The Brugada syndrome: can we predict the risk?

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ABSTRACT

Since its introduction in 1992, the Brugada syndrome has attracted great interest because of increased risk of sudden cardiac death. Risk stratification aimed at the identification of patients at risk for sudden death is an important goal of current research. Controversy exists on risk stratification particularly in asymptomatic individuals. The predictive value of the inducibility of ventricular tachyarrhythmias is also discussed controversially. Currently, an implantable cardioverter defibrillator is the only proven effective treatment for the disease.

Key words: Brugada syndrome, risk stratification

In 1992, Brugada and Brugada described a new syndrome consisted of right bundle-branch block, ST segment elevation in the right precordial electrocardiogram (ECG) leads and an increased risk of sudden cardiac death (1). The syndrome is most prevalent in South-east Asia. In the Western world the prevalence is much lower. Brugada syndrome has a male dominance (8:1 ratio) and arrhythmic events tend to manifest around third and fourth decades of life. A coved type ST segment elevation ≥ 2 mm and a negative T wave in right precordial leads are diagnostic of Brugada Syndrome. The ECG pattern may be dynamic and is often concealed. The ECG manifestations of Brugada syndrome, when concealed can be unmasked primarily by sodium channel blocker administration but also during a febrile state or with vagotonic agents.

Different groups have presented data on the long-term follow-up and outcome of individuals with Brugada syndrome (2-5). In all reports concerning risk stratification of patients with Brugada syndrome, the history of aborted sudden cardiac death (SCD) and syncope are major parameters in predicting future events. In addition spontaneous presence of a type 1 ECG (compared with drug-induced) is considered important for increased risk for future events (syncope, SCD, or implantable cardioverter defibrillator (ICD) shock) in different series (2-5).

According to Brugada et al. (2) symptomatic patients with a history of syncope or aborted SCD were estimated to have a mean recurrence rate of 11% per year. Priori et al. (4) presented data of 200 patients with Brugada syndrome. Patients with syncope demonstrated 13% event rate during a follow-up of 34±44 months. They also found that in Brugada patients with spontaneously diagnostic basal ECG, the history of syncope demonstrated a significant increase of the risk of SCD with a hazard ratio of 6.4. The most recent publication about long term prognosis of patients with Brugada Syndrome was presented by Eckardt et al. (5). During 40±50 months of follow up of 212 patients they found that symptomatic individuals with aborted SCD and syncope had 17% and 6% event rate. Asymptomatic patients had a benign outcome during the follow-up with only one first arrhythmic event out of 123 patients (5).

Spontaneous diagnostic ECG is one of the important parameters in predicting outcome in all publications regarding risk stratification in Brugada syndrome. In a recent publication by Brugada et al. (1), follow-up data of 547 patients without previous SCD were presented. Spontaneous type 1 ECG, independently of history of syncope, predicted a higher risk in experiencing SCD than a non-diagnostic ECG which converted to coved-type ECG by exposure to sodium channel blockers during a mean follow-up of 24±32 months. Priori et al. (4) classified patients with spontaneous type 1 ECG as having intermediate risk for SCD with a hazard ratio of 2.1. Spontaneous type 1 ECG was also a predictor for a severe arrhythmic event during follow-up comparing with drug-induced type 1 ECG in the study of Eckardt et al. (5).

It is well known that the ECG in Brugada syndrome is variable from day to day and changes between diagnostic, non-diagnostic and normal forms. Veltmann et al. (6) investigated spontaneous fluctuations between diagnostic and non-diagnostic ECGs in Brugada syndrome in a prospective study. Of 43 consecutive patients, only one patient had a type 1 ECG consistently, whereas in others, diagnostic basal ECG disappeared transiently during follow-up (33%), converted from non-diagnostic basal type to non-diagnostic type (19%), or was only inducible by drugs (47%). The main finding of this prospective study was that 51% of the patients diagnosed with Brugada syndrome presented fluctuations between diagnostic and non-diagnostic ECGs (6). The obvious impact of this finding is that a patient’s risk for future events may be underestimated if it is based only on an initial non-diagnostic ECG (7).

The predictive value of the inducibility of ventricular tachyarrhythmias is controversial (2-5). Gehi et al. (8) performed a meta-analysis of prognostic studies of patients with a Brugada ECG to assess predictors of events recently and retrieved 30
prospective studies with data on 1545 patients. The overall event rate at an average of 32 months follow-up was 10%. The relative risk (RR) of an event (SCD, syncope, ICD shock) was increased in patients with a history of SCD or syncope (RR 3.24), in men compared with women (RR 3.47), and in patients with a spontaneous form compared with sodium channel blocker-induced type I ECG (RR 4.65). The RR of events was not significantly increased in patients with a family history SCD (p=0.97) or a mutation of the SCN5A gene (p=0.18). The RR of events was also not significantly increased in inducible patients compared with non-inducible patients (RR 1.88, p=0.27). However there was significant heterogeneity of the studies included.

Currently, an ICD is the only proven effective treatment for the disease. Symptomatic patients displaying the type 1 Brugada ECG (either spontaneously or after sodium channel blockade) who present with aborted sudden death should receive an ICD without additional need for electrophysiological study (EPS). Similar patients presenting with syncope, seizure, or nocturnal agonal respiration also should undergo ICD implantation after noncardiac causes of these symptoms have been ruled out.

Asymptomatic patients displaying a type 1 Brugada ECG (either spontaneously or after sodium channel blockade) should undergo EPS if a family history of sudden cardiac death is suspected to be the result of Brugada syndrome. The EPS is justified if the type 1 ECG occurs spontaneously in an asymptomatic patient with negative family history for sudden cardiac death. If inducible, then the patient receives an ICD. Asymptomatic patients who have no family history and who develop a type 1 ECG only after sodium channel blockade should be closely followed up (8).

References