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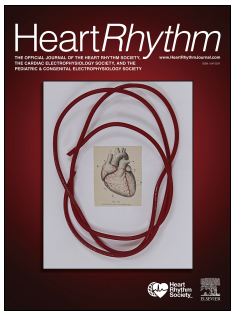

Long-term clinical outcomes of asymptomatic patients with spontaneous type 1 Brugada electrocardiographic pattern undergoing electrophysiological study for risk stratification

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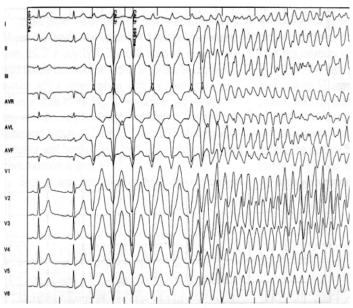
Long-term clinical outcomes of asymptomatic patients with spontaneous type 1 Brugada electrocardiographic pattern undergoing electrophysiological study for risk stratification

N = 165

Asymptomatic patients with spontaneous type-1 BrS ECG followed for a median time of 90 months



undergoing electrophysiological study for risk stratification evaluation

Outcome

✓ Major arrhythmic risk (1.8% patients; median annual event rate 0.15%)

✓ Patients who experienced arrhythmic events had significantly more often:

- a family history of BrS
- first-degree AV block
- prolonged QRS duration

Electrophysiological Study

✓ High negative predictive value (99%)

✓ Low positive predictive value (4.8%)

BrS: Brugada syndrome; AV: atrio-ventricular

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Long-term clinical outcomes of asymptomatic patients with spontaneous type 1 Brugada electrocardiographic pattern undergoing electrophysiological study for risk stratification

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Electrophysiological study (EPS) remains controversial for risk stratification in asymptomatic patients with Brugada syndrome (BrS) (1-3). This multicentre study aimed to evaluate the life-threatening event rate in asymptomatic patients with spontaneous type 1 BrS electrocardiographic (ECG) pattern undergoing EPS and its potential role in risk stratification. The study population consisted of 165 asymptomatic patients with a spontaneous type 1 BrS ECG pattern who underwent EPS. The patients were enrolled at eight centers between July 1996 and February 2023. Programmed electrical stimulation (PVS) was performed at the apex and outflow tract at two pacing cycle lengths and up to two (n=63) or three (n=102) ventricular extrastimuli with a minimum coupling interval of 200 ms. Differences between groups were evaluated with the X^2-test or Fisher exact test as appropriate. Continuous variables were compared with the Mann–Whitney U-test. A $p<0.05$ was considered statistically significant. The registry was ethically approved by the local institution and was conducted according to the Helsinki Declaration.

First-degree atrioventricular (AV) block and prolonged QRS duration were significantly more frequent in patients with a SCN5A variant (n=10/21,48% vs n=0/54,0%; P<0.001; n=7/21,33% vs n=2/54,4%;P<0.001). Forty-two (26%) patients were inducible at PVS. Fifty-three (32%) patients received a prophylactic ICD. Patients who had a positive EPS were significantly more often male (P=0.03), showed a prolonged HV interval (P=0.03), QRS duration (P=0.02) and prominent S-wave in lead I (P=0.005) at the basal ECG (Table 1). The median follow-up period was 90 (40–150) months. Only 3 patients (1.8%) experienced ≥1 major arrhythmic event (MAE) (0.2%/year; median annual event rate: 0.15%, which consisted of sudden cardiac death (n=1;0.6%) and appropriate ICD interventions on VF (n=2;1.2%). The mean time to the first event after EPS was 40±19 months. The median annual event rate in patients with a positive EPS was similar to that in patients with a negative EPS: 0.54 (0.07-1.96 vs 0.06 (0.002-0.32); P=0.16 (Table 1). Patients who experienced MAEs had more often a family history of BrS

(P=0.02), first-degree AV block (P=0.03) and prolonged QRS duration in lead II (P=0.017). There was no significant difference between patients who experienced MAEs during follow-up and those who did not, with respect to the presence of an SCN5A variant (P=0.08). Positive and negative predictive values of EPS were respectively 4.8% and 99%.

Risk predictive scores in BrS have been previously developed with varying levels of performance (5). In our study population, patients who experienced major adverse events (MAEs) had higher mean values of the Sieira score (3±2 vs. 2±1; P=0.04) and the Shanghai score (5±1 vs. 3±1; P=0.001). No significant differences were observed between patients who experienced MAEs during follow-up and those who did not, in relation to the PAT score and the Brugada-Risk score (P=0.83 and P=0.5, respectively).

Our main findings are: (i) MAEs often occurred several years after EPS; (ii) the median annual event rate in patients with a positive EPS was low and similar to that in patients with a negative EPS; therefore, ICD implantation should not be based solely on the positive EPS result due to the significant risk of complications over time (4); (iii) patients who experienced MAEs had more often a family history of BrS, first-degree AV block, prolonged QRS duration at basal ECG; (iv) among the three patients who reported MAEs, two were SCN5A+ confirming the possible role of genetic on risk stratification.

The present study has limitations predominantly related to the low event rate, relatively limited follow-up period and retrospective design. Our findings indicate that asymptomatic patients with a spontaneous type 1 ECG pattern of BrS should not be classified as "high risk" solely based on a positive EPS. Therefore, prophylactic ICD implantation or epicardial ablation should not be recommended without further consideration including an assessment of the risks and benefits of catheter ablation. A refined, multiparametric approach to risk stratification,

integrating ECG findings with clinical, genetic information and possible advanced risk scores could improve current models for BrS and warrants further investigation.

TABLE

Table 1. Patient's characteristics according to a positive or negative electrophysiological study

	Overall (n=165)	**EPS + (n=42)**	**EPS - (n=123)**	**P-value**
Age, years	43 (34-53)	46 (34-55)	43 (34-51)	0.48
Male gender	124 (76)	37 (88)	88 (72)	0.03
Family history				
Family history of BrS	34 (28)	13 (31)	34 (28)	0.7
Family history of SCD	51 (31)	14 (33)	37 (30)	0.7
History of atrial fibrillation	9 (6)	2 (5)	7 (6)	1
Genetic testing	75 (45)	15 (36)	60 (49)	
SCN5A variant	21 (28)	6 (40)	15 (25)	0.34
AH interval, ms	100 (85-111)	100 (85-126)	100 (82-110)	0.20
HV interval, ms	50 (43-60)	55 (45-61)	50 (42-58)	0.03
EPS protocol				
Up to three extrastimuli	102 (62)	30 (71)	72 (58)	0.14
Up to two extrastimuli	63 (38)	12 (29)	51 (42)	0.14
Electrocardiographic features				
Early repolarization	23 (14)	7 (17)	11 (9)	0.25
QTc prolongation	4 (3)	1 (2)	3 (2)	0.9
QTc duration, ms	410 (400-420)	423 (418-440)	430 (410-440)	0.8
First-degree AV block	18 (11)	7 (17)	11 (9)	0.2
f-QRS	11 (7)	6 (14)	5 (4)	0.03
Prolonged QRS duration	15 (9)	8 (19)	7 (6)	0.02
QRS duration, ms	100 (100-105)	100 (95-124)	100 (95-105)	0.05
S-wave in lead I	64 (39)	24 (57)	40 (33)	0.005
Left anterior fascicular block	14 (9)	3 (7)	11 (9)	1
Major arrhythmic event during follow-up	3 (2)	2 (5)	1 (1)	0.2
Median annual event rate,%	0.15 (0.03-0.44)	0.54 (0.07-1.96)	0.06 (0.002-0.32)	0.16 *
Duration of follow up, months	90 (40-150)	93 (40-155)	87 (41-143)	0.67

Continuous variables are given median (interquartile range).Categorical variables are given as numbers (percentage).AV:atrioventricular;BrS: Brugada syndrome;EPS:electrophysiological study;f-QRS:fragmented QRS;ICD:implantable cardioverter defibrillator;QTc:corrected QT interval;SCD:sudden cardiac death. *Analysis was made using the Kaplan-Meier method, and the distributions of the groups were compared by means of a log-rank test.

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