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Prevalence of Brugada-type electrocardiogram pattern by recording right precordial leads at higher intercostal spaces

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Aims Recording electrocardiograms (ECGs) by placing the right precordial leads at higher intercostal spaces (ICSs) increases the sensitivity for detecting Brugada-type ECG pattern (BTEP). Published studies unfortunately used standard lead positions for recording ECGs and underestimated the true prevalence of BTEP. Therefore, by placing right precordial leads at higher ICS, we aimed to find out the true prevalence of BTEP in our population.

Methods and results Healthy male volunteers ($n = 504$) between 18 and 55 years of age (37.3 ± 10.7 years) without known cardiac or metabolic disorders were enrolled into the study. After the standard ECG recording, two other recordings were obtained by placing the right precordial leads to the third and second ICS. Electrocardiograms were stratified by two independent reviewers for the presence of BTEP. There were 15 subjects (3%) who displayed BTEP on their standard ECG recordings. Number of cases displaying BTEP increased to 25 (5%) and 38 (7.5%) when the right precordial leads were moved to third and second ICS, respectively. Although none of the subjects displayed type 1 BTEP on their standard ECGs, three subjects displayed type 1 BTEP on the third and four subjects displayed type 1 BTEP on the second ICS.

Conclusions Our study revealed that the prevalence of BTEP in healthy male subjects was 7.5% by placing the right precordial leads to higher ICS. Instead of standard lead locations that are not sensitive enough for detection of BTEP we recommend high right ICS recording in further prevalence studies.

Keywords Brugada syndrome • Brugada pattern • Prevalence • ECG • Diagnosis • Epidemiology

Introduction

Brugada syndrome (BrS) is an important hereditary ion channel disorder associated with ventricular arrhythmias and sudden cardiac death in subjects without structural heart disease. Brugada syndrome is thought to be responsible for at least 4% of all sudden deaths and at least 20% of sudden deaths in patients with structurally normal hearts. Men are affected more than women because of genetic and hormonal background. The prevalence of the disease is estimated to be 5/10 000; however, due to fluctuating nature of ECG pattern it is difficult to estimate the true prevalence of the disease in the general population.[1] Three different types of ST-segment elevation patterns which are defined as 'Brugada-type ECG pattern (BTEP)' may be observed during ECG recording.[2] In a Japanese study, type 1 BTEP specific for BrS was observed in only 12/10 000 inhabitants; type 2 and 3 BTEP which are not diagnostic for BrS were much more prevalent appearing in 58/10 000 inhabitants.[3] Recent studies, however, highlighted the importance of recording right precordial leads at a higher intercostal space (ICS) for increasing the sensitivity of detecting or unmasking type 1 BTEP.[4–8] However, the true prevalence of BTEP in healthy subjects by placing the leads and recording ECGs at high right ICS is unknown. Only one small sample-sized study investigated the prevalence of type 1 BTEP in Korean male healthy subjects by using this simple and more sensitive method.[6] Since there is a lack of data about the true prevalence of BTEP in our population, we intended to find out its prevalence in healthy men by placing the right precordial leads to higher ICS.

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Methods

Healthy students, medical staff, and personnel at our institution as well as subjects who came in for check-up and found to be otherwise healthy volunteered to participate in the present study. They were enrolled between January and September 2011. They did not describe any systemic complaints and history of cardiac or metabolic disorders. Subjects on any medication and/or with any abnormal finding on physical examination were excluded from the study. Other exclusion criteria were history of syncope, family history of sudden cardiac death, history of any disease that may be associated with electrocardiographic ST/T changes, complete right and left bundle branch block, and/or atrial fibrillation on their ECGs. After exclusion criteria were applied, the study population consisted of 504 healthy male volunteer subjects whose age range was between 18 and 55 years (mean 37.3 $\pm$ 10.7 years). Twelve-lead ECGs were obtained from all subjects in a supine position at a paper speed of 25 mm/s and a calibration of 10 mm/mV. Electrocardiograms were obtained by the same investigator with the same ECG recorder (Nihon Kohden ECG-9020K, Japan). After the standard ECG recording two other recordings were obtained by placing the right precordial V_1–V_3 leads to the third and second ICS, respectively. All ECG recordings were carried out by the same investigator and were evaluated by two independent reviewers for the presence of BTEP according to the Second Brugada Consensus Conference criteria.[2] The diagnosis of BTEP was made only when both investigators agreed on the classification of the ECG abnormalities. The study complies with the declaration of Helsinki and was approved by the local ethics committee. All subjects gave written informed consent to participate in the study.

Statistical analysis

The age, gender, and ECG findings of the subjects were recorded by Statistical Package for Social Sciences 16.0 software (SPSS Inc., Chicago, IL, USA). Data were expressed as mean $\pm$ SD (standard deviation) and percentage (%). Significance of differences regarding BTEP frequencies among age groups were tested by χ^2 test. To minimize errors in the evaluation process ECGs were assessed for inter-observer variability using 'Cohen's kappa statistic'. The kappa value was 0.896 [95% confidence interval (0.694–1) (kappa: 0.8–1 = almost perfect)]. There was also a high statistical agreement between the observers [agreement: 98% (standard error: 0.103)].

Results

There were 15 subjects (3%) who displayed BTEP on their standard ECG recordings. Number of cases displaying BTEP increased to 25 (5%) and 38 (7.5%) when V_1–V_3 leads were moved to third and second ICS, respectively (*Table 1*). Although none of the subjects displayed type 1 BTEP on their standard ECGs, three subjects displayed

Table 1 Frequency of Brugada-type electrocardiogram pattern on standard and high intercostal space electrocardiogram recordings

BTEP	Fourth ICS, *n* (%)	Third ICS, *n* (%)	Second ICS, *n* (%)
Type 1	0	3 (0.6)	4 (0.8)
Type 2	5 (1)	5 (1)	10 (2)
Type 3	10 (2)	17 (3.4)	24 (4.8)
Total	15 (3)	25 (5)	38 (7.5)

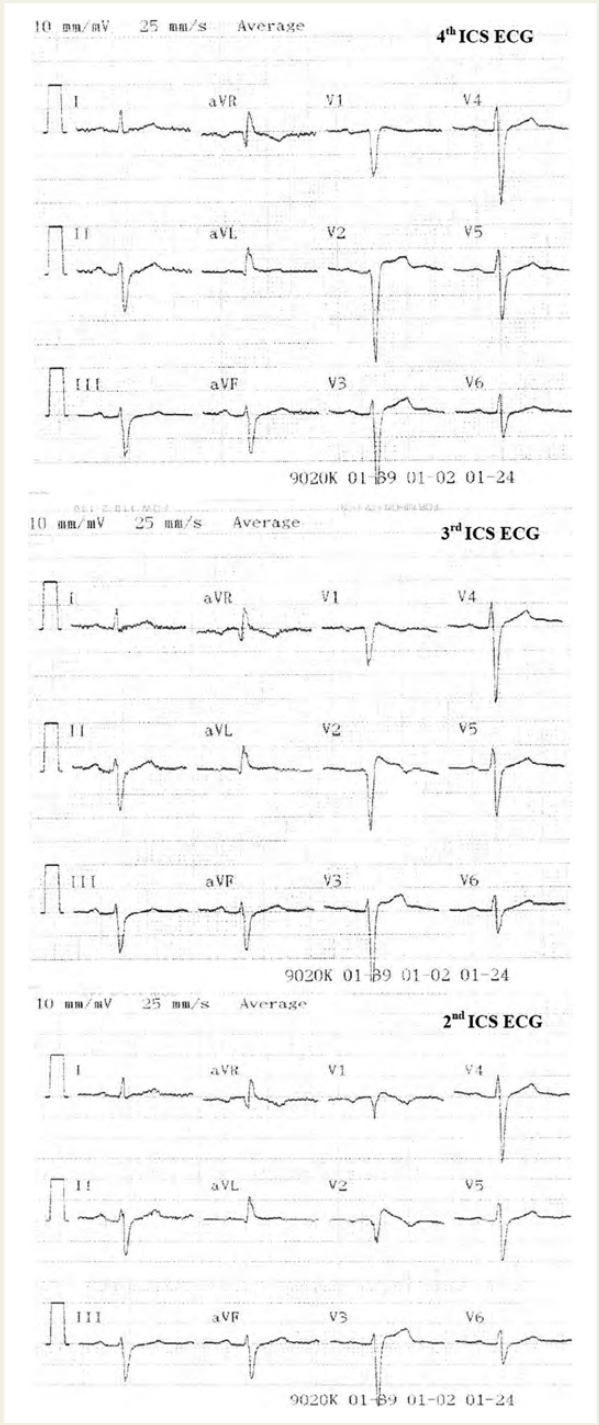

Figure 1 Electrocardiograms of a 39-year-old man recorded from the fourth, third, and second intercostal spaces. This subject displayed type 1 Brugada-type electrocardiogram pattern on second intercostal space electrocardiogram despite the absence of type 1 Brugada-type electrocardiogram pattern on fourth intercostal space recording.

type 1 BTEP on the third and four subjects displayed type 1 BTEP on the second ICS (*Figure 1*). None of the subjects without evidence of any BTEP on their second ICS ECG displayed BTEP on their third ICS or standard ECG. As right precordial leads were moved to higher ICS, subjects were observed to display a progressively increasing degree of BTEP (*Tables 2, 3* and *4*). As it is shown in *Table 5*, there were no significant differences between age groups regarding the prevalence of BTEP on standard and higher ICS ECG recordings.

Discussion

The present study revealed that the true prevalence of BTEP in healthy Turkish men were 7.5% when ECGs were recorded at higher ICS. However, when the standard lead locations were used, the prevalence was found to be 3%. We observed type 1 BTEP in four (0.8%) new subjects when the ECGs were recorded at high right ICS. In addition, we were unable to find any specific age range associated with increased frequency of BTEP. The frequency and degree of BTEP progressively increased as right precordial leads were moved from standard fourth to third and second ICSs. It is obvious that placing the right precordial leads to higher ICS is more sensitive than standard lead positions for detecting BTEP. Majority of the previous studies were designed and conducted according to standard lead positions and possibly underestimated the true prevalence of BTEP.

In subjects without structural heart disease BTEP has been suggested to be a marker for sudden cardiac death.[2] However, the epidemiology and clinical outcome of BTEP in asymptomatic general population is not homogenous. Studies investigating the prevalence of BTEP in general population have reported discordant rates between 0.2 and 6%.[9] The reasons for those inhomogeneous results might be small sample sized studies, fluctuating nature of BTEP, application of different diagnostic criteria and concurrently used medications. Ethnicity may also be a concern, since BrS is known to be more prevalent in Asian populations. If we consider gender, it is well known that men are more affected with BrS and more often display BTEP than women because the myocardial amount of transient potassium outward channels especially on the right ventricular epicardium is much more pronounced in male subjects.[10] In a recent study investigating the prevalence and significance of BTEP in 12012 healthy European subjects, Gallagher *et al.*[9] found 31 (0.3%) subjects with BTEP. Only two subjects displayed

Table 2 Brugada-type electrocardiogram on third and fourth intercostal space electrocardiograms of four patients who displayed type 1 Brugada-type electrocardiogram on second intercostal space

Age (years)	Fourth ICS ECG	Third ICS ECG	Second ICS ECG
51	Type 2	Type 2	Type 1
47	Type 2	Type 1	Type 1
39	Type 3	Type 1	Type 1
51	Type 3	Type 1	Type 1

Table 3 Brugada-type electrocardiogram on third and fourth intercostal space electrocardiograms of 10 patients who displayed type 2 Brugada-type electrocardiogram on second intercostal space

Age (years)	Fourth ICS ECG	Third ICS ECG	Second ICS ECG
29	None	None	Type 2
55	Type 2	Type 2	Type 2
30	None	None	Type 2
52	None	Type 2	Type 2
52	None	None	Type 2
51	Type 2	Type 2	Type 2
24	Type 3	Type 3	Type 2
39	None	None	Type 2
26	Type 3	Type 3	Type 2
42	Type 2	Type 2	Type 2

Table 4 Brugada-type electrocardiogram on third and fourth intercostal space electrocardiograms of 24 patients who displayed type 3 Brugada-type electrocardiogram on second intercostal space

Age (years)	Fourth ICS ECG	Third ICS ECG	Second ICS ECG
42	None	Type 3	Type 3
18	None	Type 3	Type 3
36	None	None	Type 3
55	None	None	Type 3
20	None	None	Type 3
30	None	None	Type 3
36	None	Type 3	Type 3
44	Type 3	Type 3	Type 3
53	None	None	Type 3
21	None	None	Type 3
24	None	Type 3	Type 3
32	Type 3	Type 3	Type 3
47	None	Type 3	Type 3
45	None	None	Type 3
35	Type 3	Type 3	Type 3
20	Type 3	Type 3	Type 3
47	None	Type 3	Type 3
31	None	None	Type 3
45	None	Type 3	Type 3
47	Type 3	Type 3	Type 3
55	None	Type 3	Type 3
37	None	None	Type 3
28	Type 3	Type 3	Type 3
45	None	Type 3	Type 3

Table 5 Prevalence of Brugada-type electrocardiogram on fourth intercostal space ICS*, third intercostal space **, and second intercostal space * electrocardiograms as well as their distribution among different age groups**

Age (years)	BTEP absent			BTEP present			Total
	Fourth ICS, *n* (%)	Third ICS, *n* (%)	Second ICS, *n* (%)	Fourth ICS, *n* (%)	Third ICS, *n* (%)	Second ICS, *n* (%)	
18–25	83 (17)	81 (17)	79 (16)	2 (0.4)	4 (0.8)	6 (1.2)	85
26–35	152 (30)	152 (30)	148 (29)	4 (0.8)	4 (0.8)	8 (1.6)	156
36–45	111 (22)	107 (21)	103 (20)	3 (0.6)	7 (1.3)	11 (2.2)	114
46–55	143 (28)	139 (27)	136 (27)	6 (1.2)	10 (2)	13 (2.6)	149
Total	489 (97)	479 (95)	466 (92)	15 (3)	25 (5)	38 (8)	504

*$P = 0.84$, **$P = 0.35$, and ***$P = 0.50$ for comparison of frequencies among age groups. Statistics were computed with χ^2 test.

type 1 BTEP. Another study investigated the prevalence and significance of BTEP in a young and middle-aged Finnish population and reported a prevalence rate of 0.6%.[11] There were no subjects with type 1 BTEP in that study. In two major studies Japanese authors reported different prevalence rates of type 1 and type 2/3 BTEP as 0.27–0.54% and 0.51–0.94%, respectively.[12,13] Hermida *et al.*[14] found a prevalence rate of 6% for concave ST elevation in 1000 European men whereas prevalence rate for convex ST elevation was 0.1%. Monroe and Littmann[15] found 52 cases with BTEP among ~12 000 unselected non-cardiac hospitalized patients. However, only two cases were reported to display convex pattern of ST elevation in that study. Viskin *et al.*[16] reported no cases of definitive BTEP in 592 healthy patients referred to their hospital, whereas 1% of these patients displayed a questionable BTEP. Holst *et al.*[17] published a recent study conducted in Denmark and found 1.1 definite BrS cases per 100 000 inhabitants. In the only study investigating the frequency of BTEP among asymptomatic Turkish male and female subjects, Bozkurt *et al.*[18] reported a frequency rate of 0.48% (6 out of 1238 subjects). Three of those subjects (0.24%) displayed type 2 and two displayed type 3 (0.24%), whereas only one subject (0.08%) showed type 1 BTEP. Young males between 17 and 24 years of age had the highest frequency in that study. All of these aforementioned studies used standard lead positions at fourth ICS and most of them included female subjects. Therefore, our study is somewhat different from the previous studies in terms of using a more sensitive recording method and including only male subjects. In our study, we were able to find BTEP only in 15 (3%) subjects at standard lead positions. However, the frequency of detecting BTEP was dramatically increased when ECGs were recorded at higher right ICS. Four new subjects demonstrated diagnostic type 1 BTEP at high ICS emphasizing the importance of high right precordial ECG recording. In contrast with results of Bozkurt *et al.*,[18] we were unable to detect any specific age range associated with increased frequency of BTEP. Since we included only men in our study and used a more sensitive method, we were able to detect a much higher rate of BTEP than they found in their study.

Placement of the right precordial leads in a higher position has been suggested to increase the sensitivity of the ECG for detecting BTEP both with and without a drug challenge. In the only study published so far that investigated the prevalence of BTEP recorded from higher ICS in healthy Korean men, Shin *et al.*[6] found that 3 of 225 subjects had a BTEP on higher ICS ECG while there was no subject with BTEP on standard ECG. All BTEPs were type 2 in that study. In contrast, the prevalences of BTEP in our study were 5 and 7.5% at third and second ICS, respectively. These frequencies were considerably higher than the frequencies found by Shin *et al.*[6] A plausible explanation for this might be the larger sample size of our study or the different ethnic origin of subjects included in both studies.

Limitations

A potential limitation of our study would be including a less number of subjects in the age group between 18 and 25 years than the other age groups. That might potentially lead to an incorrect estimation of a non-significant difference between age groups. It should also be mentioned that the subjects with BTEP have not been followed up regarding their prognosis. One other factor that should be taken into account is the possibility of overdiagnosing or misdiagnosing every subject with BTEP as real BrS patient by recording ECGs at higher right ICS without considering additional diagnostic criteria. However, subjects detected with BTEP by this novel ECG recording technique might be regarded as silent carrier of a gene mutation specific for BrS or asymptomatic cases of BrS. Therefore, we recommend that they be warned against certain triggering factors such as fever and medications as well as handled with caution.

Conclusions

The present study revealed that the prevalence of BTEP by recording ECGs at higher right ICS is 7.5% in Turkish men. Four new subjects developed type 1 BTEP at high right precordial ECG recording as opposed to standard lead positions. Placement of right precordial leads on higher ICS increases the sensitivity and detection rate of BTEP in asymptomatic subjects. Finally, we suggest that prospective trials about the prevalence of BTEP should better use high right precordial ECG recording for preventing a possible underestimation of BTEP prevalence in general population.

Conflict of interest: none declared.

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