

Surveillance after cardiac arrest in patients with Brugada syndrome without an implantable defibrillator: An alarm effect of the previous syncope[☆]



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ABSTRACT

Background: Debate regarding the prognosis of asymptomatic patients with Brugada syndrome (BrS) is possibly affected by the selection bias of survivors of sudden cardiac arrest (SCA). We aimed to determine variables influencing surveillance after SCA.

Methods: We analyzed a BrS cohort of 145 patients belonging to 37 families. We compared the clinical data and circumstances surrounding SCA (i.e., place of occurrence and people accompanying the subject) in 10 patients who survived an episode of SCA (Group A) vs. 27 deceased relatives (first or second degree) who suffered sudden cardiac death (SCD; Group B). Information concerning Group B was agreed upon by at least 3 relatives. A sub-analysis was performed considering families carrying a mutation in *SCN5A* (Group B-Mutant).

Results: Syncope was unique in predicting SCA in the BrS cohort. Comparing Groups A vs. B, there were no differences in the mean age at time of SCA/SCD (46.2 [SD 17.1] vs. 39.9 [SD 14.5] years; $p = 0.271$), gender (male 60% vs. 74.1%; $p = 0.442$), prior cardiomyopathy (0%), administration of cardiovascular treatments (anti-hypertensive and lipid-lowering drugs; 20% vs. 14.8%; $p = 0.653$) or conventional cardiovascular risk factors. Environmental circumstances surrounding the SCA/SCD were not significantly different between groups. Prior syncope was more frequent in Group A (80% vs. 3.7%; $p < 0.001$) and unique in predicting surveillance ($p < 0.001$). Group B-Mutant displayed equivalent data.

Conclusions: A previous syncope, as an alarm symptom, might contribute to better surveillance of SCA compared with subjects with SCA as the debut of BrS. The latter might behave as a factor of selection bias.

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1. Introduction

The sudden death toll in the general population as a result of lethal arrhythmic events attributed to Brugada syndrome (BrS) is unknown. Therefore, although syncope is a risk factor of sudden death (SDth) [1], it is controversial how selection bias of survivors of sudden cardiac arrest (SCA) could influence the characterization of these and other clinical variables [2]. Under this perspective, the prognosis of asymptomatic

patients with BrS remains in question. Recent reports highlight that the risk is not as low as previously reported [3], but efforts to discern which patients will eventually benefit from interventional preventive therapies (i.e., inducibility of ventricular fibrillation by programmed stimulation) failed to achieve conclusive results [4,5].

Data from international and multicenter registries shows that the percentage of patients with BrS receiving appropriate therapies from implantable defibrillators continues to increase with increasing follow-up time [6]. In addition, this behavior seems to replicate in asymptomatic patients, frequently represented by young people with long life expectancy [3]. Preventive measurements (i.e., lifestyle measurements, avoidance of drugs with potential adverse effects and prompt treatment of fever episodes) and close follow-up of patients, with a particular emphasis on the occurrence of new episodes of

[☆] The authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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malignant syncope, might eventually help to reduce the risk of SDth [7]. However, the question about true prognosis of asymptomatic patients has not been resolved, and the selection bias of survivors limits the ability to provide conclusive data. As an approximation to the problem of selection bias effect, in this study we aimed to compare the clinical variables and circumstances of SDth of two groups: patients with BrS who survived an episode of cardiac arrest (Group A) vs. those patients, possibly affected by the syndrome, who did not survive (Group B).

2. Methods

2.1. Population and data recording

We studied a BrS cohort of 145 living patients belonging to a total of 37 families (Fig. 1). Among them, Group A was defined as those patients with BrS who had survived an episode of SCA in the absence of an implantable defibrillator. All of the patients in the BrS cohort were questioned about first- and second-degree relatives who had experienced SDth (did not survive the episode). Of those, Group B comprised those cases fulfilling the criteria established or probable sudden cardiac death (Est-SCD and Prob-SCD, respectively; see below: definitions) [8]. For most patients in Group B, it was not possible to confirm the diagnosis of BrS according to guidelines [9]. However, to increase the probability that patients in Group B had been affected by BrS, we performed an additional analysis considering those families carrying a mutation in the *SCN5A* gene causing BrS, which is inherited in an autosomal dominant pattern (Group B-Mutant).

Each patient from Group A was directly asked about the clinical features, symptoms and environmental circumstances of the cardiac arrest following a structured interview comprising 14 consecutive questions summarized in Table 1. An experienced physician performed the questions and additional explanation were given if necessary (i.e., for clarifying what the “syncope” means). For cases from Group B, data were obtained from their relatives. Given the ambiguity introduced by the impossibility for direct interview with patients in Group B (deceased), we established as a criterion of validity the consensus of at least 3 family members regarding each of the questioned data. Informed consent was obtained from living patients and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

2.2. Definitions

The term SCA was used to describe SDth cases in which specific resuscitation records were available or the individual had survived the cardiac arrest event [8]. Est-SCD was defined as an unexpected death

Table 1
Structured interview.

Question	Possible responses
Are you a smoker or have you smoked during the last 10 years?	Yes vs. no
Have you ever been made aware by your doctor that you are affected by hypertension? Or, are you under pharmacological treatment for hypertension?	Yes vs. no
Have you ever been made aware by your doctor that you are affected by diabetes? Or, are you under pharmacological treatment for diabetes?	Yes vs. no
Have you ever been made aware by your doctor that you are affected by dyslipidemia? Or, are you under pharmacological treatment for dyslipidemia?	Yes vs. no
Have you ever been made aware by your doctor that you are affected by any cardiac disease confirmed by echocardiography, cardiac catheterization or other diagnostic methods?	Yes vs. no If yes, please describe.
Have you ever been made aware by your doctor that you are affected by any non-cardiac disease that puts you under risk of SDth? (i.e., severe chronic lung disease, pulmonary embolism, cerebral aneurism, etc.)	Yes vs. no If yes, please describe.
Are you taking chronic oral medication?	Yes vs. no If yes, please describe.
Did you experience syncope any time before the episode of SDth?	Yes vs. no
Have you ever been under medical evaluation because of syncope before the episode of SDth occurs?	Yes vs. no
Did the SDth occur during daytime or nighttime?	Daytime vs. nighttime
If the SD occurred during daytime, was it during the morning or during the afternoon?	Morning vs. afternoon
Did the SDth occur during rest/seated or while performing any physical activity?	At rest vs. physical activity
Did the SDth occur at wakefulness or while sleeping?	Wakefulness vs. sleep
Did the SDth occur while accompanied by people who were aware of your medical conditions (friends or family)?	Yes vs. no
When the SDth occurred, were you in a public space surrounded by other people? (Whether they were friends/family)	Yes vs. no

Description of the structured interview regarding clinical features, symptoms and environmental circumstances of the cardiac arrest. The same questions were posed to relatives to explore the data regarding cases included in Group B. SDth: sudden death.

without obvious extracardiac cause, occurring with a rapid witnessed collapse, or if unwitnessed, occurring within 1 h after the onset of symptoms. Prob-SCD was defined as an unexpected death without obvious extracardiac cause that occurred within the previous 24 h. In any situation, the death should not occur in the setting of a prior terminal condition, such as a malignancy that was not in remission or end-stage chronic obstructive lung disease [8]. Syncope was defined as transient

Flowchart of patients included for analysis

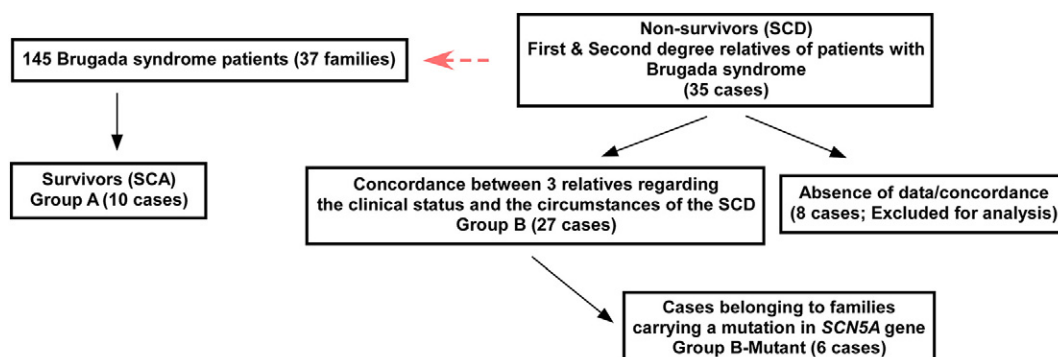


Fig. 1. Flowchart of patients included for analysis.

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