Evaluation complaints of palpitations in patients with Fibromyalgia Syndrome

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Research Article

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Abstract

Objective

To research the effect of Fibromyalgia Syndrome (FMS) on the cardiac conduction system and evaluate the feasibility of ECG parameters in estimating arrhythmia development with 24-hour ambulatory Holter ECG monitoring.

Method

ECG was taken for all participants of the study. ECG parameters were measured. 24-hour ambulatory Holter ECG monitoring was made and analyzed.

Result

90 patients with FMS and 70 controls were enrolled in the study. The average age of the patient group was 38.3 ± 6.3 years, and the female patient population (73.3%) was almost three times the number of male patients ($p = 0.032$). In terms of clinical features such as age ($p = 0.301$), height ($p = 0.789$), weight ($p = 0.628$), and body mass index (BMI) ($p = 0.770$), there was no significant difference between the study and control groups. There was no significant difference between the groups in terms of heart rate ($p = 0.800$), systolic blood pressure ($p = 0.394$), and dyslipidemia ($p = 0.133$). In terms of routine blood tests, there was no significant difference between the study and control groups ($p > 0.05$). In the comparison of ECG parameters, Pmax, QTd, and QTcd were statistically significant in the study group compared to the control group ($p < 0.05$). In terms of Pmin and Pdis, there was no significant difference between the two groups ($p > 0.05$). There was no significant relationship between the study group and the control group in terms of 24-hour Holter ECG recording results ($p = 0.182$).

Conclusion

Although FM patients complain of palpitations, the outcomes of the study showed that the risk of arrhythmias was not increased.

İntroduction

Fibromyalgia syndrome is non-inflammatory soft-tissue rheumatism with characteristic symptoms such as common musculoskeletal pain, morning stiffness, sleep disturbance, fatigue, anxiety, and depression [1, 2].

It can occur at any age, even though it is most common in women between the ages of 20–45 [3]. The diagnosis is delayed because the complaints concern more than one clinician [4]. Usually, the time it

takes for patients to get a diagnosis after contacting a medical institution might be delayed by an average of 2–3 years due to the inability of clinicians to adequately understand FMS [5]. During this time, multiple doctors have been visited.

Patients apply to the cardiology outpatient clinic with palpitations, chest pain, and back pain. Patients without cardiac pathology are usually referred to a Physiotherapy and Rehabilitation specialist and diagnosed with FMS however, patients whose palpitations continue are referred to a cardiologist for re-evaluation. Chronic stress, together with autonomic nervous system disorder and neuroendocrine anomalies, is responsible for pathogenesis [6, 7]. P-wave, QT, and QTc dispersions which are measured non-invasively on surface ECG could predict the development of atrial and ventricular arrhythmias (8).

In our study, we investigated the effect of FMS on the cardiac conduction system by using parameters of ECG and evaluated the feasibility of ECG parameters in estimating the development of arrhythmia with 24-hour ambulatory Holter ECG monitoring.

Material And Methods

Study Design and Subjects

The study population was formed of patients diagnosed between 2017 and 2021 according to the criteria of the American College of Rheumatology (ACR 2010).

Hypertension, thyroid dysfunction, structural cardiac disease, dysrhythmia, pregnancies, malignancy, using medications including beta-blockers or antiarrhythmics, smoking, COPD, asthma, chronic renal disease, diabetes mellitus, obesity, anxiety, vitamin deficiency, electrolyte disorder, alcohol use, and any inflammatory diseases were excluded from the study.

98 patients who were diagnosed with FMS as a result of presenting to the Physical Therapy and Rehabilitation polyclinic with palpitations, back and chest pain and who were referred to the cardiology polyclinic after the complaints of palpitations did not go away were included in the study. 8 patients whose data could not be reached were not included from the study.70 patients were enrolled in the control group.

The current research was carried out in accordance with the Helsinki Declaration (2013).

Study protocol

Routine blood tests of the patients were studied. ECG recording was performed at 25 mm/sec with 10 mm/mV amplitude using the Nihon-Kohden Corporation Electrocardiograph type EKG-1350K device. ECGs were magnified with the help of a magnifying glass and dispersions were measured manually. By subtracting the minimum P-wave duration from the maximum P-wave duration, the P-dispersion was calculated. (9).

The QT interval was calculated from the onset of the QRS to the end of the T-wave. The research eliminated patients who did not have a T-wave on their ECG. In those with T waves with two peaks, the end of the T-wave was regarded as the moment where the big peak reached the isoelectric line. The minimum QT duration was subtracted from the maximum QT duration to calculate QT dispersion. Similarly, the QTc dispersion was calculated (10).

The patients were evaluated by taking 24-hour standard 3-channel (lead V1, II, and V5) ambulatory Holter ECG (Northeast Monitoring, Maynard, MA) recordings.

Statistical Analysis

IBM SPSS 24.0 package program was used for analysis. Clinical characteristics and laboratory data of fibromyalgia patients and the control group were analyzed. The difference between the ECG findings of the patients and the frequency of arrhythmia seen in the 24-hour Holter ECG between the two groups was investigated. Baseline continuous variables were presented as median with mean ± standard deviations or first and third quartiles (Q1–Q3) depending on the distribution of data. Categorical variables were expressed as frequency and percentage. Whether the variables were normally distributed was analyzed by Kolmogorov-Smirnov or Shapiro-Wilk tests. Continuous variables were compared using the T-test or Mann-Whitney U-test as appropriate. Univariate analysis was used for continuous variables, Chi-Square or Fisher's exact test was used for categorical variables. A p-value of < 0.05 was considered statistically significant for all tests.

Results

The average age of the study patient group was 38.3 ± 6.3 years, and the female patient population (73.3%) was almost three times the number of male patients. In terms of clinical characteristics like age, height, weight, and BMI, there was no significant difference between the study group and the control group. In terms of heart rate, systolic blood pressure, and dyslipidemia, there was no significant difference between the groups (Table 1).

Table 1
Demographic characteristics of the patients

PARAMETERS	Study group, 90 (%)	Control group, 70 (%)	P-Value
Age (Years)	38.3 ± 6.3	37.4 ± 5.3	0.301
Gender, female, n (%)	66 (73.3)	40 (57.1)	**0.032**
Weight (kg)	76.8 ± 13.5	75.7 ± 13.7	0.628
Height (cm)	166 ± 7.1	165.5 ± 7.5	0.789
BMI (kg/m²)	27.8 ± 4.0	27.6 ± 3.7	0.770
SBP (mmHg)	122.5 ± 17.1	124.7 ± 13.7	0.394
Heart Rate (beat/min.)	89.6 ± 18.4	90.3 ± 18.6	0.800
DL, n (%)	27 (30)	29 (41.4)	0.133

Data are presented as mean SD, number (percentage), or median (interquartile range). BMI: Body mass index, SBP: Systolic blood pressure, DL: Dyslipidemia.

In terms of routine blood tests, there was no significant difference between the study and control groups (Table 2).

Table 2
Laboratory findings of patients

PARAMETERS	Study group, 90 (%)	Control group, 70 (%)	P-Value
White blood cell count (× 10^3 µL)	9.6 ± 3.2	9.9 ± 3.6	0.596
Hemoglobin (g/dl)	13.3 ± 1.9	13.9 ± 2.2	0.091
AST (U/L)	18 (13)	20 (13.5)	0.321
ALT (U/L)	16 (17)	18 (17.2)	0.406
Glucose (mg/dl) [IQR]	89 (30)	86.5 (29.5)	0.811
Total cholesterol (mg/dl) [IQR]	186.9 ± 55.9	178.3 ± 44.1	0.289
Triglyserides (mg/dl)	156 (117.7)	142.5 (99.5)	0.135
LDL (mg/dl) [IQR]	106.5 ± 39.4	105.9 ± 36.7	0.921
HDL (mg/dl) [IQR]	39.9 ± 8.8	41.3 ± 13.0	0.426
CRP (mg/dl) [IQR]	0.3 (0.3)	0.3 (0.2)	0.745
eGFR	95.4 ± 30.8	99.8 ± 22.3	0.314

Values are presented as mean ± SD and median [interquartile range]. AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDL: low-density lipoprotein, HDL high-density lipoprotein, CRP: C-reactive protein, eGFR: Estimated glomerular filtration rate.

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In the comparison of ECG parameters, Pmax, QTd, and QTcd were statistically significant in the study group compared to the control group. In terms of Pmin and Pd, there was no significant difference between the two groups (Table 3).

Table 3
Comparison of ECG parameters between groups.

ECG Parameters	Study group, n (%)	Control group, n (%)	P-Value
Pmax (ms)	120.8 ± 7.8	118.3 ± 7.3	**0.040**
Pmin (ms)	72.7 ± 8.2	72.0 ± 11.0	0.646
Pd (ms)	51.1 ± 9.1	48.3 ± 13.6	0.129
QTd (ms)	54.0 ± 6.6	50.3 ± 8.1	**0.002**
QTcd (ms)	68.6 ± 8.1	65.0 ± 8.8	**0.008**

Values are presented as mean ± SD and median [interquartile range]. Pmax: P-wave maximum duration, Pmin: P-wave minimum duration, Pd: P-wave dispersion, QTd: QT dispersion, QTcd: Corrected QT dispersion.

In terms of 24-hour Holter ECG recording findings, there was no significant difference between the study and control groups (p = 0.182) (Table 4).

Table 4
24-hour Holter ECG recording results

Abnormal Holter ECG findings	Study group (n)	Control group (n)
Sinus tachycardia	4	5
Abnormal ST-T wave	0	1
Left anterior fascicular block	0	1
Complete right bundle branch block	0	1
First-degree AV block	1	0
QT interval prolongation	1	0
Pre-mature atrial contraction (<%10)	1	1
Pre-mature atrial contraction (>%10)	1	1

Discussion

In our study, P-wave dispersion was similar between the groups, however, FM patients had higher QT and QTc dispersions than the control group. Although fibromyalgia patients presented with complaints of chest pain and palpitations, no arrhythmia or ischemic ST-T wave changes consistent with clinical symptoms were observed in the Holter ECG recordings.

Fibromyalgia is a chronic, non-inflammatory locomotor system disorder marked by common pain and sensitive points throughout the body and sleep disturbances, anxiety, back pain, chest pain, and palpitations. Although it is seen in 2% of the society, the diagnosis is delayed because the complaints concern more than one clinician. This period lasts for 2–3 years on average and the patients' life quality decreases considerably. It is more common in women and in our study, it was observed in women with a rate of 73.3% ($p = 0.032$). Patients with FMS had an average age of 38.3 ± 6.3 years.

Sympathetic hyperactivation and parasympathetic dysfunction develop due to autonomic nervous system disorder. As a result of excessive stress, sleep disorders, tender points, and exercise intolerance develop [11]. The etiology and pathogenesis of FMS are clarified yet, although central and peripheral nervous system disorders, immunological and hormonal anomalies, genetic predisposition, and psychiatric factors are considered to have a role [12]. Serotonin, noradrenaline, dopamine, and endorphin levels in the brain are low in fibromyalgia patients, whereas substance P levels in the cerebrospinal fluid are high. Our study did not examine hormonal testing, but hematological and biochemical tests revealed no significant differences between the study and control groups ($p > 0.005$).

Chest pain and palpitations are examples of somatic complaints related to the cardiovascular system. Cohen et al. argued that physical fatigue and psychological stress increase the symptoms, while Furlan et al. reported that the symptoms increased with sympathetic hyperactivity during rest [6, 13]. The Covid-19 process, which included the results of both studies, showed that increased stress may worsen FMS symptoms and FMS may develop after covid-19 [14, 15, 16]. During the covid-19 process, many acute coronary syndromes have been observed due to increased stress [17]. In addition, in the study of AL-Shamri et al., fibromyalgia was found at a high rate (18%) in patients with ischemic heart disease [18]. Yunus et al. reported that FMS is more common in the elderly, women, and patients with anxiety [19]. Sedentary lifestyle, increased prevalence of metabolic syndrome, high blood pressure levels, increased stress, high resting heart rate have been reported as the key causals for the increase in cardiovascular diseases (CVD) [20, 21, 22]. In our study, there was no significant difference in systolic blood pressure ($p = 0.394$), heart rate ($p = 0.800$), BMI ($p = 0.770$), or the rate of dyslipidemia ($p = 0.133$) between FM and control patients.

Patients usually complain of palpitations [23]. Fluctuations in heart rate have been reported as a result of increased autonomic activity. However, there is conflicting information about the development of arrhythmia [11]. Dogru et al. reported that sympathetic activity increased and the rate of supraventricular tachycardia increased compared to control patients [24]. It has been reported that there is more palpitation at night than during the day, and therefore sleep disorders develop in patients [25]. Dursun et al. emphasized that the heart rate did not change in women with FMS [26]. Invasive (electrophysiological study) and noninvasive (P-wave and QT dispersions in ECG) methods can be used to determine atrial and ventricular conduction durations [27]. We can easily predict the development of arrhythmia with the non-invasive method.

P-wave dispersion has an independent predictive value for PAF. Dogan et al. in patients with Behcet's disease, Yavuzkır et al. in patients with RA, Ahlehoff et al. in Psoriasis reported that the P-wave dispersion duration due to inflammation was prolonged and the risk of developing atrial fibrillation increased [28, 29, 30]. In previous studies, changes in P-wave duration were longer in FM patients these findings support a greater risk of developing AF in the FM patient group [31]. Sarıfakıoğlu et al. reported that the risk of AF increased in FM patients [32]. In contrast, Kulshreshta et al. reported that cardiac autonomic function was normal and the risk of arrhythmia did not develop [33]. We found that P-wave dispersion was the same in FM and control patients ($p = 0.129$), similar to the results of Yolbaş et al [34].

Arrhythmia and CVD mortality are both predicted by QT dispersion [35]. Furthermore, QT dispersion duration is longer in several rheumatic diseases, including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), juvenile idiopathic arthritis, systemic sclerosis, and Behçet's disease, and CVD risk is higher. In our study, QTd, and QTcd were statistically significant between the groups ($p < 0.05$). Yolbaş et al. reported that QT dispersion was the same in FM patients and control patients [34].

Aşkın et al. performed an electrophysiological study (EPS) on FM patients who came with palpitations, and they did not find a relationship between complaints of palpitations and arrhythmia [36]. Thus, they proved that the predictive power of arrhythmia development with a non-invasive method is low. Therefore, they did not feel the need to perform 24-hour Holter ECG monitoring in their study.

Holter ECG recording is the simplest method to reveal whether the risk of arrhythmia will develop in patients with a long duration of Pd, QTd, and QTcd. In our study, although QT and QTc dispersions were significant in the study group, no arrhythmia was found in the 24-hour ambulatory Holter ECG recordings ($p = 0.182$). Sinus tachycardia was observed in 4 patients in the study group and 5 in the control group. Only one patient in each group was observed with more than 10% premature atrial contraction.

Limitation

It was difficult to establish a patient population according to exclusion criteria and the study was retrospective. In our study, the patient population was small. ECG and Holter-ECG data were analyzed, but an electrophysiological study was not performed. Cardiac magnetic resonance imaging was not performed for myocardial fibrosis and involvement.

Conclusion

In our study, we found that the P wave distribution was normal in FM patients with heart palpitations, but the QT and QTc distribution was higher than in control patients. However, we found that prolonged ECG parameters in the 24-hour Holter ECG recordings were not posing a risk of arrhythmia. Therefore, it should be kept in mind the risk of arrhythmias is not increased in fibromyalgia.

Declarations

Ethical approval

The study protocol was authorized by the local ethics committee (Gazi Yasargil Training and Research Hospital No: 2022-40 Date: 25/02/2022), and it followed the Declaration of Helsinki's ethics rules for human experimentation.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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