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Inappropriate implantable cardioverter-defibrillator shocks in Brugada syndrome: Pattern in primary and secondary prevention

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ABSTRACT

Background: Inappropriate implantable cardioverter-defibrillator (ICD) shocks is a common complication in Brugada syndrome. However, the incidence in recipients of ICD for primary and secondary prevention is unknown.

Method and results: We compared the rate of inappropriate shocks in patients with Brugada syndrome that had an ICD for primary and secondary prevention. We studied 51 patients, 86.5% of whom were males. Their mean age at diagnosis was 47 ± 11 years. Eighteen (35%) were asymptomatic, while 25 (49%) experienced syncope prior to implantation. Eight (16%) patients were resuscitated from ventricular fibrillation before implantation. During a mean follow-up of 78 ± 46 months, none of the asymptomatic patients experienced appropriate therapy, whereas 21.6% of symptomatic patients had ≥1 shock. Inappropriate shock occurred in 7 (13.7%) patients, with a mean IS of 6.57 ± 6.94 shocks per patient occurring 16.14 ± 10.38 months after implantation. There was a trend towards higher incidence of inappropriate shock in the asymptomatic group ($p = 0.09$). The interval from implantation to inappropriate shock occurrence was 13.91 ± 12.98 months. The risk of IS at 3 years was 13.7%, which eventually plateaued over the time.

Conclusion: Inappropriate shock is common in Brugada syndrome during the early periods after an ICD implantation, and seems to be more likely in asymptomatic patients. This finding may warrant a review of the indications for ICD implantation, especially in the young and apparently healthy population of patients with Brugada syndrome.

1. Introduction

Brugada syndrome (BrS) is a life-threatening arrhythmogenic disorder requiring implantation of cardioverter-defibrillator (ICD) in some patients to prevent sudden cardiac death (SCD) [1,2]. From the discovery of the disease until recent years, ICD has been implanted almost systematically in asymptomatic BrS carriers with ≥1 risk factors such as spontaneous type 1 ECG (Fig. 1), inducible ventricular fibrillation (VF) during programmed electrical stimulation (PES), and family history of premature death without strong evidence of the rationale for this preventive approach. Because of the low event rates observed on ICD-stored electrograms over a long period of follow-up after implantation, two contending views with regard to appropriateness or otherwise of primary prevention by ICD in BrS have emerged [3–10]. The aim of our study was to compare the rates of inappropriate shock (IS) in the setting of primary and secondary prevention in BrS recipients of ICD.

2. Methods

2.1. Study population

Consecutive patients diagnosed with BrS who underwent ICD

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implantation from 1999 to 2013 in four centers were followed-up and ICD therapy, whether appropriate shock (AS) or IS documented. The patients were divided into 2 categories of asymptomatic (group A), and symptomatic (syncope or cardiac arrest, group B) subjects prior to implantation. Diagnosis of BrS was made based on an episode of aborted sudden cardiac arrest (SCA) or during evaluation of syncope, occurrence of spontaneous ECG pattern consistent with BrS in asymptomatice subjects undergoing routine evaluation, or during screening of kindred of patient diagnosed with BrS. This registry was approved by institutional review committees, and the subjects gave informed consent.

2.2. Diagnosis, clinical data, and diagnostic workup

The following clinical data were collected in the participating centers: circumstances and age at the time of diagnosis, gender, family history of SCD before the age of 45 years, presence of atrial fibrillation (AF) and ventricular tachycardia (VT) before ICD implantation, results of pharmacological testing for unmasking the characteristic coved-type ECG pattern, results of invasive electrophysiological study (EPS), and indication for ICD implantation.

Diagnosis of BrS was made in accordance with the recommendations of the second consensus conference [11]. Patients had to have a prominent coved-type ST-segment elevation (Fig. 1) displaying J-wave amplitude or ST-segment elevation$\geq$0.2 mV at its peak, followed by a negative T wave [11]. In subjects with type 2 or type 3 ECG pattern and other reasons for suspecting the BrS, 1.0 mg/kg of ajmaline (a class I antiarrhythmic drug) was administered intravenously at a rate of 10 mg per minute, and a 12-lead ECG monitored for ST-segment changes of the coved-type BrS pattern. Patients with a history of presumed arrhythmic syncope, documented sustained VT, or aborted SCA were considered symptomatic.

We excluded conditions mimicking BrS by undertaking the following investigations: laboratory tests to exclude acute cardiac ischemia as well as metabolic and electrolyte disturbances; echocardiography and stress testing where indicated; coronary and/or right ventricular angiography, radionuclide ventriculography and cardiac magnetic resonance imaging to rule out structural heart disease. The decision to implant an ICD or not was made at the behest of an experienced electrophysiologist. Until 2010, ICD was implanted in asymptomatic patients in whom sustained VF was induced by any level of programmed stimulation.

2.3. ICD follow-up

In the absence of symptoms or device therapy, patients were routinely seen for ICD interrogation every 3–6 months (depending of physician's protocol). ICD programming consisted of a single detection (VF) zone above 200 to 220 bpm. Appropriate therapies were defined as shocks or antitachycardia pacing delivered for VT or VF. Inappropriate shock was defined as shock delivered in the absence of documented ventricular arrhythmias. We first counted overall occurrence of arrhythmic events (self-terminating ventricular arrhythmias, anti-tachycardia pacing and appropriate shocks) and IS. Afterwards, we compared event rates between both groups. Quinidine hydrochloride (300 mg twice daily) was added for supraventricular tachyarrhythmia or electrical storm during follow-up.

2.4. Statistical analysis

Continuous variables were expressed as the mean $\pm$ SD or the median and interquartile range for non-normally distributed data. Categorical variables were expressed in percentage and compared using the Chi-square test while continuous variables were compared using the Student's t-test. Conditions of validity of tests were checked and in case they were not verified we performed non-parametric tests (Fisher exact, and Mann-Whitney). The event-rate curve was determined using the Kaplan-Meier method. The differences in the rate of appropriate therapy and IS-free survival were analysed with the Log-rank test. To assess the contribution of baseline patient characteristics to the prediction of the likelihood of first IS during follow-up, multivariable Cox proportional hazard regression analysis was used. Adjustment variables were age at diagnosis, the coved type ECG pattern, the history ofAF, and the treatment with quinidine which was analysed in intention-to-treat fashion. Given the low incidence and prevalence of BrS in the general population [12], we assumed the choice of 10% α level for

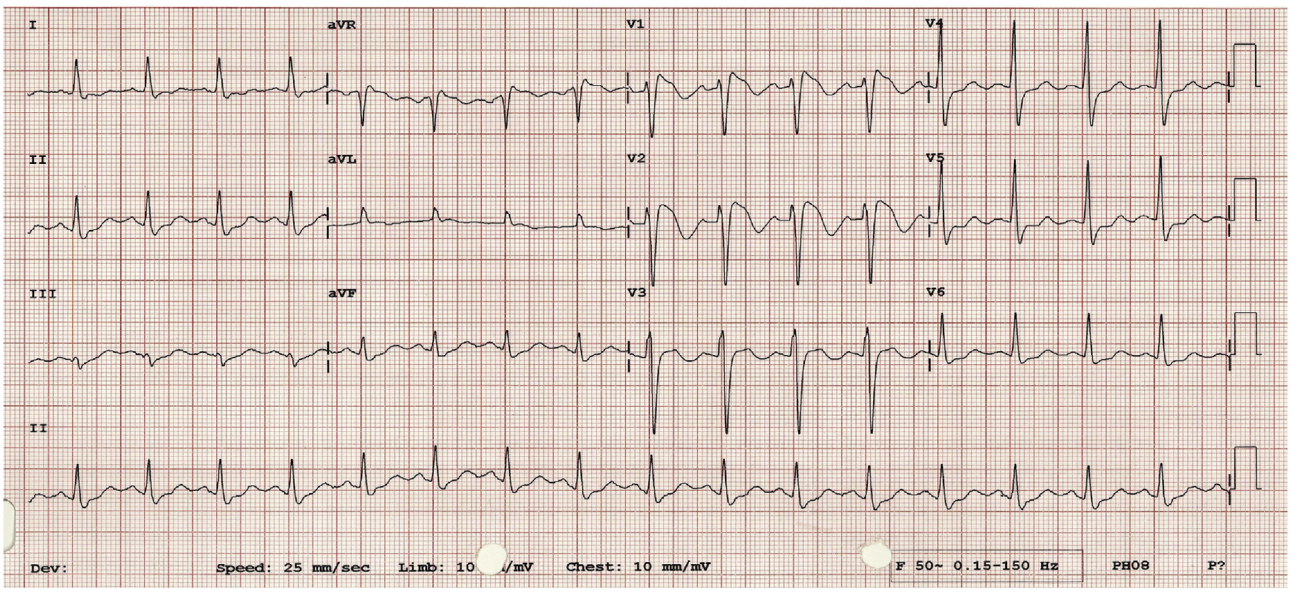

Fig. 1. Diagnostic ECG pattern of Brugada syndrome. Spontaneous coved-type S-T elevation in right precordial leads (mostly in V_1 and V_2 rather than V_3) is the hallmark of Brugada syndrome.

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