while events occurred only in patients with 2 or 3 risk factors. These results were confirmed either in patients with spontaneous or with a drug-induced Brugada type 1 ECG. Similar results were reported by Okamura *et al.*[9] in 2015. In 2017, Sieira *et al.*[10] proposed a score model to predict the risk of events in patients with Brugada Syndrome. This model encompasses several risk factors: spontaneous type 1 ECG (1 point), early familiar SCD (1 point), positive electrophysiological study (2 points), syncope (2 points), sinus node dysfunction (3 points) and previous aborted SCD (4 points): a significantly increased risk was observed in subjects with more than 2 points.

Therefore, is it always justified to carry out a pharmacological test in each patient with type 2 pattern without risk factors? About that, Zorzi *et al*.[11] found that the long-term risk of patients with BrS diagnosed by this test is significantly lower than the risk of patients with spontaneous type 1. Therefore, a wide indication for flecainide or ajmaline challenge does not seem to be scientifically justified nowadays. On the other hand, asymptomatic type 2 patients with a family history for BrS or SCD, or with symptoms possibly related to the syndrome, should be informed of the availability of a sodium channel blocker challenge test to provide a more definitive diagnosis. However, patients should be also informed about the risk of the test and about the emotional consequences of having a positive test not followed by definitive therapy.[12, 13]

For all these reasons, extensive use of the drug test is not easily shared, but the decision to undergo the drug challenge ultimately should be left up to a well-informed patient. In the latter scenario, the cardiologist must have the ability to clearly explain to subjects with type 2 Brugada

pattern and without any other risk factor that they have a negligible risk of SCD, and their life does not require any particular limitation.

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