Frequency of Brugada-Type ECG Pattern (Brugada Sign) in Southern Turkey

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SUMMARY

The frequency of Brugada sign was found to differ among ethnic groups. Yet, there is no data regarding the prevalence of Brugada syndrome and sign in our country. The aim of this study was to determine the frequency of a Brugada-type electrocardiogram (ECG) pattern in southern Turkey.

A total of 1238 subjects (males, 671, females, 567) were included in the study. The previously archived ECGs of 807 subjects without any evidence of structural heart disease were chosen randomly and evaluated. In addition, prospective analysis of the ECGs of 431 subjects (males, 293, females, 138) randomly chosen from healthy university students were also included. The mean age was 38.9 ± 17.6 years. Six subjects (0.48%) had a Brugada-type ECG pattern. One (0.08%) of them had the coved-type and 5 (0.40%) had the saddleback-type. All subjects were asymptomatic.

A Brugada-type ECG pattern was obtained in 1 (0.17%) female and in 5 (0.74%) males (OR: 4.2 CI: 0.5-36.4, $P = 0.2$). The Brugada-type ECG pattern frequency was 0.12% in subjects ≥ 25 years old and 1.16% in subjects between 17-24 years old (OR: 9.4 CI: 1.1-81.2, $P = 0.02$). Young males between 17-24 years had the highest (1.70%) frequency.

The results indicate that the frequency of the Brugada-type ECG pattern was 0.48% in the general population, being more prevalent in young males in our region. These results are similar to the findings of studies performed in other countries. (Int Heart J 2006; 47: 541-547)

Key words: Brugada-type ECG pattern (Brugada sign), Frequency

BRUGADA syndrome is a cardiac channel abnormality that is associated with high risk of ventricular arrhythmias and sudden cardiac death (SCD) without structural heart disease. It is characterized by a typical electrocardiographic (ECG) pattern, including right bundle branch block and transient or persistent ST segment elevation in leads V_1 toV_3.[1,2)] The first description of the syndrome was a series of 8 patients presented by Brugada, *et al*.[1)] Symptoms usually appear in

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the 3rd or 4th decade of life.[3] The disease is inherited in an autosomal dominant fashion in approximately 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 obtained in 15-30% of the cases.[4] The ST segment elevation in this syndrome is the coved type. A change to a saddleback type or normalization is common, which leads to underdiagnosis.[1,3] 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 the Brugada sign.[5,6] The frequency of a Brugada type ECG pattern or sign has been reported to be 0.02% and 6.1%.[5,7] No data regarding the frequency of Brugada syndrome or sign exist in a Turkish population. The aim of this study was to determine the frequency of a Brugada-type ECG pattern in southern Turkey.

METHODS

Subjects: After obtaining approval from the Ethics Committee, 1238 subjects (671 males, 567 females, mean age, 38.9 ± 17.6 years) were included in the study. The files of 1500 subjects with a 12-lead ECG (at a paper speed of 25 mm/s and 1 mV/100 mm standard gain) recorded between October 2004 and March 2005 were randomly selected from the archives of our hospital and evaluated retrospectively. A total of 807 cases (378 males, 429 females, mean age, 48.4 ± 14.7 years) with ECG recordings and no structural cardiac disease were included in the study. Between November 2004 and March 2005, 431 university students (293 males, 138 females, mean age, 21.1 ± 1.8 years) were also randomly selected and their ECGs were recorded with the same equipment by the same person.

Electrocardiogram: All ECG recordings were evaluated by 2 cardiologists. ECGs were examined for the presence of sinus rhythm abnormality (bradycardia defined as a heart rate of < 60 beats/min and tachycardia > 100 beats/min), bundle branch block, ventricular hypertrophy, ST segment and T wave changes, ectopic beats, QRS axis, atrioventricular (AV) conduction disturbance, atrial fibrillation and pre-excitation syndromes. A Brugada-type ECG pattern was determined according to the criteria recommended by European Heart Association Molecular Basis of Arrhythmias Study Group.[3] The criteria used for classifying ECG abnormalities into type 1, 2 or 3 are shown in Table I. The diagnosis of a Brugada-type ECG pattern was considered to be positive only when the 2 cardiologists agreed on the classification of the ECG abnormalities.

Echocardiography: Subjects suspected of having structural heart disease or a Brugada-type ECG pattern were invited to undergo an M-mode and 2-dimensional echocardiographic examination. In addition, 24-hour Holter monitoring was performed in subjects with a Brugada-type ECG pattern.

Statistical analysis: The age, gender, and ECG findings of the cases were recorded with SPSS 9.0 software. A Kappa analysis was performed to evaluate

Table I. Criteria for Brugada-type ECG Patterns (3)

	Type 1	Type 2	Type 3
J-wave amplitude	≥ 2 mm	≥ 2 mm	≥ 2 mm
T-wave	negative	positive or biphasic	positive
ST configuration	coved	saddleback	saddleback
ST segment elevation	gradually descending	≥ 1 mm	< 1mm

Table II. Electrocardiographic Abnormalities of Subjects (*n* = 270)

Electrocardiographic abnormality	*n* (%)
Left ventricular hypertrophy voltage criteria	33 (2.66)
Left atrial abnormality	13 (1.00)
ST-T changes	7 (0.56)
Conduction disturbances	97 (7.83)
Right bundle branch block	40 (3.24)
Complete	3 (0.24)
Incomplete	37 (3.00)
Left bundle branch block	17 (1.37)
Complete	2 (0.16)
SASH	15 (1.21)
Incomplete right bundle block + SASH	3 (0.24)
AV conduction disturbances	7 (0.56)
First degree block	7 (0.56)
QRS axis deviations	30 (2.42)
Left axis	24 (1.92)
Right axis	4 (0.32)
Undetermined	2 (0.16)
Rhythm disturbances	99 (7.99)
Premature beats	11 (0.90)
Supraventricular	6 (0.48)
Ventricular	5 (0.40)
Sinus arrhythmias	81 (6.54)
Tachycardia	43 (3.47)
Bradycardia	37 (3.00)
Sinoatrial block	1 (0.08)
Atrial fibrillation	4 (0.32)
Supraventricular rhythm (atrial/nodal)	3 (0.24)
Myocardial infarction (silent)	2 (0.16)
Pre-excitation	13 (1.05)
LGL	11 (0.89)
WPW	2 (0.16)
Brugada-type ECG pattern	6 (0.48)
Type 1 (coved)	1 (0.08)
Type 2	3 (0.24)
Type 3	2 (0.16)

SASH indicates left anterior superior hemiblock, LGL, Lown-Ganong-Levine syndrome; and WPW, Wolff-Parkinson-White syndrome.

the consistency between the cardiologists. The ratios for age and gender groups were evaluated by using Fisher's exact test and OR (95% CI). Values are expressed as the mean ± SD (standard deviation), n value, and percentage (%).

RESULTS

ECG abnormalities were found in a total of 270 (21.8%) subjects. The most frequently encountered abnormalities were rhythm (7.99%) and conduction (7.83%) disturbances. Only 3 of 33 subjects with left ventricular hypertrophy on ECG had left ventricular hypertrophy on echocardiography. Forty subjects with complete and incomplete right bundle branch block had normal echocardiographic results. The ECG abnormalities observed in the subjects are shown in

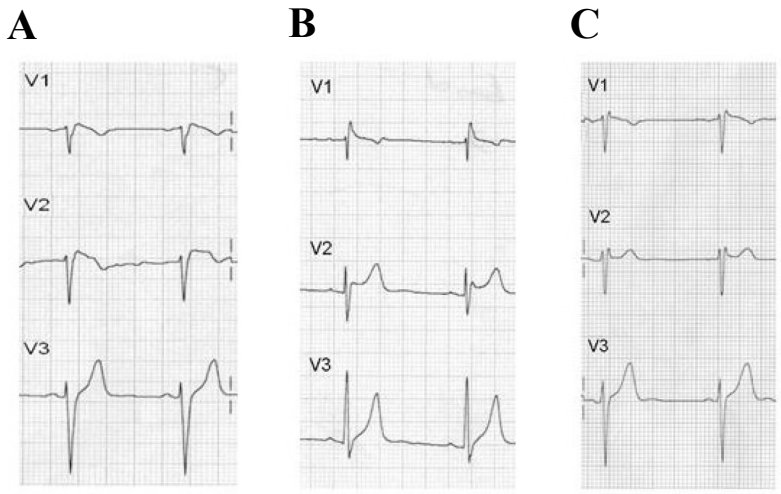


Figure. **A:** Type 1 (coved type), **B:** Type 2, **C:** Type 3 of Brugada sign.

Table III. Distribution of Brugada-Type ECG Pattern According Age and Gender

	Brugada-type ECG pattern		
	Yes *n* (%)	No *n*	*P*
Age			
17-24 years	5 (1.16)	426	0.02
≥ 25 years	1 (0.12)	806	
Gender			
Male	5 (0.74)	666	0.2
Female	1 (0.17)	566	
Total	6 (0.48)	1232	

Table II.

Among the 1238 subjects, 6 (0.48%) had a Brugada-type ECG pattern. One of these 6 subjects had coved type (0.08%) (Figure A), whereas 5 (0.40%) had the saddleback type (Figure B, C), 3 of which were type 2 (0.24%) and 2 type 3 (0.16%). Two subjects were excluded because of the lack of interobserver agreement. No cardiac symptoms or family history of sudden cardiac death were found in any of the subjects. A moderator band in the right ventricle was found in 3 of the 6 cases. No other pathology was found. In addition, 24-hour Holter monitoring did not reveal any pathological rhythm-conduction abnormality.

The incidence of a Brugada-type ECG pattern was 0.12% (1/807) in subjects ≥ 25 years and 1.16% (5/431) in subjects between 17-24 years (OR: 9.4 CI: 1.1-81.2, $P = 0.02$). Young males between the ages of 17-24 years had the highest (1.70%) frequency. The distribution of a Brugada-type ECG pattern according to age and gender is shown in Table III. In the young group, all cases with a Brugada-type ECG pattern were male. A Brugada-type ECG pattern was obtained in one (0.17%) female and in 5 (0.74%) males (OR: 4.2 CI: 0.5-36.4, $P = 0.2$). Only 1 (0.17%) female had the saddleback type. One (0.15%) coved type and 4 (0.59%) saddleback type ECG patterns were seen in males.

DISCUSSION

Frequency of Brugada sign: The frequency of Brugada sign differs among ethnic groups. In a Japanese urban population, the frequency in males was found to be 0.38% for the coved type and 2.14% for the saddleback type.[8] Furuhashi, *et al*[9] 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 0.14-0.70% in middle-aged healthy populations.[10-13] In a retrospective study conducted with 1000 patients in France, the frequency was found to be 6.1% in the middle-aged group.[7] However, the authors noted that the high frequency obtained in the study could be due to early repolarization and the difficulties in differential diagnosis. In Israel, the frequency of the Brugada sign was found to be 0%, while that of suspected Brugada sign was 1% among 592 healthy individuals.[14] These ratios were 21% and 5%, respectively, in 39 cases of idiopathic ventricular fibrillation. Brugada sign frequency was reported to be 0.61% and 0.55% in 2 different age groups consisting of only males in Finland.[6] However, there are no data regarding the prevalence of Brugada syndrome and sign in Turkish populations. The frequency of 0.48% obtained in our study is similar to those found in other European countries, with the exception of one study reporting a frequency of 6.1%.[7]

Distribution of the frequency according to age and gender: Brugada syndrome is

8 times more common in males than in females.[5,13,15] Junttila, *et al*[6] reported a ratio of 0.61% in 2479 young males aged between 18-30 years, and 0.55% in 542 individuals aged between 40-60 years. In Japan, the frequency in males has been reported to vary between 0.14-2.41% and 0.04% in females.[8-13] In our study population, the frequency was 0.74% in males and 0.17% in females. However, we did not find any significant gender difference. This finding could be due to the small number of subjects with a Brugada type ECG pattern. In the younger group aged between 17-24 years, the incidence of a Brugada type ECG pattern was significantly higher.

Types of Brugada sign: In one study in Finland, no subject had type 1.[6] In Japan, the frequency was found to be 2.14% for the saddleback type and 0.14-0.37% for the coved type in males.[8,11,13] In our study, the frequencies were 0.08% for the coved type and 0.40% for the saddleback type. In males, the coved type had a frequency of 0.15%, whereas it was 0.59% for the saddleback type. The corresponding ratios were 0.34% and 1.36%, respectively, in young males. We found that the frequency of Brugada sign in young Turkish males was lower than that in Japan, and higher than some European countries.

Clinical significance of Brugada type ECG pattern: It has been shown that subjects with a Brugada type 1 ECG pattern and symptoms are at higher risk of sudden cardiac death.[1-3,13] However, type 2 and type 3, characterized with "saddleback" type ST segment elevation, were reported to have a good prognosis.[6,8,11,12] In a 19-year long retrospective follow-up involving 31 cases without symptoms, paroxysmal atrial fibrillation was found only in one case, and no cardiovascular events were observed in the remaining subjects.[6] In addition, arrhythmic events were not observed during 9 to 84 months of follow-up in 57 cases without symptoms or a family history.[11,12] It was reported that type 2 and type 3 Brugada signs in particular 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.[6] We did not detect any symptoms or family history of sudden death and arrhythmias in subjects with a Brugada type ECG pattern. We are planning a long-term follow-up of our subjects.

Limitations: Since the frequency obtained in our study was collected from a heterogenous population and not from a community-based sample, it may not be a reflection of the actual prevalence. This is the most important limitation of our study. For this reason, the results would be more reliable if the frequency of Brugada sign in the 2 subgroups was taken into consideration. In addition, some limitations influencing these findings exist. Since the ECG pattern may return to normal, the ratio we have determined might be lower than the true frequency. However, this limitation is due to the syndrome itself and the properties of the ECG pattern of Brugada syndrome. This limitation is valid for all studies. We

were not able to evaluate pharmacological stress testing or the inducibility of ventricular tachycardia/fibrillation in subjects with a Brugada type ECG pattern. However, as mentioned above, since the individuals were asymptomatic with no history of Brugada-related death in the family and the saddleback type had good prognosis, stress tests were not performed.

Conclusion: The frequency of a Brugada-type ECG pattern was 0.48% in the general population in southern Turkey and was more prevalent in young males. These results are similar to those of previous studies performed in other countries.

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