Spontaneous electrocardiographic fluctuations in Brugada syndrome: does it matter?

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This editorial refers to 'A prospective study on spontaneous fluctuations between diagnostic and non-diagnostic ECGs in Brugada syndrome: implications for correct phenotyping and risk stratification' by C. Veltmann et al., on page 2544

Brugada syndrome is increasingly recognized as a disease entity associated with sudden cardiac death in generally relatively young individuals without structural heart disease. Right precordial ST-segment elevation is considered the hallmark of the Brugada ECG, but discrete prolongation of various conduction parameters is also frequently encountered. It is well known that the ECG is variable from day to day and varies between the three defined ECG types (types 1, 2, and 3).1,2 Type 1, i.e. the 'coved-type' ST-segment, is mandatory for the diagnosis. Type 2 is referred to as the 'saddle-back' type and type 3, a right precordial saddle-back type ST-segment with minor deviation from the isoelectric segment, cannot be distinguished from normal. When associated with documented (or inducible) ventricular arrhythmias or premature sudden cardiac death or diagnostic ECGs in family members or nocturnal agonal respiration, Brugada syndrome is diagnosed.1,2 In the absence of a baseline type 1 ECG, exposure to sodium channel blockers (i.e. flecainide and ajmaline i.v.) can unmask the required ECG. A genetic diagnosis, encountered by the identification of SCN5a mutations in up to 30% of patients, is not mandatory for the diagnosis.

The risk for malignant ventricular arrhythmias in patients with a spontaneous or drug-induced coved-type ECG is ill-defined. However, in different series, symptoms and the spontaneous presence of a type 1 ECG (compared with drug-induced) are considered important for increased risk for future events (syncope, sudden cardiac death, or ICD shock). Both variables also show up, in addition to the male gender, in a recent meta-analysis on this topic.3 Veltmann et al.4 quantify the number of patients that do not present initially with a diagnostic ECG. Actually, of 43 consecutive patients, only one patient consistently had a type 1 ECG, whereas in others, it disappeared transiently during follow-up (33%), was, at some time, spontaneously present (19%), or was only inducible by drugs (47%).4 Of note, this series contained 16 female patients, i.e. more females than usually encountered in Brugada patients series.

The obvious impact of this finding is that a patient’s risk for future events may be underestimated if it based only on an initial non-diagnostic ECG. In that respect, the most interesting group is the group in which the ECG turned spontaneously into a diagnostic ECG during follow-up (from non-diagnostic at baseline, group C). It is not likely that the diagnosis will be missed in these patients because, in all cases, ajmaline (not flecainide) elicits a type 1 ECG. However, it could take as long as 66 days before a spontaneous type 1 ECG was recorded (with a mean of more than five ECGs made). Such a patient would lack a spontaneous diagnostic ECG for 2 months and be wrongly classified as far as risk is concerned. Furthermore, data from a relatively small Japanese series provide evidence that daily fluctuations in the magnitude of the right precordial ST-segment elevations (and in the appearance of late potentials), in particular, might possess predictive power for future events.5,6 These data are potentially also relevant for group A (one-third of the patients) in which a diagnostic ECG turned spontaneously into a non-diagnostic ECG.

An obvious potential caveat with repeated ECGs over time is that placement of the precordial leads is not always similar. This could significantly affect the ECG pattern, including R-wave and ST-segment amplitude. Excluding the ECGs with different right precordial R-wave amplitudes (>0.1 mV difference), as Veltmann et al.4 have done, is probably sufficient to assure that the electrodes were placed in similar positions. Other reasons for the spontaneous variations are, as the authors have acknowledged, the use of drugs (controlled), body temperature (not controlled, but likely to be generally stable), and the relation with meals. The latter is uncontrolled and very likely plays a role in spontaneous ST-segment amplitude variation. A positive ‘full stomach test’ (augmentation of ST-segment amplitude after a large meal) has even been proposed as a new risk factor.7 It would have been interesting to see whether patients would remain in the same group based on the ECG at the time of the electrophysiological study, when all patients are fasting and confounding by meals can be excluded. Unfortunately, the present data do not include genetic results. Whether right precordial ST-segments in

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SCN5a-related Brugada syndrome, generally associated with longer conduction intervals,\(^8\) fluctuate as much as in non-SCN5a-related Brugada syndrome is therefore unknown. The relatively short PQ intervals in the group of patients without a spontaneous diagnostic ECG (group D) might reflect under-representation of SCN5a-related patients in this group.

These present data add further complexity to the issue of risk stratification in patients with Brugada syndrome. At this point in time, symptoms and the spontaneous presence of a diagnostic type 1 ECG are considered of importance.\(^2,3\) But what about an initial non-diagnostic ECG that turns spontaneously into a diagnostic ECG after 2 months? Other risk stratifiers are controversial, including the role of programmed electrical stimulation,\(^9\) or hard to interpret because of a relatively short follow-up. It is clear that further studies will be needed to settle this issue. In particular, a longer follow-up duration is obligatory before sound conclusions can be drawn. It is desirable that in such studies, much attention is paid to non-invasive markers, including the promising spontaneous variations in various electrocardiographic markers.

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References