Risk Stratification of Individuals with the Brugada Electrocardiogram: A Myth or a Reality?

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Editorial Comment

One of the leading causes of death in young adults in some countries, Brugada syndrome has been the focus of many clinical and research investigations since 1992. Large prospective cohort studies have advanced our knowledge of this syndrome. We now know that Brugada syndrome is an autosomal dominant disease characterized by mutations in the cardiac sodium channel (e.g., SCN5A) that result in overt or concealed ST-segment elevation in the right precordial leads and a high risk of sudden cardiac death in young and otherwise healthy adults. Many factors have shown promise for predicting sudden cardiac death in such patients; however, observations in this regard have not been entirely consistent even in the three largest prospective studies of the natural history of this syndrome.1-4

One study2 included 200 patients with Brugada syndrome (130 probands and 70 family members). An electrophysiology study (EPS) was performed in 86 patients and genetic analysis was done in all patients. Cardiac arrest occurred in 11% of patients. The risk of cardiac arrest was highest in patients with spontaneous ST-segment elevation in leads V1 through V3 and a history of syncope. Inducible ventricular arrhythmias on EPS were not predictive of cardiac arrest. The presence of an SCN5A mutation showed 32% sensitivity and 57% specificity in predicting the occurrence of cardiac arrest.2

Another study3 included 547 patients with the Brugada electrocardiogram and no prior cardiac arrest. During a mean follow-up of 24 months, 8% of patients had sudden death or documented ventricular fibrillation. The risk of these events was significantly higher in patients with a history of syncope and those with inducible sustained ventricular arrhythmias on EPS. The risk appeared to be highest in patients who had suffered at least one episode of syncope, had a spontaneously abnormal electrocardiogram, and were inducible on EPS.3

A third study4 included 212 patients with an electrocardiogram characteristic of Brugada syndrome. During a mean follow-up of 40 months, 9% of patients with previous syncope or cardiac arrest had a ventricular arrhythmic event versus 0.8% in asymptomatic patients. Significant predictors of arrhythmic events were a history of aborted sudden death or syncope and spontaneous coved ST-segment elevation in the right precordial leads. Although inducible ventricular arrhythmias on EPS were not found to be a significant predictor of arrhythmic events, the number of events that occurred in this study was too small to allow definitive conclusions in this regard.3

In this issue of the Journal, we are fortunate to have an article that refines previous knowledge of risk in patients with Brugada syndrome.5 In a meta-analysis of 30 prospective prognostic studies (including the three studies mentioned above), Gehi and colleagues5 assessed predictors of sudden cardiac death, syncope, or implantable cardioverter defibrillator (ICD) shocks in 1,545 patients with Brugada electrocardiogram. They found an overall event rate of 10% within a mean follow-up of 32 months. Significant predictors of events included a history of syncope or sudden cardiac death, male gender, and spontaneous compared with induced type I Brugada electrocardiogram. The risk of events was not higher in patients with a family history of sudden cardiac death, a mutation of the SCN5A gene, or inducible sustained ventricular arrhythmias on EPS.5

These results confirm that a history of syncope and a spontaneously abnormal electrocardiogram are strong indicators of future occurrence of arrhythmic events in patients with Brugada syndrome. Because Gehi and colleagues pooled data on EPS from six studies that were quite heterogeneous, the role of EPS in the risk stratification of patients with Brugada syndrome remains uncertain.5 Through sensitivity analyses, the authors could have excluded studies with different programmed electrical stimulation protocols and/or interpretation of EPS results; however, verification of protocol data and EPS results may not have been possible. The large prospective PROgrammed Electrical stimUlation preDictivE study will provide some answers to this ongoing debate.6

In the clinical arena, knowledge of risk is only important if it can alter therapy. Thus, one should ask the question: now that we know about risk, what can we do about it? Currently, the ICD is the only effective therapy for Brugada syndrome. There is consensus that patients who suffered a cardiac arrest and those who had syncope and spontaneously abnormal ECG should receive an ICD.1 The results of Gehi’s meta-analysis support this recommendation.

The treatment of asymptomatic patients displaying spontaneous type I Brugada ECG is controversial. In the report of the second consensus conference on Brugada syndrome, an EPS is deemed necessary in these patients, especially if they have a family history of sudden cardiac death and an ICD is recommended when sustained ventricular arrhythmias are induced. These recommendations are not supported by the results of Gehi’s meta-analysis as in his analysis, neither family history of sudden cardiac death nor inducibility on EPS had any predictive value. Asymptomatic patients with provoked type I Brugada ECG seem to be at low risk for arrhythmic events, so an ICD is currently not recommended in these patients.
The studies by Priori, Brugada, Eckardt, and Gehi provide important information on risk stratification of patients with Brugada syndrome. Future studies should use this information to determine the best therapy for patients with various manifestations of this syndrome. Although clinical trials are the best mainstay for clinical guidelines, conducting large clinical trials in patients with Brugada electrocardiogram may not be possible, especially in countries where the prevalence of this disease is low. As such, the importance of national and international registries of patients with Brugada syndrome cannot be overemphasized.

References