

## IMAGES IN CARDIOLOGY

### Programmed Ventricular Stimulation in Brugada Syndrome: An Irrefusable Offer or an Inaccurate Tool for Patients with Absent or Doubtful Symptoms?

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#### Abstract

A case of a patient with Brugada pattern on ECG is presented with dubious symptoms whose management was guided by an electrophysiology (EP) study where programmed ventricular stimulation easily induced ventricular fibrillation with only two ventricular extrastimuli and facilitated a decision to implant a defibrillator for sudden death protection. Images of the EP tracings are provided that illustrate the findings and the pros and cons of such an approach are herein discussed. *Rhythm* 2019;14(3):55-57.

**Key Words:** Brugada syndrome; sudden cardiac death; ventricular fibrillation; electrophysiology study; programmed ventricular stimulation; implantable cardioverter defibrillator

**Abbreviations:** ECG = electrocardiogram; EPS = electrophysiology study; ICD = implantable cardioverter defibrillator; RV = right ventricular; SCD = sudden cardiac death; VA = ventricular arrhythmia; VF = ventricular fibrillation

A 51-year-old gentleman was told of a suspect electrocardiogram (ECG) showing Brugada pattern 7 years earlier when he experienced an episode of palpitations accompanied by dizziness and lightheadedness, but records were not available. Three months before this referral he had a febrile episode during which a recorded ECG was compatible with coved type I Brugada pattern. Other subsequent ECGs and ambulatory recordings showed either type I (Fig. 1) or type II Brugada pattern.

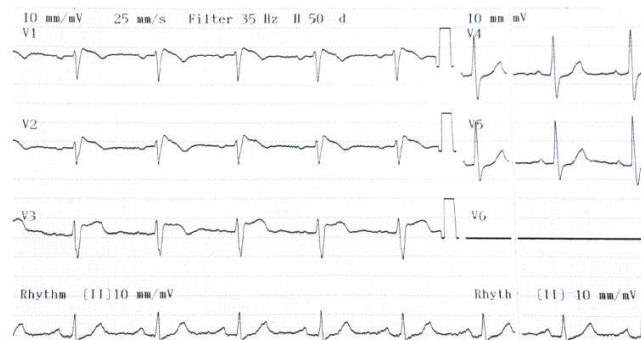


Figure 1

Except for this single spell of palpitations and dizziness in the remote past, the patient denied syncopal episodes or disturbed sleep. Past medical history was significant for smoking and hyperlipidemia treated with a statin. Physical

examination was unrevealing. Echocardiographic examination was reported within normal limits.

For further risk stratification, an electrophysiology study (EPS) with programmed ventricular stimulation (PVS) was recommended. During the EPS, a prolonged HV interval of 70 ms was recorded (Fig. 2), while the PVS



Figure 2

with use of double ventricular extrastimuli (coupling intervals 220/160 ms) at the right ventricular (RV) apex induced ventricular fibrillation (VF) (Fig. 3) which was promptly electrically cardioverted (Fig. 4). The patient was subsequently recommended, consented to and received an implantable cardioverter defibrillator (ICD) device for sudden cardiac death (SCD) protection. Over the ensuing 3 years, the patient has remained asymptomatic with no activation of the device as yet.

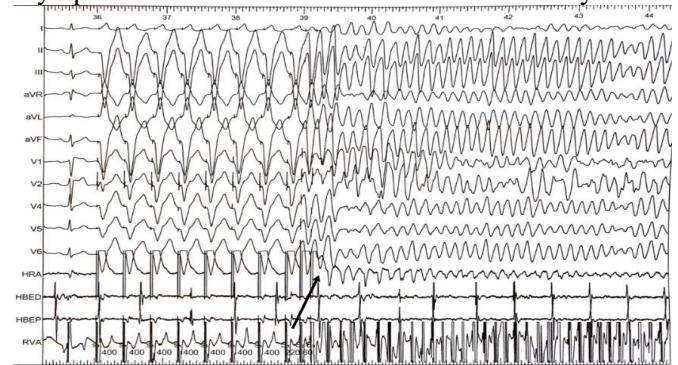


Figure 3

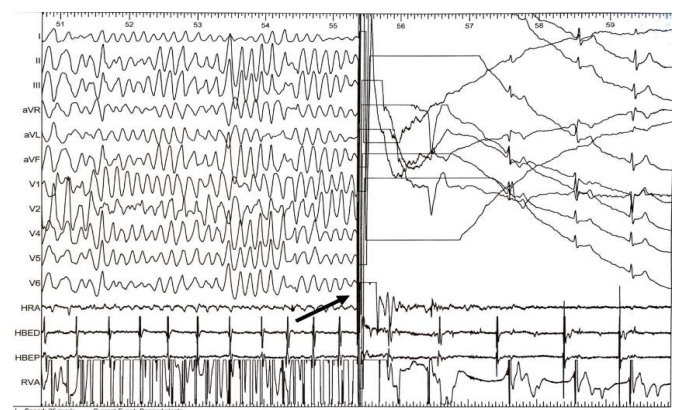


Figure 4

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Symptomatic patients with spontaneous type I Brugada pattern (Brugada syndrome) do not require further risk stratification and they should have an ICD implanted for protection of SCD.<sup>1, 2</sup> However, asymptomatic patients or patients with equivocal symptoms will need further risk stratification. The role of PVS for risk stratification of asymptomatic Brugada patients remains controversial.<sup>1, 2</sup> Sustained VF can be induced in up to 40-50% of Brugada syndrome patients (up to 34% in asymptomatic patients vs 70% in symptomatic patients) (*Figures 3 & 4*), which is much higher than the induction rate encountered in normal individuals.<sup>3, 4</sup> However, many factors seem to determine inducibility with the type and aggressiveness of the specific PVS protocol employed as the most important determinant; the number of ventricular extrastimuli (two or three), the site of RV pacing (RV apex and/or RV outflow tract), the minimal coupling interval of the extrasystoles, induction attempts and drive cycle lengths employed (two or three), and the autonomic nervous system status of the patient, all play a significant role in VF inducibility. The more aggressive the protocol the higher the rate of inducible VF and thus the lower the specificity of the test. Other important pertinent questions relate to the value and clinical utility of a negative test; does it identify truly low-risk patients?<sup>5</sup> A two-extra-stimuli PVS protocol would probably be the most conservative approach for risk stratification.<sup>1, 2, 6</sup> What about reproducibility? If a patient has inducible VF with use of 3 extrastimuli, should one accept the result as positive or should one proceed to test for reproducibility and only if reproducible accept it as true positive? Finally, should one take into account other findings of the EPS in addition to VF inducibility, like refractory periods,<sup>3</sup> sinus node dysfunction and/or prolonged HV interval suggestive of conduction disturbance. Thus, all these issues have not been settled.

In the FINGER registry of 1029 (654 asymptomatic) patients, a higher event rate was found in patients with inducible ventricular arrhythmia (VA) (both symptomatic and asymptomatic), which was nonsignificant on multivariate analysis, with an overall low incidence of 0.5% (cardiac event rate) in asymptomatic patients.<sup>7</sup> Similarly, in the PRELUDE registry of 308 Brugada patients (273 asymptomatic), there was no significant difference in event rates between patients with inducible and noninducible VAs.<sup>3</sup> However, in the study by Brugada brothers, inducibility was a powerful predictor of arrhythmic events during follow-up; 60 (28%) of 217 inducible patients had spontaneous VF compared with 5

(2%) of 221 noninducible patients ( $P = 0.0001$ ).<sup>4</sup> Their PVS protocol included a minimum of two basic pacing cycle lengths with two extrasystoles from the RV apex.

A systematic review and pooled analysis of 8 studies comprising 1312 patients evaluating the role of PVS (527 with induced arrhythmia with up to 3 extrastimuli) in identifying patients with Brugada syndrome at the highest risk for SCD, indicated that induction was associated with cardiac events during follow-up (hazard ratio, 2.66,  $P < 0.001$ ), with the greatest risk observed among those induced with single or double extrastimuli.<sup>8</sup> The lowest risk occurred in individuals without syncope and with drug-induced type 1 patterns (0.23% for no induced arrhythmia with up to double extrastimuli; 0.45% for induced arrhythmia), and the highest risk occurred in individuals with syncope and spontaneous type 1 patterns (2.55%, for no induced arrhythmia; 5.60%, for induced arrhythmia). The authors concluded that in patients with Brugada syndrome, arrhythmias induced with PVS are associated with future VA risk. Induction with fewer extrastimuli is associated with higher risk. However, clinical risk factors are important determinants of arrhythmia risk, and lack of induction does not necessarily portend low VA risk, particularly in patients with high-risk clinical features.

In a most recent meta-analysis of 6 studies including 1138 asymptomatic patients with Brugada syndrome, of the patients with inducible VA at EPS ( $n=390$  or 34.3%), 13 total arrhythmic events occurred (3.3% of the patients with inducible VA).<sup>9</sup> In asymptomatic patients with Brugada syndrome, 748 patients did not have inducible VA at EPS. There were 12 total arrhythmic events in this population (1.6% of the patients with noninducible VA). This results in an odds ratio (OR) of 2.3 ( $p=0.20$ ) for major arrhythmic events in asymptomatic patients with Brugada syndrome and inducible VA at EPS. A recent pooled analysis of 4 studies assessing risk stratification in 1338 Brugada patients indicated that a spontaneous type-1 Brugada pattern on the ECG is associated with a worse prognosis when combined with positive EPS,<sup>10</sup> which fits the description of our case presented herein. Hence, EPS served as the most decisive tool in risk stratification in our patient.

In summary, in view of a lack of other reliable risk stratifiers in Brugada patients who do not have or have doubtful symptoms, as in our case, the suggestion to perform an EPS practically finds no rival in risk stratification tools to use for these patients. The question remains about the type of specific PVS protocol to employ during the EPS, however, induction of VF with up to two extrastimuli, as in our case, is met with general agreement

as an acceptable guide to recommend ICD implantation ; in cases of VF induced with three extrastimuli, one may consider repeating the stimulation for purpose of reproducibility, however, this remains speculative.

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