Prevalence of Brugada sign in patients presenting with palpitation in southern Iran

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Aims Brugada syndrome is a cardiac channel abnormality that is associated with a high risk of ventricular fibrillation and sudden cardiac death and characterized by an electrocardiographic pattern of right bundle branch block and transient or persistent ST-segment elevation in leads V1–V3. No data regarding the frequency of Brugada syndrome exist in an Iranian population. The aim of this study was to determine the frequency of Brugada-type ECG pattern in southern Iran.

Methods and results All patients presenting with palpitation were enrolled in the study. A Brugada-type ECG pattern was determined according to the criteria recommended by European Heart Association Molecular Basis of Arrhythmias Study Group. A total of 3895 patients (mean age 38.2 ± 11.9 years, 54% women) met all study criteria. One hundred patients (2.56%) had Brugada-type ECG pattern. Of these, 21 patients (0.54%) had definite Brugada sign (Type 1 or Types 2 and 3 with conversion to Type 1 following procainamide test). Of 21 patients with definite Brugada sign, eight had Brugada syndrome, four had history of syncope, two had coved-type ECG in the family, one had polymorphic ventricular tachycardia, and one had history of sudden cardiac death in the family. Five patients underwent ICD implantation. The incidence of a Brugada-type ECG pattern was 2.43% in subjects between 17 and 30 years and 0.13% in subjects >30 years ($P = 0.01$).

Conclusion Frequency of Brugada sign in an Iranian population presenting with palpitation is greater than some European countries and lower than a Japanese urban population.

KEYWORDS Arrhythmia; Brugada Syndrome; Palpitation

Introduction

Brugada syndrome is a cardiac channel abnormality that is associated with a high risk of ventricular fibrillation and sudden cardiac death. It is characterized by a typical electrocardiographic (ECG) pattern of right bundle branch block and transient or persistent ST-segment elevation in leads V1–V3.1–10 It accounts for ~20% of all cases of sudden cardiac death in patients with structurally normal hearts and appears to be more frequent in Southeast Asia than in other regions.5 The disease is inherited in an autosomal dominant fashion in ~50% of the cases.1,2 A mutation in the gene SCN-5A encoding the alpha subunit of the sodium channels of the heart has been defined in 15–30% of the cases.5 Symptoms including palpitation, syncope, and sudden cardiac death, usually appear in the third or fourth decade of life.7 Recently, the presence of a Brugada-type ECG pattern despite the absence of symptoms and a family history of sudden cardiac death has been defined as a Brugada sign.11,12 No data regarding the frequency of the Brugada syndrome and Brugada sign exist in the Iranian population. The aim of this study was to determine the frequency of Brugada sign in patients presenting with palpitation in southern Iran.

Methods

From September 2004 to October 2006, all patients presenting with palpitation were enrolled in the study and gave informed written consent. Clinical data were recorded. A 12-lead ECG (at a paper speed of 25 mm/s and 1 mV/100 mm standard gain) was recorded from each subject. All ECG recordings were evaluated by two cardiologists. Brugada-type ECG pattern was defined as Type 1, 2, or 3. Type 1 pattern has coved ST-segment, elevation of 2 mm or greater, followed by an inverted T-wave, with little or no isoelectric separation (Figure 1). Type 2 pattern also has a high-takeoff ST-segment, elevation of 2 mm or greater with gradually descending ST-segment elevation (remaining ≥1 mm above the baseline), followed by a positive or biphasic T-wave resulting in a saddleback configuration (Figure 2). Type 3 pattern has either coved or saddleback appearance with right precordial ST-segment elevation of <1 mm ($P < 0.001$) (Figure 3). Type 1 pattern is diagnostic of the Brugada sign, whereas Types 2 and 3 patterns require conversion to the...
Type 1 pattern after challenge with a sodium channel blocking agent to be diagnostic. Brugada syndrome is definitively diagnosed when a Type 1 ST-segment elevation is observed in more than one right precordial lead (V1–V3) in the presence or absence of a sodium channel-blocking agent, and in conjunction with one of the following: documented ventricular fibrillation, polymorphic ventricular tachycardia, a family history of sudden cardiac death at 45-years-old, coved-type ECGs in family members, inducibility of VT with programmed electrical stimulation, syncope, or nocturnal agonal respiration. The diagnosis of a Brugada-type ECG pattern was considered to be positive only when the two cardiologists agreed on the classification of the ECG abnormalities. All patients underwent 24-h Holter monitoring. To detect structural heart disease, transthoracic echocardiography was performed on each patient. Patients with structural heart disease were excluded from the study. If the standard 12-lead ECG showed Type 2 or 3 Brugada pattern, 10 mg/kg of procainamide was intravenously administered in 10 min, with the patient being continuously monitored in the intensive care unit. Conversion of Type 2 or 3 to Type 1 following procainamide was considered diagnostic of the Brugada sign.

Statistical analysis

The age, gender, and ECG findings of the cases were recorded with SPSS (Chicago, IL, USA) 9.0 software. A Kappa analysis was performed to evaluate the consistency...
between the cardiologists. Continuous variables are presented as means ± SD. Categorical variables are displayed as percentages (%). Student's t-test was used for comparison of data between the two groups. A value of P < 0.05 was considered statistically significant.

Results

A total of 3895 patients (mean age 38.2 ± 11.9 years, 54% women) met all study criteria and consented to participate. Rhythm and conduction disturbances were found in 506 (13%) and 182 (4.6%) subjects, respectively. The ECG abnormalities observed in the subjects are shown in Table 1. Analysis of the 24-hour Holter monitoring revealed that the most common abnormalities were supraventricular premature beats (34%) and sinus tachycardia (18%); atrial fibrillation was found in 71 (1.8%) patients and 3 (0.07%) patients had episodes of ventricular tachycardia.

Type 1 Brugada ECG pattern

Fourteen patients (mean age 29.2 ± 13.9 years, 78% male) had Type 1 ECG pattern. Of these, three had episodes of syncope, one had a family history of sudden cardiac death at <45 years old, one had polymorphic ventricular tachycardia on 24-hour Holter monitoring, and one had coved-type ECGs in family members (Table 2).

Type 2 Brugada ECG pattern

Fifty-six patients (mean age 31.4 ± 11.6 years, 67% male) had Type 2 Brugada ECG pattern in whom procainamide testing was performed and unmasked Type 1 ECG in five. One of these five patients had episodes of syncope and one had coved-type ECGs in family members (Table 2).

Type 3 Brugada ECG pattern

Thirty patients (mean age 32.1 ± 12.3 years, 56% male) had Type 3 Brugada ECG pattern in whom procainamide testing was performed and unmasked Type 1 ECG in two patients (Table 2).

Therefore, with amalgamation of the above data, 100 patients (2.56%) had Brugada-type ECG pattern in the study population. Of these, 21 patients (0.54%) had definite Brugada sign (Type 1 or Types 2 and 3 with conversion to Type 1 following procainamide test). Of 21 patients with definite Brugada sign, eight had Brugada syndrome as four patients had history of syncope, two had coved-type ECG in family, one had polymorphic ventricular tachycardia, and one had history of sudden cardiac death in their family. The incidence of a Brugada-type ECG pattern was 2.43% in subjects between 17–30 years and 0.13% in subjects >30 years (P = 0.01).

ICD implantation

Currently, an implantable cardioverter defibrillator (ICD) is the only proven effective treatment for the disease. Symptomatic patients displaying the Type 1 Brugada ECG (either spontaneously or after sodium channel blockade) who present with aborted sudden death should receive an ICD without additional need for electrophysiological study (EPS). Similar patients presenting with related symptoms

### Table 1 Electrocardiographic abnormalities of patients presenting with palpitation (n = 3895)

Electrocardiographic abnormality & n (%) &
--- & --- &
Rhythm disturbances & 506 (13) &
Premature beats & 135 (3.4) &
Supraventricular & 97 (2.5) &
Ventricular & 38 (0.9) &
Sinus node arrhythmia & 221 (5.6) &
Tachycardia & 213 (5.4) &
Bradycardia & 85 (2.1) &
Atrial fibrillation & 56 (1.4) &
Supraventricular rhythm (atrial/nodal) & 91 (2.3) &
Ventricular rhythm & 3 (0.07) &
Conduction disturbances & 182 (4.6) &
AV block & 74 (1.9) &
First degree & 16 (0.4) &
Second degree & 53 (1.36) &
Mobitz I & 46 (1.1) &
Mobitz II & 7 (0.17) &
Third degree & 5 (0.12) &
Right bundle branch block & 43 (1.1) &
Left bundle branch block & 13 (0.3) &
Hemiblocks & 52 (1.33) &
Pre-excitation & 45 (1.1) &

### Table 2 Characteristics of patients with Brugada-Type ECG pattern

<table>
<thead>
<tr>
<th>Type</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (n)</td>
<td>14</td>
<td>56</td>
<td>30</td>
</tr>
<tr>
<td>Male (n)</td>
<td>11</td>
<td>38</td>
<td>17</td>
</tr>
<tr>
<td>Age (Mean ± SD)</td>
<td>29.2 ± 13.9</td>
<td>31.4 ± 11.6</td>
<td>32.1 ± 12.3</td>
</tr>
<tr>
<td>Ventricular fibrillation (n)</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Polymorphic VT (n)</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Syncope (n)</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>SCD in family (n)</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Coved-type ECG in family (n)</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Nocturnal agonal respiration (n)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Positive procainamide testa</td>
<td>–</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>ICD implantation</td>
<td>4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*aIf Type 2 or 3 converted to Type 1 following procainamide test, the test was considered positive.

SCD, sudden cardiac death; VT, ventricular tachycardia.
such as syncope, seizure, or nocturnal agonal respiration also should undergo ICD implantation after non-cardiac causes of these symptoms have been carefully ruled out. Asymptomatic patients displaying a Type 1 Brugada ECG (either spontaneously or after sodium channel blockade) should undergo EPS if a family history of sudden cardiac death is suspected to be the result of Brugada syndrome. Asymptomatic patients who have no family history and who develop a Type 1 ECG only after sodium channel blockade should be closely followed up. In our study, ICD implantation was done in a total of five patients: three patients had spontaneous Type 1 ECG and episodes of ventricular tachycardia and one patient with history of syncope who had Type 1 ECG after sodium channel blockade.

Discussion

The frequency of Brugada sign differs among ethnic groups. In a Japanese urban population, the frequency was found to be 0.38% for the coved type and 2.14% for the saddleback type. Furuhashi et al. reported the frequency of ST segment elevation as 0.14% in 8612 asymptomatic subjects with a mean age of 49 years. In recent years, the frequency of Brugada sign has been reported to range between 0.14 and 0.70 percent in middle-aged healthy populations. In a retrospective study conducted with 1000 patients in France, the frequency was found to be 6.1% in a middle-aged group. However, the authors noted that the high frequency obtained in the study could be due to early repolarization. In Israel, the frequency of the Brugada sign was found to be 0% among 592 healthy individuals. Prevalence of Brugada sign was reported to be 0.61 and 0.55% in two different age groups in Finland. However, there are no data regarding the prevalence of Brugada syndrome and Brugada sign in Iranian populations. In our study, the frequency of Brugada-type ECG pattern was 2.56%. The prevalence of Brugada sign was 0.54% in our study population, which is greater than those found in European countries and lower than those found in the Japanese urban population.

Types of Brugada ECG pattern

In one study in Finland, no subject had Type 1. In Japan, the frequency was found to be 2.14% for the saddleback type and 0.14–0.37% for the coved type. In our study, Types 1, 2, and 3 were found in 0.14, 0.56, and 0.30% of patients, respectively.

Clinical significance of Brugada-type ECG pattern

It has been shown that symptomatic subjects with Brugada Type 1 ECG pattern are at higher risk of sudden cardiac death. However, Types 2 and 3 were reported to have a good prognosis. It was reported that Type 2 or 3 in asymptomatic patients with no family history of sudden cardiac death could be considered as a normal variant, rather than a predictor of sudden death.

Conclusion

We found that the frequency of Brugada sign in an Iranian population presenting with palpitation is greater than some European countries and lower than the Japanese urban population.

References