RESEARCH ARTICLE / *Araştırma Makalesi*

The Relations of Brugada ECG Pattern and Fraqmented QRS in Patient with Schizophrenia

Şizofreni Hastalarında Brugada EKG Paterni ve Fraqmente QRS İlişkisi

Osman Bektaş[1], Ahmet Kaya[1], Esra Yancar Demir[2], Seçkin Dereli[1]

[1] Department of Cardiology, Ordu University Medical School, Ordu, Turkey
[2] Department of Psychiatry, Ordu University Medical School, Ordu, Turkey

Yazışma Adresi / *Correspondence:*
Osman Bektaş

Ordu University Medical School, Department of Cardiology, 52000, Ordu, Turkey
T: **+90 452 225 23 42** E-mail **: bektas7960@gmail.com**

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Orcid :

Osman Bektaş https://orcid.org/0000-0002-6616-9891
Ahmet Kaya https://orcid.org/0000-0001-9845-7938
Esra Yancar Demir https://orcid.org/0000-0002-9639-6649
Seçkin Dereli https://orcid.org/0000-0003-0090-3835

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Abstract

Objective	Schizophrenia is a psychiatric disease with high risk of fatal rhythm disorders and sudden cardiac death. A previous study reported that Brugada syndrome was highly prevelant in patients with schizophrenia. In this study we aimed to investigate the prevelance of Brugada syndrome and fraqmanted QRS in patients with schizophrenia.
Materials and Methods	Two hundred and fifty patients with schizophrenia who were followed up in the psychiatry clinic, and 400 age- and sex-matched non schizophrenia controls were included. Standart ECGs and high intercostal ECGs with V1 and V2 derivation above two intercostal intervals were taken.
Results	In schizophrenia patients, Type 1 Brugada syndrome was not observed, Type 2 Brugada was identified in one subject and Type 3 Brugada was observed in two patients. In the control group, Type 2 Brugada pattern was identified in one subject and again one control had Type 3 Brugada pattern(p=0.320). The fragmented QRS (fQRS) incidence, QRS duration and corrected QT were observed to be higher in the schizophrenia group compared to the control group (p=0.001, p=0.003, p<0.001, respectively).
Conclusion	There is no increased prevalence of Brugada-ECG pattern in patients with schizophrenia. Importantly, the prevelance of fQRS was significantly higher in patients with schizophrenia compared to the control group. Fqrs can be used to estimate the frequency of cardiovascular events in patients with schizophrenia.
Keywords	Schizophrenia; Brugada Syndrome; fragmented QRS

Öz

Amaç	*Şizofreni, ölümcül ritim bozuklukları ve ani kardiyak ölüm riski yüksek olan psikiyatrik bir hastalıktır. Brugada sendromunun şizofreni hastalarında oldukça yaygın olduğunu düşünülmektedir. Bu çalışmada şizofreni hastalarında Brugada sendromu ve fraqmante QRS sıklığını araştırmayı amaçladık.*
Gereç ve Yöntemler	*Psikiyatri kliniğinde izlenen iki yüz elli şizofreni hastası ve 400 yaş ve cinsiyet uyumlu şizofreni olmayan kontrol grubu çalışmaya dahil edildi. Standart EKG'ler ve iki interkostal aralığın üzerinde V1 ve V2 derivasyonu olan yüksek interkostal EKG'ler alındı.*
Bulgular	*Şizofreni hastalarında Tip 1 Brugada sendromu gözlenmedi, bir hastada Tip 2 Brugada, iki hastada Tip 3 Brugada gözlendi. Kontrol grubunda bir hastada Tip 2 Brugada paterni belirlendi ve yine bir kontrol hastasında Tip 3 Brugada paterni vardı (p = 0.320). Fragmente QRS (fQRS) insidansı, QRS süresi ve düzeltilmiş QT'nin şizofreni grubunda kontrol grubuna göre daha yüksek olduğu gözlendi (sırasıyla p = 0.001, p = 0.003, p <0.001).*
Sonuç	*Şizofreni hastalarında Brugada EKG paterninin sıklığında artış yoktur. Şizofreni hastalarında fQRS sıklığı kontrol grubuna göre anlamlı olarak daha yüksekti. fQRS bulunan şizofreni hastalarının kardiyovasküler olay sıklığını öngörmede kullanılabilir.*
Anahtar Kelimeler	*Şizofreni; Brugada Sendromu; fragmente QRS*

INTRODUCTION

Brugada syndrome is an autosomal dominant inherited genetic syndrome and known to have an increased risk of sudden death linked to rapid polymorphic ventricular tachycardia or ventricular fibrillation.[1] Recent studies showed that fragmented QRS (fQRS) is a reliable electrocardiogram (ECG) finding with the importance of an indicator of myocardial fibrosis and scarring.[2]

One of the common causes of sudden cardiac death in schizophrenia is thought to be cardiac arrhythmia. Although the cause of the increase in the incidence of cardiac arrhythmia is uncertain, medications used or genetic variations identified in schizophrenia patients are thought to affect the electrophysiology of the heart through sodium channels.[3] A previous study reported that there was a very high rate (11.6%) of Brugada syndrome, which has a genetic inheritance and high risk of sudden cardiac death, in patients with schizophrenia.[4]

In this study we aimed to investigate the frequency of Brugada syndrome and fQRS in patients with schizophrenia.

MATERIALS and METHODS

This study is a descriptive study. Our study included a total of 250 patients being monitored in the psychiatry clinic for the diagnosis of schizophrenia according to the Diagnostic Statistical Manual of Mental Disorders – IV classification. Patients who did not give permission for electrocardiography (ECG), patients with advanced heart failure, valve disease and bundle branch block were excluded from the study. The study was approved by Ordu University ethic committee(03.06.2016, no:2016/54) and all participants provided written informed consent. The study also included an age- and sex-matched control group of 400 individuals applying to the psychiatry clinic without diagnosis of schizophrenia.

ECG Analysis

Standard ECGs and high intercostal ECGs with V1 and V2 derivations above two intercostal intervals were obtained from all participants. All ECGs were screened for Type 1 (At the end of QRS, an ascending and quick slope with a high take-off ≥2mm followed by concave or rectilinear downsloping ST), Type 2 and Type 3 Brugada syndrome ECG characteristics by a cardiologist blind to the patients' diagnoses .Fragmented QRS (fQRS) was defined as narrow QRS complex (duration <120 ms) with R wave notching, S wave notching, RSR' pattern or more than one R' in at least two consecutive derivations. The diagnosis of Brugada Syndrome requires typical ST-segment elevations in right precordial ECG leads and events suggestive of cardiac arrhythmia or a family history of Brugada.[1]

Statistical analysis

SPSS (SPSS 20.0 software) packet program was used for statistical analysis. Continuous variables were given as mean standard deviation (SD) and categorical variables were given as percentages. Pearson chi-square analysis and Fisher's Exact test were used to compare categorical variables. A p value <0.05 was considered statistically significant.

RESULTS

The demographic characteristics of the groups included in our study are shown in Table 1. The ECG parameters of the groups are shown in Table 2. The fQRS frequency, QRS duration and QTc were observed to be higher in the schizophrenia group compared to the control group (p=0.001, p=0.003, p<0.001, respectively). Both mild and severe QTc prolongation were observed more often in the schizophrenia group (p<0.001, p<0.001, respectively). In subgroup analysis, fQRS (Fig.1) was found to be more common in male sex (p<0.011) and in those with fQRS, QTc was observed to be higher (425.7±42.4 vs. 397.6±25.4; p<0.001).

Table 1: Clinical and demographic characteristics of the study population

		Schizophrenia Group (n: 250)	Control Group (n: 400)	p
Age, mean±SD (years)		44.33 ± 14.7	45.6 ± 9.8	0.164
Male, n(%)		130(52)	230(57.5)	0.169
Diabetes Mellitus, n(%)		10(4)	30 (7.5)	0.070
Hypertension, n(%)		25(10)	45 (11.2)	0.616
Hyperlipidemia, n(%)		20(8)	41(10.1)	0.338
Heart Rate, mean± SD(beat/min.)		78.4± 14.1	77.6± 16.1	0.509
Sodium channel blockers, n(%)		85 (34)	-	-
QT-interval–prolonging drugs, n(%)		190 (76)	-	-
Selective serotonin reuptake inhibitors,n(%)		38 (15.2)	30 (7.5)	0.002
Tricyclic antidepressants, n(%)		40 (16)	25 (6.2)	<0.001
Antipsychotics	Clozapine, n(%)	150 (60)	-	-
	Olanzapine, n(%)	50 (20)		
	Aripiprazol, n(%)	15 (6)		
	Risperidon, n(%)	15 (6)		
	Quetiapine, n(%)	5 (2)		

Table 2: Comparison of ECG parameters between Schizophrenia and Control Group

		Schizophrenia Group (n:250)	Control Group (n:400)	p
Brugada	Type 1, n(%)	-	-	0.320
	Type 2, n(%)	1(0.4))	1(0.25)	
	Type 3, n(%)	2(0.8))	1(0.25)	
Mild Prolongation of QTc-interval, n(%)		31(12.4)	1(0.25)	<0.001
Severe Prolongation of QTc-interval, n(%)		21(8.4)	-	<0.001
QTc duration, mean±SD (ms)		413.0 ± 31.4	390.4 ± 23.1	<0.001
QRS duration, mean±SD (ms)		102.1 ± 24.1	92.3 ± 14.1	0.003
fQRS, n(%)		50(20)	39 (9.8)	0.001
Heart Rate, mean±SD(beat/min.)		78.4 ± 14.1	77.6 ± 16.1	0.509

QTc: Corrected QT, fQRS: Fragmented QRS

DISCUSSION

According to the results of our study; The Brugada ECG frequency was similar to schizophrenia patients and non-schizophrenia control group. Importantly, the prevalence of fQRS was significantly higher in patients with schizophrenia compared to the control group.

Previous studies have shown that schizophrenia patients have higher mortality secondary to sudden cardiac death and cardiac arrhythmia compared to the normal population.[5-6] The most important cause of this is considered to be the arrhythmogenic potential of the medications used and the possibility of genetic ion defects shown in this patient population that may affect cardiac electrophysiology.[3] Brugada syndrome is a rare clinical entity with high risk of sudden cardiac death1 and a study by Bloom et al. found high rates of Brugada syndrome among schizophrenia patients in their population (north Holland). They suggested that the higher prevalence of Brugada syndrome may be responsible for the increased mortality rate in schizophrenia patients.[4] Bloom et al. identified a higher incidence of sudden cardiac death in their study population. However the association between higher prevalence of Brugada syndrome and increased rate of sudden cardiac death was only an observation far from being just an established clinical cause-effect relationship.[4] Again, Bloom et al. proposed that the antipsychotics especially Na channel blockers used by schizophrenia patients may provoke Brugada syndrome.[4] Contrary to the results of the study of Bloom et al, schizophrenia patients using antipsychotics and Na channel blockers were not found to have a higher prevalence of Brugada syndrome in our study. However, in line with the previous studies the QTc prolongation was identified to be higher in our patient population.[7-8]

In the European countries such as Germany and Denmark, the prevalence of Brugada Pattern on ECG was low with the rates of <0.05% (<1 in 2000), while in Turkey it was reported to be ≥0.05% (≥1 in 2000) (Type 1 Brugada pattern 0.08%, Type 2-3 Brugada pattern 0.40%).[9] The study by

Bloom et al. revealed that the prevalence of Brugada syndrome among patients monitored for schizophrenia was higher than the control group (11.6% vs. 1.1% and 2.4%).[4] Although the prevalence of Brugada syndrome in Turkey is known to be higher compared to European countries[10], the present study demonstrated that the prevalence of Brugada syndrome was not higher among schizophrenia patients when compared to controls in Turkey (p:0.320) contrary to the results of the study of Bloom et al. which was conducted in north Holland. Although Brugada syndrome is an autosomal inherited disease, it is known to occur 8-10 times more often in men compared to women.[10] In our study 52% of the patiens were male, while in the study by Bloom et al. this rate was 70.9%. Consequently the Brugada prevalence found in the study by Bloom et al. was very high and we believe that larger prospective studies are required to explain this difference.

Yap et al. found a weak correlation between the manifestation of Brugada syndrome and increase in sudden cardiac death risk with the use of sodium channel blockers.[11] In our study the prevalence of Brugada was not increased among schizophrenia patients, leading to the consideration that there was no effect of the medications used. Previous studies of schizophrenia patients have focused on the fact that genetic variations in ion channels may affect cardiac electrophysiology and may trigger arrhythmic deaths.[1,3,4] Unfortunately we did not perform any genetic study in our research.

Many studies have shown that the presence of fQRS on ECG is related to myocardial fibrosis and and increases the risk of sudden cardiac death[12] Many causes including cardiac ischemia, myocarditis or increased sympathetic activity may cause development of myocardial fibrosis.[12-13] Myocardial fibrosis disrupts the electrical activity of the heart and increases the risk of arrhythmic death.[12-14] The antipsychotic medications used in the treatment of schizophrenia are known to cause myocarditis and increase sympathetic activity.[15-16] In our study we found that the frequency of fQRS, which is a strong predictor of cardiac fibrosis was significantly higher in patients with schizophrenia. We suggest that this may be due to the cardiac effects of medications used or the neurohormonal changes in schizophrenia. fQRS, which is easy to assess with surface ECG, shows electrical heterogeneity secondary to myocardial fibrosis[17] and may be beneficial to predict sudden cardiac arrhythmias. We believe that it will be valuable to determine whether there is a correlation between presence of fQRS on ECG and mortality in patients with schizophrenia with prospective studies.

Study Limitations

Our study had a cross-sectional design with no prospective monitoring of patients. Patients were not monitored to show the correlation between presence of fQRS and mortality. Lack of echocardiographic evaluation, magnetic resonance imaging or histological assessment in order to demonstrate myocardial fibrosis can also be considered as a limitation. Drug use of the patient group can also be considered as study limitations. However, the obligation of patients with schizophrenia to receive treatment is a part of their lives.

CONCLUSION

We found that the prevalence of Brugada ECG pattern was not higher in patients with schizophrenia. Many factors such as the low prevalence of Brugada syndrome in the general population, geography, genetics and sex may have affected the results of our study. The higher prevelance of fQRS in schizophrenia patients in our study leads to the consideration that myocardial involvement than the genetic transmission may be more frequent in these subjects. For the use of fQRS as a marker of cardiac risk in schizophrenia patients, there is a need for large scale studies in different geographical regions.

Disclosure statement

The authors declare that they have no competing interests.

Conflict of interest

The authors have no conflicts of interest to declare.

Financial Disclosure

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