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Title: More evidence-based data are required for a consensus on the so called Brugada syndrome

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More evidence-based data are required for a consensus on the so called Brugada syndrome.

The Consensus report (1) on the syndrome of sudden death, right bundle branch block and ST segment elevation, is important, since the authors 1) do not firmly assume that this is a functional syndrome related to abnormal repolarization, 2) admit that "structural abnormalities may only be found at the time of autopsy", 3) state that "discrimination from ARVC should receive due attention". These assumptions, which we have proposed since 1988, and were recently scarcely debated (2,3,4), have not received adequate analysis and need further elucidation on an evidenced based approach, before this report should be considered as a consensus document.

Moreover, the choice of terms and the historical review should be more accurate. In 1953 Osher (5) did not report a syndrome but an ECG abnormality (Osher ECG). The term "syndrome" should be limited to clinical events associated with abnormal findings, such as the ECG pattern of ST segment elevation in V_1-V_3 in patients who have a clinical event. Using this definition, the syndrome was first described by Nava (Nava and not Brugada sign) (6-9). As noted by Surawicz (10) and by others, "patients with such characteristics were described, before the Brugada brothers reported their findings". However, this was barely mentioned in this report. Forgetting that at least six articles in the literature preceded Brugada's article (6-9,11).

Why weren't these articles, which would have enhanced and not diminished Brugada's accomplishments, discussed or at least referenced in this official European document on the syndrome ?

This document paid little attention to different diagnostic criteria to exclude organic heart disease. Despite a lack of contrast angiographic data as well as nuclear magnetic resonance and electron-beam tomography data, and insufficient (or absent) pathologic material (2), the limited value of genetic evaluation, electrophysiological testing and drug challenge in this disease was highlighted . Although the term channelopathy is becoming popular (not yet in this report), to classify this syndrome, it should be noted that SCN5A was reported to be present in only a small proportion (10-30%) of patient's with the Brugada syndrome, and is almost nonexistent in some high risk groups (12). A recent relevant study showed that the SCNA abnormality may be so diffuse in some populations to reduce its specificity (13). Again, the experimental studies on the role of SCN5A channels and its effect on the ECG pattern, particularly on the ST segment elevation have not yet reached an evidence-based clinical explanation in this report.

This indicates that there is a need to search for other chromosomal loci or genes (14,15). Hopefully these investigations should avoid insertion of an ICD in an asymptomatic individual based solely on the results of a blood test or drug infusion that was thought to indicate a high risk individual with this syndrome.

Finally, there is some confusion regarding the electrocardiographic patterns of the syndrome, all well described in 1989 (9). As previously noted (16), and reaffirmed in this consensus document, many ECG patterns have been described, ranging from a typical complete RBBB pattern, to minor ST segment abnormalities (8,9,17).

Much attention has been given to the ECG "types of repolarization patterns", but these were insufficiently linked to the "depolarization abnormalities". The committee describes prolonged RBBB, PR and HV intervals, left axis deviation and late potentials as typical features of the syndrome, without giving any patho-physiological explanations, and neglecting the fact that clinical-anatomical correlations are not absent (see ref. 24,25 of the report). The presence of a prolonged QRS complex in precordial or all leads (in this latter case there are minor changes due to vector orientation), and of late potentials both at averaging or at the RV outflow tract coincident with the ST segment elevation, is a clear sign of organic altered depolarization, as we have noted in our earlier papers (8,9), and concurred by Antzelevitch (18). This does not diminish the importance of the elegant and evidence-based experiments by Antzelevitch that illustrate a different hypothesis based on transmural voltage gradients. Nevertheless, these theories have not been confirmed in evidence-based clinical practice, despite well-illustrated drawings.

The pathogenetic interpretation of a QRS disturbances with persistent or dynamic ST segment abnormalities of the precordial, but (often) not left or limbs leads, requires more than a laboratory experiment or an ECG analysis, and should stimulate evidence-based research (using signal averaged studies, surface and endocardial mapping, anatomical correlations etc.) (19,20) to define the borders between clear organic electrical cardiac abnormalities, and functional causes of a strange ECG abnormality.

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