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RESEARCH LETTER

# Characteristics of Patients with Spontaneous Versus Drug-Induced Brugada Electrocardiogram: Sub-Analysis From the SABRUS

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Patients with Brugada syndrome (BrS) may display either a spontaneous (S) or a drug-induced (DI) ECG pattern. The latter group is considered at a lower risk of arrhythmic events (AE) and sudden cardiac death (SCD). The only study that compared these 2 groups in BrS associated with AEs comprised a small cohort of 44 patients.[1]

The SABRUS study (Survey on Arrhythmic events in Brugada Syndrome) gathers the largest cohort of patients with BrS and AEs published to date.[2] The data that support the findings of this study are available from the corresponding author upon reasonable request. Patients were divided into 2 groups according to their AE presentation: group A presented with aborted cardiac arrest before diagnosis of BrS and group B were Brugada patients implanted prophylactically with an ICD, which proved to be justified during follow-up. The present study compares DI-BrS and S-BrS patients from SABRUS. The study was approved by the Institutional Committee on Human Research at the Tel Aviv Sourasky Medical Center. Continuous variables are presented as mean±SD or median (interquartile range) and compared using the student *t* test or Mann-Whitney U test as appropriate. Categorical variables are presented by absolute numbers and proportions and compared using the $\chi^2$ test or Fisher exact test. All tests were 2-tailed, and a $P<0.05$ was considered statistically significant.

Of the 678 SABRUS patients, 451 (66.5%) had S-BrS ECG and 227 (33.5%) had DI-BrS ECG (Table 1). Females predominated in the DI-ECG group (15.4% versus 5.3% in the S-ECG group, $P<0.001$), with less Asians than Whites (33.9% versus 42.8% in the S-ECG group, $P=0.036$). Higher inducibility rates of ventricular fibrillation (VF) at electrophysiologic study (EPS) were found in the S-ECG group (67.3% versus 55%.7 in the DI-ECG groups, respectively, $P=0.022$), with a similar rate of EPS performed in both groups (61.7% in the DI-ECG group versus 57.6% in the S-ECG group, $P=0.315$). There were no differences between DI-BrS ECG and S-BrS ECG patients regarding age at AE, proband status, history of syncope, AE presentation, family history of sudden cardiac death, fever-related events, and genetic analysis.

**Key Words:** Brugada syndrome ■ electrocardiography ■ heart arrest ■ syncope ■ ventricular fibrillation

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## Nonstandard Abbreviations and Acronyms

| | |
|---|---|
| **AE** | arrhythmic events |
| **BrS** | Brugada syndrome |
| **DI** | drug-induced |
| **ICD** | implantable cardiac defibrillator |
| **S** | spontaneous |
| **SABRUS** | Survey on Arrhythmic events in Brugada Syndrome |
| **VF** | ventricular fibrillation |

To the best of our knowledge, this is the first study comparing BrS patients with S-ECG and DI-ECG in a large population cohort with AEs. Although a previous article by Tadros et al[3] showed that 8% of patients tested by drug provocation for BrS could have false positive results, we assume, based on our findings of the SABRUS cohort,[4] that all our patients with DI-ECG have proven BrS, and that the results of our study should be taken in this context only.

Syncope combined with a spontaneous type 1 Brugada ECG has been shown to be useful for identifying Brugada patients at risk for AE. However, this is not relevant when a DI-ECG is encountered. In addition, the use of programmed ventricular stimulation has shown conflicting results. In a large series of patients with DI-BrS ECG, Sieira et al[5] showed that VF inducibility rate was significantly lower than in patients with S-BrS ECG (13.2% versus 42.4%, respectively, $P<0.01$); however their cohort comprised a minority of patients with AEs. In our cohort comprising only patients with AEs, the lower inducibility rate is confirmed (55.7% versus 67.3%, respectively, $P=0.022$). These findings suggest that EPS is less useful for the management of BrS patients with DI-ECG, and do not inform necessarily on risk stratification strategies. These findings could actually represent a difference in the mechanism of arrhythmia generation of the 2 subgroups of Brugada patients, and future studies should test whether this could explain the lower arrhythmic risk of DI-ECG patients.

Females predominated in our DI-ECG group. This is in line with the study by Nagayama et al[1] in a smaller cohort.

For the first time, SABRUS showed that Asians with AEs displayed significantly less DI-ECG compared with whites. This may suggest that a genetic predisposition of Asians plays a role in the occurrence of the S-BrS ECG type.

No difference in the presence of *SCN5A* gene mutation was found between the DI-ECG and S-ECG groups. These findings agree with those reported by Nagayama et al[1] in a similar, although significantly smaller patient cohort.

**Table 1. Patient Characteristics According to Brugada ECG Type**

| | Drug-Induced BrECG | Spontaneous BrECG | |
|---|---|---|---|
| | n=227 (33.5%) | n=451 (66.5%) | *P* |
| Age at AE, y (mean±SD) | 42±14 | 42±15 | 0.969 |
| Age at AE ≤16 | 9 (4) | 23 (5.1) | 0.532 |
| Age at AE >16 | 218 (96) | 428 (94.9) | |
| Gender | | | |
| Men | 192 (84.6) | 427 (94.7) | <0.001 |
| Women | 35 (15.4) | 24 (5.3) | |
| Ethnicity | | | |
| White | 130 (57.3) | 234 (51.9) | 0.036 |
| Asian | 77 (33.9) | 193 (42.8) | |
| Other/unknown | 20 (8.8) | 24 (5.3) | |
| Arrhythmic event documentation | | | |
| Group A | 150 (66.1) | 276 (61.2) | 0.214 |
| Group B | 77 (33.9) | 175 (38.8) | |
| Proband status | 181 (85.4) | 361 (86.4) | 0.736 |
| History of syncope | 82 (36.1) | 183 (40.6) | 0.262 |
| Fever during AE | 11 (5.9) | 24 (6) | 0.961 |
| Family history of SCD | | | |
| Yes | 46 (20.3) | 99 (22) | 0.851 |
| No | 158 (69.6) | 310 (68.7) | |
| Unknown | 23 (10.1) | 42 (9.3) | |
| EPS performed | 140 (61.7) | 260 (57.6) | 0.315 |
| VF inducibility during EPS | 78 (55.7) | 175 (67.3) | 0.022 |
| Genetic analysis performed | 158 (69.6) | 327 (72.5) | 0.429 |
| SCN5A mutation present | 41 (25.9) | 102 (31.2) | 0.235 |

AE indicates arrhythmic event; BrECG, Brugada electrocardiogram; EPS, electrophysiologic study; SCD, sudden cardiac death; and VF, ventricular fibrillation.

In conclusion, DI-BrS patients represented a third of BrS cohort with AEs. They differed from S-BrS patients in gender, ethnicity, and VF inducibility rates. The most important observation is that this group of patients is less studied, and identifying high-risk DI-BrS patients is not an easy task. We encourage seeking new risk markers in this group in future studies.

## ARTICLE INFORMATION

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## Disclosures

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